Cardiology Procedures

A Clinical Primer

Robert C. Hendel
Carey Kimmelstiel
Editors

Second Edition

Springer

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To our past, current, and future trainees, who continue to inspire us, with the hope that this book will help set a foundation of excellence in cardiovascular medicine. And to our families, friends, and colleagues who have supported us through this endeavor.

Robert C. Hendel, Carey Kimmelstiel

To Judy, Adam, and Jason for your unwavering love, patience, and support.

And to my patients and fellows from Miami, Chicago, and New Orleans, who provide reason for all that I do professionally.

Robert C. Hendel

To Laurie, Dana, Matt, and Frankie for understanding Cardiology is a calling.

To my parents, Albert and Jacqueline, for instilling in me the love of learning.

And to my brother, Fred, for being the best human I know.

Carey Kimmelstiel

Foreword

I was happy to hear that Robert Hendel and Carey Kimmelstiel were in the process of preparing edition number two of *Cardiology Procedures.* I keep the first edition of this excellent text on my desk for easy access. While teaching residents and students or answering questions from hospitalists, primary care physicians, and nurse practitioners, it is not rare for one of them to ask what a particular cardiovascular test involves. The answer is easy: I show them Hendel and Kimmelstiel's first edition of *Cardiology Procedures* and refer them to the appropriate chapter. The material in this first-rate primer is clearly written with easy-to-understand figures and diagrams.

The cardiovascular world is constantly changing with new technology and innovative protocols appearing almost every month. Rapid progress makes it challenging for trainees and practitioners who are attempting to understand why the attending cardiologist had ordered a CT coronary angiogram for patient X, while requesting a pharmacologic nuclear stress test for patient Y. *Cardiology Procedures*, edition two, provides succinct and lucid answers to all these queries. The editors are to be congratulated for producing this outstanding update which enlarges and extends the scope that was so well-done in the first edition.

The material covered is comprehensive and subdivided into four parts. The first part covers various non-invasive procedures, starting with echocardiography and followed by stress testing and imaging. Part II describes practices done in critically ill patients, while Part III covers the ever-expanding area of electrophysiology. The final part deals with many techniques employed by interventional cardiologists.

Clinicians will welcome this second edition of Hendel and Kimmelstiel's excellent and valuable primer. This book will find widespread use in medical schools, clinics, and hospitals.

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Part I

Non-invasive Cardiology

Transthoracic Echocardiography

1

Eddy Karnabi

Echocardiography is a widely used imaging procedure in patients with cardiovascular disease. The basis of echocardiography relies on the transmission and reflection of ultrasound waves from a transducer and interaction with different tissue interfaces to generate a digital image. The images obtained include M-Mode, 2D, 3D and Doppler (CW: continuous wave, PW: pulse wave, color and tissue Doppler) to define both normal and abnormal structures and pathologies. The uses include evaluation of the structures of the cardiac chamber walls, the systolic and diastolic performances of the ventricles, the structure and function of the native or prosthetic cardiac valves, evidence of pericardial effusion and constriction, the appearance of the proximal great vessels and inferior vena cava, and the presence of abnormal intracardiac shunting.

Indications

The American College of Cardiology (ACC) and American Heart Association (AHA) initially published guidelines for the clinical application of echocardiography in 1997 (with an update in 2003 and 2019) for various cardiovascular conditions [1, 2]. In 2011, followed by an update in 2019, the ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR Appropriate Use Criteria for Echocardiography were published with the level of appropriateness to guide physicians [3, 4]. These indications are extensive and generally includes usefulness in the acute setting and in patients with cardiac signs and symptoms, patients with valvular heart disease, hypertension, heart failure and cardiomyopathies, cardiac masses and pericardial diseases, suspected cardiovascular sources of emboli, and aortic diseases (Table 1.1).

Contraindications

Transthoracic echocardiography has no contraindications, as the use of ultrasound has no adverse effects when used for cardiac imaging. However, ultrasound waves have the potential to cause thermal bioeffects depending on the intensity and length of exposure that are determined by the frequency, focus, power output, depth, perfusion, tissue density; these bioeffects are considered minimal.

Ultrasound enhancing agents or UEAs (contrast agents), when used, include the following contraindication:

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Table 1.1 Appropriate indications for transthoracic echocardiography

1.	Symptoms or conditions potentially related to suspected cardiac etiology including but not limited to chest pain, shortness of breath, palpitations, TIA (transient ischemia attack), stroke, or peripheral embolic event
2.	Prior testing that is concerning for heart disease or structural abnormality Initial evaluation of suspected hypertensive heart disease
3.	Frequent VPCs (ventricular premature contractions) or exercise-induced VPCs, Sustained or non-sustained atrial fibrillation, SVT (supraventricular tachycardia), or VT (ventricular tachycardia). Newly diagnosed LBBB (Left bundle branch block)
4.	Clinical symptoms or signs consistent with a cardiac diagnosis known to cause lightheadedness/presyncope/syncope
5.	Evaluation of suspected pulmonary hypertension including evaluation of right ventricular function and estimated pulmonary artery pressure, Routine surveillance (>1 year) of known pulmonary hypertension without change in clinical status or cardiac exam,
6.	Hypotension or hemodynamic instability of uncertain or suspected cardiac etiology. Assessment of volume status in a critically ill patient
7.	Acute chest pain with suspected myocardial infarction (MI) and non-diagnostic ECG. Initial evaluation of ventricular function following ACS Suspected complication of myocardial ischemia/infarction, including but not limited to acute mitral regurgitation, ventricular septal defect, free-wall rupture/tamponade, shock, right ventricular involvement, HF, or thrombus
8.	Exertional shortness of breath/dyspnea or Respiratory failure or hypoxemia of uncertain etiology
9.	Known acute pulmonary embolism to guide therapy (e.g., thrombectomy and thrombolytics), Re-evaluation of known pulmonary embolism after thrombolysis or thrombectomy for assessment of change in right ventricular function and/or pulmonary artery pressure
10.	Re-evaluation of known valvular heart disease with a change in clinical status or cardiac exam or to guide therapy Routine surveillance (>3 years) of mild valvular stenosis without a change in clinical status or cardiac exam, Routine surveillance (>1 year) of moderate or severe valvular stenosis without a change in clinical status or cardiac exam. Routine surveillance (>1 year) of moderate or severe valvular regurgitation without a change in clinical status or cardiac exam Initial postoperative evaluation of prosthetic valve for establishment of baseline, Routine surveillance (>3 years after valve implantation) of prosthetic valve if no known or suspected valve dysfunction, Evaluation of prosthetic valve with suspected dysfunction or a change in clinical status or cardiac Exam, Re-evaluation of known prosthetic valve dysfunction when it would change management or guide therapy
11.	Participation assessment of an asymptomatic athlete with >1 of the following: abnormal examination, abnormal ECG, or definite (or high suspicion for) family history of inheritable heart disease
12.	Initial evaluation of suspected infective endocarditis with positive blood cultures or a new murmur, Re-evaluation of infective endocarditis at high risk for progression or complication or with a change in clinical status or cardiac exam
13.	Initial evaluation of cardiac mass, suspected tumor or thrombus or potential cardiac source of emboli.
14.	Initial evaluation of patient to exclude cardiac origin of TIA or ischemic stroke including provocative maneuvers (Valsalva, cough) to assess for the presence of Right-to-left intracardiac shunt with the use of agitated bubble saline study.
15.	Suspected pericardial conditions, re-evaluation of known pericardial effusion to guide management or therapy, evaluation for pericardial constriction
16.	Evaluation of the ascending aorta in the setting of a known or suspected connective tissue disease or genetic condition that predisposes to aortic aneurysm or dissection (e.g., Marfan syndrome),
17.	Initial evaluation of known or suspected HF (systolic or diastolic) based on symptoms, signs, or abnormal test results, Re-evaluation of known HF (systolic or diastolic) with a change in clinical status or cardiac exam without a clear precipitating change in medication or diet, or to guide therapy
18.	Initial evaluation or re-evaluation after revascularization and/or optimal medical therapy to determine candidacy for device therapy and/or to determine optimal choice of device
19.	Known implanted pacing device with symptoms possibly due to device complication or suboptimal pacing device settings
20.	To determine candidacy for ventricular assist device, Optimization of ventricular assist device settings, Re-evaluation for signs/symptoms suggestive of ventricular assist device-related complications

Table 1.1 (continued)

21.	Cardiac structure and function evaluation in a potential heart donor. Monitoring for rejection or coronary arteriopathy in a cardiac transplant recipient
22.	Re-evaluation of known cardiomyopathy with a change in clinical status or cardiac exam or to guide therapy
23.	Screening evaluation for structure and function in first-degree relatives of a patient with an inherited or acquired cardiomyopathy (e.g., restrictive, infiltrative, dilated, hypertrophic)
24.	Baseline and serial re-evaluations in a patient undergoing therapy with cardiotoxic agents
25.	Initial evaluation of known or suspected adult congenital heart disease, known adult congenital heart disease with a change in clinical status or cardiac exam, Re-evaluation to guide therapy in known adult congenital heart disease
26.	Guidance of percutaneous noncoronary cardiac procedures including but not limited to pericardiocentesis, septal ablation, or right ventricular biopsy. Pre/peri/post-procedural evaluation for closure of PFO (patent foramen ovale), atrial septal defect, and LAA (left atrial appendage) Occlusion

1. Hypersensitivity to contrast agents.

The previous contraindications of

(a) Clinical instability with hypotension in such cases as acute myocardial infarction, worsening or clinically unstable heart failure, life threatening ventricular arrhythmias, respiratory failure, severe emphysema, pulmonary embolism;
(b) Right-left, bidirectional, or transient right-to-left cardiac shunts.

Have been removed by the FDA and changed to warning. For additional details about contrast agents, please see Chap. 3 (Contrast Echocardiography).

Equipment

The necessary equipment for performing an echocardiographic exam includes the portable echocardiography unit, a suitable ultrasound transducer (typically 2–4 MHz) and an experienced sonographer or physician. The ultrasound transducer uses a piezoelectric crystal (such as quartz or titanate ceramic) to generate and receive ultrasound waves. The received waves are converted to electrical signals and displayed on the echocardiographic machine. The equipment is portable and allows examination in multiple locations aside from the echocardiography laboratories.

Technique

The echocardiographic examination starts by connecting the ECG electrodes and positioning the patient comfortably in the left lateral decubitus position to obtain optimal images (Obtaining images in supine position are possible if patients are unable to lie on their side and is used for the subcostal and suprasternal notch views). The ultrasound transducer is applied (using a water soluble gel) to the parasternal, apical, subcostal and suprasternal notch to obtain the usual images of an echocardiographic protocol. Parasternal long axis (PLAX), parasternal short axis (PSAX), apical four (A4C), two (A2C), and three-chamber (A3C or long axis), subcostal (SC), and suprasternal notch (SSN) images are obtained. Doppler echocardiography (color flow, continuous and pulsed wave) is used to determine regurgitant and stenotic flow across valves and measure the velocity, pressure gradients, and volumetric flow. Tissue Doppler (mitral annulus) is used in determining diastolic function.

1. The parasternal long axis view (PLAX) (Fig. 1.1) with the transducer slightly left of the sternum (third or fourth intercostal space) with the marker on the probe pointing towards the right shoulder, is initiated with the 2D evaluation of a sagittal view of the left ventricle (LV) (long axis view). This view allows evaluation of the structure and systolic function of the LV including LV outflow tract, left

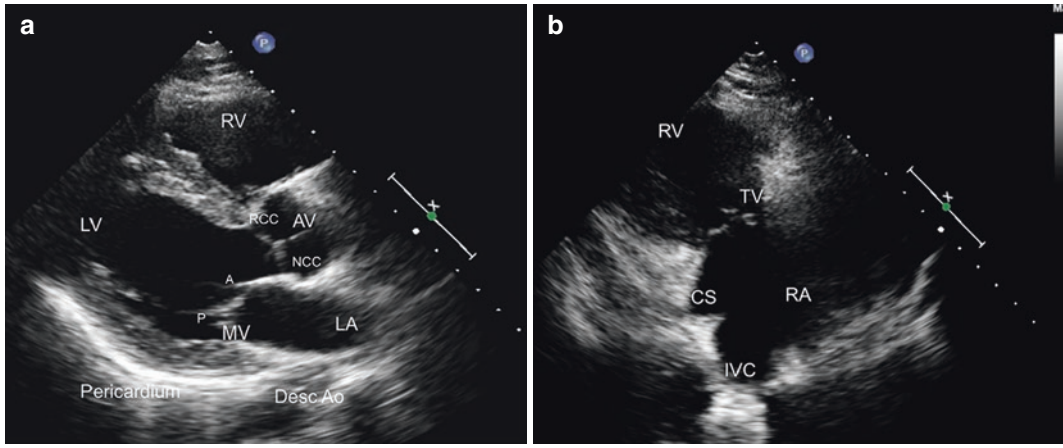

Fig. 1.1 Parasternal long axis (PLAX) views: (**a**) shows PLAX with the LA, LV, MV-mitral valve with anterior and posterior leaflets, AV—aortic valve with RCC—right coronary cusp and NCC—non-coronary cusp. The RV lies anteriorly and posteriorly the pericardium and descending aorta are seen. In the PLAX, the anteroseptal and inferolateral walls of the LV are evaluated for any wall motion abnormalities. Panel (**b**) shows an RV inflow view with the RV, RA, the TV—tricuspid valve as well as the ostia of the IVC—inferior vena cava and the CS—coronary sinus

atrium (LA), the structure and motion of the aortic valve (AV) right and usually non-coronary cusps, the proximal aortic size and wall characteristics, and a portion of the right ventricular outflow. The posterior pericardium can also be evaluated for thickening or presence of pericardial effusion and more posteriorly pleural effusion. The septum is visualized and information can be obtained on the presence of a ventricular septal defect (VSD).

2. A parasternal right ventricular (RV) inflow (Fig. 1.1) view can be obtained by medial angulation of the transducer from the parasternal long axis position. This allows visualization of the tricuspid valve (TV), right atrium (RA), coronary sinus (CS), and RV inflow tract. Tricuspid regurgitation can be evaluated and using continuous flow (CW) Doppler, right ventricular systolic pressure (RSVP) can be calculated.
3. Parasternal short axis view (PSAX) (Fig. 1.2) is orthogonal to the long axis view. It is obtained by rotating the transducer 90° with the probe marker pointing to the left shoulder. Cross sectional evaluation of the LV, mitral valve (MV), AV, and LA are obtained, as well as views of the interatrial septum, RA, TV, RV outflow tract, PV, proximal PA and main PA branches. Doppler studies allow assessment of aortic regurgitation, tricuspid regurgitation, PA velocity, and the presence of pulmonic stenosis or regurgitation. Shunts that can be assessed in this view include membranous and supracristal VSD, patent ductus arteriosus (PDA), atrial septal defects (ASD) and patent foramen ovale (PFO).
4. Apical four chamber (A4C) view (Fig. 1.3): The transducer is placed on the left side of the chest as far inferiorly and laterally as possible to obtain views of the four chambers, including the mitral and tricuspid valves. This view allows assessment of the LV apex, inferoseptal and anterolateral walls and the lateral RV wall. The view is useful for evaluation of global LV systolic performance and the presence of LV apical aneurysm and thrombus. The RV size and function can be assessed in this view. Diastolic performance can be determined by Doppler assessment of mitral inflow, pulmonary vein, and mitral annular (tissue Doppler) motion. This is the best view for assessing the presence and degree of mitral and tricuspid stenosis and regurgitation and is useful for assessing the extent of pericardial effusion, and respirophasic characteristics of mitral

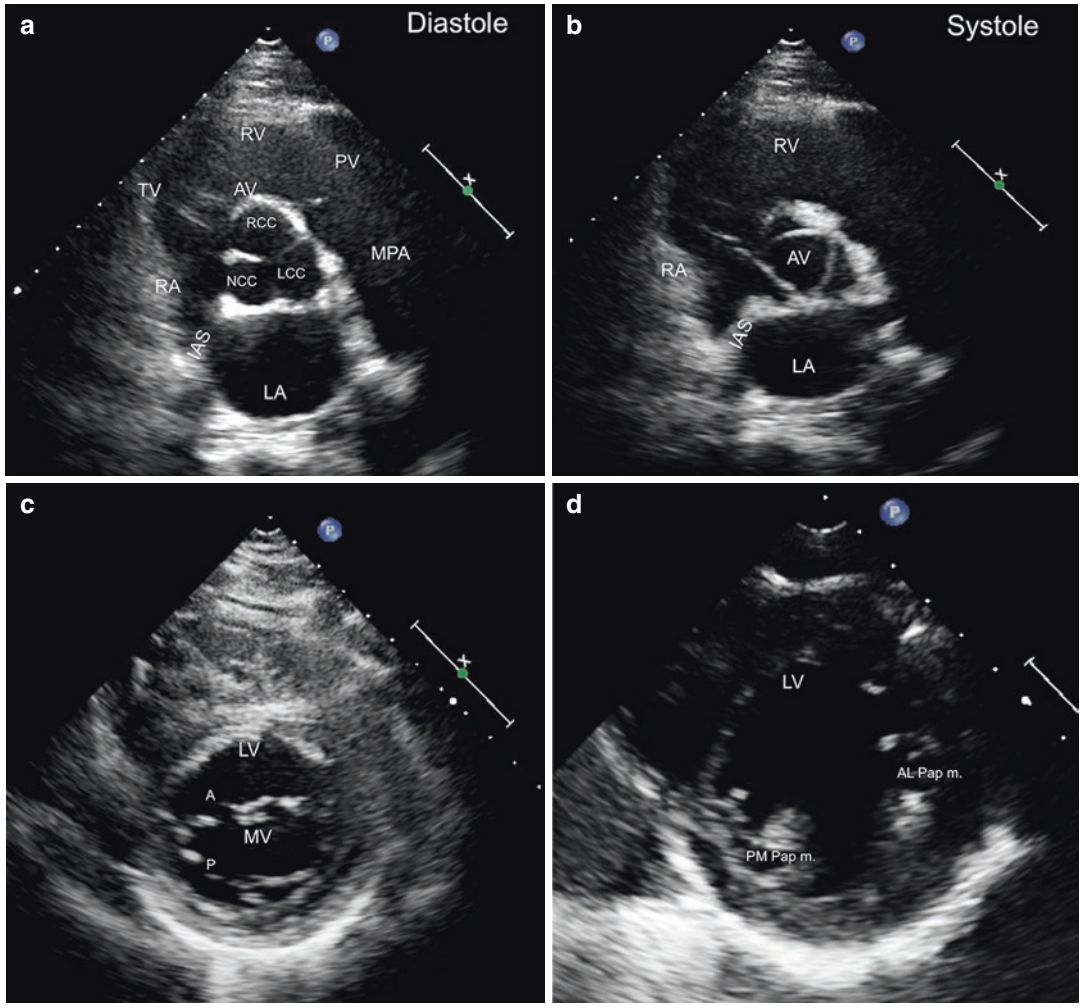

Fig. 1.2 Parasternal short axis (PSAX) views: (**a**, **b**) At the aortic level in diastole (AV closed) and systole (AV open). Note the three cusps: RCC, LCC, and NCC (located at the IAS—interatrial septum). Also seen are the LA, RA, IAS with slight dropout, RV outflow, PV—pulmonary vein and MPA—main pulmonary artery. Panel (**c**) shows short axis of the LV at the mitral valve level showing the anterior and posterior leaflets. Panel (**d**) shows a short axis of the LV at the papillary muscle level with the AL—anterolateral and PM—posteromedial papillary muscles from [1]

and tricuspid characteristics that may include pericardial tamponade. RV and RA invagination or compression also suggesting tamponade can be seen in these views. Doppler interrogation for muscular VSD is best accomplished in this view. Saline intravenous injections for R-L shunts are best determined in this view.

Since three-dimensional imaging has become widely available, 3D imaging for an accurate evaluation of the LV size, systolic function and measuring ejection fraction has become standard in most laboratories and is usually obtained from the A4C to obtain the 3D volume set.

5. Apical two chamber (A2C) view (Fig. 1.3): Rotation of the transducer 60° counterclockwise provides visualization of the LV, MV, and LA. This view allows evaluation of the LV inferior and anterior walls, further evaluation for mitral regurgitation, and may be the best view for demonstration of LV pseudoaneurysm, which usually involves the inferior wall.

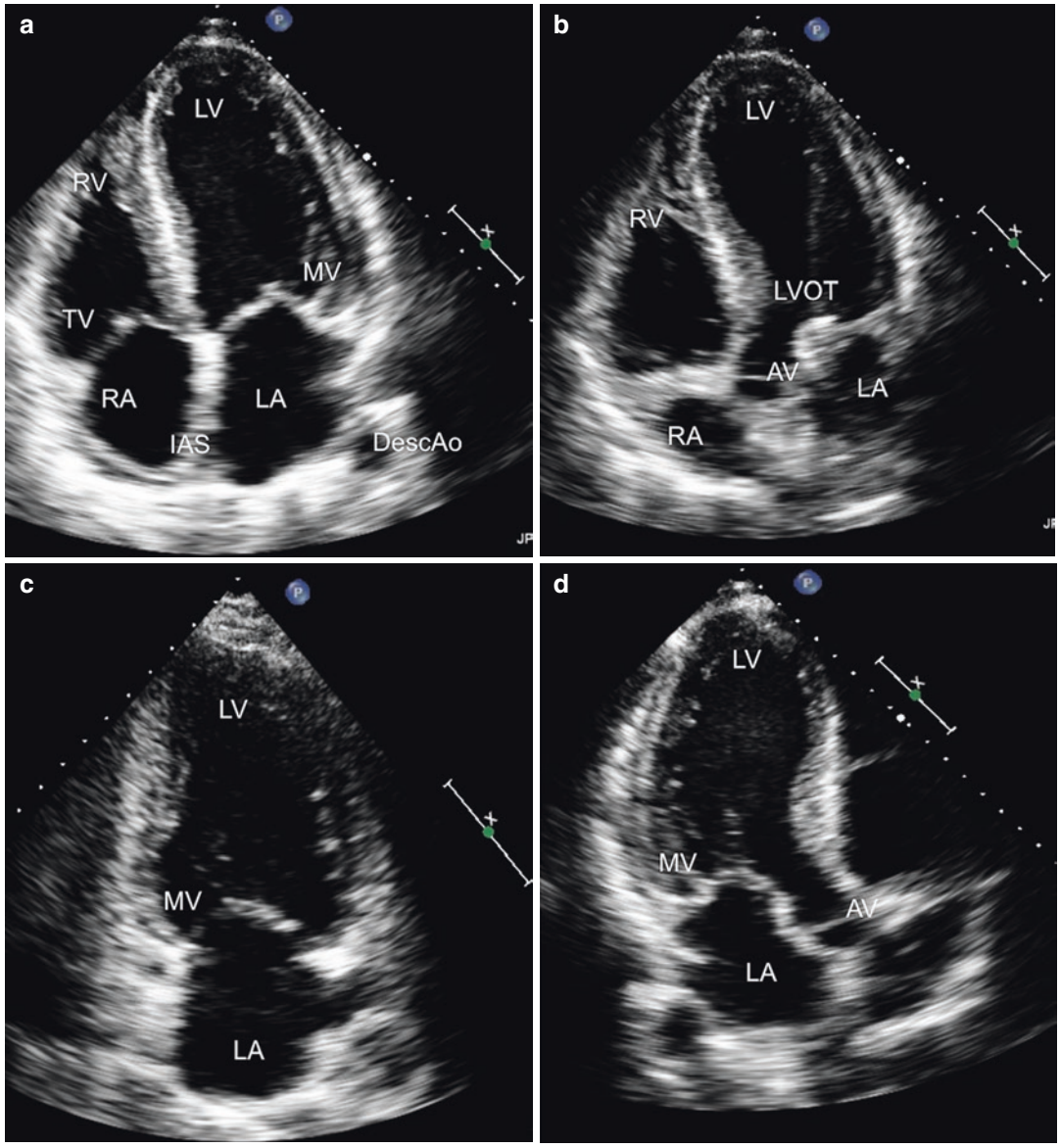

Fig. 1.3 Apical views. (**a**) Apical four chamber (A4C) view showing the LA, RA, RV, LV (anterolateral and inferoseptal walls), and the MV/TV. (**b**) Apical five chamber (A5C) with slight anterior angulation of the transducer, the aorta is opened and the aortic valve can be seen and interrogated with CW to evaluate for AS, and PW of the LVOT to measure the SV—stroke volume. (**c**) Apical two chamber (A2C) showing the LA, MV and LV (Anterior and inferior walls). (**d**) Long axis (A3C) showing the LA, LV, MV, and AV. Similar to the PLAX, the anteroseptal and inferolateral walls of the LV are seen from [5]

6. Apical three chamber (A3C) view (Fig. 1.3): Rotating the transducer 60° clockwise and tilting is slightly anteriorly allows visualization of the LV, MV, LA, LV outflow tract, AV and proximal aorta. It is the best view for Doppler interrogation for aortic stenosis, subaortic stenosis and aortic regurgitation.
7. Subcostal view (Fig. 1.4): The transducer is placed in the epigastrium just below the subxiphoid process. It is the best view for

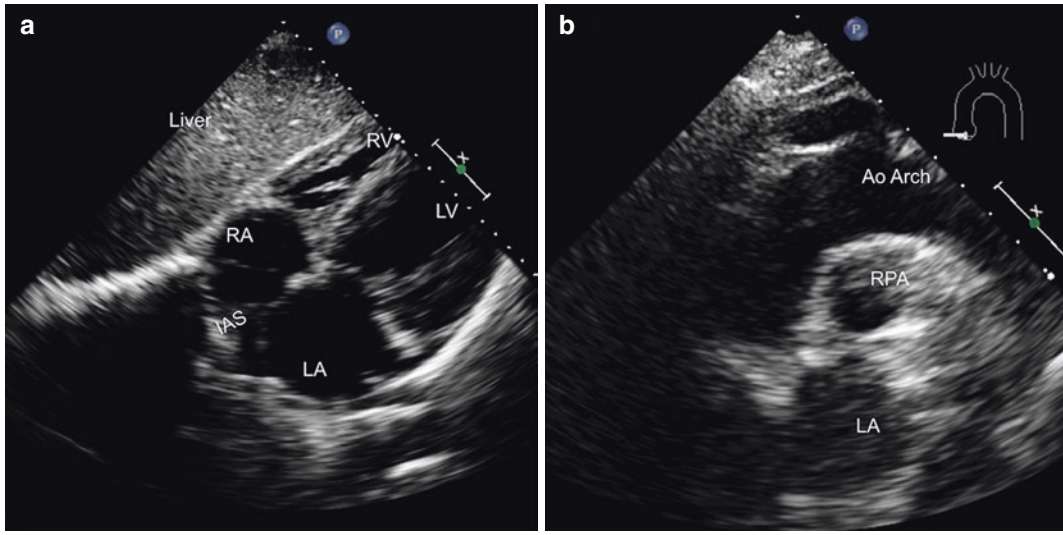

Fig. 1.4 Subcostal and suprasternal TTE views: (**a**) A subcostal view with the four chambers LA, LV, RA, and RV are seen. This is the best view to evaluate for the presence of IAS—interatrial septal defects such as ASDs or PFOs using color flow Doppler. (**b**) Suprasternal notch view showing the aortic arch, RPA—right pulmonary artery and LA. This view is used to evaluate for the presence of aortic coarctation and diastolic flow reversal to determine the severity of aortic regurgitation

evaluating RA and RV free wall motion, and presence of PFO or ASD. The inferior vena cava is best viewed in this location. The diameter of which is measured and used to estimate RA pressure. The abdominal aorta can be seen several centimeters below the diaphragm, which allows the evaluation of aneurysms or dissection at this level.

8. Suprasternal view (Fig. 1.4): This view allows Doppler assessment of the ascending aortic velocities in aortic stenosis an can provide 2D imaging of the transverse and proximal descending thoracic aorta. Doppler assessment of the descending aorta in this view may be useful for the diagnosis of PDA and coarctation.

In general, standard images can be obtained in most patients with limitations in those with extremes of weight, with severe lung hyperinflation (i.e. severe COPD), or in patients in which access to the chest wall is precluded in setting of thoracic bone malformations, open-heart surgery or other thoracic surgeries. In difficult to image patients, ultrasound contrast agents are used to improve image quality.

Data Interpretation

Physicians with specialized training should perform data interpretation as established by competency guidelines from the ACC/AHA/ASE to generate a formal report. It is important to use a consistent systemic approach with special attention directed to the clinical question.

A systemic approach includes the following:

- Left Ventricle: Chamber dimension, wall thickness, fractional shortening (FS), ejection fraction, regional wall motion abnormalities, stroke volume, diastolic characteristics and presence of VSD [5].

- Right Ventricle: Chamber dimension, wall thickness and global function.
- Left atrium: Size, presence of masses or cor triatriatum.
- Right atrium: Size, abnormal motion suggesting pericardial tamponade.
- Proximal aorta: Size, evidence of dissection and fibrocalcific changes.
- Proximal PA: Size, presence of PDA.
- Valves: Stenosis, regurgitation, vegetations, calcification, prolapse, bicuspid and other AV abnormalities.
- Congenital anomalies: PFO, ASD, VSD, cor triatriatum, Ebstein anomaly, transposition of ventricles and other congenital abnormalities.
- Pericardium: Pericardial effusion, tamponade, constriction.
- Hemodynamic: Hemodynamics play an important role in echocardiography and is helpful in evaluating the degree of right to left or left to right shunting, degree of mitral and aortic stenosis, regurgitant flow, PA systolic pressure.

Flows can be calculated using the formula

$$\text{Flow Rate} = \text{Area}\left(\pi r^2\right) \times \text{Vmax}.$$

πr^2 represents the area across a circle assuming the left ventricular outflow tract (LVOT) is circular in shape. The volume is calculated as

$$\text{Volume} = \text{Area}\left(\pi r^2\right) \times \text{VTI}$$

(Velocity time integral: measured by tracing the CW or PW signal).

The stroke volume (SV) can be calculated using multiple methods, with the use of the LVOT being the most accurate:

$$\text{SV} = \text{Area}\left(\text{LVOT}\right) \times \text{VTI}\left(\text{PW LVOT}\right).$$

The SV can also be calculated by SV = EDV − ESV by tracing the LV in end diastole and end systole and using the biplane summation method to calculate volumes.

The pressure gradients across valves can be calculated using the modified Bernoulli equation:

$$\Delta p = 4\,\text{V}^2.$$

Another method to evaluate aortic stenosis is by measuring the mean pressure gradient (PG) by tracing the CW AV signal (or approximating it by calculating 2/3 or 0.7 of max PG). The aortic valve area (AVA) is calculated using Newton's Second law of conservation of energy (Flow in = flow out), therefore,

$$\text{AVA} \times \text{VTI} = \text{CSA}\left(\text{LVOT}\right) \times \text{VTI}\left(\text{PW at LVOT}\right).$$

CSA of LVOT = πr^2. R = radius of the LVOT, CSA = Cross sectional area, VTI = Velocity time integral.

Lastly, a dimensionless index defined as DVI = VTI (LVOT) divided by VTI (AV) is used to estimate severity with a value less than 0.25 signifying severe. This method avoids the error of measuring the LVOT diameter because LVOT squared results in squaring any error obtained.

Table 1.2 shows the classification of the severity of aortic stenosis.

Mitral stenosis can be evaluated with several methods including the determination of the mean pressure gradient by tracing the CW signal across the mitral valve or by calculating the mitral valve area (MVA) by planimetry using the parasternal short axis at the mitral valve level. Additionally, MVA may also be determined by pressure half time (PHT), which is defined as the time for the LA to LV pressure gradient to fall to half its peak. A deceleration time (DT) can be calculated from the slope and PHT = 0.29 × DT and MVA = 220/PHT (Table 1.3).

Quantification of valvular regurgitation can be achieved using volumetric methods or PISA. The

Table 1.2 Recommendations for classification of AS severity [6, 7]

	Aortic sclerosis	Mild	Moderate	Severe
Aortic jet velocity (m/s)	<2.5	2.6–2.9	3.0–4.0	>4.0
Mean PG (mm Hg)	–	<20	20–40	>40
AVA (cm^2)	–	>1.5	1.0–1.5	<1.0
Indexed AVA (cm^2/m^2)	–	>0.85	0.60–0.85	<0.6
Velocity ratio	–	>0.50	0.25–0.50	<0.25

PG pressure gradient, *AVA* aortic valve area

Table 1.3 Recommendations for classification of MS severity [6]

	Mild	Moderate	Severe
Valve area MVA	>1.5	1.0–1.5	<1.0
Mean PG (mm Hg)	<5	5–10	>10
PA pressure (mm Hg)	<30	30–50	>50

The above recommendations are based on the ASE guidelines, however, the AHA/ACC guidelines; define an area >1.5 as progressive, <1.5 as severe, and an area <1.0 as very severe

MVA mitral valve area, *PG* pressure gradient, *PA* pulmonary artery

volumetric methods, uses the principle of "What goes in, must come out". Therefore, the regurgitant volume (RV) across the

$$\text{MV RV}(\text{MR}) = \text{SV}(\text{MV}) - \text{SV}(\text{LVOT})$$

and

$$\text{RV}(\text{AI}) = \text{SV}(\text{LVOT}) - \text{SV}(\text{MR}).$$

The ERO (Effective regurgitant orifice) can be calculated by dividing the regurgitant volume (RV) by the VTI of the regurgitant valve (MR or AI). The regurgitant fraction is calculate by dividing the RV by the SV at the valve i.e., if MR then SV of MV and if AI then SV LVOT. Using the PISA method, by adjusting the aliasing velocity and creating a hemisphere of isovelocity, calculations can be made to quantify regurgitation with the ERO measuring lesion severity and RV measuring volume overload from the regurgitation.

$$\text{ERO} = 2\pi r^2 \times \text{Va}(\text{Aliasing velocity}) / \text{Vmax of MR, RV} = \text{ERO} \times \text{MR VTI, and RF} = \text{RV} / \text{SV of mitral valve.}$$

Similar calculations are made for aortic regurgitation. Tables 1.4 and 1.5 demonstrate the ASE criteria for classification of mitral and aortic regurgitation.

The RVSP and PASP can be estimated. The right atrial pressure (RAP) is estimated using the size or diameter of the IVC. If the IVC diameter is <2.1 cm, the RAP is given a value of 3 mmHg. If the IVC diameter is >2.1 cm and collapses by 50% with a sniff or <2.1 cm and is non-collapsed, then a value of 8 mmHg is given. If the IVC is >2.1 cm and is non-collapsed, then a value of 15 mmHg is given. The RVSP can be calculated using the TR velocity by applying the Bernoulli equation with RVSP = 4 V^2 (TR) + RAP. The pulmonary artery systolic pressure (PASP) is estimated to be equal to the RVSP unless pulmonary stenosis is present.

Finally, shunts such as ASD and VSD can be estimated using the Qp/Qs ratio. The formula to calculate the shunt is

$$\text{Qp} / \text{Qs} = \text{RVOT CSA} \times \text{RVOT VTI} / \text{LVOT CSA} \times \text{LVOT VTI}.$$

The assessment of diastolic dysfunction is an integral part of a routine echocardiographic examination especially in heart failure patients [9]. The most recent diastolic guidelines simplified the algorithm to key variables for the assessment of LV diastolic function grade include mitral inflow velocities (and peak early filling (E-wave) and late diastolic filling (A-wave) velocities, E/A ratio), mitral annular e′ velocity, E/e′ ratio, peak velocity of TR jet, and LA maximum volume index (Fig. 1.5). The algorithm is divided into patients with normal LVEF (left ventricular ejection fraction) and patients with an abnormal LVEF or normal LVEF but with evidence of myocardial disease.

In normal LVEF, if <50% of the below variable are present, then there is normal diastolic function. If >50%, then abnormal diastolic function is present. If 50% or 2/4 variables are satisfied, indeterminate diastolic function id defined.

1. Average E/e' > 14
2. Septal e' velocity < 7 cm/s or Lateral e' velocity <10 cm/s
3. TR velocity > 2.8 m/s
4. LA volume index >34 ml/m^2

In abnormal LVEF or normal LVEF with evidence of myocardial disease, if E/A ≤ 0.8 + E ≤ 50 cm/s, there is normal LAP or left atrial pressure with Grade I Diastolic Dysfunction. On the contrary, if E/A ≥ 2, then there is

increased LAP and Grade III Diastolic Dysfunction. If E/A ≤ 0.8 + E > 50 cm/s, or E/A > 0.8 − <2, then three criteria would need to be evaluated: (1) Average E/e' > 14, (2) TR velocity > 2.8 m/s, (3) LA Vol. index >34 ml/m^2. If two of three or three of three are negative, then there is normal LAP and Grade I diastolic dysfunction. If two criteria are positive, then there is Grade II diastolic dysfunction. When 1/3 criteria are positive, then we cannot determine LAP and Diastolic Dysfunction Grade and other parameters can be looked at such as pulmonary S/D ratio if <1 to determine elevated LAP [9]. In general, left sided filling pressures can be estimated using the E/e' ratio. If E/e' > 14, left sided filling pressures are high and if the E/e' ratio <9, filling pressures are generally normal.

3D echocardiography provided a major advantage in the field of echocardiography and has been able to overcome the limitations of 2D echocardiography by acquiring a pyramidal three-dimensional dataset which avoids the geometrical assumptions from missing the third dimension in 2D and avoiding foreshortened apical views resulting in a more accurate and reproducible evaluation of cardiac chamber size, volume, and function. In fact, multiple studies have shown that 3D volume measurements correlated closely with cardiac MRI which is consider the gold standard. In transthoracic echocardiography, it has become routine to obtain a 3D dataset for evaluation of left ventricle and left atrial volumes, and calculation of a left ventricular ejection fraction (LVEF) (Fig. 1.6).

Table 1.4 Qualitative and quantitative parameters in grading mitral regurgitation severity [8]

	Mild	Moderate	Severe
LA and LV size	Normal	Normal or dilated	Usually dilated
Color flow jet area	Small, central jet	Variable	Large jet (>10 cm^2 or >40% of LA)
Mitral inflow-PW	A wave dominant	Variable	E wave dominant
Jet density-CW	Faint	Dense	Dense
Jet contour-CW	Parabolic	Usually parabolic	Early peaking-triangular
Pulmonary vein flow	Systolic dominance	Systolic blunting	Systolic flow reversal
VC width (cm)	<0.3	0.3–0.69	>0.7
RV (ml)	<30	30–59	>60
RF (%)	<30	30–49	>50
EROA (cm^2)	<0.2	0.2–0.39	>0.4

LA left atrium, *LV* left ventricle, *PW* pulse wave, *CW* continuous wave, *VC* vena contracta, *RV* regurgitant volume, *RF* regurgitant fraction, *EROA* effective regurgitant orifice area

Table 1.5 Qualitative and quantitative parameters in grading aortic regurgitation severity [8]

	Mild	Moderate	Severe
LA and LV size	Normal	Normal or dilated	Usually dilated
Jet width in LVOT-color flow	Small, central jet	Intermediate	Large jet
Jet density-CW	Faint	Dense	Dense
Jet deceleration rate-CW (PHT, ms)	>500	500–200	<200
Diastolic flow reversal in descending aorta-PW	Brief early diastolic reversal	Intermediate	Prominent holodiastolic reversal
VC width (cm)	<0.3	0.3–0.6	>0.6
Jet width/LVOT width, %	<25	25–64	>65
Jet CSA/LVOT CSA, %	<5	5–59	>60
RV (ml)	<30	30–59	>60
RF (%)	<30	30–49	>50
EROA (cm^2)	<0.1	0.1–0.29	>0.3

LA left atrium, *LV* left ventricle, *LVOT* left ventricular outflow tract, *PHT* pressure half time, *PW* pulse wave, *CW* continuous wave, *VC* vena contracta, *RV* regurgitant volume, *RF* regurgitant fraction, *EROA* effective regurgitant orifice area

Strain Imaging has become standard in evaluation of certain disease conditions. The most useful is the use of longitudinal strain obtained by 2D speckle-tracking derived from apical imaging. The protocol involves obtaining apical two, three, and four chamber images to calculate peak systolic strain of the segments of the left ventricle and display the results as a bull's-eye map and averaged longitudinal strain calculated (Fig. 1.6). According to the AUC criteria, strain imaging is quite useful in the initial evaluation prior to exposure to medications/radiation that could result in cardiotoxicity/heart failure, periodic re-evaluation in patient undergoing therapy with cardiotoxic agents and worsening symptoms, evaluation of suspected hypertrophic cardiomyopathy or infiltrative cardiomyopathy such as cardiac amyloidosis (cherry on top pattern with apical sparing) [2].

Complications

As mentioned, echocardiography is generally very safe with no complications. The key procedural complications are usually related to ultrasound enhancing agents or contrast administration or inaccuracy of data.

Clinical Vignettes

Case 1

Sixty-five-year-old male with history of hypertension, hyperlipidemia and heavy alcohol and tobacco use was admitted with 2 weeks of worsening dyspnea on exertion, orthopnea and cough with clear sputum production. His vitals include a blood pressure (BP) of 80/44, heart rate (HR) 126 and respiratory rate (RR) of 22. Physical

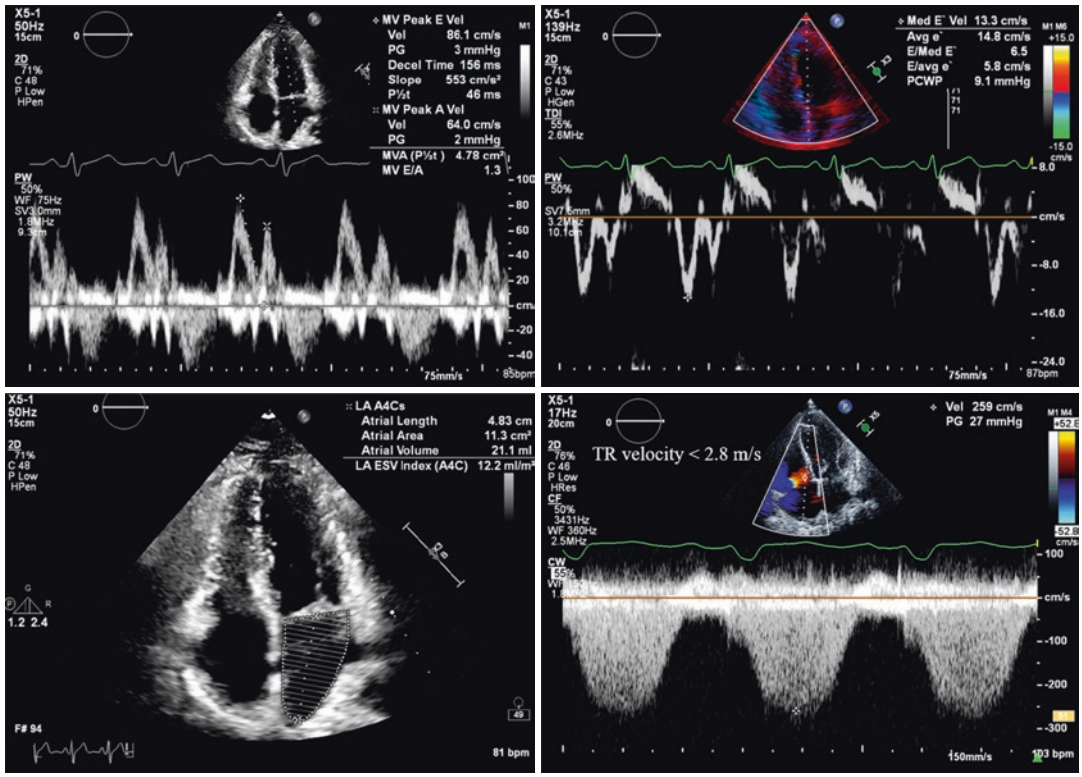

Fig. 1.5 Normal diastolic function with the four variables (E/A ratio, septal e' velocity, E/e' ratio, LA volume index, and TR velocity) to assess diastolic function being normal

exam is significant for distant heart sounds, few crackles and lower extremity edema. ECG is remarkable for low voltage and electrical alternans. 2D transthoracic images are shown in Fig. 1.7.

The TTE images clearly show a large circumferential pericardial effusion that is causing hemodynamic compromise and tamponade. Pericardial effusions are classified as small (less than 1 cm), moderate (1–2 cm), and large (>2 cm). In this case, the effusion is 3–4 cm with diastolic collapse or invagination of the right-sided chambers. The treatment of choice is emergent pericardiocentesis.

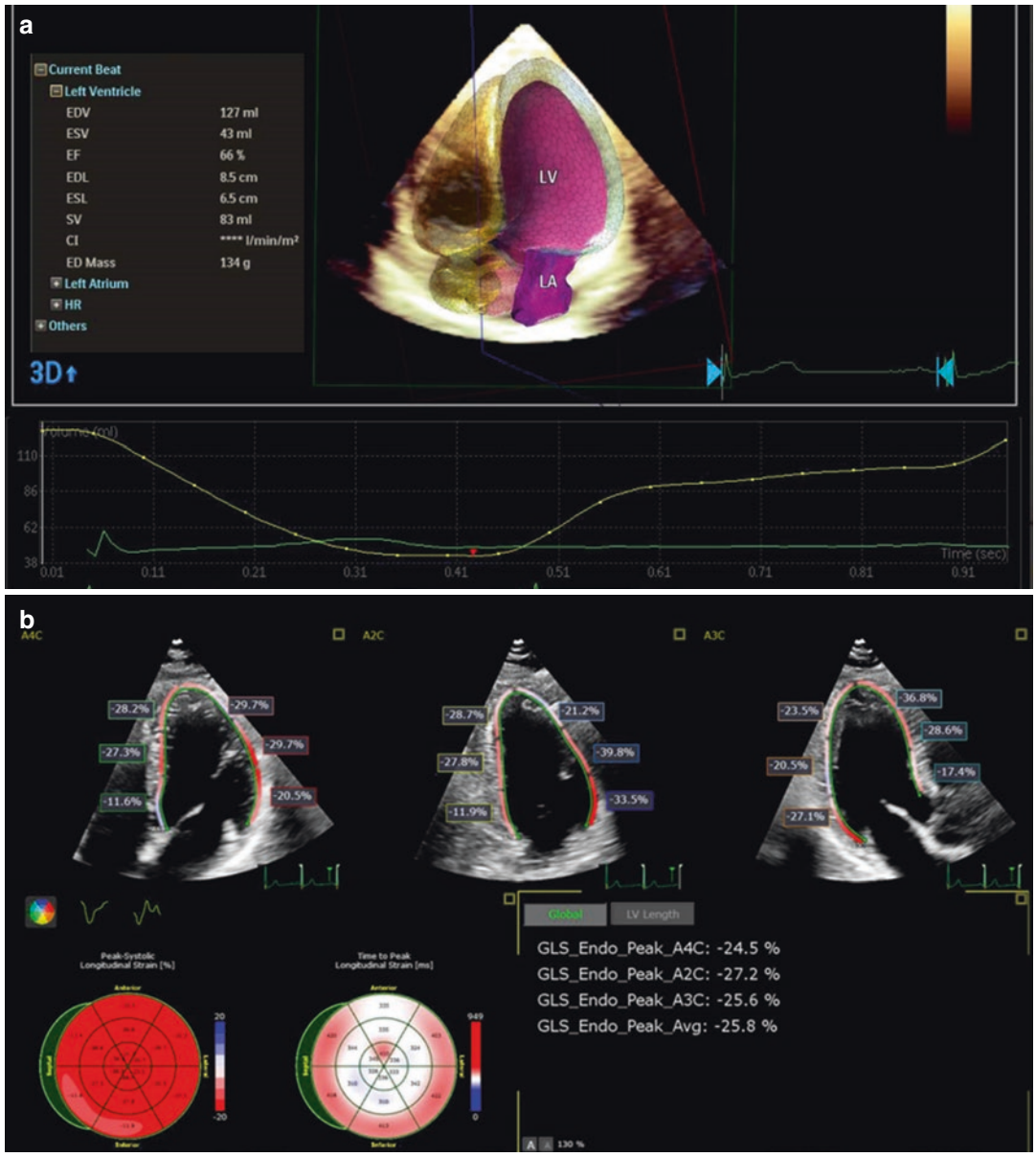

Fig. 1.6 (**a**) 3D echocardiography using a full volume Heart Model to calculate LV end diastolic volume (EDV), end systolic volume (ESV), stroke volume (SV), and Left ventricular ejection fraction (LVEF). Left atrial volume can also be calculated using 3D echocardiography. (**b**) Normal strain imaging using speckle tracking with the Apical four, two and three chamber images and a bulls eye map of normal strain values in a healthy subject

Case 2

Eighty-five year old male with hypertension, hyperlipidemia, prostate cancer s/p radiation and surgery presented with worsening clinical status over the last year with episodes of chest pain, dyspnea and an episode of syncope that prompt the admission. His Vitals are stable. Physical examination is notable for a grade 3/6 systolic murmur at the right upper sternal border with radiation to the carotids, S2 is diminished, lungs bibasilar crackles. ECG evidence of LVH. Transthoracic echocardiographic images are shown in Fig. 1.8.

The TTE images show severe calcifications of the aortic valve with a slit like opening during systole indicating the presence of severe aortic stenosis (As shown in the upper panels). The lower panels show a continuous wave through the aortic valve, a pulse wave at the LVOT level, and a CW of the aortic regurgitation $\Delta p = 4(4\ m/s)^2$ is 64 mmHg. The mean PG is calculated by tracing the CW across the aortic valve or 2/3 of the Peak PG. AVA is calculated at 0.9 cm^2 indicative of severe AS per guidelines (AVA < 1 cm^2) and in symptomatic patients should be referred for aortic valve replacement.

Case 3

Seventy-three-year-old male with multiple cardiovascular risk factors including hypertension, hyperlipidemia, diabetes, active tobacco use, and family history of coronary artery disease who developed chest pain approximately 10 days prior to presentation with typical features during the night that persisted for 3 days. On the day of presentation to the ER, the patient

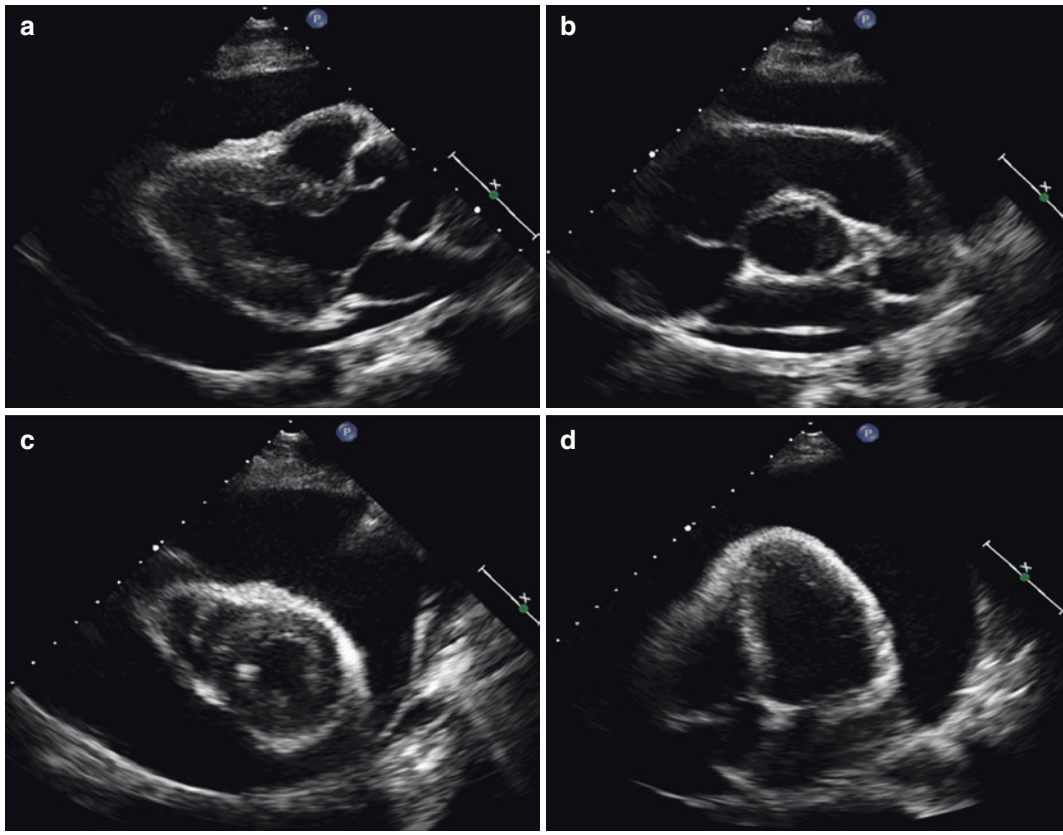

Fig. 1.7 Case #1. (**a**) Parasternal long axis; (**b**, **c**) Short axis, (**d**) Four chamber view (see text for details)

started experiencing significant dyspnea. Vitals were concerning for hypotension, tachycardia and a loud, harsh holosystolic murmur at the apex and left lower sternal border and lung crackles. An ECG showed sinus tachycardia with Q waves in anterior leads. A stat echocardiogram was performed with the images shown below (Fig. 1.9):

Case 4

Fifty-two-year-old female without known prior significant history other than morbid obesity presented to the emergency department with cough, dyspnea on exertion, hemoptysis, and lower extremity edema for the last few months. She also has had unintentional 20-pound weight loss. A TTE was ordered with the images showed below (Fig. 1.10):

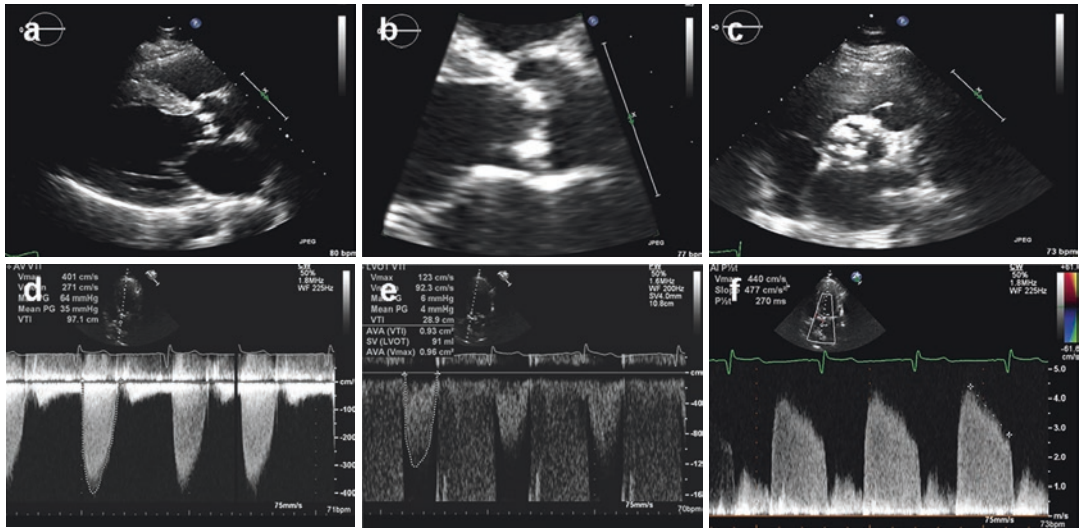

Fig. 1.8 (**a**) Parasternal long axis (severe calcification of the aortic valve). (**b**) Zoom on aortic valve. (**c**) Parasternal short axis. (**d**) Continuous wave Doppler through the aortic valve to measure the peak and mean aortic stenosis gradients. (**e**) Pulse wave Doppler at the LVOT to calculate the aortic stroke volume. (**f**) Continuous wave Doppler through the aortic valve to quantify the pressure half time of aortic regurgitation

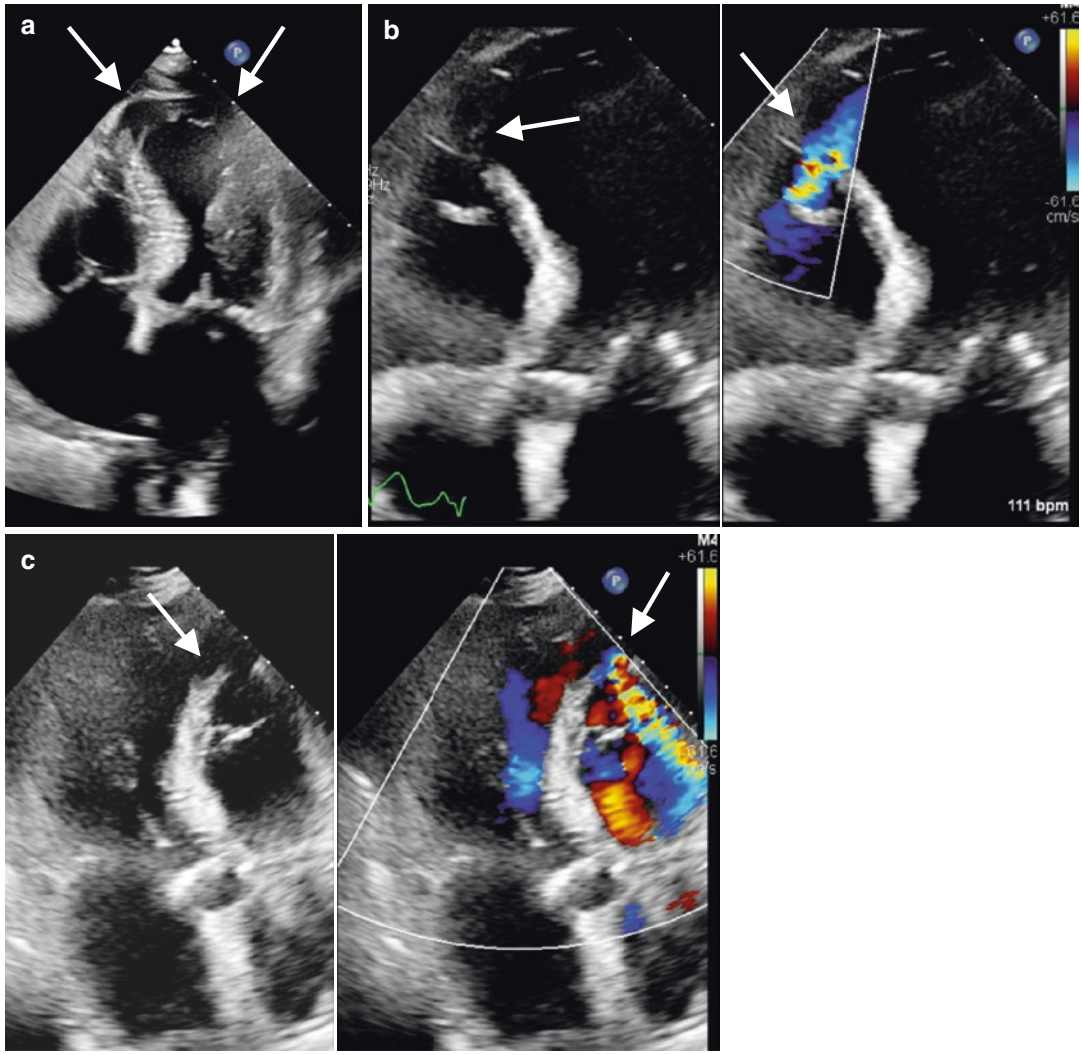

Fig. 1.9 The TTE images show sequela of a large myocardial infarction with panel (**a**) showing apical four chamber image with akinesis of the mid to apical walls and panels (**b, c**) color Doppler of a large interventricular muscular ventricular septal defect (VSD) with left to right shunting. This is a potentially lethal mechanical complication from a presumed late presentation anterior STEMI. Treatment should include stabilization from the cardiogenic shock and surgical repair

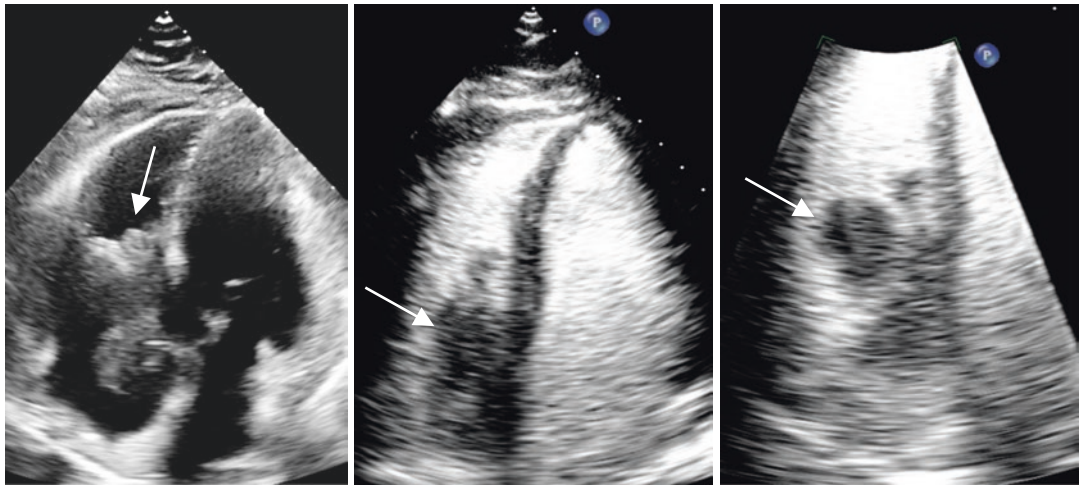

Fig. 1.10 The most likely explanation for the patient's symptoms is a pulmonary embolism that was confirmed on a contrast chest CT. The above echocardiogram images show a large mass prolapsing across the tricuspid valve in the right atrium and ventricle. The use of ultrasound enhancing agents (contrast) clearly demarcates the mass in the right sided chambers. Further images confirmed the extension into the inferior vena cava and along with the patient's history of weight loss prompt further investigations to diagnose a "Tumor Thrombus" which is commonly associated with malignancy such as renal cell carcinoma and hepatocellular carcinoma

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2 Transesophageal Echocardiography

Eddy Karnabi

Transesophageal echocardiography (TEE), in comparison to transthoracic echocardiography (TTE), provides superior image resolution/quality and has become the test of choice in many circumstances. Improved image quality is due to the decreased distance and the absence of bone or lung between the transducer and the heart. However, it is an invasive procedure and hence, should be reserved for indications where TTE provides inadequate diagnostic information.

Indications

The most common indications for TEE are as follows: detection of a cardiac source of embolism as in atrial fibrillation or stroke; evaluating the left atrial appendage (LAA) for a thrombus; endocarditis (vegetations) and its complications; valvular disorders, diagnosing atrial septal defects (ASD) and patent foramen ovale (PFO); evaluating the thoracic aorta (dissection); evaluating acute complications post myocardial infarction; evaluating intracardiac masses/tumors; and guidance for percutaneous cardiac procedures. Table 2.1 shows a list of the appropriate indications of TEE based on the ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR Appropriate Use Criteria [1, 2]:

Contraindications

Absolute contraindications	Relative contraindications
Perforated viscous	Restricted cervical mobility such as atlantoaxial joint disease
Esophageal pathology (stricture, tumor, diverticulum, scleroderma, Mallory-Weiss tear)	Recent upper GI bleeding
Active upper GI bleeding	History of GI surgery
Recent upper GI surgery	Esophagitis, peptic ulcer disease
Esophagectomy	Barrett's esophagitis
	History of dysphagia
	Prior radiation to the chest
	Coagulopathy, thrombocytopenia
	Thoracoabdominal aneurysm
	Symptomatic hiatal hernia

Equipment

Similar to a TTE, the necessary equipment's are the portable echocardiography unit; an ultrasound probe with multiplane imaging capabilities and trained

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Table 2.1 Indications for transesophageal echocardiography [1–3]

1.	Use of TEE when there is a high likelihood of a nondiagnostic TTE due to patient characteristics or inadequate visualization of relevant structures
2.	Evaluation for cardiovascular source of embolus with no identified noncardiac source. Initial evaluation of cardiac mass, suspected tumor, or thrombus
3.	To diagnose infective endocarditis with a moderate or high pretest probability (e.g., staph bacteremia, fungemia, prosthetic heart valve, or intracardiac device)
4.	Evaluation of valvular structure and function to assess suitability for, and assist in planning of, an intervention
5.	Guidance during percutaneous noncoronary cardiac interventions including but not limited to closure device placement, radiofrequency ablation, and percutaneous valve procedures
6.	Suspected acute aortic pathology including but not limited to dissection/transection. Evaluation of the aortic sinuses, Sino-tubular junction, or ascending aorta in patients with bicuspid aortic valve when morphology cannot be assessed on TTE.
7.	Re-evaluation of prior TEE finding for interval change (e.g., resolution of thrombus after anticoagulation, resolution of vegetation after antibiotic therapy) when a change in therapy is anticipated
8.	Evaluation to facilitate clinical decision making with regards to anticoagulation, cardioversion, and/or radiofrequency ablation
9.	Suspected complications of myocardial ischemia/infarction such as acute mitral regurgitation, VSD, free-wall rupture/tamponade, shock, right ventricular involvement, HF, or intraventricular thrombus

personnel in sedation and transesophageal echocardiography based on the ACC/AHA competency guidelines. The TEE probe is a modified gastroesophageal probe with a 3–7 MHz ultrasound transducer at its tip. The diameter of an adult transducer is 9–14 mm and can be maneuvered in a left-right direction and retroflexion/anteflexion using a rotating knob/wheel at the proximal operator end. The transducer tip is equipped with a multiplane that can be rotated from 0° to 180°.

The TEE room should be equipped with vitals monitor to record BP, HR, pulse oximeter, oxygen supply, oral suction, bite guard, pillow wedge to position the patient, and a cardiopulmonary resuscitation crash cart.

In addition to the physician, at least two additional personnel are required: a sonographer to operate the echocardiographic machine, optimize and acquire the images, and a nurse that will be monitoring the patient vitals (BP, HR, RR, oxygen saturation), administering sedatives/analgesics, and suctioning the oropharynx.

Technique

The procedure starts with patient and room preparation. The room should be equipped with all the supplies/medications required as indicated above. TEE is considered a semi-invasive procedure and a thorough conversation should be performed with the patient explaining the indications, alternatives, and possible complications; informed consent should then be obtained. To avoid or reduce the risk of aspiration, the patient should be NPO for at least 6–8 h. Prior to the start of the procedure, a review of the patients' history, medications, allergies, and laboratory data should be performed. A physical exam should also be performed with attention made to the respiratory, cardiovascular system and the Mallampati score (Class I–IV) (Also see Chap. 17). The physical status classification according to the American Society of Anesthesiologists (ASA) should be performed, Classes I–VI, with a level of III and above requiring anesthesiology support. A recent coagulation profile should be reviewed and if patients are on anticoagulation, those agents can be held hours or days prior depending on the type of agent.

The patient is positioned in left lateral decubitus position at a 30–45° inclination to reduce the risk of aspiration. Local anesthesia spray is then performed using tongue depressors to numb the

oropharynx. A bite guard is placed to protect the TEE probe from inadvertent biting. Two techniques have been described for the esophageal intubation: hands-in or hands-out techniques. Using the hands-in technique, two fingers are placed inside the oropharynx and are used to depress the tongue and guide the probe (transducer ultrasound facing towards the tongue) towards the posterior pharynx. If patient is under conscious sedation, he/she can be asked to swallow which assists the probe to easily intubate the esophagus. If resistance is encountered at any point, the probe should not be forced further. The probe has markings to help with localization (distance from incisors to mid esophagus approx. 30–35 cm and distance to the stomach 40–45 cm). Throughout the procedure, the vital signs should be monitored, and the oropharynx suctioned as necessary.

A comprehensive TEE examination is then performed to answer the indication of the study as described below in data interpretation. A key to performing a TEE examination is understanding the terminology of probe manipulation: advancing or withdrawing the probe, flex to the right or left, and anteflexing anteriorly or retroflexing posteriorly. Once the procedure is done, the probe is removed and sent for proper cleaning and the patient monitored for at least 2 h NPO until the gag reflex has returned and the patient recovered from the sedation. If the procedure is elective/outpatient study, he/she is suitable for discharge under the care of a responsible adult with avoidance of driving for at least 12 h.

Data Interpretation

According to the American Society of Echocardiography (ASE), a comprehensive TEE examination includes 28 views [3]. The three primary positions used are upper esophageal (UE), midesophageal (ME), and transgastric (TG). At the ME level, a five chamber (5C) at transducer angle 0–10°, 4C at angle 0–10° slight retroflexion, 2C angle 50–70°, and 3C or long axis views at an angle of 120–140° are obtained (Fig. 2.1). At the UE level, a transducer angle of 25–45° will show the aortic valve in short axis, 50–70° shows the pulmonic valve, 90–110° shows the bicaval view and the interatrial septum (Fig. 2.2). The left atrial appendage (LAA) is usually seen at an angle of 60° with slight counterclockwise rotation (Fig. 2.2). In the TG views, a transducer angle of 0–20° will show the LV

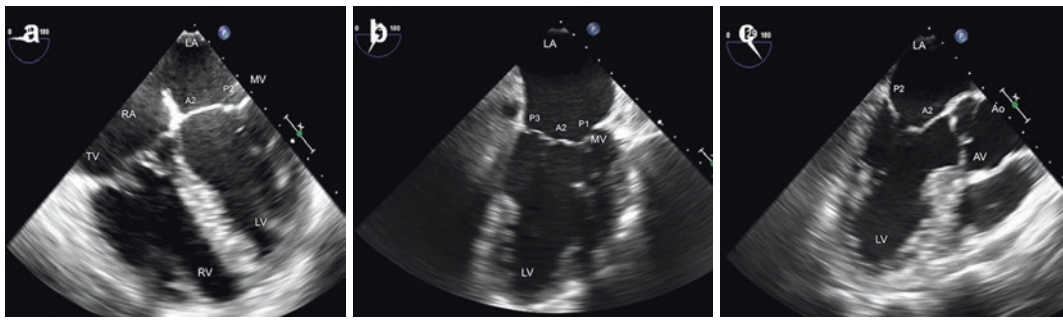

Fig. 2.1 ME (Mid esophageal) TEE images: (**a**) Four chamber view (0–10°) showing the LA, LV, RA, RV with the mitral and tricuspid valve. Note that the mitral valve is divided into anterior (A1–3) and posterior scallops (P1–3). In this view, A2 and P2 are seen. (**b**) Two chamber view (50–70°) showing the LA and LV with the mitral valves and P1, A2, and P3 scallops. (**c**) Three chamber view or long axis (120–140°) showing the LA, LV, mitral valve (A2, P2 scallops) and the aorta with the aortic valve

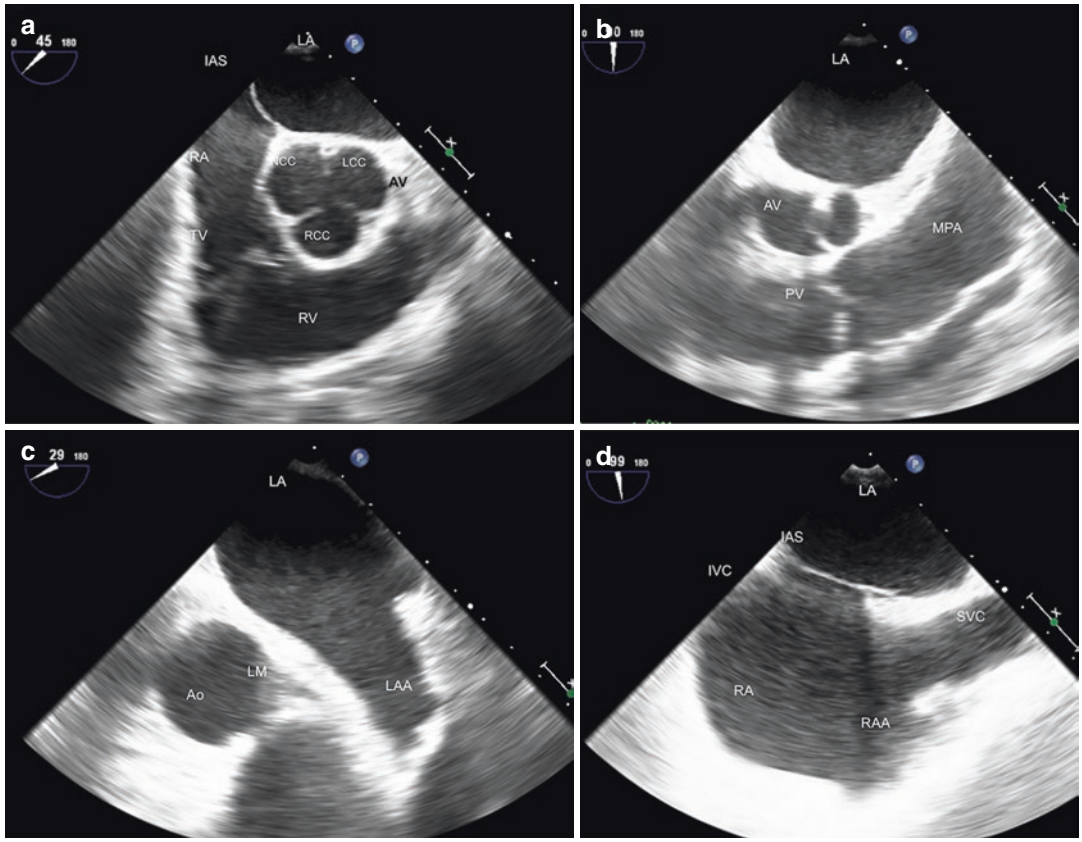

Fig. 2.2 UE (Upper Esophageal) TEE images: (**a**) Short axis of the aortic valve 25–45° showing a tricuspid aortic valve with non-coronary cusp—NCC (at the interatrial septum-IAS), LCC—left coronary cusp, and RCC—right coronary cusp. Note the LA is most posterior and closer to the probe. IAS—inter atrial septum is seen separating the LA and RA. TV-tricuspid valve and the RV outflow tract. (**b**) The PV-pulmonary valve and MPA-main pulmonary arteries are seen with slight increase in the multiplane to 50–70°. (**c**) The probe is withdrawn slightly to above the aortic valve level where the LAA-left atrial appendage can be seen with pectinate muscles at its apex. (**d**) A bicaval view is shown at 90–110° with clockwise rotation with the IAS—interatrial septum, foramen ovale, and RAA—right atrial appendage. Note the location of SVC—superior vena cava and IVC—inferior vena cava

in short axis at the mitral valve and papillary levels, an angle of 90° shows the LV, mitral valve, and papillary muscles in long axis (Fig. 2.3). Clockwise rotation of the probe will reveal the right side including the RV and the tricuspid valve (Fig. 2.3). In cases of aortic stenosis, the aortic valve velocity can be obtained in the TG either at 0° deep TG or at 120° TG (Fig. 2.4). Finally, the aortic views are obtained by rotating the probe 180° degrees either clockwise or counterclockwise so that the probe is facing posteriorly to image the descending aorta and distal aortic arch (Fig. 2.5). An example in which TEE is extremely useful is in evaluation of mitral valve prolapse as shown in (Fig. 2.6).

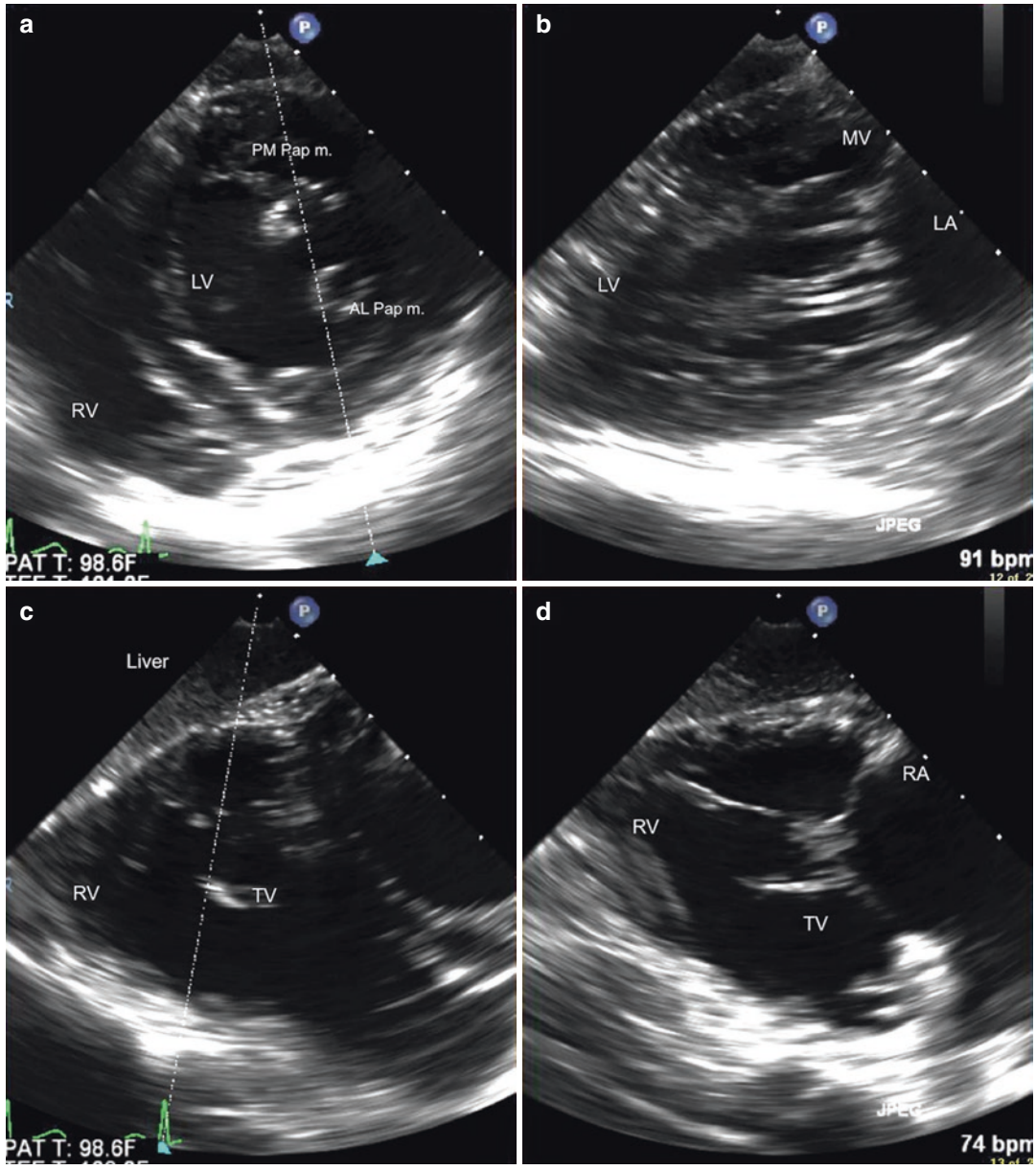

Fig. 2.3 TG (Transgastric) TEE images: (**a**) Short axis view (0°) of the LV showing the Al-anterolateral and PM-posteromedial papillary muscles. (**b**) X-plane through the short axis or multiplane at 90° shows the LV in long axis with mitral valve posterior and anterior leaflets. (**c**, **d**) Right sided views from the TG level are obtained by clockwise rotation of the probe. Panel (**c**) shows the TV-tricuspid valve in short axis and (**d**) in long axis

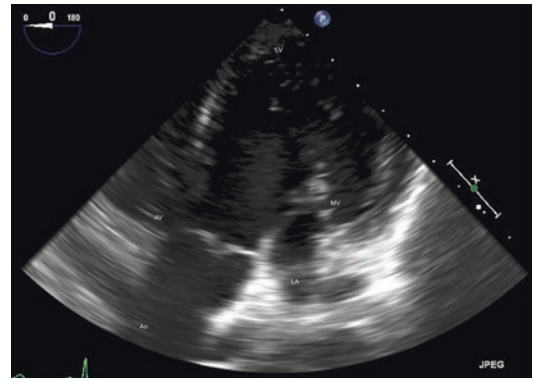

Fig. 2.4 TG TEE view of the aortic valve at 0° deep TG. Alternatively, the aortic valve velocity can be evaluated at 120° TG. These are the two views that are used in cases of aortic valve stenosis that produces the most parallel angle to the transducer for continuous wave flow interrogation

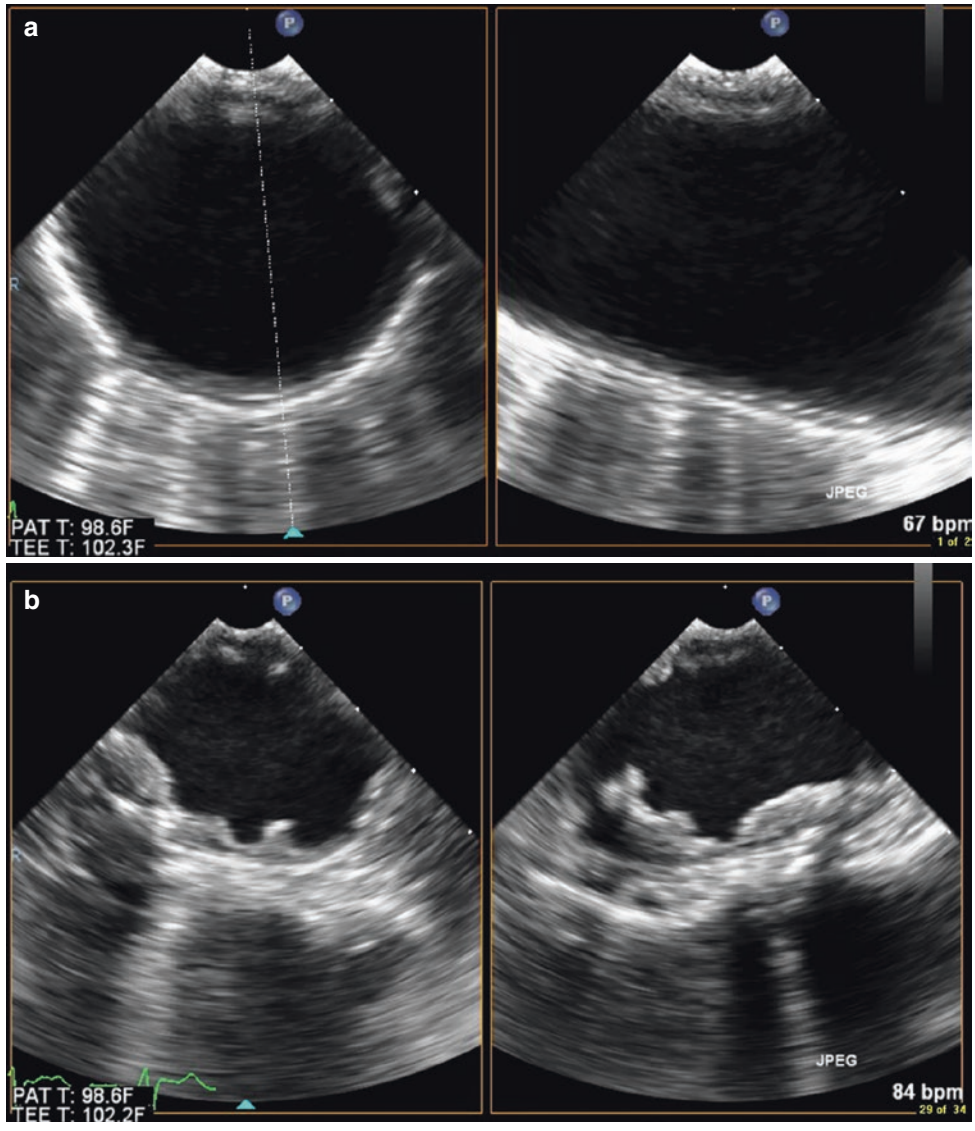

Fig. 2.5 Aortic TEE images: (**a**) Descending aorta in short axis (0°) and long axis (90°) showing absence of atherosclerosis. In comparison, panel (**b**) shows a severely diseased descending aorta with ulcerated atherosclerotic plaques

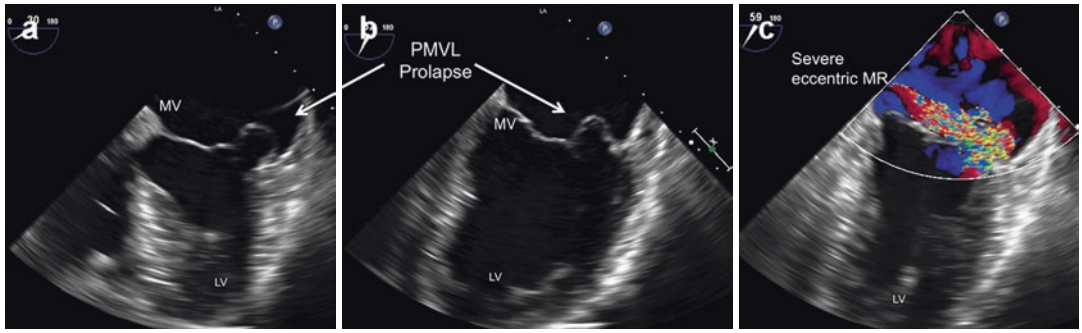

Fig. 2.6 Mitral valve prolapse images: (**a**, **b**) show severe prolapse of the posterior mitral valve leaflet (shown in *arrow*). Panel (**c**) shows severe eccentric mitral regurgitation with an anteriorly directed jet

Complications

Rates of major TEE complications range from 0.2 to 0.5% and the rate of TEE associated mortality is estimated to be less than 0.01% [4]. The risk with the use of local anesthetics to numb the oropharynx using benzocaines include methemoglobinemia that presents as central cyanosis, oxygen desaturation, and brownish color to a blood sample. The risks associated with esophageal intubation include trauma to the oropharynx such as dental trauma, laryngeal/pharyngeal lacerations, bleeding, sore throat and hoarseness, laryngospasm/bronchospasm, and inadvertent tracheal intubation. Similarly, esophageal or gastric trauma, laceration, bleeding, perforation and rupture can occur. The risk associated with sedation whether conscious sedation, MAC (Monitored anesthesia care), or general sedation include hypotension, respiratory depression, aspiration, arrhythmias, and even death. The risks of complications can be reduced dramatically by appropriate patient selection, careful manipulation of the probe during insertion and study, and experience in conscious sedation and the assistance of anesthesiology. Reversal agents should be available bedside in cases such as methemoglobinemia or respiratory depression. The reversal agents are methylene blue (1–2 mg/kg IV ×1) for methemoglobinemia, flumazenil (0.2 mg IV qmin) for benzodiazepines and naloxone (0.4–2 mg IV q2–3 min) for opioid overdose/reversal.

Clinical Vignettes

Case 1

Sixty-four-year-old female with a history of ovarian cancer, hyperlipidemia has been experiencing occasional palpitations over the last 3 months associated with occasional lightheadedness. Two weeks ago, the palpitations became more frequent and were associated with a few pre-syncopal episodes. In the ER, she was noted to be in atrial fibrillation with rapid ventricular response. TEE images are shown in Fig. 2.7.

The TEE images show the upper esophageal views of the LAA-left atrial appendage that clearly demonstrate a small thrombus (arrow). Therefore, cardioversion and catheter ablation are contraindicated. Thrombolytics have no role in treatment of LAA thrombi. The patient should receive at least 4 weeks of anticoagulation, followed up by re-evaluation and possible cardioversion.

Case 2

Forty-two-year-old male with a history of polysubstance abuse and intravenous drug use (IVDU) presented to the ER with fever, shills, shortness of breath, with unstable vitals: hypotension (BP 70/35) and tachycardic (HR 135). A 2D echo was performed, followed by a TEE (Fig. 2.8).

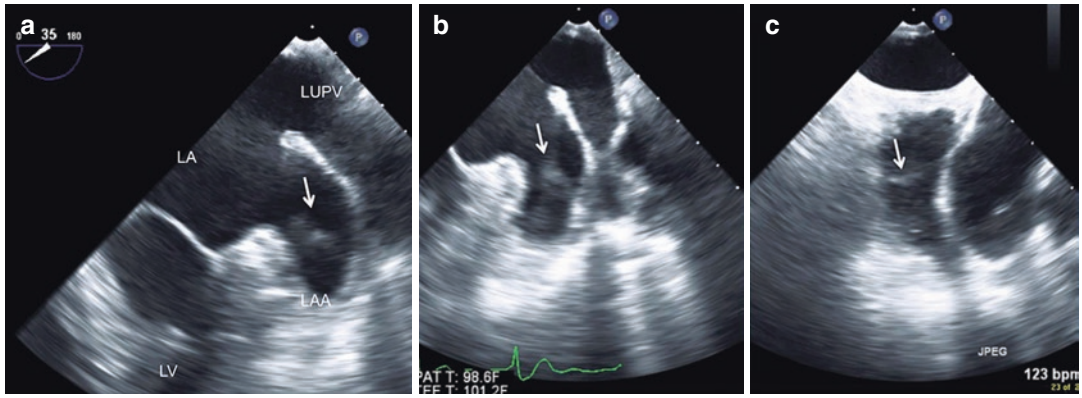

Fig. 2.7 (**a**)–(**c**) TEE views of the left atrial appendage in multi-plane angulations showing the presence of a thrombus

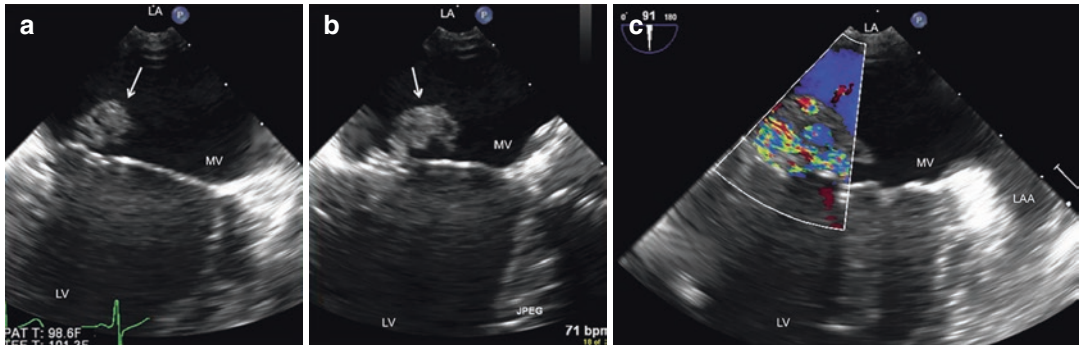

Fig. 2.8 (**a**, **b**) Two chamber views showing the presence of a large vegetation on the mitral valve (**c**). Using color Doppler, severe eccentric mitral regurgitation can be visualized as a consequence of the vegetation

The patient is presenting with hemodynamically unstable septic shock due to mitral valve endocarditis with a large vegetation (arrow) on the posterior mitral leaflet causing severe eccentric mitral regurgitation. The source is most likely due to IV drug use. The patient should be treated for antibiotics, however, considering the size of the vegetation, the severity of associated mitral regurgitation, he should be evaluated by cardiothoracic surgery.

Case 3

Forty-six-year-old female with prior history of hypertension developed acute episode of facial droop and dysarthria. She presented to the emergency department with a CT scan showing an acute stroke. A transesophageal echocardiogram was performed the next day with the images shown in Fig. 2.9.

The transesophageal echocardiogram images show a mid-esophageal bi-caval view with an X-plane and a 1.5 cm round mass attached on a stalk to the septum on the left atrial side, which is rather classic for an atrial myoma. This is beautifully shown on the 3D TEE rendering. The patient had no cardiovascular symptoms but did experience evidence of systemic embolization and surgical removal is usually recommended.

Case 4

Eighty-year-old female with prior history of aortic and mitral stenosis status-post bioprosthetic replacements 12 years prior, atrial fibril-

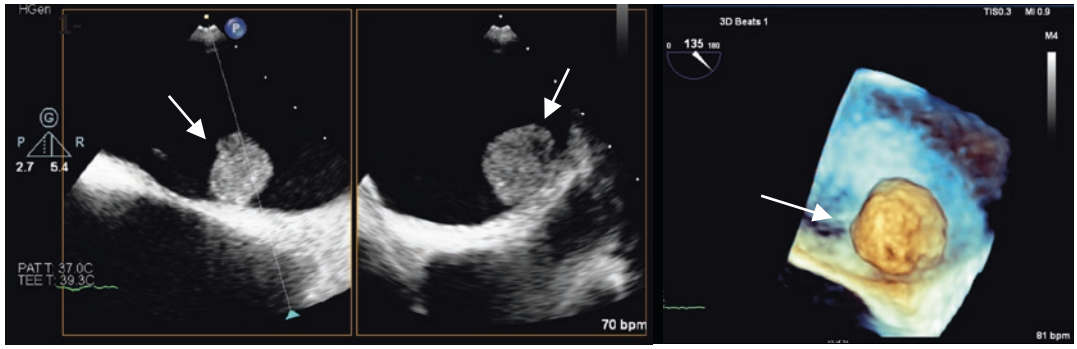

Fig. 2.9 Case 3#: 2D and 3D Transesophageal images showing a 1.5 cm round mass attached to the septum representing an atrial myxoma

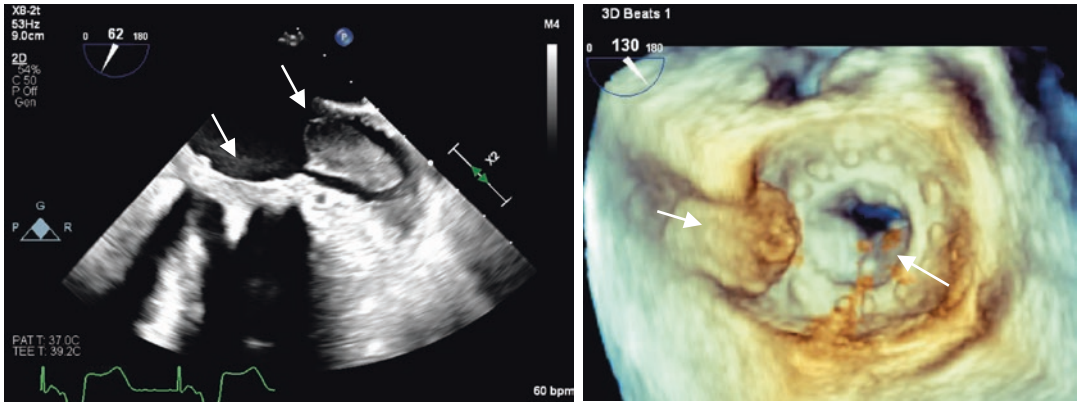

Fig. 2.10 Case #4: 2D and 3D Transesophageal images showing a large left atrial appendage thrombus protruding into the left atrium with a layered thrombus on the mitral prosthesis with resultant mitral valve stenosis (see text for details)

lation, hypertension, diabetes presented to the hospital with significant dyspnea on exertion along with orthopnea, lower extremity edema over the last 6 months. A transthoracic echocardiogram showed evidence of increased gradients of both the mitral and aortic prosthesis consistent with stenosis. A transesophageal echocardiogram was ordered to assess the stenosis with images shown in Fig. 2.10.

The transesophageal echocardiogram show a mid-esophageal view of the mitral valve and left atrial appendage with a large thrombus extending out of the left atrial appendage into the left atrium along with stenosis of the mitral valve prosthesis with layered thrombus on two of the leaflets with restricted opening. The treatment should include anticoagulation and possible surgical intervention.

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Contrast Echocardiography

3

Cesia Gallegos and Robert C. Hendel

Despite the development of improved imaging techniques, contrast echocardiography (CE) remains indispensable for ventricular delineation, enhancement of endocardial border visualization, and assessment of intracardiac structures.

In 2018, the term *ultrasound contrast agents* was replaced by *ultrasound enhancing agents* (UEA) [1, 2] to help distinguish these substances from those that are iodine or gadolinium based. The mechanism of the use of UEA with echocardiography lies in the principle of acoustic impedance, where the change in density from one medium to another causes reflection of sound waves, reason for the use of microbubble contrast agents since gas is less dense than blood. It is important to note that the only FDA approved use for UEAs is for left ventricular opacification (LVO). However, there are other off label uses of UEAs including assessment of myocardial perfusion and viability, guidance of intracoronary injection during alcohol septal ablation in hypertrophic cardiomyopathy patients, as well as enhancement of Doppler signal [2].

There are two types of microbubble contrast agents that will be discussed in the following sections: agitated saline contrast and enhancing agents for LV opacification. Both types must meet the following requirements: small enough to pass through capillaries, strong reflector of ultrasound, long lasting, metabolically inert, and safe [2].

Indications

The assessment of left ventricular (LV) function is the most common indication for UEA use particularly for LVO in patients with suboptimal images, which happens in about 5–10% of cases. It is also the only FDA approved indication. The endpoint is to enhance the endocardial border definition (EBD), for accurate assessment of dimensions, volume, and wall motion.

Indications for the use of UEAs include [1]:

1. To reduce variability in the quantification of LV volumes, LV ejection fraction (LVEF), and wall motion abnormalities (WMA).
2. Assessment of LV function at rest, especially when two or more segments are not seen on non-contrast images mainly due to respiration and increased heart rate and/or in settings in which the study indication requires accurate analysis of WMA.
3. For definite diagnosis when the following are suspected: apical variant of hypertrophic cardiomyopathy, ventricular non-compaction,

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apical thrombus, and complications of myocardial infarction such as LV aneurysm, pseudoaneurysm, and myocardial rupture.
4. For use with stress echocardiography when two or more segments of the LV are not well identified during stress, for the assessment of wall motion abnormalities, to increase accuracy, and increase the reader's confidence.
5. Detection and identification of intracardiac masses including tumors and thrombi.
6. To enhance Doppler signals when spectral profiles cannot be obtained with standard examination
7. To assist in right ventricular assessment.
8. Although not yet FDA approved, contrast injection can be used in myocardial perfusion imaging. It is also useful to guide alcohol septal ablation, and to differentiate between stunned or hibernating myocardium.

Agitated saline on the other hand, provides contrast in the right heart and enables detection of shunts, as the microbubbles remain in the right heart and then diffuse into the lungs, unable to access the left heart unless a right-to-left heart or extracardiac (pulmonary arteriovenous) shunt exists.

The indications for use of agitated saline use include:

1. Detection of cardiac and extracardiac shunts: atrial septal defects (ASD), ventriculoseptal defects (VSD), patient foramen ovale (PFO)
2. Structure identification, particularly the right heart
3. Doppler signal enhancement for evaluation of tricuspid regurgitation and right ventricular systolic pressure.
4. Evaluation of congenital heart disease, such as persistent left superior vena cava

Contraindications

Although generally safe and effective, UEA have some contraindications [1]:

- Hypersensitivity to an agent
- For perflutren protein type-A microspheres (Optison) or perflutren lipid microspheres (Definity) known hypersensitivity to blood, blood products, or albumin
- Fixed right to left, bidirectional or transient right to left cardiac shunts.

Equipment

Agitated saline is composed of bacteriostatic normal saline cannula agitated with 0.5 ml of room air, between two 10 ml syringes. For this, a three-way stopcock should be used, as well as a >20-gauge intravenous (IV) line, preferably in the right arm. The aim is to inject 5 ml of saline and 0.2 ml of air from one syringe to the other prior to immediate injection [3].

There are three FDA approved UEAs that are available world-wide [1]: Optison (GE Healthcare, Princeton, NJ), Lumason (Bracco Diagnostics Inc., Monroe Township, NJ; also known as SonoVue outside of the US), Definity (Luminity in Europe; Lantheus Medical Imaging, North Billerica, MA). Both Optison and Definity use perflutren gas. However, Optison's shell is made of human albumin coating, whereas Definity uses a phospholipid shell. These contrast agents are stable and small in size (2–6 μm) allowing the passage through the pulmonary capillary bed and causing the opacification of the left sided chambers. Because small lumen catheters increase bubble destruction, a 20-gauge or greater needle is usually recommended for administration. A saline flush is required for the use of contrast; therefore, it is generally better to use a three-way stopcock.

Technique

Harmonic imaging, the current standard technique for echocardiography, in its original use was to enhance the detection of contrast. Contrast microbubbles interact with the ultrasound waves in a nonlinear fashion and generate a second harmonic frequency that enhances the detection of the microbubbles. For its optimal use, the transmit power must be reduced from >1.0 to approximately 0.4–0.6. However, this gives the possibility

of contrast destruction with subsequent equivocal results in assessment of the myocardium [3]. Hence, there are contrast-specific imaging modalities, namely low-power, or low Mechanical Index (MI), which deliver best left ventricular opacification and endocardial border definition. MI in these cases is usually between 0.15 and 0.3. With the use of these techniques, less contrast is necessary, minimizing the risk for any adverse effects.

As mentioned above, an infusion pump can be used, as well as an IV bolus, or a diluted bolus, which must be set up prior to starting the procedure. During a rest study, the rate of IV bolus is usually 0.5–1.0 ml/s, with subsequent slow saline flush administration that is to be stopped when contrast is seen in the right ventricle. Repeat doses as necessary may be required. During stress, the contrast should be injected about 30 s prior to exercise termination. For the infusion method, the contrast should be diluted in a 10 ml syringe, or in a 50 ml bag of normal saline, after which the infusion rate must be adjusted. If using a 10 ml syringe, it is usually recommended to slowly push 0.5–1 ml every few minutes, whereas if the saline bag is utilized the rate will determined by the appearance of a contrast image, usually at 150–200 ml/h.

Data Interpretation

For conventional CE with agitated saline, the presence of contrast/bubbles in the left heart indicates the possibility of an intracardiac shunt. The bubbles created do not appear in the left chambers (as the size precludes its passage through the pulmonary capillaries) unless there is a communication between the right and left cardiac chambers in cases of right to left shunts. However, in case of a left to right shunt, negative contrast effect is visualized. For instance, a PFO is diagnosed when more than three bubbles pass from right to left within 3–4 cardiac cycles (Fig. 3.1). Based on the number of bubbles, the PFO is then defined as being small (3–10), medium (10–20), or large (>20 bubbles). If the bubbles are seen >5 cardiac cycles, a pulmonary

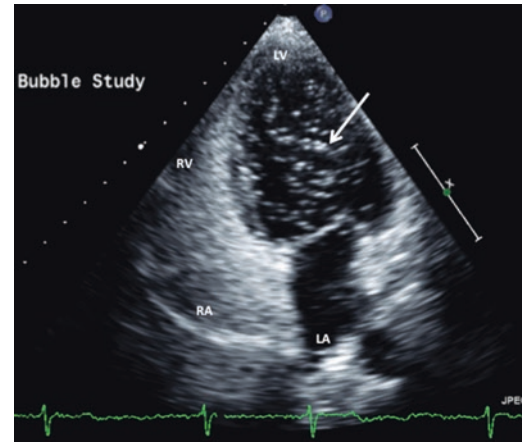

Fig. 3.1 Bubble study with saline injection showing the presence of a PFO with saline bubbles opacifying the right-sided chambers and multiple bubbles passing into the left cardiac chambers (*arrow*)

arteriovenous malformation is suggested. With transthoracic echocardiography, the apical four-chamber view is used. Injection of agitated saline from the left arm, in comparison to the usual injection from the right arm, may help detect the presence of a persistent left superior vena cava (Fig. 3.2) draining into the coronary sinus. Agitated saline bubbles strengthen the Doppler signals from the right heart chamber and augments the tricuspid regurgitation (TR) signal to record the TR gradient used to calculate the right ventricular systolic pressure (RVSP).

In particular cases, for example, in the evaluation of LV masses or thrombi, contrast agents have been shown to improve its diagnosis. A thrombus for instance, is usually seen as a non-opacified structure. Contrast is also useful for the diagnosis of non-compaction, in which the addition of an agent allows for the myocardial layers to be clearly displayed and the ratio to be calculated (2:1 non compacted to compacted myocardium is the usual finding). Contrast can be used in the identification of complications of myocardial infarction such as LV aneurysm, pseudoaneurysm, and myocardial rupture.

CE for stress testing also yields important information, given that images tend to be worse

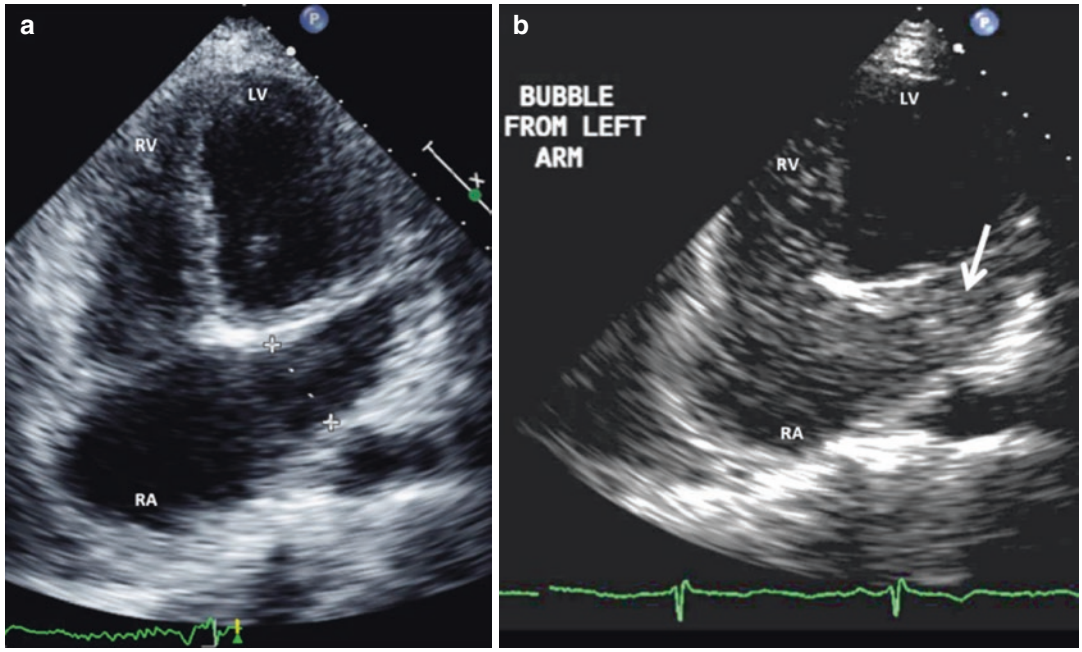

Fig. 3.2 Use of contrast in delineating unknown structures. (**a**) Four chamber view showing the presence of a persistent left SVC (PLSVC). (**b**) A bubble study with the use of saline injection from a left arm vein confirms the presence of the persistent left SVC (*arrow*) draining into the coronary sinus (enlarged). PLSVC is a common variation of the thoracic venous system. In isolation, this entity is benign, but it is frequently associated with other cardiac abnormalities

during stress. Thus, addition of contrast provides a marked improvement in images, and increases the percentage of wall motion abnormalities visualized.

Complications

As mentioned earlier, CE is generally safe, however side effects have been noted, though these tend to be mild and transient. In a small proportion, severe hypersensitivity reactions have been reported. In clinical trials, the most common side effects per contrast agents were [3]:

- SonoVue: Headache (2.1%), Nausea and chest pain (1.3%)
- Optison: Headache (5.4%), Nausea and/or vomiting (4.3%) warm sensation or flushing (3.6%), dizziness (2.5%)
- Definity (Luminity): Headache (2.0%), flushing (1.0%) Back pain (0.9%) rash, urticarial, anaphylaxis.

In summary, contrast agents are safe, effective, and recommended for use with echocardiography, improving the results of echocardiographic imaging studies [3, 4].

Clinical Vignettes

Case 1

Seventy-eight-year-old male with history or prior anterior wall myocardial infarction, hypertension, hyperlipidemia presented to the hospital with left sided weakness for 3 days duration. In ER, as part of his evaluation, a 2D echocardiogram was performed. For better assessment of LV apex, contrast was injected. Images are shown in Fig. 3.3.

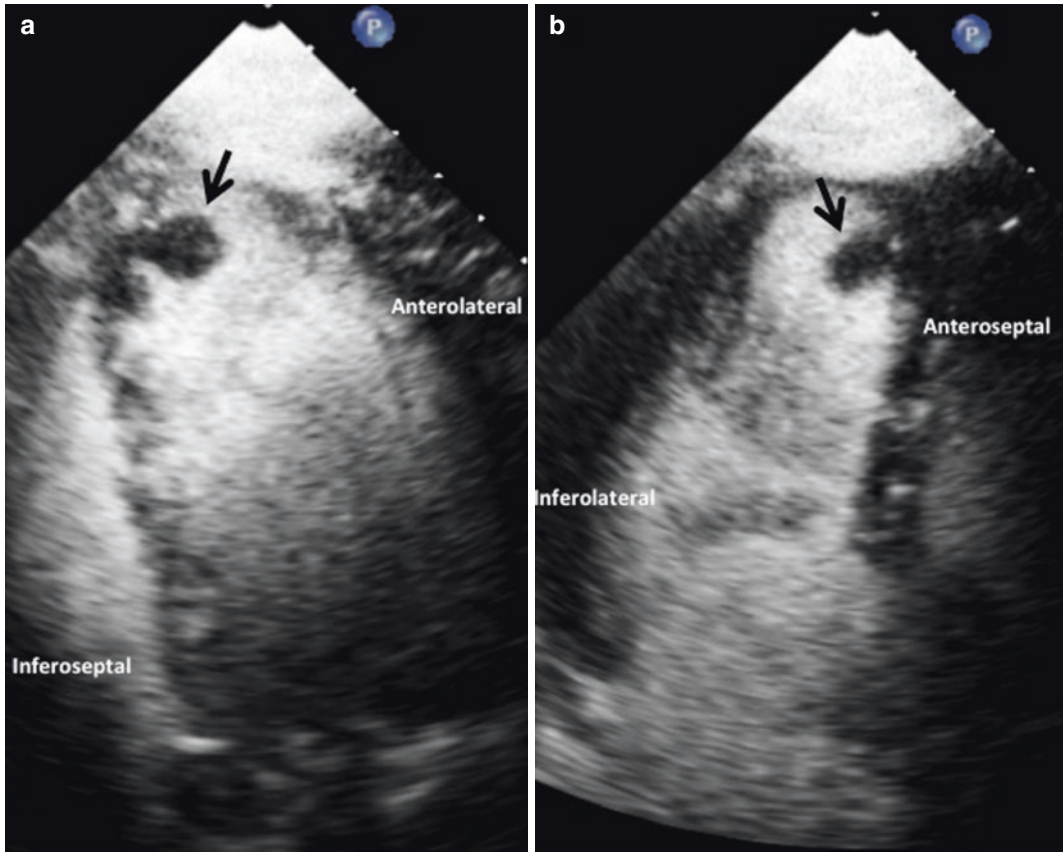

Fig. 3.3 Use of contrast in delineating area of infarction and thrombus. Panel (**a**) and (**b**) demonstrates apical aneurysm with a thrombus on a stalk (*arrow*). See Case #1 text for details

This case shows the presence of apical infarction with akinetic segment and the presence of a moderate size apical aneurysm with a thrombus on a stalk (arrow), that is clearly detected with contrast but can sometimes be missed during a standard echocardiographic examination. In such cases, anticoagulation is recommended.

Case 2

Eighty-five-year-old female with no significant cardiac history presented to the hospital with 2 weeks of chest pain and shortness of breath. While in the ER, she was noted to be in cardiogenic shock requiring inotropic and pressor support. A STAT echo performed is shown in Fig. 3.4.

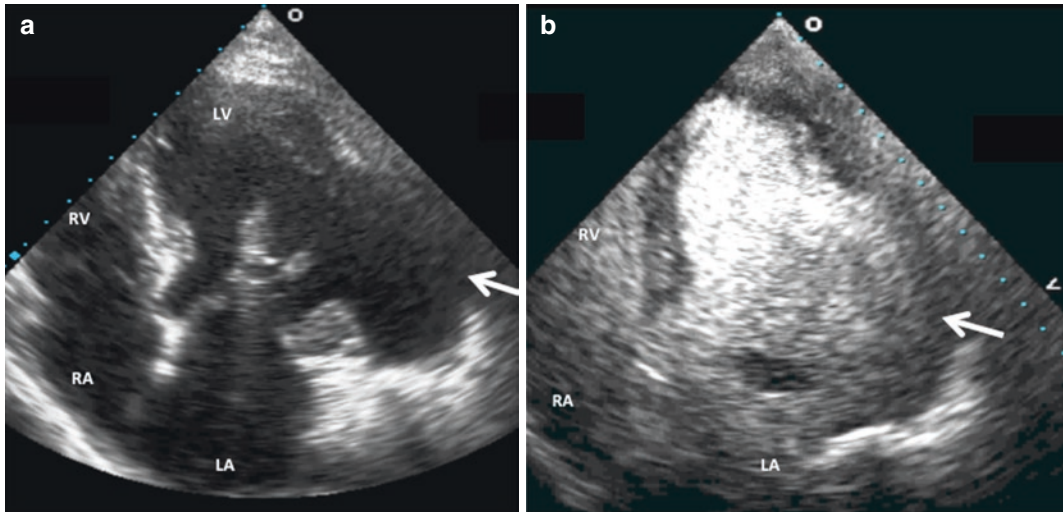

Fig. 3.4 Use of contrast in echocardiography to identify and delineate post-MI aneurysm (*arrow*). (**a**) Four-chamber view without contrast. (**b**) Anterolateral aneurysm noted with contrast. See Case #2 text for details

The images shown represent a complication of myocardial infarction with (a) without contrast and (b) with contrast. The use of contrast clearly helps in establishing the diagnosis of an anterolateral aneurysm as a complication of MI.

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Exercise ECG Stress Testing

4

Eddy Karnabi

Exercise testing (ET) is a well-validated procedure for the diagnosis of coronary artery disease (CAD) and assessing functional capacity and prognosis. Exercise stress tests may detect myocardial ischemia along the ischemic cascade (Fig. 4.1) as a result of a mismatch between myocardial oxygen delivery (from coronary blood flow impairment) and myocardial oxygen demand. It is simple and easy to perform the test, with minimal equipment required.

There are two types of exercise stress tests that can be performed: bicycle and treadmill with the latter being the most widely used in the US. The advantages that bicycle ergometry have over treadmill is the ability to be performed in patients with weight bearing problems, patients with gait/balance and orthopedic abnormalities, a cleaner (less noise) ECG for interpretation, and the ability to take direct measurements of workload in watts which has a linear relationship with myocardial oxygen consumption (MVO2).

Indications

The most common indications according to the 2002 ACC/AHA guidelines for exercise testing and the 2014 guidelines for stable ischemic heart disease [1–3] are (Table 4.1).

Most commonly, ET is used in the diagnosis of ischemic heart disease in patients with intermediate pretest probability of CAD, but may be considered for if low pretest likelihood. ET is also used stratification of patients with intermediate or high pretest probability of CAD based on age, gender, and symptoms (Table 4.2). It may also be appropriate to use ET in asymptomic, high global coronary heart disease risk.

There are several conditions in which exercise tests should be combined with an imaging modality; either myocardial perfusion imaging (MPI-SPECT or PET) or echocardiography. These conditions include: ventricular paced rhythm, left bundle branch block (LBBB), pre-excitation (Wolff-Parkinson-White syndrome), >1 mm ST depression at rest, patients taking digoxin, previous

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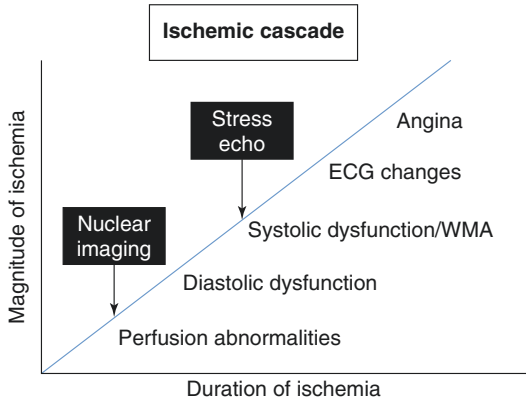

Fig. 4.1 The ischemic cascade: represent the magnitude of ischemia in relation to the increasing duration of ischemia. The initial changes seen are perfusion abnormalities detected with nuclear myocardial perfusion imaging. With increasing ischemia, diastolic dysfunction followed by systolic dysfunction occurs. At this stage, wall motion abnormalities (WMA) are detected by stress echocardiography. It is only at the late stages, that ECG changes and angina develops

Table 4.1 Indications for exercise ECG stress testing

1.	Symptoms suggestive of CAD
2.	Acute chest pain after ACS is ruled out
3.	Recent ACS not treated with coronary angioplasty
4.	Known CAD and change in clinical status
5.	Prior incomplete revascularization
6.	Valvular heart disease
7.	Newly diagnosed cardiomyopathy
8.	Certain cardiac arrhythmias
9.	Pre-op cardiac assessment prior to non-cardiac surgery

PCI/CABG, left ventricular hypertrophy (LVH), and right bundle branch block (RBBB) which precludes ST segment interpretation in leads V1–3.

ET may also be used for patients with valvular heart disease (such as mitral stenosis, aortic stenosis, and aortic regurgitation) to assess for symptoms; this is usually performed in conjunction with echocardiography.

Contraindications (Table 4.3)

Table 4.3 Contraindications to exercise stress testing [1]

Absolute contraindications to exercise stress testing
Acute myocardial infarction (within 2 days)
High risk unstable angina
Uncontrolled cardiac arrhythmias
Symptomatic severe aortic stenosis
Uncontrolled symptomatic heart failure
Acute pulmonary embolus or pulmonary infarction
Acute myocarditis or pericarditis
Acute aortic dissection
Relative contraindications to exercise stress testing
Left main coronary stenosis or it's equivalent
Moderate stenotic valvular heart disease
Electrolyte abnormalities
Severe arterial hypertension
Tachyarrhythmias or bradyarrhythmias
Hypertrophic cardiomyopathy and other forms of outflow tract obstruction
Mental or physical impairment leading to inability to exercise adequately
High degree atrioventricular block

Table 4.2 Pretest probability of CAD

Age (year)	Gender	Typical/definite angina	Atypical/probable angina	Non-anginal chest pain	Asymptomatic
30–39	Men	Intermediate	Intermediate	Low	Very low
	Women	Intermediate	Very low	Very low	Very low
40–49	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Low	Very low	Very low
50–59	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Intermediate	Low	Very low
≥60	Men	High	Intermediate	Intermediate	Low
	Women	High	Intermediate	Intermediate	Low

Equipment

The equipment for a treadmill ECG stress test includes the treadmill, ECG electrodes, BP cuff, and the recording computer system that controls the stress testing protocol being used. In addition, a physician or physician assistant/nurse practitioner should supervise the test (with a physician on site). The exercise protocols in practice are the Bruce protocol, Modified Bruce protocol, Naughton, Blake, and Cornell protocols. Each varies according to the speed and grade parameters. The Bruce protocol is the most widely used and validated; the protocol is divided into 3-min stages that increase in speed and inclination (Table 4.4).

The disadvantages of the Bruce protocol is the large variations in workload between stages and therefore, lowering the diagnostic sensitivity and reducing the value in evaluating functional capacity. The modified Bruce protocol provides a lower workload for patients with poor cardiovascular fitness and in less fit/sedentary and older individuals with stages of 0 and ½ being included at 0 and 5% grades respectively at 1.7 mph. The Naughton protocol is well suited for older debilitated patients (less intense); with the Blake protocol for younger and fit patients; In addition, the ramp protocol is especially useful in heart failure patients in conjunction with cardiopulmonary metabolic testing.

Table 4.4 Bruce protocol

Stage	Minutes	% Grade	MPH	METS
1.	3	10	1.7	5
2.	6	12	2.5	7
3.	9	14	3.4	10
4.	12	16	4.2	13
5.	15	18	5.0	15
6.	18	20	5.5	18
7.	21	22	6.0	20

Technique

The test starts with patient preparation: NPO for at least 4–6 h and instructed to bring comfortable clothing and shoes for the procedure. A thorough review of the patients' history, medications and physical exam should be performed. A proper indication as listed in Table 4.1 should be reviewed. The patient should sign an informed consent after explaining the indication, possible complications and risks of the procedure, which include a risk of 1:10,000 of a serious adverse event (MI or death), and alternative testing. If the test is being done for the diagnosis of CAD, then certain cardiovascular drugs should be withheld if possible, such as beta-blockers, non-dihydropyridine calcium channel blockers (diltiazem and verapamil), and digoxin, certain antiarrhythmics (e.g. Amiodarone and sotalol), or anti-anginal medications (nitrates); this ideally should be done after discussion and under the supervision of their supervising physician. If the test is for functional purpose or to assess symptoms or ischemia, on optimal medical treatment, then cardiovascular medications should be continued.

The next step is to choose the optimal stress test to achieve a satisfactory workload. The choice is usually between a Bruce and Modified Bruce protocol depending on the patients' ability to exercise appropriately to reach the target heart rate response, which is 85% of his/her age, predicted maximal heart rate (APMHR) (220−Age). A patient's capacity is also predicted based on the reported activity level and direct observation prior to the test. The preferred approach is a symptom-limited exercise testing and not simply achieving 85% of the APMHR.

A baseline ECG should be performed to exclude significant abnormalities that can render the ECG non-diagnostic such as: pre-excitation (Wolff-Parkinson-White syndrome), ventricular-paced rhythm, left bundle branch block (LBBB),

more than 1 mm ST depressions at rest, digoxin use with associated ST abnormalities, and left ventricular hypertrophy (LVH) with ST-T wave abnormalities. Next the patient is instructed on the body position during the treadmill exercise by walking erect, near the front of belt with the hands resting on the handrail.

Data are obtained during each stage of the protocol and in recovery with attention paid to any ST depressions or elevations and arrhythmias. Blood pressure measurements should be performed immediately prior to exercise and during the last minute of each stage, as well as during recovery. A normal hemodynamic response to exercise is an increase in systolic and decrease in diastolic pressures. The patient should be visually monitored for any signs of distress and asked frequently about the development of symptoms such as exercise limiting or non-limiting angina. As mentioned, most exercise stress tests should be symptom limited maximal stress tests. Achievement of 85% of APMHR is not an indication for termination of the test. The testing endpoints can be patient related or physician related. In general, if a patient is requesting to stop, it is usually an indication to terminate the test especially if it is associated with symptoms (such as chest pain, dyspnea, dizziness, claudication and fatigue) or arrhythmia. The clinician on the other hand, can decide to terminate the test if there are marked ST depressions or elevations, a new bundle branch block that cannot be distinguished from ventricular tachycardia (VT), new high grade AV block, sustained VT or ventricular fibrillation, increasing frequency of ventricular ectopy, and onset of supraventricular tachyarrhythmias, as well as hypotensive BP response to exercise.

Table 4.5 lists the absolute and relative indications for terminating exercise testing:

If the test is performed in conjunction with myocardial perfusion imaging, the radiopharmaceutical is injected as close to the peak exercise and the patient encouraged to exercise for at least 1 min after the injection.

Post-exercise recovery period should follow the termination of the test; the patient should be continued to be monitored until the HR < 100–110 and SBP < 160 or at the baseline level. It is common and not pathologic for the BP to fall in the immediate post-exercise period.

Table 4.5 Indications for terminating exercise testing

Absolute indications
Drop in systolic blood pressure of >10 mmHg from baseline BP despite an increase in workload, when accompanied by other evidence of ischemia
Moderate to severe angina
Increasing nervous system symptoms (e.g., ataxia, dizziness, or near-syncope)
Signs of poor perfusion (cyanosis or pallor)
Technical difficulties in monitoring ECG or systolic BP
Subject's desire to stop
Sustained ventricular tachycardia
ST elevation (≥1.0 mm) in leads without diagnostic Q-waves (other than V1 or aVR)
Relative indications
Drop in systolic BP of ≥10 mmHg from baseline BP despite an increase in workload, in the absence of other evidence of ischemia
ST or QRS changes such as excessive ST depression (>2 mm of horizontal or downsloping ST-segment depression) or marked axis shift
Arrhythmias other than sustained ventricular tachycardia, including multifocal PVCs, triplets of PVCs, supraventricular tachycardia, heart block, or bradyarrhythmias
Fatigue, shortness of breath, wheezing, leg cramps, or claudication
Development of bundle-branch block or IVCD that cannot be distinguished from ventricular tachycardia
Increasing chest pain
Hypertensive response (systolic BP of >250 mmHg and/or a diastolic BP > 115 mmHg)

Data Interpretation

Interpretation should be performed by an experienced physician. The test can be positive, negative, or non-diagnostic. A test is non-diagnostic if the patient does not achieve the target heart rate of 85% (APMHR = 220−age), or if the baseline ECG is abnormal making the ST changes uninterpretable during exercise. In such cases, the ET is combined with an imaging modality.

The data are analyzed for ECG abnormalities, arrhythmias, symptoms, and functional capacity.

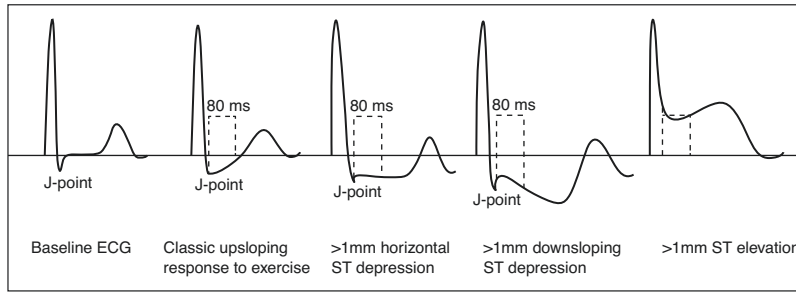

Fig. 4.2 ST segment changes at baseline and during exercise. Classic normal upsloping is seen in normal individuals if the ST segment returns to the isoelectric line by 80 ms after the J-point. Abnormal responses are >1 mm horizontal, downsloping and upsloping ST depressions 80 ms past the J-point

ECG Abnormalities

ST-segment changes deviating from the isoelectric line (determined by the PR segment) are measured 80 milliseconds (ms) beyond the J-point. A normal response to exercise is <1 mm ST horizontal or downsloping depressions, or <1.5 mm when upsloping ST depression is noted (Fig. 4.2). A few diagnostic principles for interpreting ET are: (1) The more leads with ST changes present, the higher probability of ischemia; (2) ST depressions do not localize ischemia to an area of the myocardium; (3) horizontal or downsloping ST depression >1 mm and upsloping depression of >2 mm is abnormal; (4) ischemic ST depression usually occur in the lateral leads (I, V4–6); (5) isolated inferior changes are usually false positive findings secondary to diaphragmatic motion and/or atrial repolarization; (6) changes in R wave amplitude or T wave inversion are not specific markers of ischemia; (7) ST elevation in the setting of Q-waves, represent a prior MI and is the result of abnormal wall motion such as in dyskinetic segment or aneurysm; (8) ST segment elevation represents ischemia and may localize the area of ischemic myocardium; (9) U wave inversion may be associated with ischemia.

Arrhythmias

Sustained VT and VF although rare, are abnormal findings that should prompt further evaluation.

Time to Recovery

Both ST changes and heart rate are two additional parameters to analyze. If rapid recovery (<1 min) of ST changes occurs, the less likelihood ischemia is present. Heart rate recovery is another important prognostic indicator. It is considered abnormal if the difference between maximum HR at peak stress and at 1 min into recovery is 12 beats or less.

Blood Pressure Monitoring

This is another important aspect of exercise testing for safety and diagnostic reasons. A normal hemodynamic response is an increase in systolic BP and a decrease in diastolic BP. The test can be terminated if there is a drop of systolic BP with increasing workload especially to below the resting BP (taken immediately preceding exercise) or excessive systolic BP elevation (SBP > 260). The patient's symptoms should be recorded throughout the procedure and reported.

Prognosis

The Duke Treadmill Score (DTS) calculated as: exercise minutes − (5 × maximal ST changes) − (4 × angina score) is an important predicator of mortality. The angina score is defined as no angina = 0,

non-limiting angina = 1, and limiting angina = 2. A low DTS score is >5, intermediate risk DTS −10 to <5, and high risk DTS < −10. The functional capacity is calculated based on the exercise time with an exercise period of 6 min yielding 7 METS; this is associated with a lower mortality rate independent of any ST changes.

Diagnostic Accuracy

The sensitivity of exercise stress tests is approximately 68% and specificity of 70%, which can be improved with careful patient selection. Myocardial perfusion imaging with exercise stress testing enhances the diagnostic sensitivity and specificity especially in patients with patients with resting ECG abnormalities as mentioned above.

Complications

Complications of exercise testing are rare especially in the healthy low risk patients and increases in the CAD and arrhythmia patients. Arrhythmic events are common in those with a history of prior arrhythmia and can occur in up to 10%; on the contrary, in healthy subjects the overall incidence is approximately 0.1%. The most common arrhythmia is atrial fibrillation. VT and VF are rare and occur in 6 per 10,000 tests and <1 per 10,000 test respectively. Death is extremely rare but may occur in 1 per 25,000 tests. Other cardiovascular complications include ischemia with angina and infarction, bradyarrhythmias such as bundle branch blocks and AV blocks, congestive heart failure, hypertension, hypotension and aneurysm rupture. Noncardiovascular complications include pulmonary (asthma, bronchospasm, exacerbation of underlying pulmonary disease), gastrointestinal (nausea, vomiting), neurological (dizziness, syncope, stroke), and musculoskeletal (muscle cramps, joint pain, exacerbation of musculoskeletal disease, back pain) which are more common.

Clinical Vignettes

Case 1

Fifty year old male with hypertension and hyperlipidemia who has been experiencing episodic chest discomfort during lifting and with heavy exertion. The pain is described as a sharp pain in the mid chest without any radiation. His baseline ECG was normal. His primary care physician sent him for an exercise ECG stress testing. He was able to exercise for 5:29 min at which point the test was terminated after he started experiencing non-limiting chest pain and the ECG findings as noted in Fig. 4.3. His blood pressure at peak stress was 152/68.

The case presents a patient in the intermediate risk group with atypical chest pain. According to Bayes theorem and the appropriateness criteria, he should undergo an exercise stress test especially with a normal baseline ECG. During maximal exercise, the patient experienced chest pain with >2 mm ST depressions in inferior leads and >3 mm ST depressions in lateral leads (V4–6). This is considered a positive response. The patient had a cardiac catheterization that showed 95% stenotic left circumflex artery.

Case 2

Sixty-eight-year-old female with history of left breast cancer s/p mastectomy and radiation, hypertension, tobacco use is being evaluated for pre-op testing and risk stratification prior to contralateral mastectomy. A stress test was ordered. She was able to reach stage 3 when suddenly she started feeling palpitations and lightheadedness. The tracings are shown in Fig. 4.4.

The tracings show the patient converting from sinus tachycardia to a sustained ventricular tachycardia, which is an abnormal response indicative of ischemia or infarction and is associated with a worse outcome and increased mortality. Further evaluation is warranted.

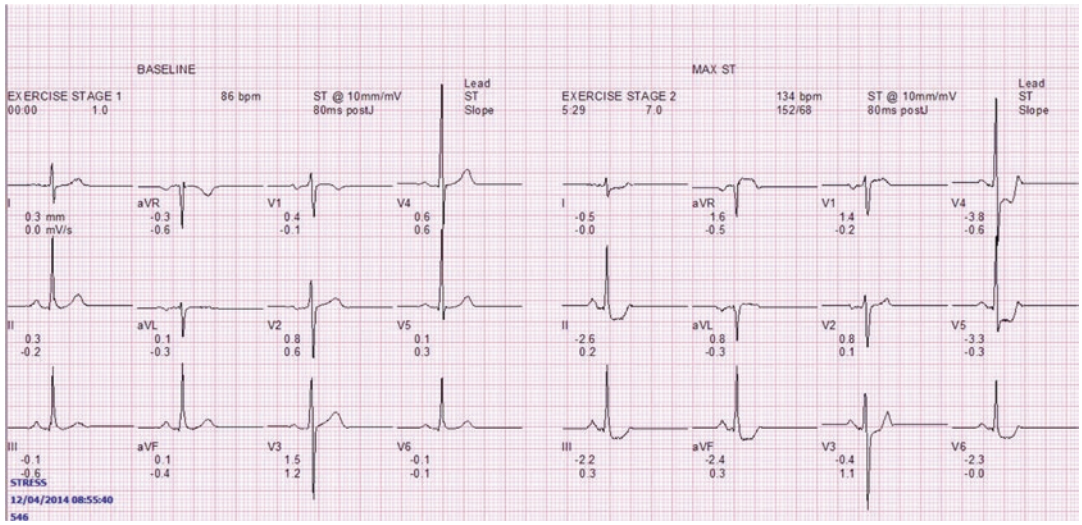

Fig. 4.3 Case #1 (see text for details)

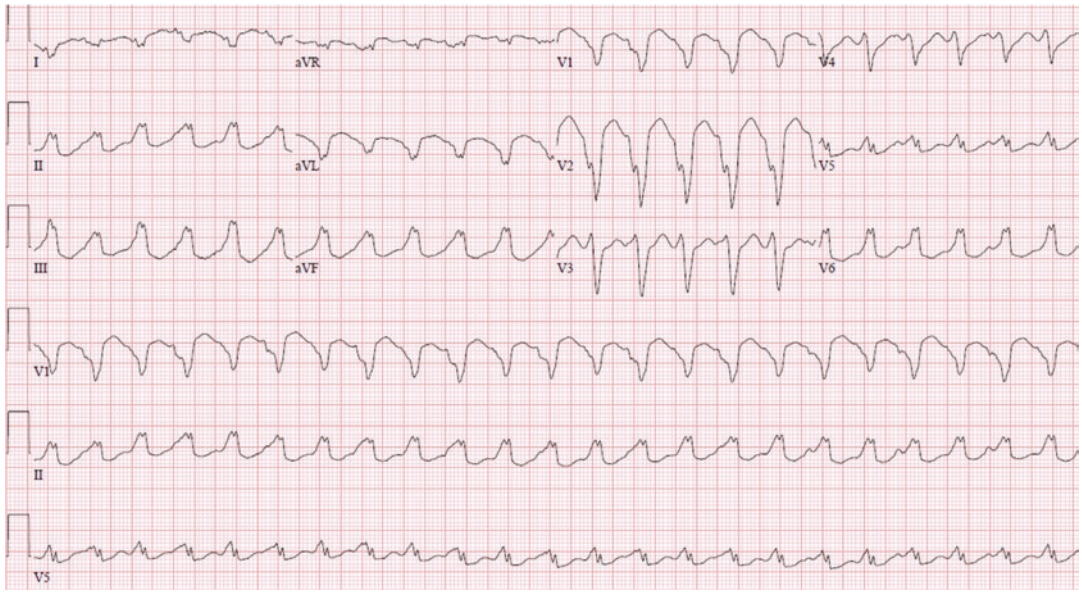

Fig. 4.4 Case #2 (see text for details)

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Cardiopulmonary Exercise Testing

5

Alexis Rodriguez

Introduction

The concomitant gas exchange measurement furthers the modality of exercise testing by estimating oxygen consumption at different exercise intensities. Oxygen consumption, in turn, can be approximated to the measurable metabolic equivalent (MET). Cardiopulmonary exercise testing (CPET) remains the sole method for the direct MET measurement. During this test, many variables are recorded including the expiratory ventilation, pulmonary gas exchange (oxygen uptake and carbon dioxide output), along with electrocardiogram (ECG) and blood pressure recordings [1].

Indications

Assessment of a patient with CPET allows for the evaluation of unexplained dyspnea, exercise intolerance, and cardiopulmonary disease extent including the evaluation of patients with heart failure. Additionally, there are new emerging applications of this diagnostic tool including the evaluation of congenital heart disease in adults, pulmonary hypertension, arrhythmia-induced heart failure, rate-response and biventricular pacemaker evaluation, disability-fitness assessment, and even prior to pulmonary resection. As more clinicians familiarize with this test, and data continue to emerge, CPET applications will continue to broaden including in the distinction and evaluation of pulmonary versus cardiac pathologies [1].

Contraindications

Absolute contraindications include acute myocardial infarction, unstable angina and arrhythmias, acute myopericarditis, severe symptomatic aortic insufficiency, acute pulmonary embolism, uncontrolled asthma, and cognitive impairment limiting subject's cooperation. The ordering clinician should also be aware of relative contraindications. These include, left main (or three-vessel) coronary disease, severe uncontrolled (pulmonary) hypertension, high degree AV block, hypertrophic cardiomyopathy, moderate valvular stenosis, pregnancy, and orthopedic impairment. Furthermore, the test should be terminated early at the patient's request, severe ischemia on ECG, extreme blood pressure responses, hypoxia, among others. On the other hand, some patients report discomfort with the facemask, mouthpiece, or nose clip. Thus, all these should be addressed before starting the test. While all these appear commonsense, they serve to prove the need for comprehensive initial patient assessment, and close monitoring during the exam.

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Equipment

The CPET aim is to progressively increase subject's workload as tolerated. This can be attained by exercising the individual on either a treadmill or cycle ergometer. The former is generally considered more appropriate for active subjects while also allowing for higher oxygen consumption. On the other hand, the latter is preferred in those at risk of falls, requires less training, and allows for blood pressure recording more expeditiously. Besides the treadmill or cycle ergometer, the patient is outfitted with either a mask or mouthpiece for the gas sampling. Blood pressure is also reordered serially throughout the test. A metabolic cart is used to measure the expire gases. For accurate recordings, this system should be monitored and meticulously calibrated to produce consistent results [2]. Figure 5.1 shows the air sealed mask used for gas analysis.

Technique

Different testing protocols have been developed for functional testing. Patient capabilities and diagnostic goals generally determine the choice of CPET and protocol modality. However, the principle is similar for all these, and requires the incremental monitored exercise effort until maximal exertion is reached. Some of these include the Balke and Ware, Naughton, and ramp protocols. Irrespective of the one used, it should be individualized and tailored to yield fatigue-limited exercise, which, in ideal circumstances, should occur between 8 and 12 min. Shorter evaluations produce unreliable non-linear relationships between oxygen uptake and work performed. Contrariwise, more protracted regiments may result in testing termination due to specific muscle fatigue, as opposed to cardiopulmonary endpoints. Finally, patients should be discouraged from significant handrail support since it alters the relationship between oxygen uptake and work, by effectively reducing the latter for any given measurement of the former.

Fig. 5.1 Air-sealed face mask with tubing connected to gas analyzer, used to determine gas flow and values during metabolic testing

Data Interpretation

During exercise, oxygen uptake (Vo_2) can be estimated by the Fick Equation:

$$Vo_2 = SV \times HR \times \left(CaO_2 - CvO_2\right)$$

SV represents the stroke volume, HR the heart rate, CaO_2 the arterial oxygen content, and CvO_2 the venous oxygen. At maximal exercise, this equation would reflect the subject's ability to take in, exchange, transport, and utilize oxygen for aerobic metabolism. The VO_2 response to exercise is linear until a maximum is reached, and then begins to plateau. With higher metabolic workloads, the arterio-venous oxygen difference increases, which is a physiologic response best noted in trained athletes. On the other hand, exercise intolerance is evidenced by any changes in the Fick equation that results in an abnormally low VO_2max, such as suboptimal maximal heart rate response, decrease stroke volume, decrease in CaO_2, or increase in CvO_2 [3].

Other important estimations include the respiratory exchange ratio (RER) and the ventilatory anaerobic threshold (VAT). The former is calculated by dividing the carbon dioxide output by the oxygen uptake. The RER is determined by the main source of metabolic fuel used; with a ratio

of 1 indicative of carbohydrates while <1 represents a mix of carbohydrates and fat, or protein. RER may increase during exercise due to either buffered lactic acid or hyperventilation. Conversely, VAT, or anaerobic threshold, is a determinant of exercise capacity. This principle relies in the fact that at lower workloads metabolism is mostly aerobic whereas there is a shift to lactate production with increasing exercise intensity. The VAT can be determined by directly measuring blood lactic acid or bicarbonate content, or less reliably through non-invasive techniques. Figures 5.2a and 5.2b shows a metabolic test graph report. Normal parameters for CPET and patterns of abnormal results are shown in Tables 5.1 and 5.2, respectively.

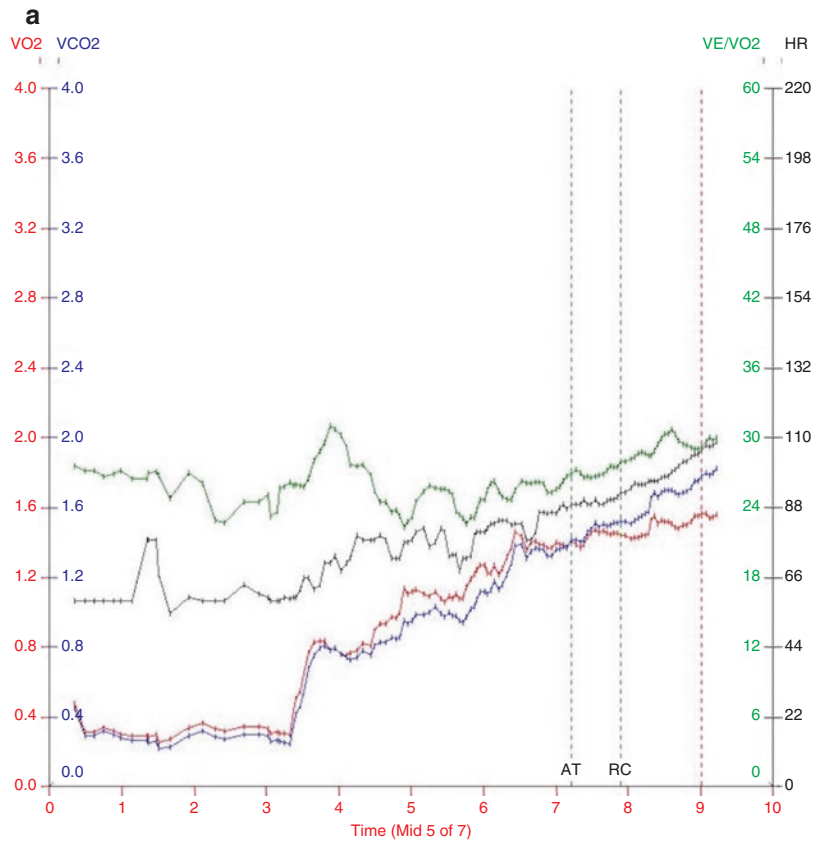

Fig. 5.2a Exercise metabolic test of a patient with history of heart failure. Panel (**a**) demonstrates the continuous calculation of metabolic information, with the horizontal axis corresponding to time in minutes. The *green curve* represents VE/V_{O2}, heart rate in *black*, V_{O2} in *red*, and V_{CO2} in *blue*. The *vertical line* labeled AT represents the aerobic threshold whereas RC represents the beginning of the recovery portion of the test. AT is reached at the point where the V_{O2} and V_{CO2} curves cross each other. From this point, V_{CO2} continues to be generated linearly whereas V_{O2} reaches a plateau

b

Spirometry						
	_	FVC	FEV1	1/FVC	MVV	_
Predicted		5.13	3.95	77	152	
Pre						
% Predicted						

Exercise						
	Rest	AT	VO2 Max	Pred	AT / VO2 Max (%)	VO2 Max/pred (%)
Time (min)	3:15	7:13	9:01			
Ex time (min)		3.56	5.44			
Speed (MPH)	1:1	2.7	2.6		104	
Grade (%)	0:0	14:0	20:9		67	
Borg PE						
---- Oxygen Cons						
VO2 (mL/kg/min)	3.0	13.7	15.2	28.7	90	53
VO2 (mL/min)	310	1407	1569	2955	90	53
VCO2 (mL/min)	256	1413	1481	3576	79	50
RER	0.83	1.00	1.14		88	
METS	0.9	3.9	4.4	8.2	90	53
---- Ventilation						
VE BTPS (L/min)	8.0	37.8	45.8	158.0	83	29
Vt BTPS (L)	0.68	2.04	2.43		84	
RR (br/min)	12	19	19		98	
BR (%)	94.9	76.1	71.0		107	
VE/VO2	26	27	29	37	92	78
VE/VCO2	31	27	26	31	104	83
VE/MVV (%)						
---- Cardiac ----						
HR (BPM)	60	89	106	167	84	64
VO2/HR (mL/beat)	5	16	15	18	107	84
sysBP (mmHg)	110	128	128		100	
diaBP (mmHg)	88	80	80		100	
SpO2 (%)						

Fig. 5.2b Panel (**b**) lists all of the quantitative data. In this patient, the exertion portion started at 3:15 min, AT was reached at 7:13 min, and maximal V_{O2} at 9:01 min. RER was 1.14, functional capacity was less than 75% of predicted, V_{O2} at anaerobic threshold was 13.7 ml/kg/min in the range of 40–49% of the predicted maximum. The heart rate reserve was high while on beta blocker, over 15%. The VE/V_{O2} was 24.4

Table 5.1 Predicted normal parameters for CPET

Variable	Predicted and normal range values
VO_2, max (ml/min)	Based on age, gender, and height
	Lower limit of normal <80% predicted
Resting VO_2, (ml/min)	150 + (6 × weight in kg)
	250–300 in larger obese individuals
Peak heart rate (bpm)	220 − age
	210 − (age × age)
	90% predicted ± 15 bpm
Oxygen pulse (ml/beat)	(Predicted VO_2, max)/(Predicted max HR)
	Normal—80% predicted (about 15 ml/beat in men, and 10 ml/beat in women)
Minute ventilation (l/min)	Peak exercise: 70–80% of MVV
Maximum tidal volume	60% of functional vital capacity
V_E/VCO_2	Early in exercise 25–35
V_E/VO_2	Early in exercise 25–35
V_D/V_T	0.25–0.35 at rest
	Should decrease with exercise
$P_{ET}CO_2$ (mmHg)	38–42
	Declines after ventilator support
$P_{ET}O_2$ (mmHg)	95–100
	Rises after ventilator support
A-a O_2 gradient	Rest: 10–20
	Peak exercise: 15–30
S_aO_2 (%)	>95% and should remain constant throughout
Respiratory exchange ratio	Rest: 0.6–1.0
	Peak exercise: 1.1–1.3

Table 5.2 Cardiopulmonary exercise testing patterns in normal and individuals with various pathologies

Cardiopulmonary exercise testing					
Variable	Normal	Cardiov. disease	COPD	Pulm. Vasc. disease	Neurom. disease
VO_2, max	Normal	Decreased	Decreased	Decreased	Decreased
Heart rate reserve	Absent to small reserve (<20 bpm)	Absent to small reserve (<20 bpm)	Large (>30 bpm)	Small (20–30 bpm)	Large (>30 bpm)
VE, max/MVV (Ventilatory reserve)	<0.8	<0.8	>0.8	<0.8	<0.8
Ventilatory threshold	Present	Present	Absent	Present	Usually present
Dead space (V_D/V_T)	Decreased	Decreased	Decreased	Stable or increased	Decreased
O_2 Sat	Within normal limits	Within normal limits	Decreased	Decreased	Within normal limits
End tidal CO_2	Decreased	Decreased	Increased or stable	Decreased	Increased or stable
Reason for early termination	Lower extremity fatigue	Lower extremity fatigue	Dyspnea	Dyspnea, lower extremity fatigue	Fatigue

CPET Complications

The most widely reported complications are those associated with exercise testing, and include fatigue, shortness of breath, cardiac arrhythmia, syncope, and bronchospasm albeit unusually. The others are more complicated and may require intervention, which can range from medications to more advanced techniques such as cardioversion for unstable arrhythmias. Intolerance of the mask may be a complication preventing adequate data collection.

Clinical Vignettes

Case 1

A 54-year-old gentleman with a history of heart failure with reduced ejection fraction (HFrEF) of non-ischemic etiology is referred by his heart failure physician. His EF has been less than 20% for the last 2 years. He is compliant with his goal-directed optimized medical regiment, and over the last year he received a bi-ventricular pacemaker, upgraded from his prior ICD. He has not been admitted for symptom exacerbation over the last 6 months, but complaints of shortness of breath with minimal exertion. He has otherwise, no significant medical comorbid conditions, and has a reliable social and family support. The patient undergoes CPET and his oxygen uptake (VO2) is calculated at 9 ml/kg/min, and his respiratory exchange ratio (RER) is estimated at 1.20.

This heart failure patient is referred for risk-stratification purposes. He still complaints of shortness of breath with minimal exertion, despite optimized medical therapy, as well as CRT-D. CPET has been used, and published trials have been reported, for the stratification of heart failure patients, and in the prediction of their mortality. His oxygen uptake is low while his respiratory exchange ratio is high. This combination is rather worrisome despite no late admissions for acutely decompensated heart failure symptomatology. This cohort of patients is classified as "very high risk." Patients with VO_2 below 10 ml/kg/min, especially with RER > 1.15, are at the highest risk for adverse cardiovascular events and their mortality rate is higher than any other heart failure group. Indeed, these results warrant further evaluation for more advanced heart failure therapies, i.e. ionotropes, ventricular devices, or cardiac transplantation.

In contrast, patients with VO_2 values ranging between 10 and 18 ml/kg/min should have their minute ventilation (VE) and carbon dioxide output (VCO_2) measured for further stratification.

The slope, or rate of change, of the curve between VE and VCO_2 is then estimated. If the slope is greater, or equal to 35 then the patient is considered to have a mortality similar to those with VO_2 below 10 ml/kg/min, which would warrant re-stratification by RER determination. In turn, those with lower slope values, less than 35, are at moderate risk. Finally, if the Vo_2 is higher than 18 ml/kg/min, these patients are deemed low risk and regular follow up with their cardiologist is indicated.

Case 2

A 45 year old lady with history of pulmonary arterial hypertension (PAH) diagnosed by echocardiography and right sided catheterization (RHC) is referred for CPET evaluation prior to starting bosentan and sildenafil. Her right ventricular systolic pressure by 2D echo and RHC was estimated at 75 and 85 mmHg respectively. She undergoes successful initial evaluation by lower extremity ergometer, and her VO2 is 9 ml/kg/min. The VE/Vco2 slope was estimated at 61.

This patient presents with an established PAH diagnosis. She is being referred prior to starting therapy for her condition. From the values obtained by echocardiography and RHC, the severity of her disease can be estimated. This is further corroborated by her low VO_2 and high V_E/VCO_2 slope, both of which are consistent with severe PAH. In fact, they are indicative of a high-risk patient, who requires aggressive expeditious intervention. There is extensive published data on the role of CPET in PAH. Serial testing is indicated after starting therapy for conditioning monitoring, and possible improvement. In patients whose CPET values trend towards normalization, so do the RHC hemodynamics, 2D echocardiography, NT-proBNP, and symptoms. While CPET has no role in the screening of this pathology as of yet, it has been suggested for high-risk patients, especially those with genetic predisposition. Neither is CPET meant to be the unique monitoring method in this patient population; however, it should be employed as another non-invasive tool, which has been extensively validated.

Case 3

A 25 year old patient is referred for evaluation of shortness of breath with exercise. His symptoms are inconsistent and at times start after half an hour of exertion, others after 10 min. An echocardiogram revealed an EF 60–65%, normal diastology. Longitudinal strain −27%. ECG is unremarkable. PFTs were normal. The patient was reassured. However, returns to clinic 3 months requesting a second opinion. CPET was ordered. The peak VO_2 was 39.5 ml/kg/min. The patient achieved 11.3 METS. Peak HR 181 bpm. Peak BP 190/88 mmHg. Peak double product 34,390. Figures 5.3 and 5.4 contains pertinent data.

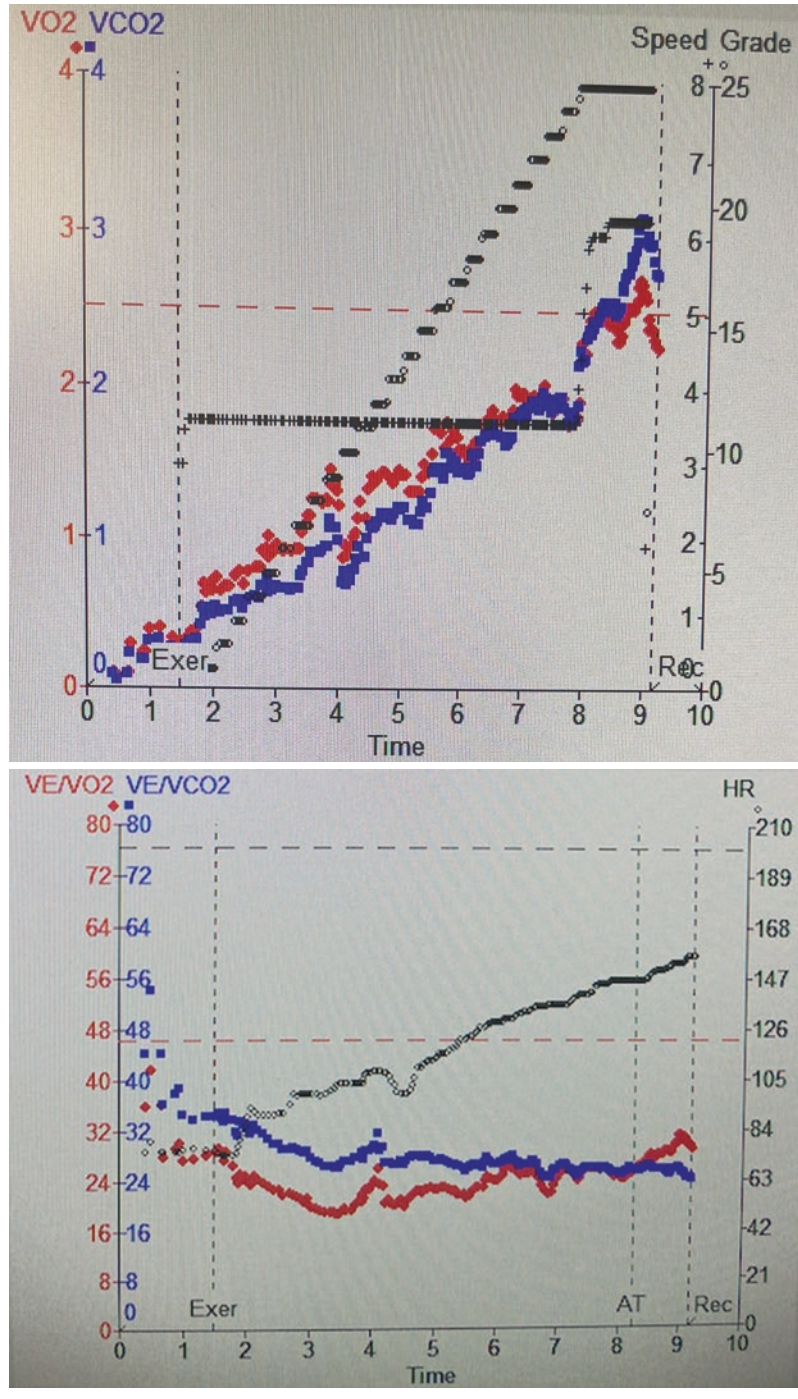

Fig. 5.3 VO2-VCO2 vs. Time

Exercise	Rest	AT	V02 Max	Pred	AT / VO2 Max (%)	VO2 Max/Pred (%)
-----WORK-----						
Time (min)	1:13	8:38	8:43			
Ex Time (min)		7:23	7:28			
Speed (MPH)		6.4	6.4		100	
Grade (%)		24.9	24.9		100	
Borg PE						
----- OXYGEN CONS						
VO2 (mL/kg/min)	3.7	38.7	39.5	33.8	98	117
VO2 (mL/min)	288	2987	3047	2606	98	117
VCO2 (mL/min)	222	2969	3200	3153	93	101
RER	0.77	0.99	1.08		95	
METS	1.1	11.1	11.3	9.7	98	116
----- VENTILATION						
VE BTPS (L/min)	8.4	80.6	83.5	126.0	96	66
Vt BTPS (L)	0.46	1.47	1.60		92	
RR (br/min)	18	55	52		105	
BR (%)	93.3	36.3	33.9		107	
VE/VO2	29	27	27	34	98	81
VE/VCO2	38	27	26	28	104	93
VE/MVV (%)						
----- CARDIAC ----						
HR (BPM)	90	159	159	201	100	79
VO2/HR (mL/beat)	3	19	19	13	98	147
sysBP (mmHg)	110	132	132		100	
diaBP (mmHg)	80	60	60		100	
SpO2 (%)						
Urinary N2 (g/day)						
Hgb (gm/dL)						

Fig. 5.4 VE/VO2 VE/VCO2 vs. time

This exam is consistent with a well-trained individual. The RER > 1.10 at WRmax. The VO_2 at anaerobic threshold was >70% of the predicted VO_2Max. The breathing reserve was also normal. The HR reserve was high. There is some systolic hypertension with exercise, and this may be a point for the patient to monitor in the future. Diastology assessment may be indicated in patients with exercised-induced shortness of breath due to elevation in the filling pressures with activity. However, this is unlikely given the normal resting echocardiogram, and normal longitudinal strain. PFTs were normal, and the patient did not have any symptoms during exercise. While exercise-induced asthma is in the differential, it is unlikely.

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Pharmacologic Stress Testing

6

Eddy Karnabi

Exercise stress testing is usually the preferred stress testing modality unless the patient is unable to exercise or achieve the target heart rate response or possess contraindications to exercise. Additionally, in the presence of LBBB or ventricular paced rhythm, pharmacological stress testing is the modality of choice. Because the sensitivity of pharmacological stress ECG alone is low, a cardiac imaging modality is needed. Pharmacological stress testing is divided into vasodilator stress with the three available agents: adenosine, dipyridamole, or regadenoson or with a catecholamine, dobutamine.

Vasodilator stress is usually in combination with myocardial perfusion imaging (SPECT-single photon emission computed tomography or PET-positron emission tomography), and less frequently with coronary artery CT and cardiac magnetic resonance. Vasodilators agents exert their effects by acting on the adenosine receptors by increasing coronary blood flow and causing a hyperemic response. The rationale behind using vasodilators is due to the significant coronary artery vasodilation that results in three- to fourfold increase in blood flow (Fig. 6.1). A normal coronary artery will exhibit a normal hyperemic response. In a stenotic coronary segment, relative flow heterogeneity is induced which is visualized with myocardial perfusion imaging, with a relative decrease tracer activity within the potentially ischemia zone of myocardium (Fig. 6.2).

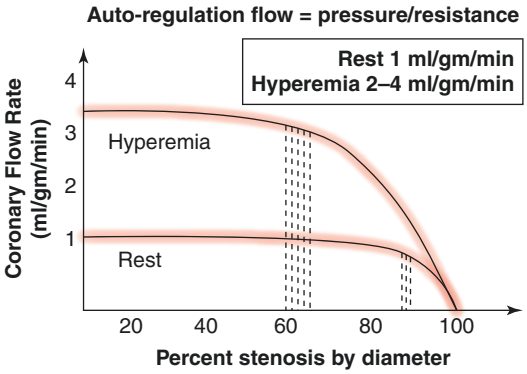

Fig. 6.1 Auto-regulation of flow in normal and hyperemic states (Adapted from Gould et al. [1]). At rest, coronary flow rate is approximately 1 ml/g/min. As coronary stenosis worsens to ~90%, symptoms develop. During vasodilator pharmacological stress testing, coronary flow rates increase two- to fourfold and coronary stenosis can be detected at 60–70% stenosis

The very short half-life of adenosine mandates that the infusion continues during the radiopharmaceutical delivery and uptake (1–2 min). However, the offset of hyperemia is also very rapid. In contrast, dipyridamole and regadenoson have a longer duration of action and may require reversal with aminophylline should side effect develop.

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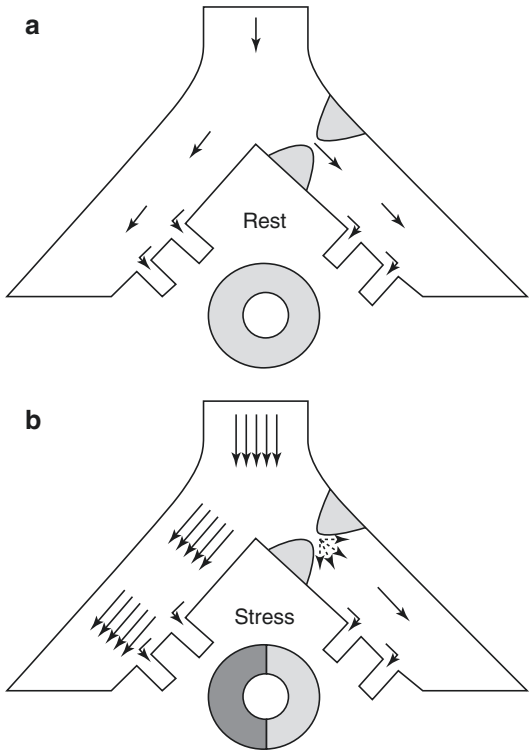

Fig. 6.2 Coronary flow in normal and stenotic arteries during rest and vasodilator stress testing. In normal state (**a**), flow distal to stenosis is compensated by vasodilation distal to the obstruction. During vasodilator stress testing (**b**), non-obstructed coronary arteries induce hyperemic response with increased flow. However, in stenotic arteries, the area distal to stenosis is already maximally dilated at rest and cannot further dilate during stress. This creates a relative hypoperfusion on MPI compared to the normally perfused myocardium

Regadenoson is a selective A2A agonist, which limits the stimulation of non-vasodilatory receptors and reduces adverse effects. Additionally, this agent does not depend on weight-based dosing.

Dobutamine is most commonly used with echocardiography but may also be used in conjunction with nuclear cardiology methods and CMR. Similar to exercise testing, dobutamine induces a positive inotropic and chronotropic response with increase in heart rate and systolic pressure, thereby, increasing myocardial oxygen consumption and induces ischemia and wall motion abnormalities or perfusion defects in the myocardium supplied by a stenotic coronary artery.

Table 6.1 Indications for stress testing

1.	Symptoms suggestive of ischemic heart disease
2.	Acute chest pain after acute coronary syndrome is ruled out
3.	Recent acute coronary syndrome not treated with coronary angioplasty
4.	Known coronary artery disease and change in clinical status
5.	Prior incomplete revascularization
6.	Newly diagnosed cardiomyopathy
7.	Certain cardiac arrhythmias: atrial fibrillation, PVCs, VT
8.	Pre-op cardiac assessment prior to non-cardiac surgery

Indications

The indications for pharmacological stress testing is similar to exercise stress testing (see Chap. 4) and according to the 2002 ACC/AHA guidelines [2] (Table 6.1).

Contraindications

All pharmacologic testing modalities should be avoided in patients with unstable clinical conditions such as hypotension, decompensated heart failure, unstable coronary syndromes or recent ACS, uncontrolled arrhythmias, and severe aortic stenosis. Absolute contraindication is hypersensitivity to any of the stress agents.

With regards to the use of vasodilator stress, the contraindications are related to the effects on the other adenosine receptors (Table 6.2).

In cases of asthma or severe COPD with ongoing wheezing, and high degree AV block, dobutamine is an acceptable alternative. Dobutamine is a positive inotropic and chronotropic agent and should be avoided in situations where the hemodynamic effects may exacerbate existing conditions (Table 6.3).

In cases of severe hypertension and uncontrolled atrial fibrillation, vasodilator stress is an acceptable alternative. Atropine, when used in conjunction with dobutamine, should be avoided in patients with glaucoma, obstructive uropathy and prostate hypertrophy, and chronic lung disease.

Table 6.2 Contraindications for vasodilator stress testing [3]

1.	Asthma or COPD with active wheezing
2.	Second or third degree AV block
3.	Profound bradycardia (<40), sick sinus syndrome
4.	Systolic blood pressure <90
5.	Use of methylxanthines (aminophylline, caffeine) in last 12 h
6.	Recent (<48 h) use of dipyridamole or dipyridamole-containing medications e.g., Aggrenox)
7.	Known hypersensitivity for the stress agent
8.	Critical aortic stenosis
9.	Use of regadenoson or adenosine in patients on chronic dipyridamole

Table 6.3 Contraindications to dobutamine stress testing

1.	Recent acute coronary syndrome
2.	Severe symptomatic aortic stenosis (Mean PG > 40)
3.	Left ventricular outflow obstruction
4.	Arrhythmias: SVT with rapid response, hx of VT
5.	Uncontrolled hypertension
6.	Aortic dissection or large aneurysm

Equipment

The equipment required are similar to those of exercise testing: room with a bed/stretcher, peripheral IV line, crash cart, ECG and BP recording, and an infusion pump for dobutamine, adenosine or dipyridamole. The monitor with vital signs and ECG recording is recorded every minute during the infusion and 3 min during recovery. In addition to the crash cart medications, an access to nitroglycerin, beta-blockers and aminophylline is required in case side effects and/or complications arise.

Technique

Vasodilator Stress

Patient preparation includes NPO status for at least 4–6 h and avoidance of caffeine and methylxanthines for at least 24 h. A careful review of history and a physical exam is performed to detect any cardiac abnormalities such as severe AS or active wheezing. Informed consent is obtained after reviewing for appropriate indications. A peripheral IV is started and ECG electrodes connected, and baseline BP recorded. ECG is reviewed to detect any contraindications for testing. Depending on the protocol, either an infusion or injection is performed (Fig. 6.3). Adenosine is given as a continuous infusion at a rate of 140 mcg/kg/min over 6 min (Fig. 6.3). The radiotracer or contrast agent is injected after 3 min. Dipyridamole is administered as 0.56 mg/kg IV over 4 min or 142 mcg/kg/min, followed by radiotracer injection after 7 min (Fig. 6.3). Regadenoson is given as a rapid injection of 0.4 mg over 10 s, followed by a saline flush (Fig. 6.3). Monitoring involves ECG recording every minute and BP every 2–3 min. If patient exhibits an adverse reaction or becomes symptomatic, either stopping the infusion (adenosine) or giving a reversal agent (dipyridamole, regadenoson), aminophylline 125 mg IV over 1 min should be done. Of note, aminophylline, if possible, should be delayed for at least 1-min post tracer/contrast administration to allow uptake, which will reflect the hyperemic state (Table 6.4).

Dobutamine Stress

Patient preparation includes NPO status for at least 4–6 h and avoidance of beta-blockers for 24 h. A careful review of history and a physical exam is performed to detect any cardiac abnormalities such as severe AS. Informed consent is obtained after reviewing for appropriate indications. A peripheral IV is started and ECG electrodes connected, and baseline BP recorded. ECG is reviewed to detect any contraindications for testing. Dobutamine is infused at gradual increasing doses from 5, 10, 20, 30, and 40 mcg/kg with the option of giving 1–2 mg atropine after 30 mcg/kg dose to achieve 85% APMHR (Fig. 6.3). The infusion should be terminated immediately with the

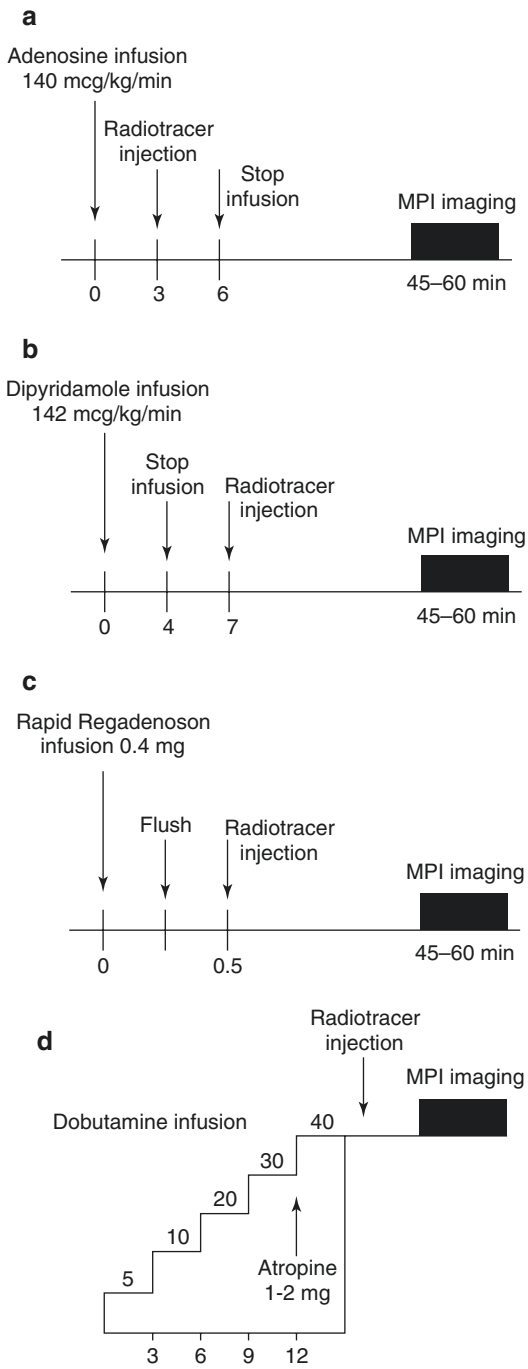

Fig. 6.3 Pharmacological stress infusion protocols [3]. (**a**) Adenosine stress infusion protocol, (**b**) Dipyridamole stress infusion protocol, (**c**) Regadenoson stress infusion protocol, (**d**) Dobutamine stress infusion protocol

Table 6.4 Indications for stopping a vasodilator

1.	Hypotension with SBP <80 or 20 mmHg fall that is accurate
2.	ST depressions >3 mm without angina or >2 mm with angina
3.	Persistent second or third AV block
4.	Severe angina, dyspnea, dizziness, headache, syncope
5.	Arrhythmias
6.	Active wheezing

development of unwanted effects and reversal with IV beta blockers is advised for continued ischemia.

Data Interpretation

Similar to the exercise testing, pharmacological stress testing may be reported as positive, negative or non-diagnostic ECG response depending on the ECG changes observed (see Chap. 4). Isolated pharmacological ECG testing has low sensitivity and is always combined with other forms of imaging especially with vasodilator stress.

Complications

Death and serious complications from pharmacological stress testing are very rare (<1/10,000) in the properly selected patients. Adverse effects, although common (50–75% incidence), are usually mild and bothersome but without major safety concerns. They are either self-limited and dissipate with the cessation if infusion or if intolerable, a reversal agent can be given (Table 6.5).

Combining low-level exercise and vasodilator stress reduces the side effects and enhances image quality and increases detection of myocardial ischemia. The exceptions are left bundle branch block and ventricular paced rhythm where the increased heart rate results in artifacts.

Table 6.5 Common adverse effects of pharmacological stress agents

Vasodilators
Flushing
Chest pain
Dizziness
Dyspnea
GI discomfort
Nausea
Headache
ST changes
AV block
Hypotension
Dobutamine
Chest pain
Headache
Palpitations
GI discomfort
Nausea
Dyspnea
ST changes
Arrhythmias
Hypertension

Clinical Vignettes

Case 1

Seventy-four-year-old female with multiple risk factors for coronary artery disease including a strong family history, active tobacco use, diabetes mellitus, hyperlipidemia with occasional chest discomfort is sent for vasodilator pharmacological stress testing. She denied any history of COPD or cardiac conduction abnormalities. Physical exam is normal with no active wheezing. ECG at baseline was normal without ST or T wave abnormalities. Adenosine stress testing was performed. Two minutes post infusion the patient started complaining of lightheadedness; the ECG obtained is shown in Fig. 6.4.

The patient had an adverse adenosine A1 receptor effect with complete AV block. The first step in urgent management should be immediately stopping the adenosine infusion and inject-

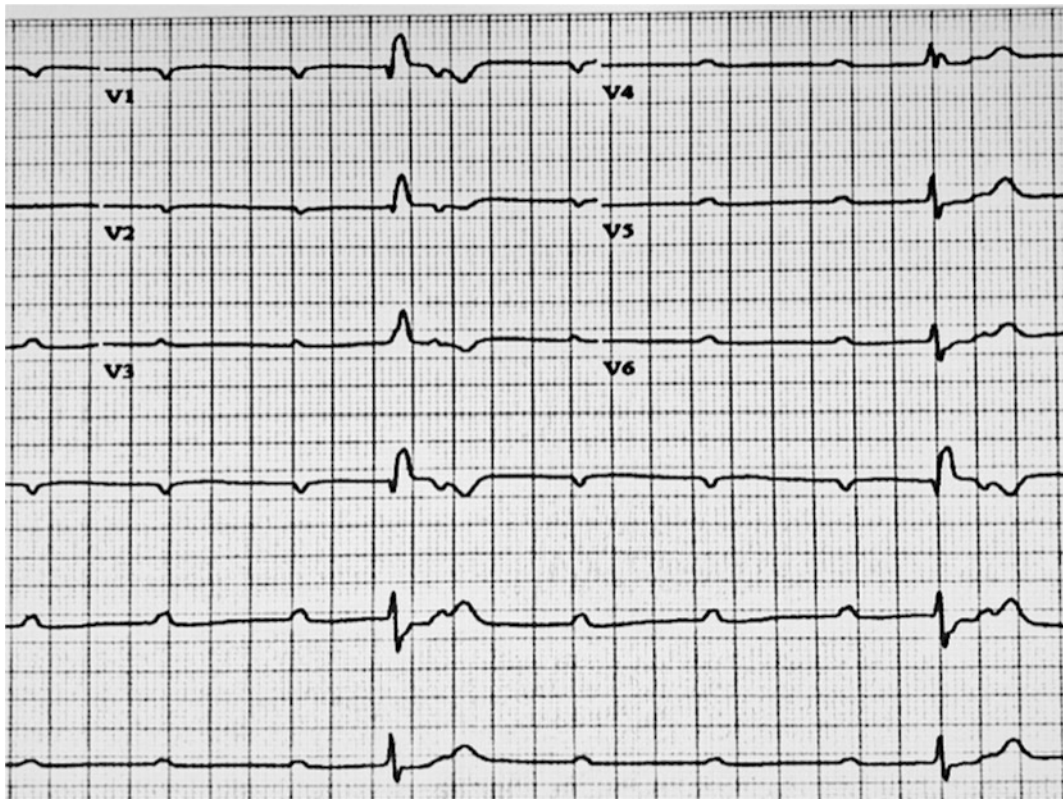

Fig. 6.4 Case #1 (see text for details)

ing 125 mg IV aminophylline if the heart block persists. With regadenoson and dipyridamole, this adverse effect usually occurs after the stress agent administration. Thus, aminophylline and additional patient monitoring is necessary.

Case 2

Fifty-four-year-old male with long standing history of smoking and cocaine use was admitted to the hospital with chest pain. He was ruled out for ACS and sent for stress testing. An exercise stress testing could not be performed due to lower extremity amputation. During the physical examination, he was actively wheezing, therefore, dobutamine stress test was performed. During the infusion, the patient complained of angina. An ECG is shown in Fig. 6.5.

The ECG shows development of ST elevations during dobutamine infusion; myocardial infarction during testing is a rare side effect that should be promptly recognized and treated urgently with cardiac catheterization. The dobutamine infusion should be terminated immediately and NTG administered. Also, a beta-blocker should be given to reduce the increased myocardial oxygen demand provoked by dobutamine.

Case 3

Sixty-four-year-old female with multiple cardiovascular risk factors admitted to the hospital with atypical chest pain. After ACS was ruled out with negative cardiac biomarkers, she underwent a pharmacological stress test with regadenoson. Following the 0.4 mg IV infusion she developed flushing, dizziness, and intractable headache. What is the next best step in management?

This case presents a common side effect of regadenoson which may include flushing, chest pain, dizziness, dyspnea, GI discomfort, nausea, headache, hypotension, ST changes and AV block. Ideally, for optimal tracer uptake, reversal agent's administration, such as aminophylline, should be delayed for 1 min to allow uptake by the myocardium. In this particular case, if the headache is intractable, aminophylline should be given, otherwise, mild symptoms can be treated with caffeine consumption.

Case 4

Forty-six-year-old male with hypertension, hyperlipidemia, below the knee amputation, and long-standing history of smoking who was

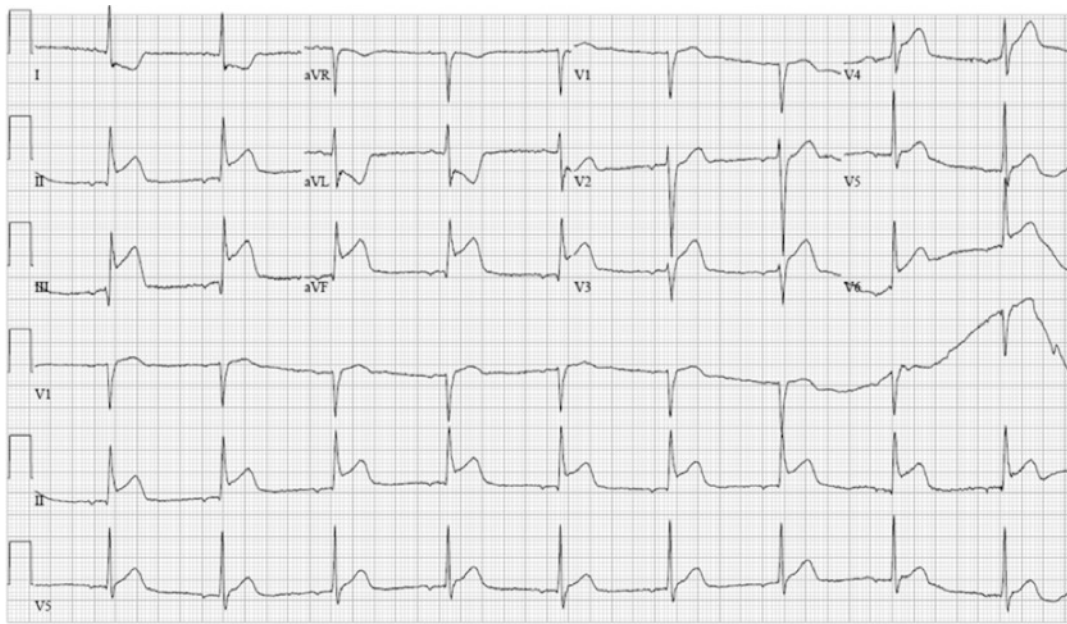

Fig. 6.5 Case #2 (see text for details)

sent by his primary care provider for stress testing due to worsening dyspnea on exertion and concern for angina equivalent. Prior to the stress testing, the patient admits to smoking few cigarettes prior to arrival and is actively wheezing.

Active wheezing is a contraindication to vasodilator stress testing and should not be performed. The best options in this patient would be to perform dobutamine stress with nuclear imaging modality such as SPECT or PET, or to change the test to dobutamine stress echocardiogram if the patient has normal LV systolic function/EF and wall motion.

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Stress Echocardiography

7

Cesia Gallegos and Robert C. Hendel

For more than 40 years, the decrease in contractile function of the heart during acute ischemia/infarction has been demonstrated with two-dimensional echocardiography. Still, it was not until the 1980s that the impact of its use with pharmacological stress became clinically obvious. Stress echocardiography (SE) is an inexpensive and relatively simple procedure with high diagnostic accuracy that may be performed either with exercise (treadmill or bicycle) or with pharmacological stress, predominantly dobutamine. Exercise is the preferred method if the patient can exercise given it mimics the physiologic electromechanical response and provides additional prognostic information [1].

Indications

Currently, there are about 50 indications for SE, which can be classified into the following categories:

- Localization of coronary ischemia and diagnosis of coronary artery disease (CAD)
- Prognosis and risk stratification in patients with an established diagnosis of CAD, including post-revascularization
- Preoperative risk assessment
- Evaluation of hemodynamic parameters in patients with valvular heart disease (aortic and mitral stenosis, mitral regurgitation)
- Special subsets comprise evaluation of hypertrophic cardiomyopathy, pulmonary hypertension, dyspnea of suspected cardiac origin, and in patients with a history of CAD scheduled for elective high-risk surgical procedures

SE is often used when the electrocardiogram (ECG) exercise stress test is non-diagnostic or in patients who have an uninterpretable baseline ECG. Table 7.1 lists some of the indications based on the 2011 Appropriate Use Criteria for Echocardiography and the 2014 Multimodality Appropriateness Criteria.

Contraindications

Contraindications for SE are the same for either exercise testing (Chap. 4) or pharmacologic stress testing (Chap. 6). Absolute contraindications for cardiac stress testing include hemodynamic instability, decompensated heart failure, acute myocardial infarction, patient with acute

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Table 7.1 Common indications for stress echocardiography and their appropriateness [2]

Indication	Appropriate use
Evaluation of ischemic equivalent/ symptoms in a patient with intermediate pretest probability	Appropriate
Acute Chest pain with low TIMI score and negative troponins	Appropriate
Acute Chest pain with definite ACS	Inappropriate
Detection of CAD in an asymptomatic patient with low CAD risk	Inappropriate
Detection of CAD in a patient with new-onset heart failure or left ventricular systolic dysfunction	Appropriate
Evaluation of arrhythmia without ischemic equivalent and no prior cardiac evaluation: Sustained VT, Ventricular fibrillation, frequent PVCs	Appropriate
Perioperative risk assessment for low-risk surgery	Inappropriate
Perioperative risk assessment for intermediate-risk surgery in a patient with moderate to good functional capacity	Inappropriate
Stress echo for risk assessment in a patient within 3 months of an ACS with no recurrent symptoms and after complete revascularization	Inappropriate
Stress echo for risk assessment in a patient within 3 months of an ACS to evaluate for inducible ischemia	Appropriate

chest pain and high pretest probability of CAD, acute aortic dissection, high-risk unstable angina, and severe symptomatic aortic stenosis or with severe left ventricle (LV) enlargement or systolic dysfunction. Absolute indications to terminate stress testing include moderate to severe angina, sustained ventricular tachycardia, near-syncope, drop in systolic pressure >10 mmHg from baseline, in addition to other signs of ischemia [3, 4].

Relative contraindications rely on the technique and patient comorbidities. In about 5% of cases, a poor acoustic window will severely limit the value of SE. A difficult resting echocardiogram serves as a cue that no interpretable results will likely be obtained during stress. Ultrasound enhancing agent (UEA) administration should be considered for improved opacification of the LV cavity (Chap. 3). Additionally, some conditions may reduce the diagnostic accuracy of the test, including preexisting wall motion abnormalities that tether adjacent segments. The evaluation of hypertrophic cardiomyopathy and other cardiomyopathies may also be challenging. Uncontrolled hypertension may also prevent attaining an adequate level of stress.

Equipment

The stress portion of this procedure may be performed with exercise or with pharmacological stressors-all required equipment should therefore be present, as outlined in previous chapters.

Use of UEAs may be needed for either exercise or pharmacological studies and should be administered when two or more segments are not well visualized to improve accuracy by opacifying the LV, enhancing the endocardial border, and reducing the frequency of equivocal findings (Chap. 3).

A blood pressure cuff is required for registering blood pressure at rest and during every stage of the test. A 12-lead ECG should be performed at rest with monitoring throughout the examination. For the echocardiographic images, an ultrasound system that permits one-to-one registration of images both during rest and stress to enable concomitant comparison is necessary. A workstation equipped with software that allows for split and quad-screen displays for concurrent comparisons of the images at the various stages of stress is required. This is essential to be able to elicit subtle wall motion changes. The advances in digital imaging also allow assessing multiple cardiac cycles during stress, hence improving interpretation analysis. Image backup should be performed. Most importantly, highly qualified professionals that are skillful in the imaging technique should perform and interpret the study.

Technique

All methods of stress testing should include standardization of protocols and monitoring of vital signs and ECG at rest and during stress. LV images are obtained from two parasternal views:

long and short, and apical-long axis, apical four- and two-chamber view both at rest and then at stress in the case of exercise, and at every dobutamine dose. A baseline echocardiogram should be performed to assess for LV function and wall motion, chamber sizes, wall thickness, aortic root and valves morphology and functionality, and to screen for contraindications for the test, significant pathology, and to ensure adequate image quality [3, 4]. If the endocardial resolution is not optimal in two or more segments, then UEA should be used as described in Chap. 3. These agents not only improve the number of interpretable LV wall segments but also the accuracy of less experienced readers and reduces the need for additional testing.

Subsequently, a comparison of rest and stress images is performed to assess LV function and regional wall motion abnormalities. Doppler imaging can also be performed for the measurement of pressure and flow gradients when assessing for valvular diseases and estimation of pulmonary artery systolic pressures, both at rest and peak stress.

The test is completed either by exercise-limiting symptoms or completion of the protocol, as with all forms of stress testing, but should also be terminated with the development of new or worsening wall motion abnormalities (i.e., akinesis of more than two LV segments-in bicycle and pharmacologic stress) in addition to the usual indications.

Exercise

When the choice of stress is the treadmill, imaging is usually not feasible during exercise and is actually performed immediately after, aiming to complete image acquisition within 1 min from the cessation of exercise. This assumes that the ischemia will persist for at least that time; hence if it recovers rapidly, false negatives occur. To achieve this, the patient must be rapidly transferred from the treadmill to the appropriate supine position. This requires patient cooperation and a well-coordinated approach by staff. If a stationary bike is used, workload is increased every 2–3 min and images in this case are obtained at peak stress. Although true stress images may also be obtained with treadmill exercise, this method is challenging and infrequently performed.

Pharmacologic Stress Testing

Dobutamine is the preferred pharmacologic stress agent for SE (Chap. 6). It is performed on patients who are unable to exercise. It involves the administration of a graded dobutamine infusion beginning at 5 μg/kg/min, with increasing dosages to a maximum of 40 μg/kg/min. If target heart rate is not achieved and /or if patient is on beta-blockers, atropine may be used in doses ranging from 0.25 to 0.5 mg to a total of 2.0 mg [3–5]. Image acquisition should occur at baseline (pre-infusion) and for each level of dobutamine stress. The endpoint of dobutamine SE is achievement of target heart rate (defined as at least 85% of age-predicted maximum heart rate). However, significant symptoms, arrhythmias, hypotension, or severe hypertension, should also prompt termination [5]. Ideally, the peak stress images should be obtained after the target heart rate is achieved.

Dipyridamole and adenosine are two vasodilator agents that can also be used in SE, particularly for myocardial perfusion contrast echocardiography. Both are contraindicated in patients with reactive airway disease [5]. Their use is beyond the scope of this chapter therefore will not be further discussed.

Data Interpretation

Grading of each of the 16 segments is performed at rest and during stress and described as normal, hyperdynamic, hypokinetic, akinetic, dyskinetic, or aneurysmal. Timing of wall motion is also considered. Table 7.2 shows the interpretation of regional wall motion abnormalities based on findings at rest and during stress.

The final report must include all the protocol information, vital signs, heart rate achieved and blood pressure response, level of stress tolerated

Table 7.2 Interpretation of regional wall motion abnormalities [6]

Rest	Stress	Interpretation
Normal wall motion and contractility	Hyperdynamic	Normal
Normal wall motion	New wall motion abnormality or lack of hyperdynamic wall motion	Ischemia
Wall motion: hypokinesis	Worsening hypokinesis akinesis or dyskinesis	Ischemia
Wall motion: hypokinesis	Unchanged	Infarction
Akinetic	Improved to hypokinesis or to normal wall motion (biphasic response)	Viable (hibernating) myocardium

and its adequacy, doses of the medications that were used, changes in ECG, presence or absence of symptoms, systolic function, and wall motion description.

Complications

Life threatening complications including asystole, acute myocardial infarction, sustained ventricular tachycardia, pulmonary edema or sudden cardiac death are rare but do occur in approximately 1/2000 studies [5]. In about 3% of cases, "bothersome" side effects such as nausea, anxiety, or tremors can lead to early termination of testing [7], as noted in Chaps. 4 and 6.

Clinical Vignettes

Case 1

A 62-year-old woman was brought to the Emergency Department with an 8-h history of atypical chest pain that began when she was notified that her husband was in critical condition after a car accident. The chest pain had resolved spontaneously. She had history of dyslipidemia, hypertension, and diet-controlled diabetes mellitus. Initial ECG demonstrated very mild ST-elevation in V1–V3 and troponins were negative. As part of her initial work-up, she underwent stress echocardiography.

Figure 7.1 demonstrates a positive stress echo study showing images at rest (a) and (b) stress: During stress, there is marked akinesis and ballooning of the apex, apical anterior/lateral/septum and inferior. The patient underwent a cardiac catheterization that showed normal coronaries consistent with apical ballooning/typical Takotsubo's cardiomyopathy.

Case 2

A 55-year-old man presented with a history of atypical chest pain that had resolved upon arrival to the Emergency Department. He had a medical history of well-controlled hypertension and dyslipidemia, but no previous cardiac history. ECG demonstrated left ventricular hypertrophy but no acute ST-T wave abnormalities. Troponins were negative. Given intermediate pretest probability for CAD and uninterpretable ECG, he underwent exercise echocardiography (Fig. 7.2). *He completed 12 min of the Bruce protocol, achieving a heart rate of 92% of the maximum predicted heart rate. ECG showed an additional 2 mm horizontal ST depression with exercise, but the patient did not develop chest pain.*

The stress echo was normal. Panels A-D show Parasternal long axis (PLAX), Parasternal short axis (PSAX), Apical four chamber (AP4) and Apical two chamber (AP2) acquired at end systole during rest and peak exercise. Note the normal systolic excursion/wall motion and thickening during peak exercise. The ST segment response to exercise was a false-positive result, likely related to the baseline ECG abnormalities.

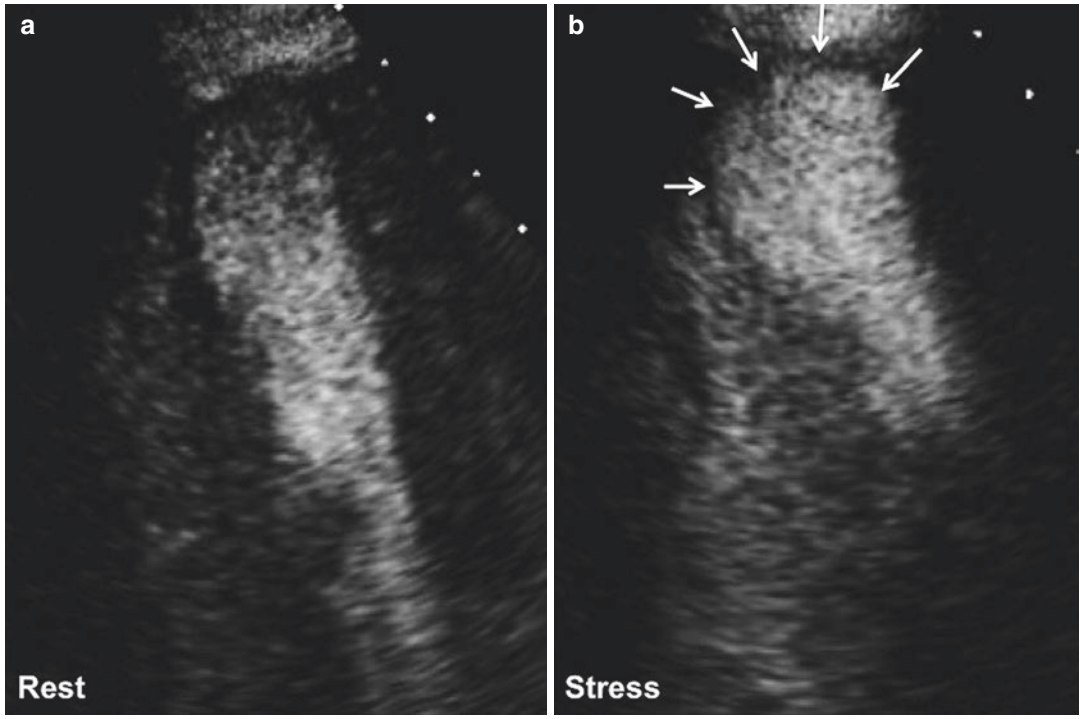

Fig. 7.1 Case #1 (see text for details)

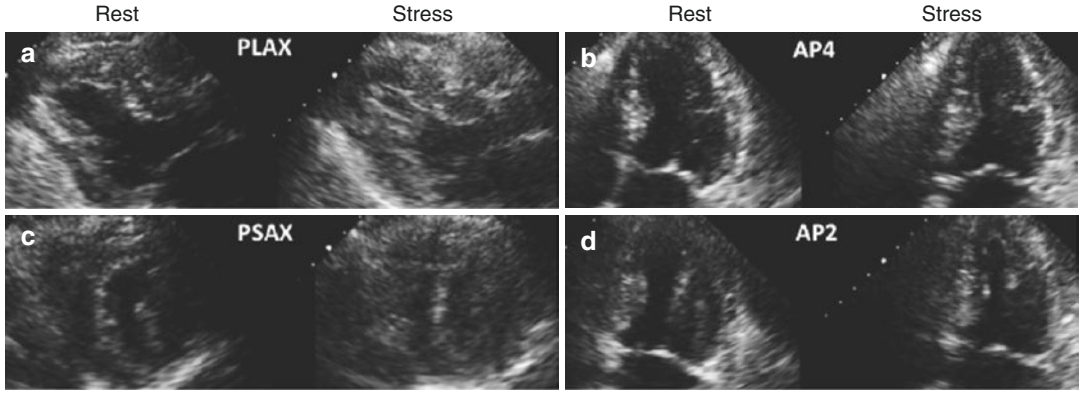

Fig. 7.2 Case #2 (see text for details)

Case 3

A 63-year-old woman presents to the echocardiography lab to complete an exercise SE ordered by her physician after she reported atypical chest pain. The protocol was explained to her, her baseline ECG was normal as were her vitals. Baseline echocardiographic images were normal without wall motion or valvular abnormalities. Her baseline LVEF was 57%. She was started on Bruce protocol. This was her ECG at Stage III at 83% of MPHR. She reported chest pressure. ECG is shown in Fig. 7.3.

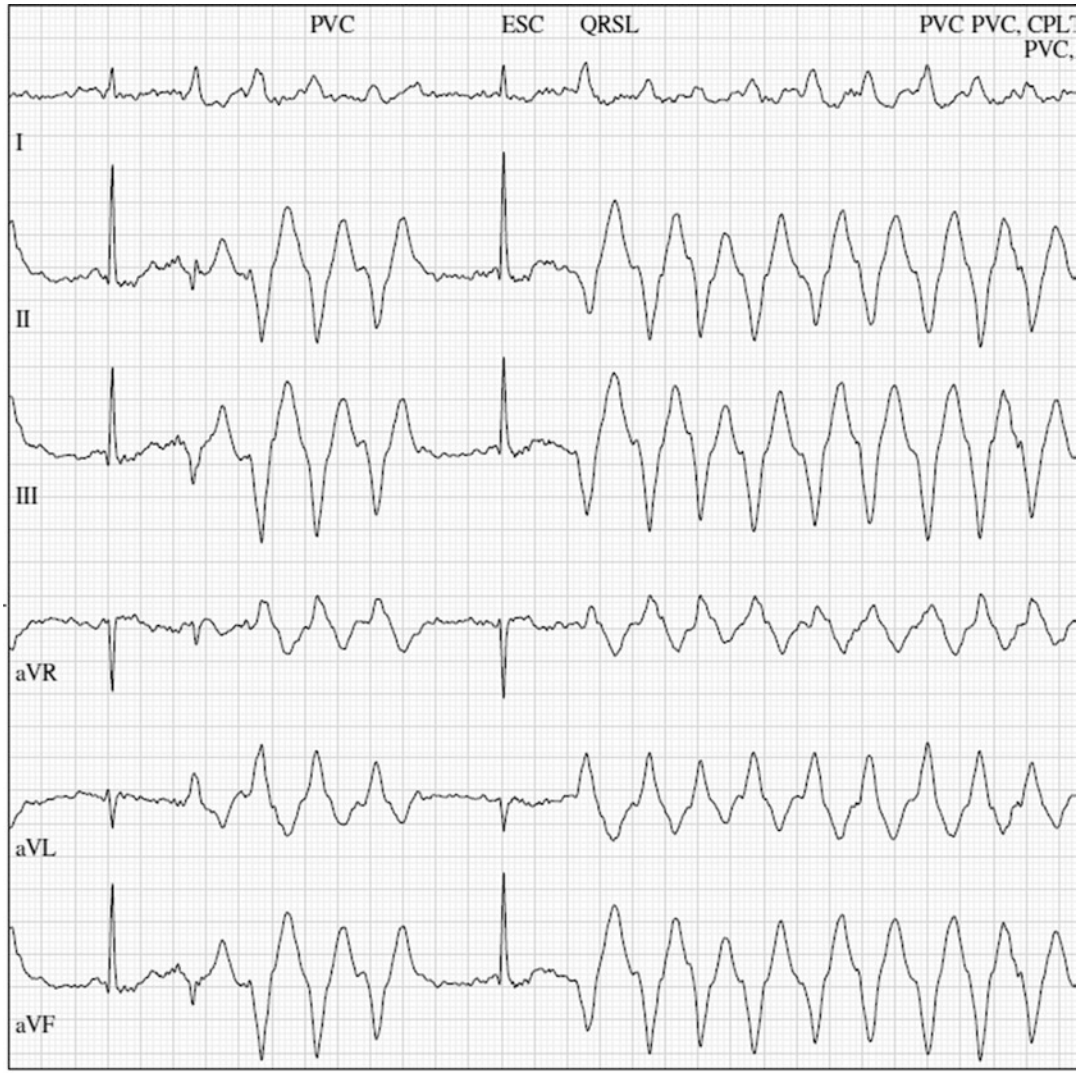

Fig. 7.3 Case 3 (see text for details)

In this setting, you stop the treadmill and obtain echocardiographic images. Patient is having ventricular tachycardia with symptoms concerning for ischemia. Therefore, stress test should be stopped, and images obtained even if heart rate goal was not achieved. If patient continues to have symptoms or arrhythmia, the laboratory must be equipped to handle BLS/ACLS.

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8 Single Photon Emission Computed Tomographic Myocardial Perfusion Imaging

Eddy Karnabi

Single-Photon Emission Computed Tomography (SPECT) is the most widely used nuclear imaging technique in cardiology, playing an important role in the detection of coronary artery disease (CAD), viability assessment, and risk stratification. Myocardial perfusion imaging (MPI) improves the sensitivity and specificity over standard exercise stress testing and provides information regarding systolic function and wall motion abnormalities with gated SPECT.

Indications

According to the appropriate use criteria [1] (Table 8.1).

Table 8.1 Appropriateness use criteria for SPECT

1	Acute chest pain (or ischemic equivalent) after definite ACS is ruled out
2	In chronic stable chest pain, patients with intermediate to high pretest probability or low pre-test probability in which the ECG is un-interpretable and unable to exercise
3	In asymptomatic patients, patients with high CHD (defined by >20% 10 year risk)
4	In asymptomatic patients with new cardiomyopathy and a depressed systolic function with no prior CAD evaluation
5	Patients with arrhythmias such as VT or new onset atrial fibrillation
6	Patients with elevated cardiac enzymes without evidence of ACS
7	Patients have an abnormal prior stress testing and present with new or worsening symptoms
8	Pre-operative evaluation in intermediate risk population or if undergoing vascular surgery if functional capacity cannot be assessed or is poor and if there are one or more risk factors for CAD.
9	In post-revascularization patients who are symptomatic or were incompletely re-vascularized
10	Asymptomatic or symptomatic CABG patients if performed >5 years prior, (Uncertain indication in asymptomatic patients >2 years post PCI)
11	Myocardial Viability study using Thalium-201 or technetium 99m radiotracer in combination with SPECT as an alternative to other imaging modalities to assess viability
12	Technetium 99m pyrophosphate (Tc-99m PYP) imaging to diagnose cardiac transthyretin amyloidosis (ATTR).

Contraindications

The contraindications to the use of exercise and pharmacological (adenosine, dipyridamole, regadenoson, dobutamine) stress testing are presented in previous chapters. The contraindications specifically for nuclear cardiology include patients who received iodine I-131 therapy within 12 h or technetium-99 studies within 48 h. In addition, due to the radiation exposure, SPECT is

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contraindicated in pregnancy and breast-feeding. Finally, uncooperative patients who are unable to lie supine for at least 30 min are not encouraged to undergo the procedure. In rare instances, it is contraindicated if there is an allergic potential to the radiopharmaceutics.

Equipment

The essential tool for performing a SPECT study is the gamma or scintillation camera that detects the gamma rays (photons) produced from the injected radiopharmaceutical agents [2].

A gamma camera consists of a single crystal, usually sodium iodide crystal (NaI), a collimator, and photomultiplier tubes (PMT). The NaI crystal is able to scintillate when subjected to ionizing radiation in form of photons. The collimator is designed to limit by attenuation, the detection of gamma rays to those traveling in certain directions. The photomultiplier tubes convert photon energy and scintillation within the crystal into electrical energy that is processed by the pulse height analyzer. The energy spectrum obtained consists of a photopeak and multiple Compton scatters. Only signals in the specific energy range of the radiotracer (the photopeak) are processed and the counts analyzed.

The basic components of the gamma camera have not changed much over the years except for upgrading from scintillation detectors to semi-conductor detectors such as Cadmium Zinc Telluride (CZT) detectors with improved count detection and thus images.

The radiopharmaceutical tracers [3, 4] used are thallium-201 and technetium-99m based agents, Tc-99m sestamibi and Tc-99m tetrofosmin, Due to the energy spectrum, effective half-life and more favorable dosimetry, the technetium agents are preferred for gated SPECT imaging. These agents emit photons with a single photopeak of 140 keV and have a half-life of 6 h. After injection, 40–60% is extracted by the myocardium and myocardial washout/redistribution is minimal requiring two injections at rest and peak exercise.

Technique

After performing an exercise or a pharmacological stress test and the injection of the pharmaceutical radiotracer, images are obtained. The images obtained by gamma cameras are two-dimensional (2D) images of a three-dimensional (3D) object. Multiple 2D planar projections are acquired from multiple angles to reconstruct a 3D image using a reconstruction algorithm.

Imaging times post injection for technetium-based agents, scanning can start 15–20 min after exercise and 45–60 min after rest or pharmacological stress testing. The routine position to acquire images is supine with arms above the head. In cases of significant inferior wall attenuation, the addition of prone images helps eliminate the inferior wall attenuation, creates more uniform breast attenuation, less motion artifact, but may cause an artifactual anteroseptal defect. The gamma camera is placed as close to the patient as possible for improved resolution with either one of the orbital types: circular or non-circular (elliptical or body contour). In a double headed camera, planar images are obtained in a 180° arc that extends from 45° right anterior oblique (RAO) to 45° left posterior oblique (LPO). The acquisition type could be a “step and shoot”, continuous, or continuous “step and shoot”. For a dual head camera, low dose studies usually take 25–30 s per step and for high dose studies 20–25 s per step which translates to approximately 12–16 min total time for the study. Using a single head camera will yield double the time to acquire the images.

Hybrid SPECT-CT systems are in use and play an essential role in attenuation correction.

Radiopharmaceutical protocols [3, 4]:

1. One day dual isotope (discouraged and less widely used due to the high radiation exposure)
2. Two-day technetium-based tracer
3. One day single isotope (Rest-stress or stress-rest)
4. Stress-first/stress-only imaging with ECG gated SPECT and attenuation correction
5. One day stress-delay thallium imaging for viability

Single isotope usually technetium based 1 day protocol is the most widely used. A rest injection is performed with low dose 8–9 mCi followed by SPECT imaging 45–60 min afterwards. After a 3-h delay, stress testing is performed and high dose 25–30 mCi is injected followed by SPECT imaging 15–30 min for exercise and 45–60 min for pharmacological stress testing (Fig. 8.1). The advantages of a single day protocol are good validation, fast tract protocol, easier image interpretation, able to determine transient ischemic dilation (TID), and validated attenuation correction. The 2-day protocols advantage is high quality rest and stress images as a result of using high dose injections with rest and stress. This is beneficial in an obese patient but requires 2 days to complete the study. A stress-first protocol permits a possible stress-only study as if the initial SPECT images are normal, the rest images are not required. The stress-only sequence reduces radiation burden and overall time required.

For SPECT viability studies, thallium-201 2.5–3.5 mCi is injected followed by rest images at 15 min post injection. Redistribution images are delayed 4 h to detect viable myocardium. Further delayed or late redistribution mages can be obtained 24 h post injection as well.

Data Interpretation

The radiotracer is distributed throughout the myocardium, however, more predominantly in the left ventricle. The standard SPECT views include the short axis from apex to base, vertical long axis, and horizontal long axis (Fig. 8.2). Data interpretation involve following a review sequence as outlined by the ASNC guidelines [5, 6] and involves: examining the unprocessed images for image quality, artifacts such as motion artifacts (vertical or horizontal), breast or subdiaphragmatic artifacts, extracardiac uptake, and increased lung uptake, followed by examining for perfusion abnormalities fixed or reversible between rest and stress images, examining the polar map or bulls eye, and examining the gated SPECT images for wall motion abnormalities and ejection fraction.

As coronary flow decreased due to coronary obstruction, less radiotracer uptake occur which translates to lower count on the perfusion images. Defects can be reversible or fixed. Fixed defects are areas with absent tracer uptake on both rest

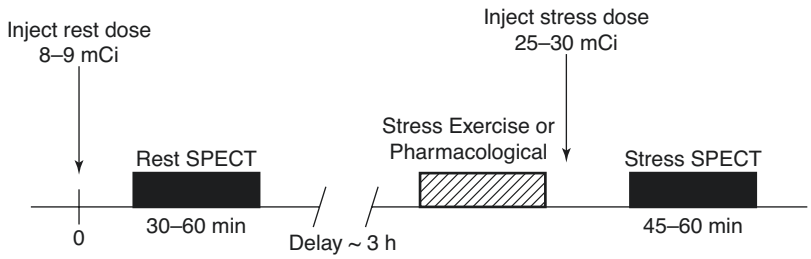


Fig. 8.1 Typical 1-day rest-stress technetium protocol. Rest dose of 8–9 mCi is injected followed by rest SPECT images 30–60 min. After a delay of approximately 3 h, the stress portion is performed followed by stress tracer injection of 25–30 mCi. After 15 min for exercise or 45–60 min for pharmacological stress testing, the stress SPECT images are obtained

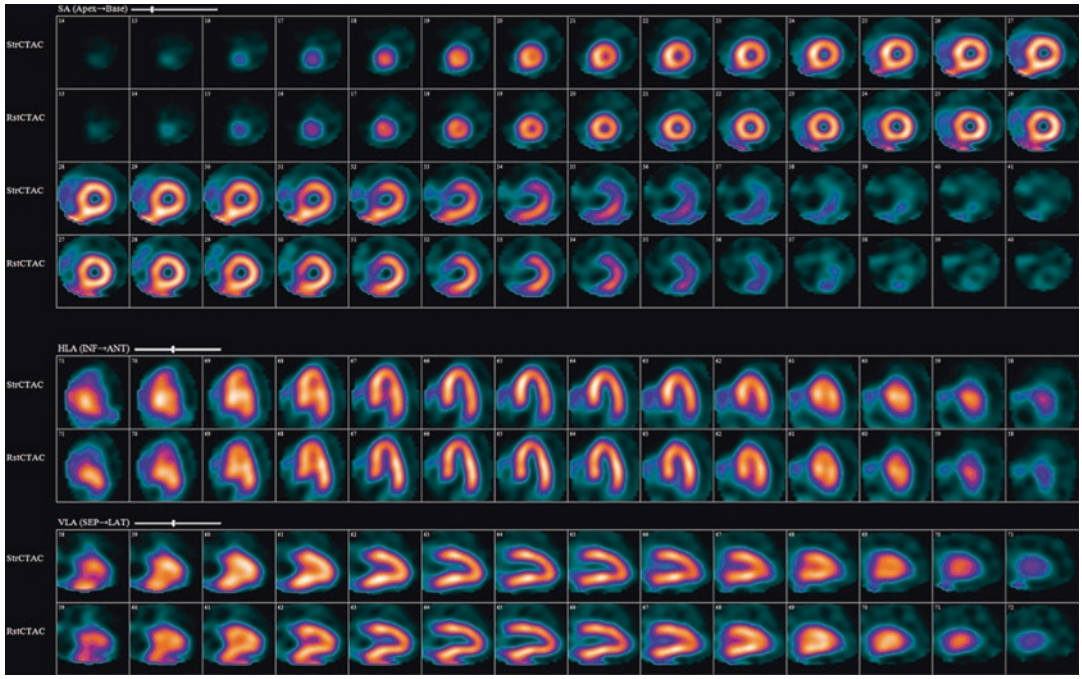


Fig. 8.2 A normal myocardial perfusion imaging showing the short axis from apex to base (usual presentation is stress images on top and rest images on bottom), horizontal long axis showing septum and lateral walls, and vertical long axis showing the anterior and inferior myocardium

and stress images. Fixed defects represent a scarred or infarcted myocardium or a viable hibernating myocardium. Differentiating a scarred myocardium from a viable myocardium requires either thallium-201 SPECT redistribution viability study or PET based study. Reversible defects are defined as normal perfusion images at rest but with decreased uptake on stress images; this pattern is consistent with ischemia.

The ischemic myocardium can usually be traced to a coronary distribution Left anterior descending (LAD), Circumflex (Cx), or Right coronary artery (RCA) (Fig. 8.3) unless multiple territories are involved. Quantitative analysis is performed by comparing count densities from the stress using the short axis images with a normal count profile from a cohort of normal patients. A bulls eye or a polar map is displayed (Fig. 8.3), however, this method should only be used in conjunction with visual analysis. Using the 17-segment model (Adapted from Cerqueira et al. [7]) (Fig. 8.4), a score may be given to each segment (Table 8.2).

Three scores are obtained: SRS summed rest score; SSS summed stress score and SDS summed difference score (SDS = SSS−SRS). The SRS shows the extent and severity of infarction, SDS extent and severity of ischemia, and SSS extent and severity of both ischemia and infarction (Table 8.3).

Similarly, the percent LV myocardium involved can be calculated by number of segments affected divided by 68 (4 points per each segment multiplied by 17 segments) × 100.

An important part in interpretation is the detection of transient ischemic dilation (TID). TID is most likely due to diffuse subendocardial ischemia. It is calculated by dividing Stress EDV (End-diastolic volume)/Rest EDV. Cutoff value of >1.22 for dual isotope and >1.12 for single isotope studies is considered significant. However, the threshold is higher for pharmacological stress testing >1.36 since the physiology in vasodilator stress is to redirect perfusion away from the endocardium. TID in combination with an abnormal perfusion images signi-

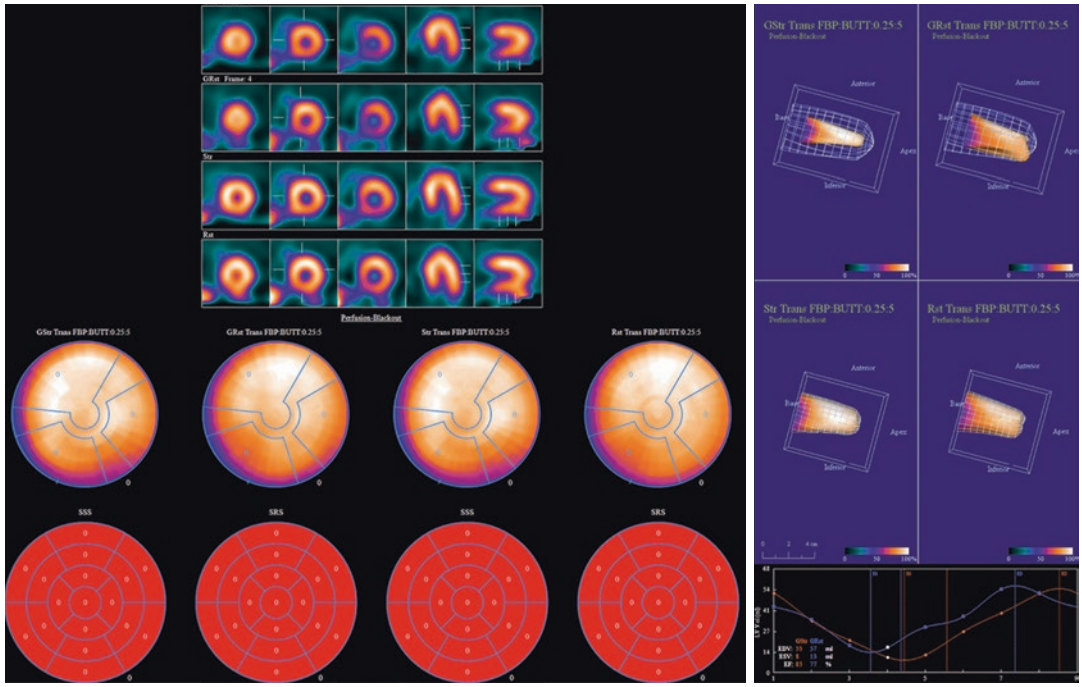
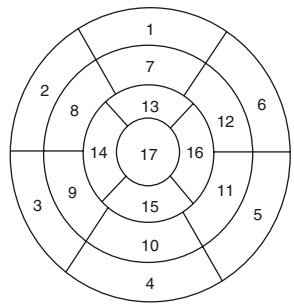


Fig. 8.3 A polar plot or bulls eye with semi-quantification using the 17-segment model. The LAD (left anterior descending) territory is between 9 and 1 O'clock, Cx (Circumflex) territory between 2 and 5 O'clock, and RCA (right coronary artery) territory between 5 and 8 O'clock. On the left, gated SPECT images are shown during diastole (*bottom*) and systole (*top*)

a

SPECT myocardial perfusion imaging
1. Basal anterior
2. Basal anteroseptal
3. Basal inferoseptal
4. Basal inferior
5. Basal inferolateral
6. Basal anterolateral
7. Mid anterior
8. Mid anteroseptal
9. Mid inferoseptal
10. Mid inferior
11. Mid inferolateral
12. Mid anterolateral
13. Apical anterior
14. Apical septal
15. Apical inferior
16. Apical lateral
17. Apex



b

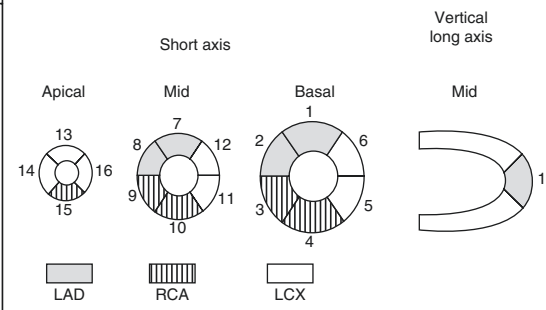


Fig. 8.4 SPECT myocardial perfusion imaging showing the 17-segment model and Coronary distribution (Adapted from the Cerqueira et al. [7]). *LAD* left anterior descending artery, *RCA* right coronary artery, *LCX* left circumflex artery. (**a**) indicates terminology of each of the 17 segments and there location on a polar map. (**b**) depicts the location of the segments on short axis and vertical long axis views and the empirically allocated vascular territory

Table 8.2 The five point model

Normal perfusion	0
Mild decreased counts	1
Moderate decreased counts	2
Severe decreased counts	3
Absent uptake	4

Table 8.3 Semiquantitative defect analysis

	Number of segments	Percent of LV
Small	1–2	5–10
Moderate	3–4	10–20
Large	>5	>20

fies extensive CAD either multi-vessel disease or proximal LAD disease and correlates with worse prognosis. However, TID in combination with normal perfusion images has low specificity for multi-vessel disease and is not associated with adverse prognosis. This is usually encountered in patients with significant left ventricular hypertrophy (LVH) especially with a hypertensive response that results in subendocardial ischemia from the thick ventricular walls.

Gated SPECT imaging improves the specificity of MPI by differentiating a fixed defect from an infarction/scar and an artifact. Wall motion abnormalities can be detected as well as an estimation of systolic function and an ejection fraction (EF).

Artifact recognition is an important part of SPECT imaging and include instrumentation-related artifacts (center-of–rotation, non-uniformity etc.) and patient-related artifacts (patient motion, attenuation, etc.).

Finally, the report should not only describe the clinical indication, the technical features of the examination, and the imaging results but also include the impression whether the study is normal or abnormal and addressing the perfusion abnormalities by noting the size, severity and location of each abnormality. Recognition of artifacts if present, addressing regional or global wall motion abnormalities with estimation of EF, inclusion of ECG findings, and integration with the clinical information to address the indication of the study.

Complications

The complications to myocardial perfusion imaging are related to the radiation exposure both to the patients and to the staff. Ionizing radiation has been linked to solid cancers and leukemia. Hence, the principle of ALARA (As low as reasonably achievable) applies.

Clinical Vignettes

Case 1

Sixty-year-old male with multiple risk factors for CAD including hypertension, hyperlipidemia, and extensive tobacco history with limited functional status due to claudication for over the past year and significant vascular disease involving the femoral artery is referred for a pharmacological stress test myocardial perfusion imaging prior to vascular surgery. The MPI images are shown in Fig. 8.5.

This case shows a normal myocardial perfusion imaging during rest and stress with a normal bulls eye or polar plot. His annual event rate is less than 1% and he should be able to proceed with the planned vascular bypass surgery.

Case 2

Seventy-eight-year-old male with hypertension, CAD with prior myocardial infarction was admitted to the hospital with chest pain. A myocardial perfusion stress testing was performed with images shown in Fig. 8.6.

This case presents a patient with a prior MI in the LAD and RCA territories and evidence of a small amount of peri-infarct ischemia in the anterior wall.

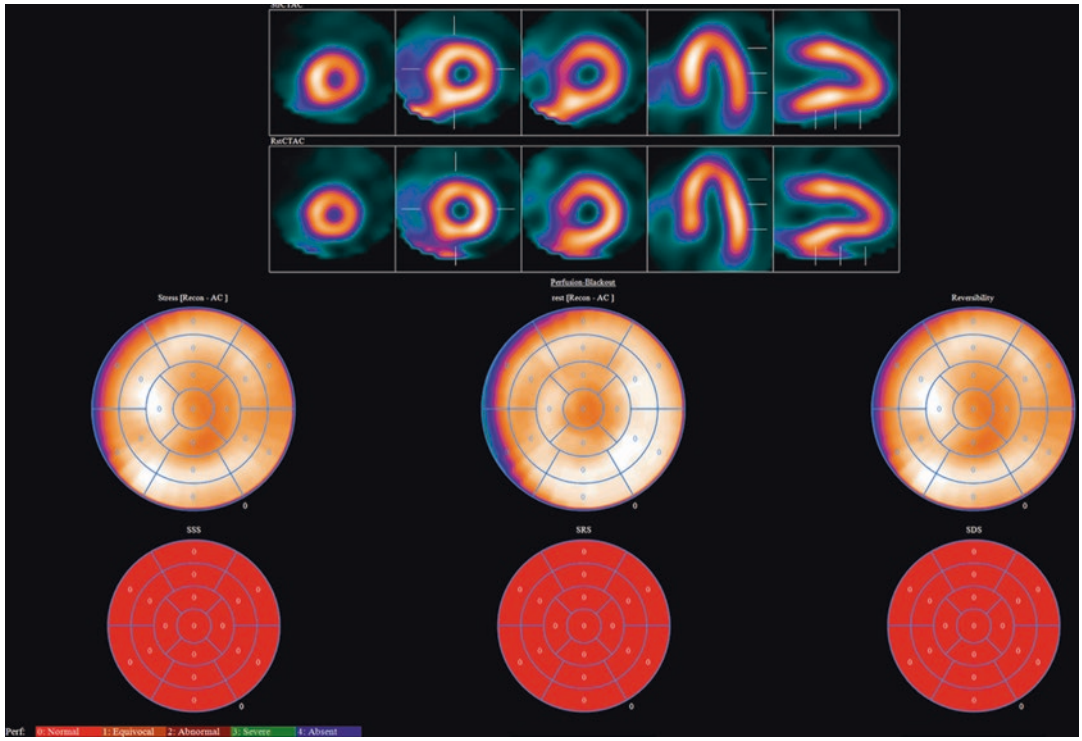


Fig. 8.5 Case #1 (see text for details)

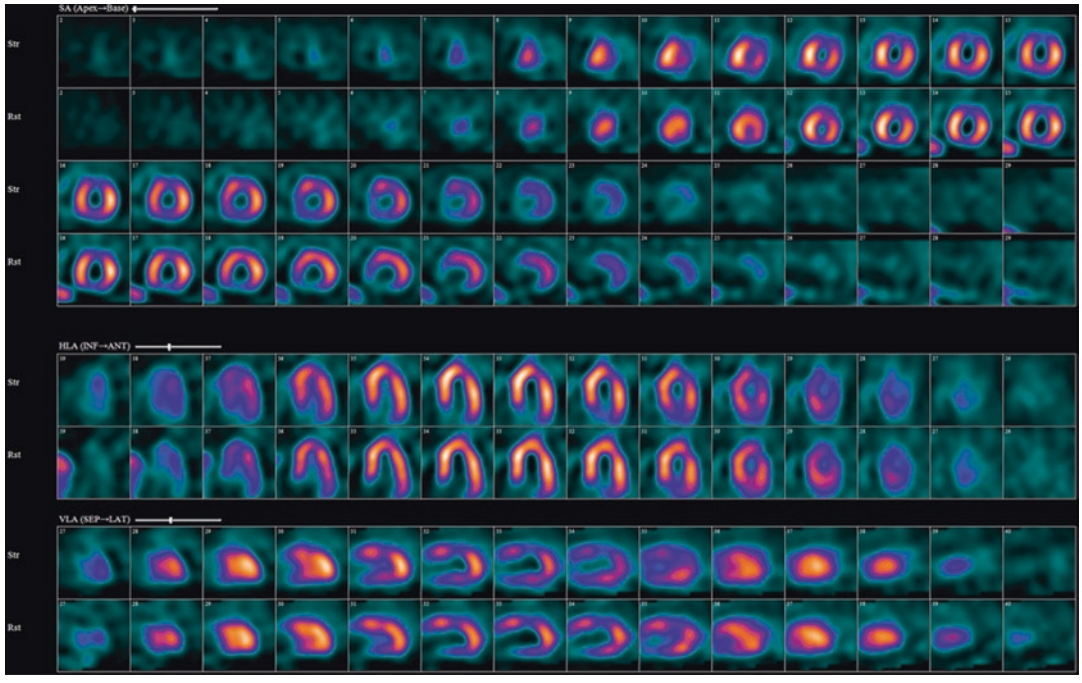


Fig. 8.6 Case #2 (see text for details)

Case 3

Fifty-nine-year-old male patient with strong family history of CAD, hyperlipidemia and prediabetes was sent for a vasodilator stress testing with SPECT imaging due to inability to exercise due to knee injury and atypical chest pain symptoms. His regadenoson ECG portion of the stress test was unremarkable. The SPECT images are shown below in Fig. 8.7a.

The above SPECT images show a large reversible perfusion defect in the apical to basal anteroseptal wall with transient ischemic dilation (TID value 1.35). TID in presence of abnormal perfusion eludes to the possibility of multivessel CAD, left main, or proximal LAD stenosis. In this case, the patient underwent a cardiac catheterization that showed >90% proximal LAD stenosis as shown in Fig. 8.7b.

Case 4

Sixty-nine-year-old gentleman with a past medical history significant for hypertension, hyperlipidemia, obstructive sleep apnea, sick sinus

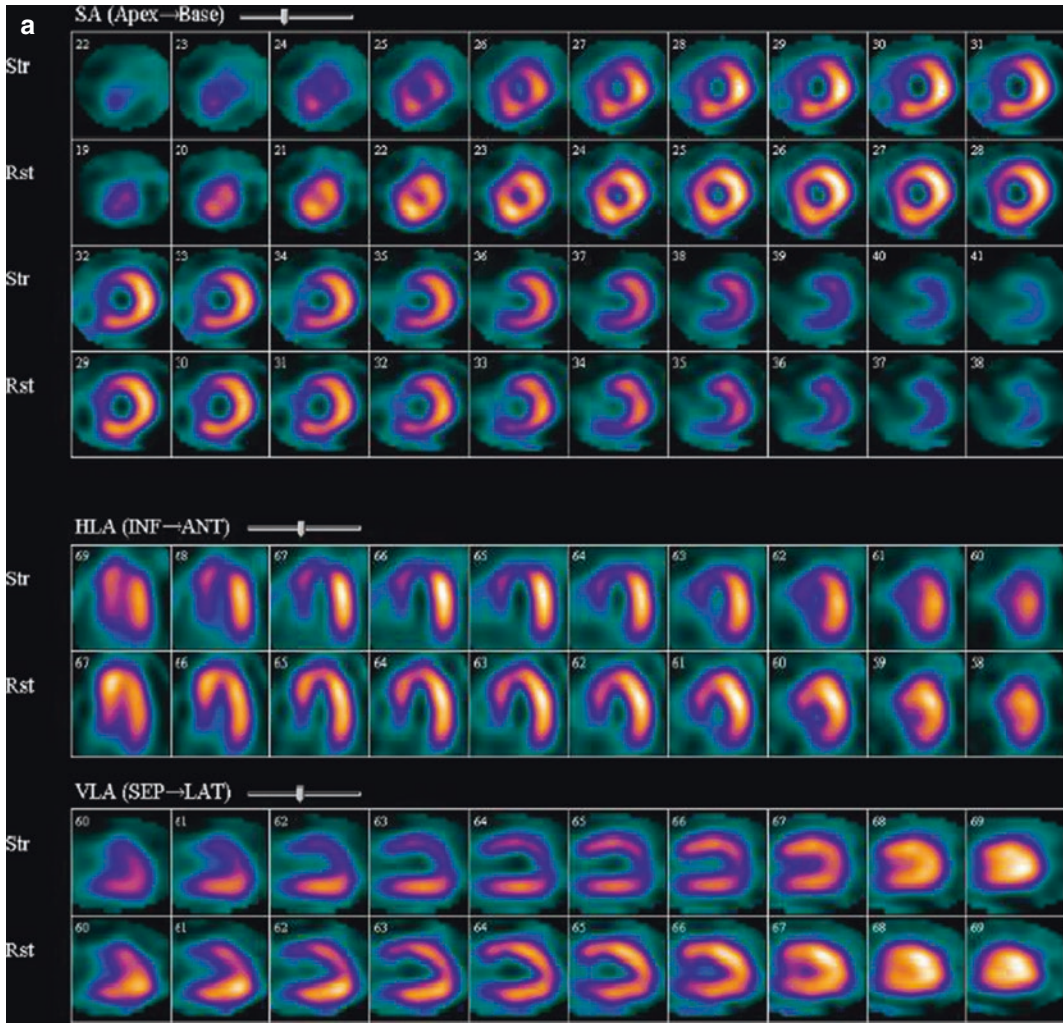


Fig. 8.7a Case #3 SPECT Images (see text for details)

syndrome status post permanent pacemaker implantation, and hydrocephalus treated with a VP shunt. For the past several months, he has noticed decreased exercise capacity and severe dyspnea on exertion performing minimal activities. He was sent for vasodilator SPECT stress testing with the images shown in Fig. 8.8: Left panel.

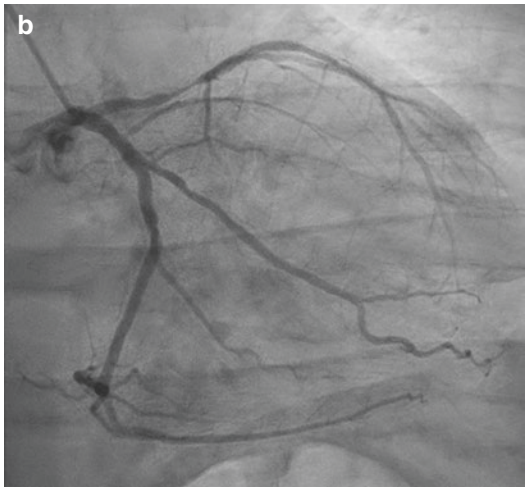


Fig. 8.7b Coronary angiogram from Case 3 (see text for details)

The SPECT images show a large mixed defect of moderate-severe intensity in the apical lateral, basal to mid anterolateral and basal to mid inferolateral segments. This could be consistent with prior infarction with peri-infarct ischemia; however, the patient underwent a cardiac catheterization that showed mild coronary disease. Review of the raw image show the cardiac chamber on the right chest. Figure 8.8 Right panel (arrow represents the left ventricular myocardium). The findings are consistent with situs inversus with dextrocardia. The septal perfusion abnormality was due to differential perfusion secondary to ventricular paced rhythm and increased heart rate on stress.

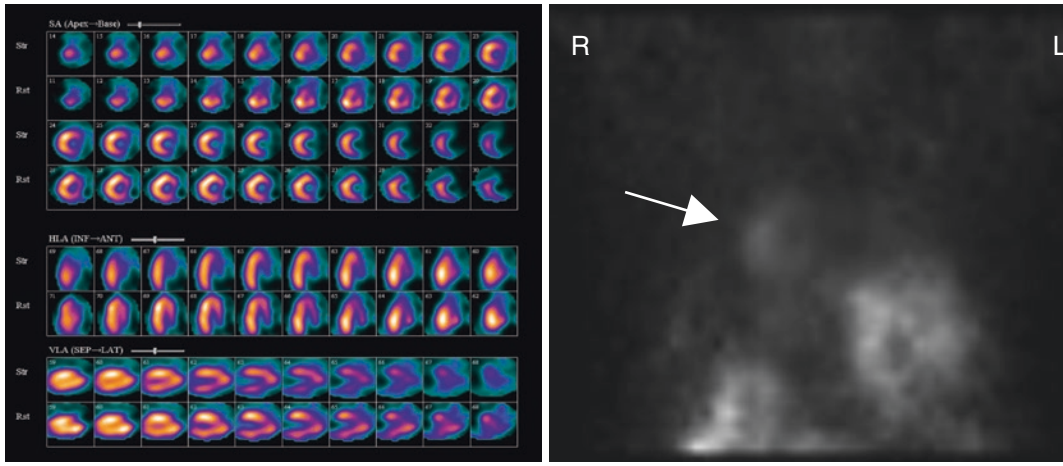


Fig. 8.8 Left panel SPECT images, Right panel: Raw images

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Positron Emission Tomography

9

Eddy Karnabi

Positron emission tomography (PET) imaging has increased substantially in recent years. PET allows noninvasive evaluation of myocardial blood flow, function, and metabolism. The advantages of cardiac PET imaging over SPECT are [1]: improved image quality (especially in obese patients) with high both temporal and spatial resolution, relatively short imaging protocols, routine attenuation correction (depth independent), providing peak stress ejection fraction (EF)-no time delay between hyperemic response and imaging and true quantification of myocardial blood flow and myocardial metabolism. In addition, PET provides equal sensitivity with higher specificity and diagnostic accuracy compared to SPECT. Furthermore, PET allows improved detection of multivessel coronary artery disease. Cardiac PET, however still faces the challenges of being less available, with a greater cost, less expertise, challenges of performing exercise stress due to the short half-life of the currently available radiotracers making pharmacological stress testing the only current option (until the availability of new radiopharmaceutical agents), and reimbursement issues.

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Indications

The indications for cardiac PET [2, 3] are similar to those for cardiac SPECT in term of myocardial perfusion imaging for the diagnosis and risk stratification of CAD. However, its role is extended to patients with an equivocal SPECT. In addition, cardiac PET is used as a viability study in patients with ischemic cardiomyopathy. Recently, there has been an increased use in heart failure and in the identification of cardiac sarcoidosis (Table 9.1).

Contraindications

The contraindications to cardiac PET are similar to SPECT (Chap. 8), which include the standard contraindications to pharmacological stress testing when PET perfusion imaging is being done. Inability to lie flat or lie still for the period of

Table 9.1 Indications for positron emission tomography

1	Intermediate likelihood of CAD and/or risk stratification in patients with intermediate and high likelihood of CAD when
	Equivocal SPECT Unable to exercise Able to exercise but ECG with LBBB or ventricular paced rhythm
2	Evaluation of myocardial viability
3	Evaluation of heart failure (Cardiac Sarcoidosis)
4	Quantification of myocardial blood flow

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acquisition, claustrophobia and extreme weight (>350–400 lbs.) are usually preferred not to undergo PET imaging. Finally, women who are pregnant or breast-feeding are contraindication.

Equipment

The equipment required for a standard cardiac PET examination includes the radionuclides and the PET camera, mostly as a hybrid (with CT) unit. The radionuclides used for PET imaging have a considerably shorter half-life as compared to SPECT tracers. PET radionuclides are produced either from a cyclotron such as fluoro-2-deoxyglucose F-18 FDG and N-13 ammonia or a generator such as rubidium Rb-82. As the name implies, PET imaging involves a positron that collides with an electron to produce two 511 keV gamma rays/photons emitted collinear to each other at 180° angle. The PET detectors are configured to only register the photon pairs if they strike opposite detectors at approximately the same time that has been termed the coincidence detection. The summations of multiple coincidence events are used to reconstruct the PET image to be used for analysis.

The CT scanner provides addition information such as coronary artery calcium scoring and/or noninvasive coronary angiography, but more importantly for PET imaging is for accurate attenuation correction.

The PET camera, similar to SPECT, is made of multiple small detector crystals arranged in a 360° ring and photomultiplier tubes to convert the scintillation events to electrical signal and digitalization to provide the counts that are used in quantification and image processing. Three types of detector crystals are available: (1) Bismuth germanate (BGO) (2) Lutetium oxyorthosilicate (LSO) (3) Gagolinium oxyorthosilicate (GSO).

The clinically available PET tracers for myocardial perfusion studies are Rb-82, and N-13 ammonia. Figure 9.1 shows the radiotracers myocardial uptake in relation to coronary blood flow with O-15 being the ideal tracer and the roll-off phenomenon seen with other tracers at higher coronary blood flows. N-13 ammonia, due to the short half-life (10 min), requires an on-site (nearby) cyclotron. It has excellent myocardial

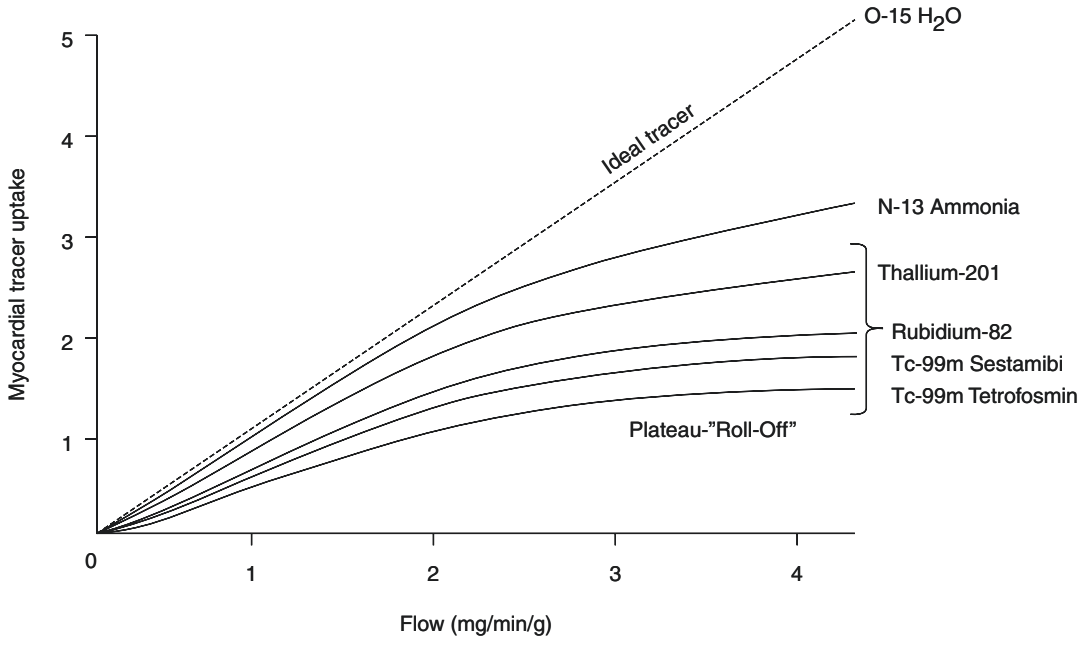


Fig. 9.1 Relationship of the myocardial uptake of the radiopharmaceutical to blood flow. O-15 water is the ideal tracer

uptake/retention with established flow quantification and applications in exercise and pharmacological stress testing. Rubidium-82 is produced on-site from a strontium-82 generator (replaced every 4 weeks) with a half-life of 76 s. Due to the short half-life, it can only be used in pharmacological stress testing. It has with high extraction at high flows (enhances the detection of moderate-severe CAD). Rb-82 is extracted by myocardial cells via the Na/K ATPase pump. The radiation dosimetry from Rb-82 varies from 1.75 to 7.5 mSv total effective dose. Depending on the left ventricular ejection fraction, typically imaging can commence 70–90 s after the injection if LVEF > 50% and delayed slightly longer (~110 s) if LVEF < 50%.

For metabolism imaging, the F-18 FDG tracer (the only FDA approved agent), an analog to glucose, is used. F-18 is produced in a cyclotron and decays with a half-life of 110 min, which allows sufficient time to be produced and distributed in a radius of several hours from the production site. FDG is transported into the cells similar to glucose and is then phosphorylated by hexokinase to FDG-6-phosphate, which is then trapped in the myocardium for PET imaging. The whole body dosimetry from 10 mCi dose is 7 mSv (Tables 9.2 and 9.3 [1]).

Table 9.2 PET radiotracers

Myocardial perfusion	Myocardial metabolism
Rubidium-82	F-18 = Glucose metabolism
Ammonia N-13	C-11 acetate = Oxidative metabolism
Water O-15	C-11 palmitate = fatty acid metabolism
F-18 agent	

Technique

Patient preparation for vasodilator stress testing and myocardial perfusion imaging is similar to what was previously described in the previous Chaps. 6 (Pharmacologic Stress) and 8 (SPECT). For myocardial perfusion imaging (Fig. 9.2), an overnight fast of at least 6 h is required. Following the stress portion, Rb-82 or N-13 is injected at peak hyperemia through a peripheral IV line and emission scans are performed.

Viability studies require a specified protocol for glucose manipulation. In order to allow the myocardium to utilize glucose, an overnight fast of at least 6–12 h (Step 1) is required as patient metabolic preparation is key to successful F-18 FDG imaging to assess viability. The most common metabolic preparation for viability imaging is the use of an oral load of glucose 25–100 g (Step 2) followed by supplemental IV insulin (Step 3) as needed.

In addition to viability imaging, F-18 FDG imaging is being used in the detection of inflammation and infection such as in the identification of active cardiac sarcoidosis and in the identification of active infections involving prosthetics (such as valves and annular rings) and device infections (including pacemakers, implantable cardiac defibrillators/ICD, and left ventricular assist devices/LVADs). The underlying mechanism is that of upregulation of glucose metabolism at the sites of inflammation or infection. The study protocol for the detection of active cardiac sarcoidosis or infection is quite similar with the exception that a rest perfusion study is required with a sarcoidosis protocol for co-localization of

Table 9.3 Properties of PET radiotracers [1]

	Tracer	Production	Half-life	Compound	Uptake/metabolism	Positron range (mm)	FDA approval
Perfusion	O-15	Cyclotron	2.1 min	H_2O	Freely diffusible	0.36	×
	N-13	Cyclotron	10 min	NH3	Extraction Na/K ATPase	0.28	✓
	Rb-82	Generator	76 s	RbCl	Extraction K channels	1.6	✓
Metabolism	C-11	Cyclotron	20.4 min	Acetate, palmitate	Active extraction	0.22	✓
	F-18	Cyclotron	110 min	Deoxyglucose	Glucose transporter	0.18	✓

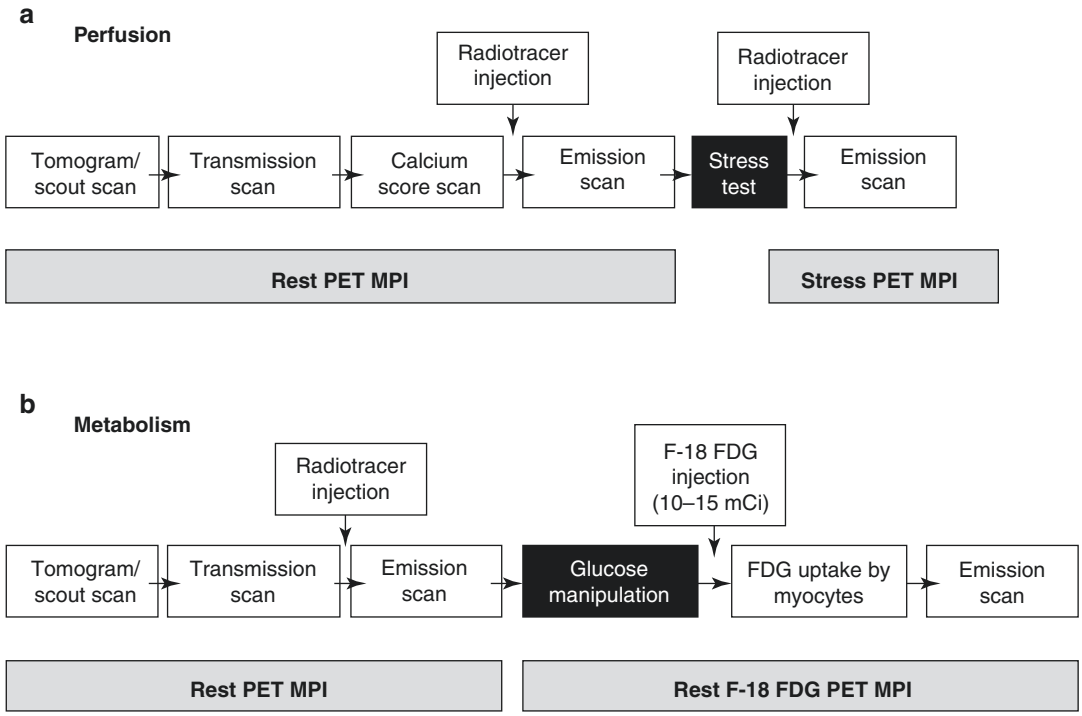


Fig. 9.2 Sample PET protocols for myocardial perfusion (**a**) and metabolism/viability (**b**)

inflammation within the myocardium and to determine whether inflammation is present in the hypoperfusion region (mismatch defect). For sarcoidosis imaging, a dietary preparation is required to suppress the physiological cardiomyocytes uptake of F-18 FDG uptake such that tracer uptake is limited to the active inflammatory cells in the myocardium. This involves avoidance of carbohydrate containing food for 24 h prior to the test with intake of high fat and protein foods for at least two meals 24 h prior followed by an overnight fast. Suppression of myocyte glucose uptake can be assisted by giving IV unfractionated heparin 15–45 min prior to F-18 FDG administration.

The imaging parameters include patient positioning supine with the arms raised above the shoulder level. To localize the heart within the field of view (FOV), a tomogram or scout CT is performed followed by a transmission scan for attenuation correction. Rest or stress emission scans are then performed. For the FDA approved radiotracers, the dose used are: for Rb-82 is 40–60 mCi, N-13 ammonia 10–20 mCi, and for F-18 FDG 5–10 mCi. The scan duration for Rb-82 is 3–7 min, N13 ammonia 10–15 min, and for F-18 FDG 10–30 min.

Of note, rest-stress MPI and viability PET protocols (Fig. 9.2) may be combined to provide information on both ischemia and viability.

Data Interpretation

As outlined by the ASNC guidelines on radionuclide imaging [4, 5], the sequence involves analyzing the raw images, followed by assessment of perfusion abnormalities, evaluation of gated images for left ventricular function, quantification of myocardial blood flow. In addition, with

hybrid PET/CT scans, coronary artery calcium and/or coronary CT angiography may be included in the report. Non-cardiac findings should be reviewed and mentioned such as pleural or pericardial effusions, aortic disease, and calcifications, mediastinal or lung masses or nodules. The rest and stress perfusion images and metabolism images should be analyzed for the extent and severity of abnormalities. Extra-cardiac findings should be carefully examined for uptake in organs other than the myocardium particularly the lungs and the mediastinum. Similar to SPECT imaging, PET images are presented in short axis from apex to base, horizontal long axis with septal and lateral walls, and vertical long axis showing the anterior and inferior walls. Interpretation of PET perfusion data (similar to what is described in Chap. 8) should be performed visually/qualitatively first with identification of location and defect severity and extent. The extent can be qualitatively described as small (5–10% of the LV), medium (10–20% of the LV), or large (>20%) of the LV. Defect severity is expressed as mild, moderate, or severe. Myocardium with stress induced perfusion abnormalities, which have normal stress imaging represent ischemia. Perfusion abnormalities present both at rest and stress i.e. fixed defects represents an area of scan or infarction. The 17-segment model with the 5-point scale (Fig. 8.4) is used for the semi-quantitative analysis as outlined in the SPECT chapter.

Absolute quantification of myocardial blood flow is an important aspect of PET imaging that helps in assessing the physiological significance of a known coronary artery stenosis especially if it is in the intermediate range. Both relative and absolute quantification is possible. Quantitative assessment of blood flow is in ml of blood per min per gram of myocardium and is validated for N-13 and Ru-82. Typical values for myocardial flow reserve >2.3 indicated a favorable prognosis whereas a ratio of less than 1.5 suggest diminished blood flow reserve and carries an elevated cardiac risk.

ECG Gated PET images at rest and peak stress provides information on LV function and volumes. Unlike post-stress SPECT, PET images are obtained at peak hyperemia and stress. Regional and global wall motion abnormalities can be identified.

Assessment of myocardial viability plays a central role in PET imaging. Viability studies are able to differentiate a scarred or infarcted myocardium from a hibernating myocardium, which upon revascularization might restore LV function. Rest perfusion imaging is compared to metabolism imaging using FDG uptake (Fig. 9.3). A myocardial perfusion abnormality in combination with no FDG uptake signifies an infarcted and scarred myocardium. An increase in FDG uptake relative to a perfusion abnormality i.e. a mismatch signifies a viable myocardium (Table 9.4).

Assessment of active cardiac sarcoidosis or inflammation involves the uptake of F-18 FDG into the inflamed or infected cells following the dietary patient preparation described [6]. In sarcoidosis imaging, a resting MPI study is obtained and compared to an F-18 FDG study side by side in a the standard short/horizontal/vertical axis views. An F-18 FDG "hot spot" indicated areas of abnormal cardiac inflammation. Different uptakes have been described including focal, diffuse uptake and focal on diffuse uptake. A typical pattern in active sarcoidosis is a "mismatch defect" in which a hot spot or diffuse uptake is localized within a hypoperfused myocardium (Fig. 9.4).

The standard reporting algorithm of myocardial perfusion and metabolism PET studies includes: patient information, indication for the study, history and key clinical findings, type of the study, summary of stress data with stress ECG interpretation, image description and interpretation for perfusion and metabolism, and final impression whether the study is normal or abnormal.

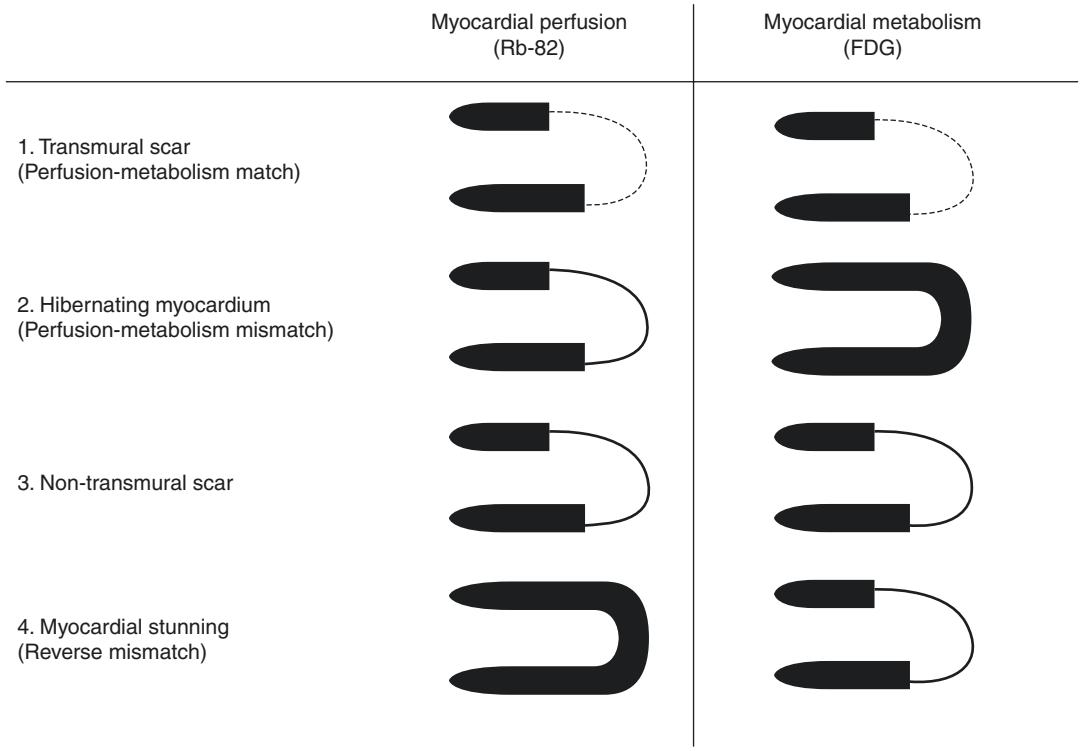


Fig. 9.3 Myocardial perfusion and metabolism patterns

Table 9.4 Myocardial perfusion and metabolism patterns

	Myocardial blood flow	Myocardial FDG glucose loaded	Regional function
Normal	Normal	Normal	Normal
Hibernating	increase	decrease	increase
Transmural scar	increase	increase	increase
Non-transmural scar	Partially increase	Partially increase	increase/Normal
Stunning	Normal	increase\decrease	increase
NICMP	Normal	Normal	increase

NICMP non ischemic cardiomyopathy, *FDG* fluorodeoxyglucose, increase\decrease

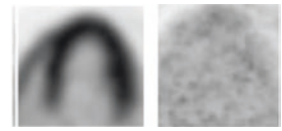
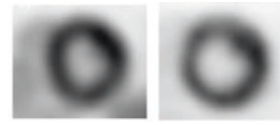
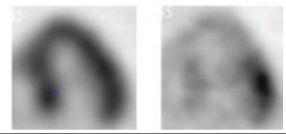
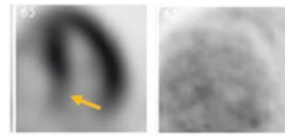
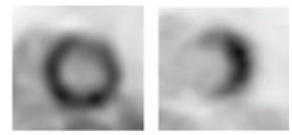
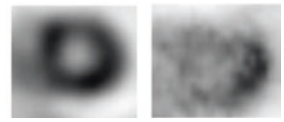
Rest Perfusion	FDG	Frequency	Example		Interpretation / Comment
			Perfusion	FDG	
Normal perfusion and metabolism					
Normal	Normal (negative)	32 (27%)			Normal
Normal	Diffuse (non-specific)	15 (12%)			Diffuse FDG most likely due to failure to suppress FDG from normal myocardium
Abnormal perfusion or metabolism					
Normal	Focal	20 (17%)			Nonspecific pattern; focal increase in FDG may represent early disease vs. normal variant
Positive	Negative	17 (14%)			Rest perfusion defect may represent scar from cardiac sarcoidosis or other etiologies
Abnormal perfusion and metabolism					
Positive	Focal increase ("mismatch pattern")	23 (19%)			Presence of active inflammation ± scar in the same location
Positive	Focal diffuse	6 (5%)			Similar to above but also areas of inability to suppress FDG from normal myocardium vs. diffuse inflammation
Positive	Focal increase (different area)	5 (4%)			Presence of both scar and inflammation but in different segments

Fig. 9.4 Assessment of cardiac sarcoidosis

Complications

The complications to pharmacological stress perfusion imaging are presented elsewhere. The risk of PET imaging includes radiation exposure and risk of solid cancers and leukemia due to stochastic effects of ionizing radiation. For instance, the total body effective dose of radiation exposure from a myocardial perfusion using rubidium Rb-82 is approximately 4.1 mSv and from F-18 fluorodeoxyglucose myocardial viability scan is approximately

7.0 mSv. In order to prevent or limit the effects of ionizing radiation, the principle of ALARA (As low as reasonably achievable) should be followed. Hence, appropriate indications for testing should be followed per the ACC/AHA and ASNC appropriate use criteria. Once a proper indication is confirmed, it is important to limit the amount of radiation and to use the lowest possible dose of radioisotopes to obtain accurate images for interpretation.

Clinical Vignettes

Case 1

Seventy-two year old man presents with mild stroke and chest pain. History includes smoking (50 pack year), elevated cholesterol, diabetes. During hospitalization, the resting ECG demonstrated mild inverted t-waves and TnI elevation, also mild. The patient was obese, BMI 35. The patient underwent a rest/ stress dipyridamole PET study with mild chest pain but no ECG changes. Images are shown in Fig. 9.5.

There was TID and two separate perfusion abnormalities. There was a medium moderate/severe completely reversible antero/lateral and inferolateral defect as well as medium moderate/severe reversible anteroseptal, apical and inferoseptal defect confined to the apical regions. These findings were consistent with two vessel ischemia, circumflex and left anterior descending arteries. The patient underwent coronary catheterization which showed LAD which was occluded in the mid region, a ramus with 60–70% stenosis and circumflex proximal 90% stenosis. This case demonstrates the ability of rest/stress PET to identify not only CAD, but the severity. The accuracy of PET to predict multivessel CAD

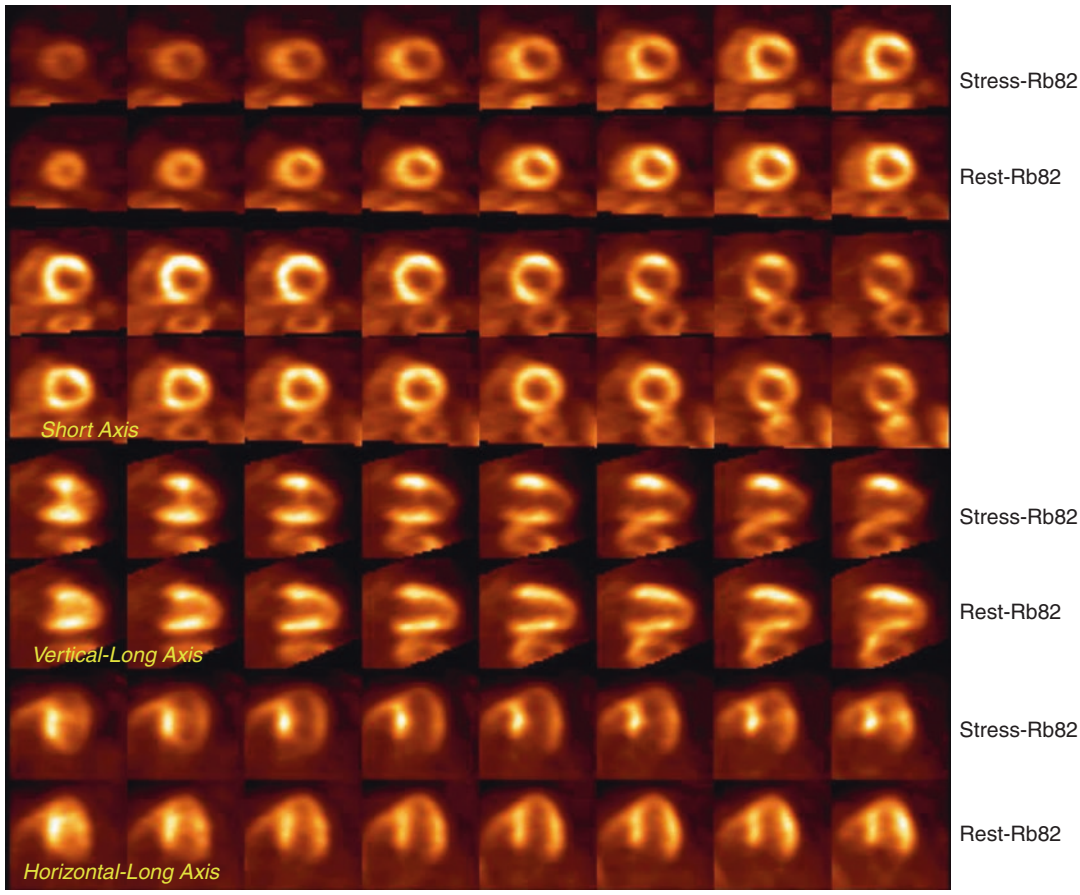


Fig. 9.5 Case #1 (see text for details)

is significantly better than SPECT (Courtesy of Gary V Heller, MD, PhD).

Case 2

Sixty-eight-year-old female patient presents with congestive heart failure and chest pain. The patient' s history includes hypertension, and prior MI several years previous. The patient had no history of diabetes. She had been stable until recent chest pain.

The patient underwent cardiac catheterization which demonstrated a 60% stenosis of the left anterior descending (LAD) artery and occluded obtuse marginal artery as well as an occluded right coronary artery with collateralization from the LAD. The patient underwent a rest/ stress dipyridamole PET protocol to evaluate for stress-induced ischemia and myocardial viability, in view of the diseased LAD and occluded vessels. The patient had no symptoms or ECG changes during the pharmacologic stress (Fig. 9.6).

Illustrates the rest/stress Rb-82 results, with an FDG viability assessment. There was normal perfusion in the anterior region with severe fixed defects in the lateral and inferior regions. Gated PET imaging revealed akinesis of portions of the lateral wall as well as inferior, with LVEF at both rest and stress of 34%. The conclusion was that there was no stress-induced-ischemia and non-viability of the inferior and lateral regions consistent with the occluded vessels. Because the ischemia work-up did not demonstrate myocardial viability in areas of concern, a cardiac PET FDG study was performed, which demonstrated marked FDG activity in both the inferior and lateral walls as well as the anterior wall ("mismatch") consistent with myocardial metabolic viability in both the circumflex and right coronary arteries.

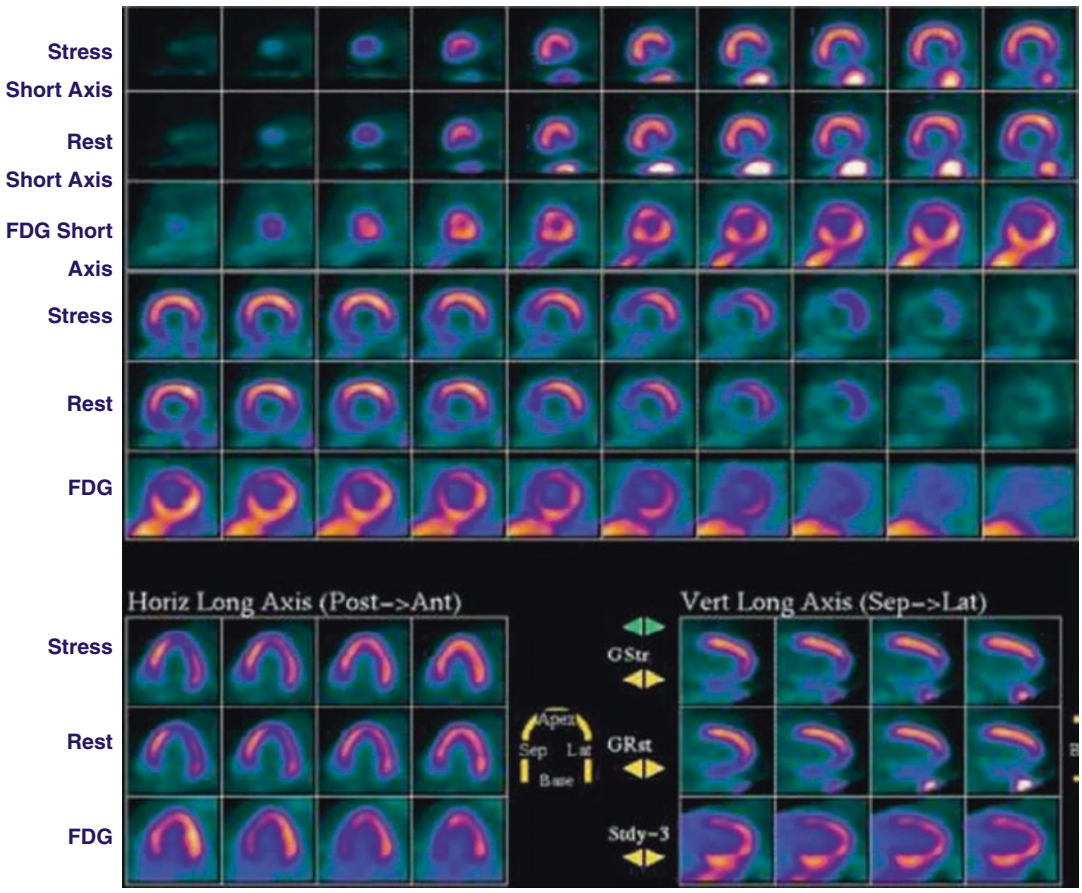


Fig. 9.6 Case #2 (see text for details)

The patient underwent successful by-pass surgery with revascularization of all three major arteries. Six months later the patient was asymptomatic and an echocardiogram revealed mild/moderate hypokinesis of the lateral/inferior walls, with a global ejection fraction of 46% (Courtesy of Gary V Heller, MD, PhD).

Case 3

Fifty-six-year-old female with history of diabetes and morbid obesity (BMI 48) presented with atypical chest pain and dyspnea on exertion for 2 weeks duration. A regadenoson stress SPECT study was ordered by her PCP and performed 10 days prior to her current presentation at an outside hospital with an equivocal stress test report mentioning a small reversible defect in the anterolateral wall that is consistent with ischemia vs differential breast tissue attenuation and a medium fixed defect in the inferior wall consistent with either a prior infarction or inferior wall attenuation. On further interview, she reports the pain as sharp left sided worsened with movement and exercise and lasting less than a minute reproducible with palpation. Due to the atypical features, obesity and equivocal SPECT study, she underwent a regadenoson PET stress test with the images shown in Fig. 9.7. The myocardial flow reserve (MFR) was calculated at 3.6.

This case represents a typical scenario comparing the superior image quality of PET compared to SPECT especially in the morbidly obese patients. The PET images show normal myocardial perfusion with normal flow reserve (>2). The perfusion defects noted on the SPECT study are most likely due to artifact. Since the quality of the pain is atypical, reproducible by palpation and the PET perfusion is normal, no further cardiac workup is necessary.

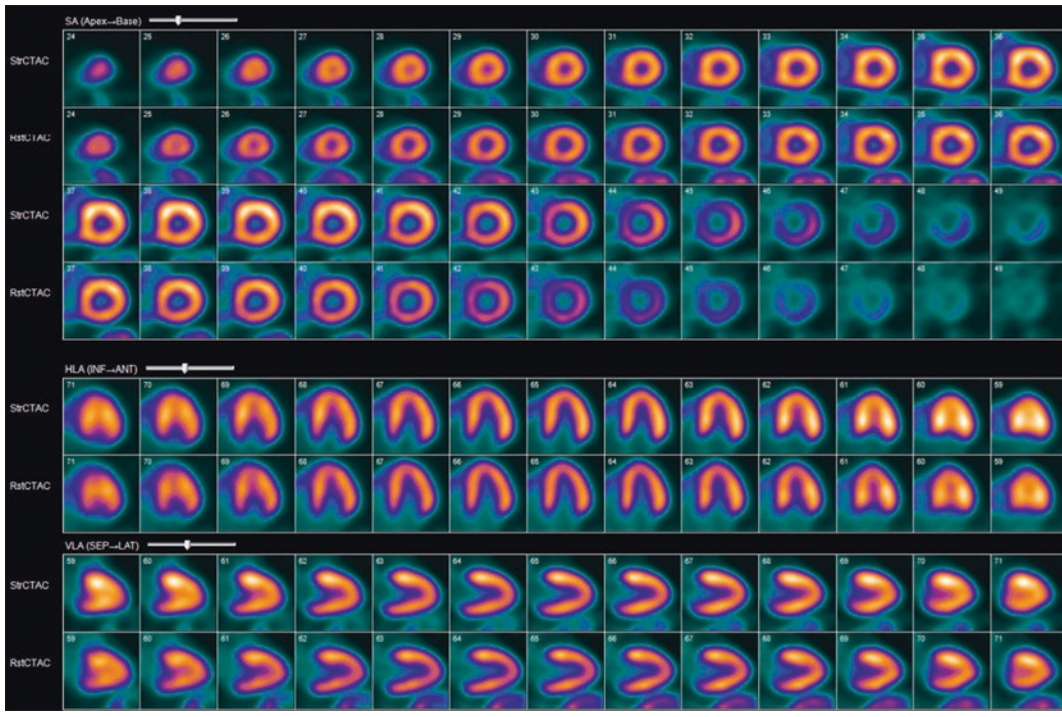


Fig. 9.7 Case #3, PET images (see text for details)

Case 4

Sixty-year-old male with a prior history of a relatively late presentation anterior myocardial infarction 20 years prior treated with thrombolytics followed by PCI who has been referred to cardiology for preoperative cardiovascular evaluation prior to vascular surgery. He is asymptomatic from a cardiac perspective but has limited ambulation with METS < 4. Due to the prior history of CAD and low METS, a regadenoson PET stress test was ordered with the images shown shown in Fig. 9.8.

The above image shows an abnormal PET perfusion study with a medium size stress perfusion defect of severe intensity in the mid to apical anterior, apical septum, apical inferior wall and LV apex that remained essentially unchanged and fixed on rest images. The findings are suggestive of prior myocardial infarction in the mid-LAD territory. No evidence of myocardial ischemia. This patient can likely undergo his surgery without the need for an invasive strategy with a cardiac catheterization. There is also no need to obtain alternate stress testing due to the good quality of the PET study.

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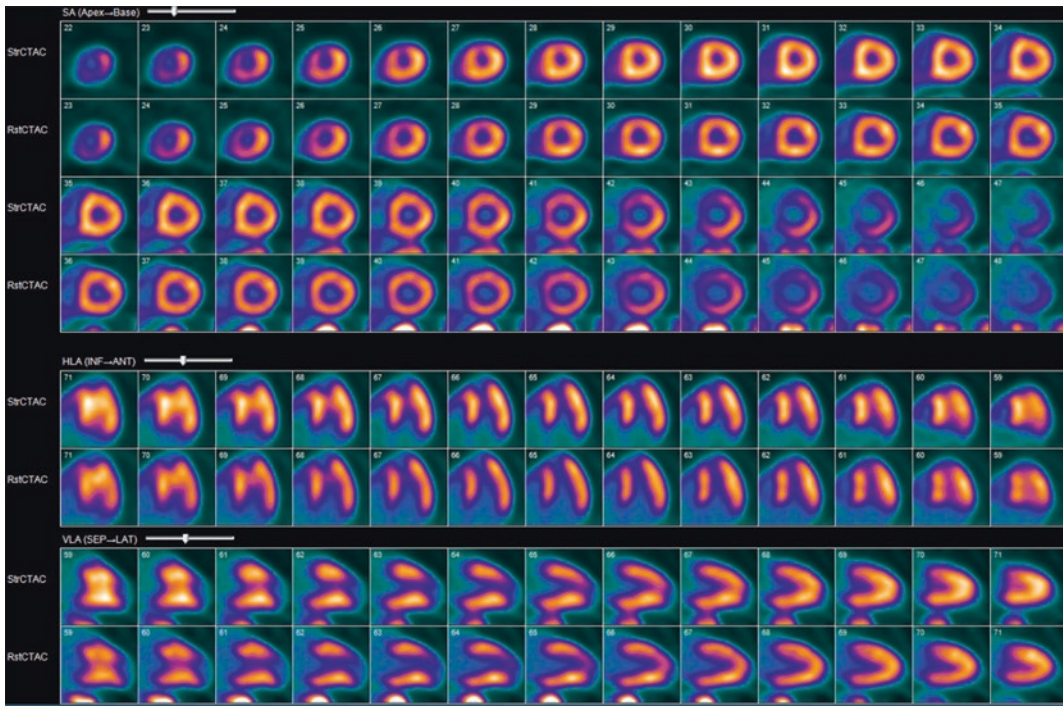

Fig. 9.8 Case #4, PET images (see text for details)

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Radionuclide Angiography

10

Cesia Gallegos

Left ventricular function is a key measure for assessing and managing cardiac conditions, especially in patients with heart failure and/or valvular disease. Several non-invasive techniques provide this information as well as the assessment of regional wall motion abnormalities.

Radionuclide angiography (RNA) is a nuclear cardiology technique first used and described in the 1970s [1, 2]. It is also known as radionuclide ventriculography (RVG), radionuclide cine angiography (RNCA), multiple gated cardiac blood pool imaging (MUGA) scan, and equilibrium radionuclide angiography (ERNA) [3]. This radioactive count-based technique provides an accurate and highly reproducible method independent of ventricular geometry and is well suited for the serial assessment of global left ventricular (LV) function. This method may also be used in conjunction with bicycle exercise, although this is now infrequently performed. Parameters obtained from RNA include global ventricular systolic function, regional wall motion, ventricular volumes, systolic and diastolic function indices, and stroke volume/cardiac output [3].

Indications [3]

1. Evaluation of cardiac function in patients receiving chemotherapy. This is the most common indication. It is beneficial for the assessment of chemotherapy-induced cardiotoxicity, such as doxorubicin, which may cause a dose-dependent impairment of the LV function, producing a severe and irreversible ventricular dysfunction before the onset of symptoms of heart failure. It provides LV quantification and can be used for risk stratification and prognosis, providing information on patients with preexisting cardiac conditions who are at greater risk of developing heart failure. Furthermore, serial evaluation of the LVEF (left ventricular ejection fraction) at rest can be performed on the patient during follow-up while on these therapies, providing essential information to guide discontinuation of doxorubicin if necessary.
2. Evaluation of function in patients with valvular heart disease for better assessment of the timing of surgery.
3. Cardiomyopathies and heart failure. RNA is helpful in the evaluation of biventricular function and its severity when other methods are not deemed accurate or cardiac magnetic resonance is not available.
4. Known or suspected coronary artery disease (CAD) with exercise or dobutamine.

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5. Other applications include evaluating right ventricular (RV) dysplasia, cardiomyopathies, candidacy for cardiac resynchronization therapy (CRT), candiday for lung transplantation, and candidacy/monitoring of heart transplantation.

Contraindications

1. Pregnancy
2. Breast-feeding, depending on the technique used for labeling red blood cells (RBCs). For instance, for in vivo labeling, it is recommended to stop breastfeeding for at least 12–24 h after the injection.
3. Patients with cardiac arrhythmias as an irregular heartbeat may limit interpretation. Although the RR variability can be corrected with "list mode acquisition," the results may still be unreliable.
4. For exercise testing, the same stress test contraindications apply [3].

Equipment

RNA is performed by labeling a patient's red blood cells with a radionuclide, technetium-99m-pertechnate (Tc99m), or human serum albumin (HSA). Therefore, standard IV supplies are required. The labeling of RBCs (explained in the next section) with Tc-99m is performed using FDA-approved kits for the in vitro preparation of the Tc-99m labeling. Its content is not administered to the patient. Each kit consists of three separate nonradioactive components: A 10 ml reaction vial with stannous chloride, dextrose, and sodium citrate, a syringe with sodium hypochlorite that must be protected from light to prevent degradation of the solution, and a second syringe with citric acid, sodium citrate, and dextrose. RBCs are prepared with the solutions in the kit. RBCs are then labeled with Tc-99m and subsequently injected into the patient within 30 min.

Image acquisition requires a standard gamma camera equipped with appropriate collimation. However, for first-pass RNA, a dedicated gamma camera with a high counting efficiency is used for best results. Images will require a workstation for post-processing. In addition, EKG leads are used for monitoring and gated image acquisition. Basic life support and resuscitative drugs must be available [3].

Technique

A complete history and physical examination are performed, focusing on indications for testing, current medications, allergies/side-effects, cardiac risk factors, current symptoms, and prior cardiac procedures, physical limitations, and special precautions. Women should be asked about pregnancy and lactation given the above considerations. An EKG must be obtained before the study to assess heart rate variability as it may limit the ability to interpret the test. Additionally, Occupational Safety and Health Administration (OSHA) guidelines for handling of blood products and radioactive material must be followed [3].

RBC labeling can be performed in vivo, modified in vivo, or in vitro, with the in vitro method being used most often. The in vitro method is performed by drawing blood from the patient, and then the stannous ions are injected into the blood with the subsequent addition of the Tc-99m to the mixture [3]. While in the in vivo method, two consecutive injections are required: the ions are injected directly to the patient's bloodstream, followed by the injection of the Tc-99m pertechnetate about 20–30 min later. The newly developed in vivo labeling technique, called modified in vivo, isolates the pre-tinned RBCs and Tc-99m from other body compartments during labeling. Tc-99m radiolabeled human albumin is an alternative. However, the resulting images are of lower quality. The usually administered activity is 555–1110 MBq.

RNA can be performed as "first-pass" or as "equilibrium" [4, 5]. In the first-pass approach, a bolus of Tc-99m pertechnetate or Tc-99m diethylenetriaminepentaacetic acid (DTPA) passes from the right to the left heart, sampling multiple cardiac cycles to determine the changes of radioactivity over time. This generates time-activity curves that provide ejection fraction (EF) measurements of both the right and left ventricles as

well as accurate quantitation of regurgitant lesions. For the right ventricular (RV) phase, 2–5 cycles are summed, and for the LV, 5–7 cycles are calculated from which LVEF and RVEF are derived. This approach is also well suited for shunt detection and evaluation of RV function but requires specialized cameras with high count rate capability and is very infrequently performed.

Equilibrium studies can be performed during rest or stress and can be acquired by both planar and SPECT (single photon computer tomography) methods. For this, Tc-99m pertechnate bound to RBCs is the most widely used [3]. The acquisition time range is 5–10 min per view, involving hundreds to thousands of heartbeats, which are synchronized with the QRS complex. Every cardiac cycle is divided into frames and all the frames within a given RR interval.

Equilibrium RNA uses the best septal left anterior oblique (LAO) projection, whereby the intraventricular septum is as vertical as possible. Lateral and anterior views are then obtained, each approximately 45° from the LAO projection (Fig. 10.1). For LVEF measurement, the LAO pro-

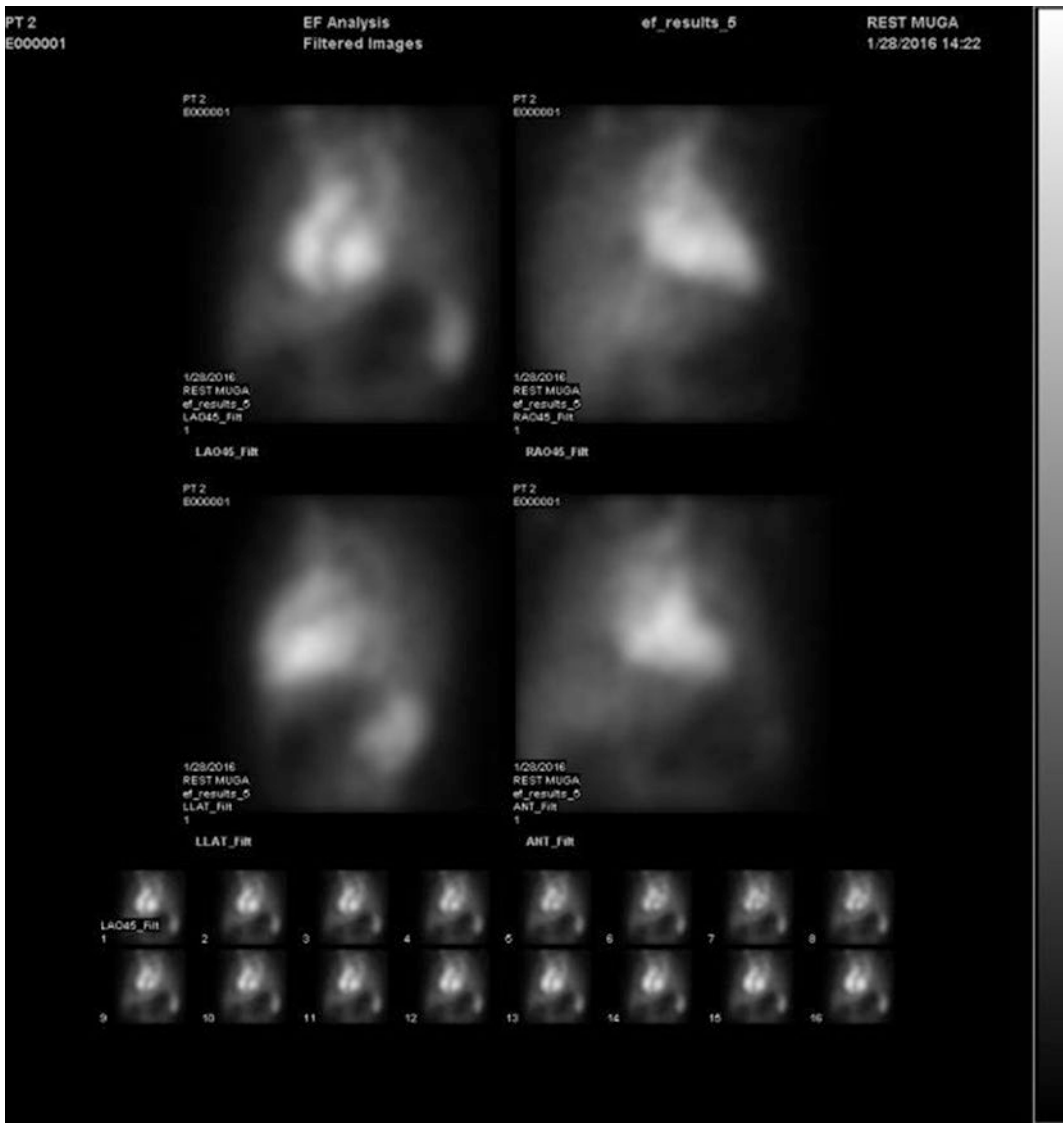

Fig. 10.1 A screenshot obtained at end-diastole demonstrating LAO (*upper left*), anterior (*upper right*), and lateral (*lower left*) planar projections. Regional wall motion is also displayed in the LAO image

vides the best measurement since this projection separates the RV and LV and identifies anterolateral, posterolateral, and septal LV motion. Regional wall motion may also be assessed (Fig. 10.2). Quantification of volumes, as well as systolic and diastolic function, is derived from the ventricular time-activity curve [3].

Data Interpretation

The findings obtained from an RNA scan should be interpreted and reported in a clear and systematic way. The essential components are [3]:

1. Cardiac Morphology: Size, orientation, and morphology of various cardiac chambers, ventricular wall thickness, as well as the pericardial silhouette, which may all be evaluated subjectively and reported. When measured, absolute volumes should be included.
2. Systolic function: All LV segments should be assessed qualitatively and global LV function should be compared to calculated EF. Reprocessing may be necessary if there are discrepancies with measurements. Abnormalities should be reported as mild, moderate or severe, hypokinesia, dyskinesia, or akinesia. It is optional to report diastolic filling indices or systolic emptying indices.
3. Stress images: These should be displayed side-by-side to the rest images in cinematic mode. Baseline, peak, and recovery LVEF should be reported as well as any alteration in regional wall motion, RV and LV function, and volumes. Cardiac morphology should be reported in a similar way as in a rest study.
4. Comparison to other studies: Prior studies should be reviewed and compared.

With an acquisition greater than 16 frames per cardiac cycle, diastolic function may also be assessed, although this is infrequently performed at the current time. Indices such as peak filling rates and time to peak filling may be quantitatively determined.

Complications

RNA is a safe, non-invasive procedure. However, there are a few scenarios that require particular caution.

1. Arrhythmias, in particular during or after stress/exercise as heart rate response during these is unpredictable.
2. Incorrect handling of RBCs during in vitro, which may result in administration of the labeled cells to the wrong patient.

Clinical Vignettes

Case 1

A 43-year-old woman was recently diagnosed with breast cancer, treated with lumpectomy and radiation therapy. She will begin chemotherapy with a variety of agents, including doxorubicin. An RNA was performed to obtain a quantitative assessment of LV function.

Figure 10.2 demonstrates a single static screen capture including most of the key information needed to assess cardiac function and subsequently begin chemotherapy. This depicts a study with a 16 frame per cardiac cycle acquisition. The time-activity curve at the bottom shows LV filling during the cardiac cycle and even demonstrates the atrial contribution near the end of diastole. The ED and ES frames illustrate the LV area during end-systole and end-diastole, with the adjacent region used for background counts. Our patient's quantitative LVEF was 73%.

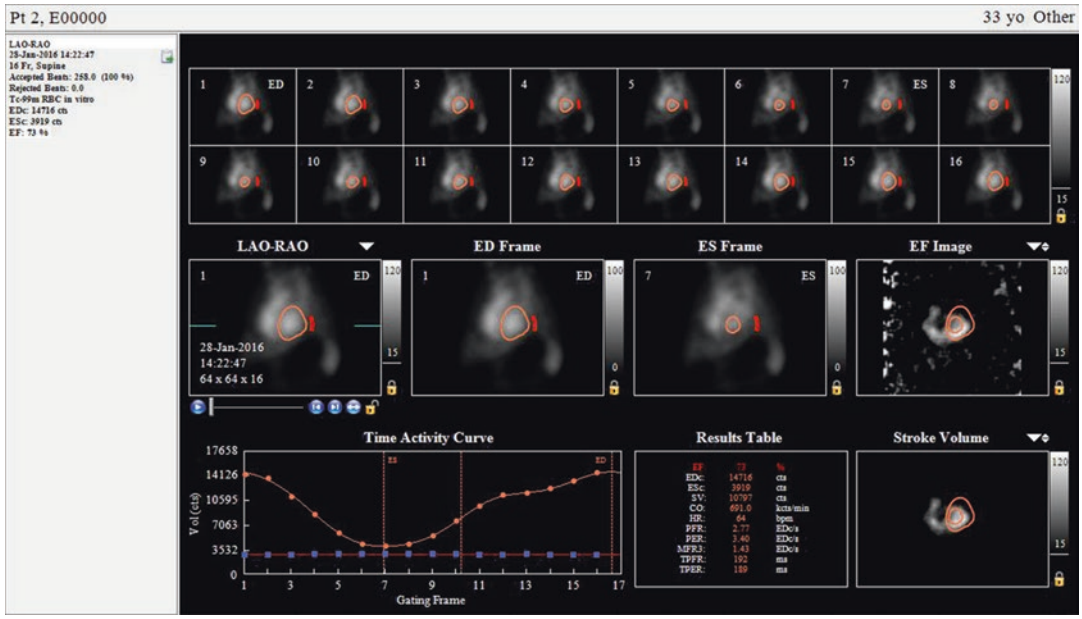

Fig. 10.2 Case 1 (see text for details)

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Amyloid Imaging

11

Adam Horblitt

Introduction

Amyloidosis is an infiltrative disease that can affect multiple organ systems, and is caused by abnormal protein deposition of insoluble amyloid fibrils within tissue substrate. Cardiac amyloidosis is characterized by protein deposition within the interstitial space of the myocardium, resulting in progressive myocardial wall thickening, diastolic dysfunction, and ultimately a restrictive cardiomyopathy in the later phases. Greater than 95% of CA cases are due to two different precursor proteins, immunoglobulin light-chain derived (AL) or liver-derived transthyretin (ATTR) amyloid fibrils. AL amyloidosis is associated with multiple myeloma in 15% of cases and carries an overall poor prognosis in comparison to ATTR amyloidosis. ATTR amyloidosis can occur as either a hereditary mutant (variant) or a wild (senile) type [3]. Amyloidosis remains an underdiagnosed disease, for which true incidence has yet to be determined. Several novel and effective treatments have been established, placing significant interest in early and accurate diagnosis [1].

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Indications

In 2019, a multi-societal expert consensus put forth recommendations to establish standardized methods of imaging, diagnostic criteria, and appropriate utilization. Currently it is recommended that all patients with clinical symptoms suspicious of amyloidosis including heart failure, peripheral/autonomic neuropathy, macroglossia, carpal tunnel syndrome, periorbital bruising, stroke, atrial fibrillation, postural hypotension, fatigue, weight loss, pedal edema, renal dysfunction, diarrhea, and constipation be evaluated. Additionally, for those patients whom have already received a diagnosis and are undergoing therapy, there may be future indications to assess response to therapy with serial imaging [2].

Techniques

Echocardiography

Both two dimensional and Doppler echocardiography play a significant role in the non-invasive assessment of CA. Its ability to assess cardiac structure and function make echocardiography the initial imaging method of choice. Echocardiography focuses on the morphological findings associated with amyloid infiltration including thickened left ventricle walls (>1.2 cm) in absence of other causes, biatrial enlargement/

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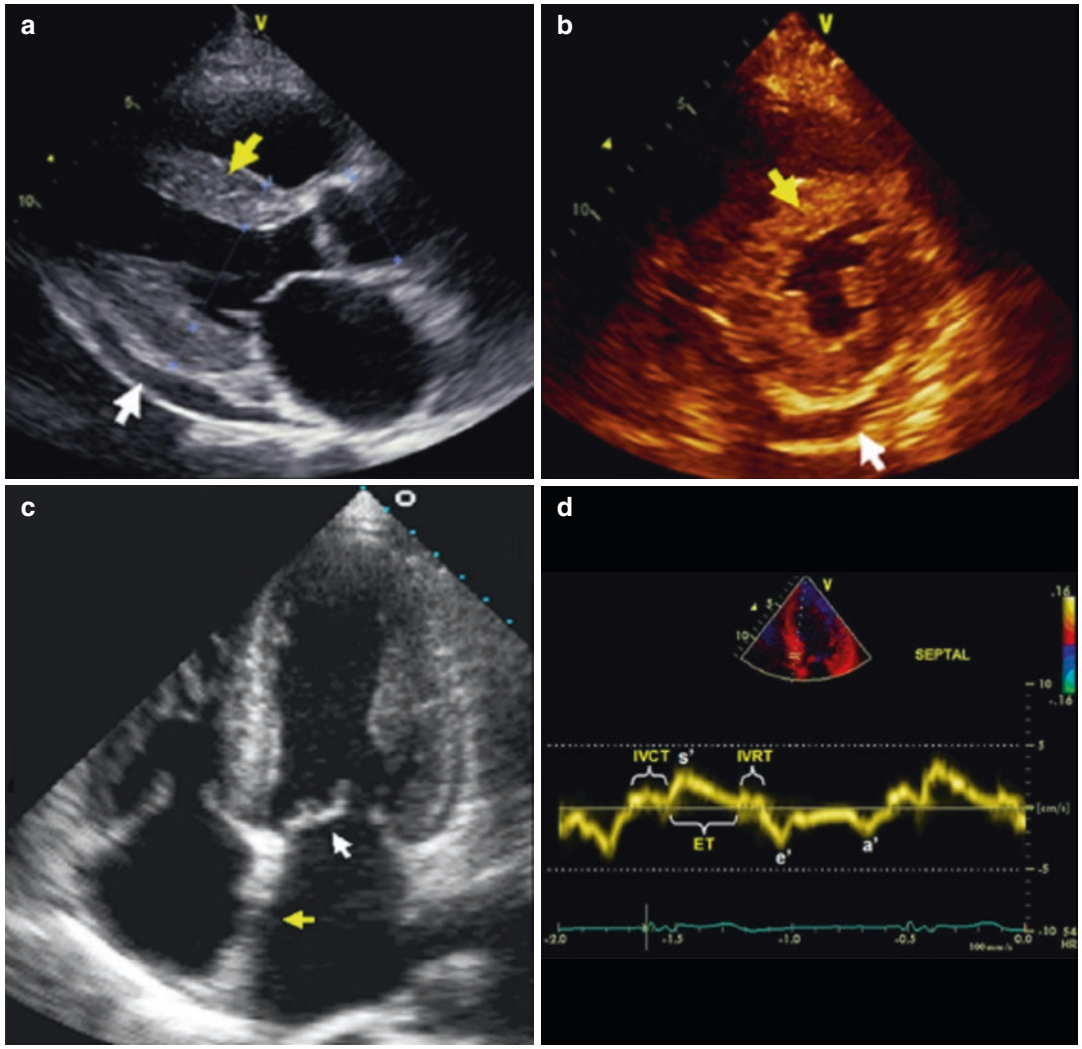

Fig. 11.1 Characteristic appearance of cardiac amyloidosis on echocardiography. (**a**) (Parasternal long axis) and (**b**) (parasternal short axis) demonstrate increased LV wall thickness with a sparkling texture of the myocardium (yellow arrows) in a patient with primary (AL) cardiac amyloidosis. A small pericardial effusion is present (white arrows). (**c**) (Apical four-chamber view) demonstrates increased biventricular wall thickness, biatrial enlargement, and increased thickening of the interatrial septum (yellow arrow) and mitral valve leaflets (white arrow) in a patient with wild-type transthyretin cardiac amyloidosis. (**d**) TDI tracing taken at the septal mitral annulus in a patient with ATTR cardiac amyloidosis. The TDI tracings shows the "5-5-5" sign (s^0 [systolic], e^0 [early diastolic], and a^0 [late (atrial) diastolic] tissue velocities are all <5 cm/s), which is seen in patients with more advanced cardiac amyloidosis [1]. (Figure and caption reproduced with permission from Dorbala, et al. Journal of Nuclear Cardiology 2020;27:659–73)

dysfunction, pericardial effusion, and restrictive transmitral filling pattern on doppler (Fig. 11.1). However, the appearance of some of these findings are uncommon until the late phases of the disease. A sparkling appearance of the myocardial walls can be appreciated with CA, but it is not considered a highly specific finding and can be observed with other conditions. Patients with CA typically show reduced velocities with tissue Doppler across all standard measurements typically less than 5 cm/s referred to as the "5-5-5" sign. When AL and ATTR CA patients demon-

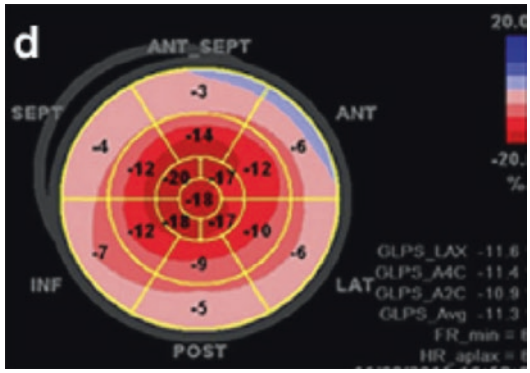

Fig. 11.2 Characteristic appearance of cardiac amyloidosis on echocardiography. Bullseye map of the longitudinal strain pattern throughout the left ventricle with the "cherry-on-the-top" sign (red denotes normal longitudinal strain at the apex and pink/blue denotes abnormal longitudinal strain at the mid/basal left ventricle). (Figure and caption reproduced with permission from Dorbala, et al. Journal of Nuclear Cardiology 2020;27:659–73)

strate a typical pattern of longitudinal strain, in which the basal portion of the left ventricular segments are severely impaired while apical segments are relatively spared, this is classically referred to as "apical sparing" or the "cherry-on-top" sign. This associated with 93% sensitivity and 82% specificity in identifying patients with CA (Fig. 11.2) [1].

Cardiac Magnetic Resonance

Cardiac magnetic resonance (CMR) provides excellent functional and morphological assessment of the heart in addition to characterization of the myocardium. CMR is able to characterize myocardial tissue with the use of gadolinium-based contrasts. Late gadolinium enhancement (LGE) is typically assessed during T1 weighted sequences. The result is regional differences in myocardial extracellular volumes as well as differential uptake and washout patterns within the extracellular space. Multiple LGE patterns have been described in association with CA; subendocardial and transmural LGE patterns predominate, with neither pattern being exclusive to ATTR or AL amyloidosis. Despite significant technical requirements, previous meta-analysis estimates the sensitivity and specificity of CMR with LGE at 85% and 92%, respectively, for diagnosing CA [2].

Radionuclide Imaging

A variety of bone-avid Tc-99m-labeled radiopharmaceuticals including diphosphonate (DPD) and Pyrophosphophate (PYP) compounds have been shown to be highly sensitive and specific in diagnosing ATTR CA. In the United States, Tc-99m-PYP is the only clinically available compound. Typical procedure includes injection of Tc-99m-PYP, with planar and single photon emission computed tomography (SPECT) obtained 2 h post radiotracer infusion. Should blood pooling persist, additional imaging may be performed. One benefit of radionuclide imaging is the potential for concurrent whole-body imaging, providing physicians and patients the ability to determine the extent of systemic involvement. For semi-quantitative assessment, interpretation of the uptake of radiotracer within the myocardium is compared with that of the ribs visually and graded from 0 (no uptake) to 3 (uptake greater than rib uptake) (Table 11.1). The presence of grade 2 or higher in combination with the absence of monoclonal proteins in blood or urine, a diagnosis of ATTR CA can be made with specificity in excess of 98%. Quantitative analysis is performed by calculating the mean counts of an area placed over the heart (a region of interest, ROI), and directly comparing it with a similar-sized area placed over the contralateral chest (Fig. 11.3). A heart/contralateral chest ratio >1.5 with the absence of monoclonal proteins in blood or urine is diagnostic of ATTR CA. In

Table 11.1 Semi-quantitative visual grading of myocardial 99MTC-PYP uptake by comparison to bone uptake

Grade	Myocardial ^{99m}Tc-PYP Uptake
Grade 0	No uptake and normal bone uptake
Grade 1	Uptake less than rib uptake
Grade 2	Uptake equal to rib uptake
Grade 3	Uptake greater than rib uptake with mild/absent rib uptake

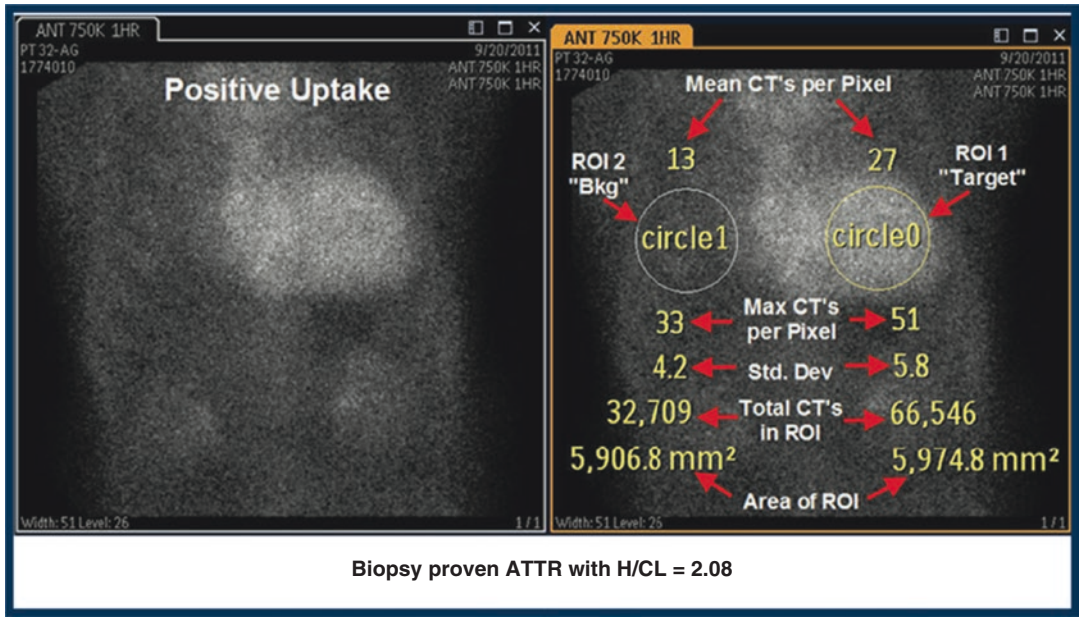

Fig. 11.3 Quantitative interpretation of ^{99m}Tc-PYP scan using heart to contralateral lung ratio (H/CL). "^{99m}Technetium-pyrophosphate Imaging for Transthyretin Cardiac Amyloidosis" by Dorbala et al., 2019, ASNC Cardiac Amyloidosis Practice Points. Copyright © 2019 by American Society of Nuclear Cardiology. Reprinted with permission

addition to bone avid radiotracers, additional agents have been developed for use with positron emission tomography and are highly specific for both ATTR and AL amyloid [1].

Contraindications

As it pertains to CMR, the main contraindications may include implanted metallic devices (ferrous), such as pacemakers, the inability to be still or obey/follow breathing instructions which can affect study quality, claustrophobia, and body habitus which exceeds equipment limits. Additionally, CMR requires the use of gadolinium contrast agents which are contraindicated in patients with chronic kidney disease/renal disease, patients on dialysis, patients at risk for nephrogenic systemic fibrosis, patients whom have experienced adverse reaction to similar contrasts agents, and lastly patients whom maybe pregnant. Technetium (99mTc-pyrophosphate) carries an FDA pregnancy classification of class C [1].

Clinical Vignette

Case 1

A 67-year-old male with past medical history of heart failure with preserved ejection fraction, obesity, atrial fibrillation, hypertension, chronic kidney disease, and hyperlipidemia presents to clinic after being referred by his primary care physician. The patient complains of worsening dyspnea on exertion, lower extremity edema, and exercise tolerance over the last 2 months. His medications include atorvastatin 40 mg, furosemide 40 mg twice daily, metoprolol succinate 100 mg, apixaban 2.5 mg twice daily. An echocardiogram obtained by his primary physician shows an LVEF of 45%, global hypokinesis, thickened left ventricular walls, and global longitudinal strain pattern in which the apex is preserved but the base strain is abnormal. EKG shows sinus rhythm with low voltage. Previous workup including nuclear stress test, basic metabolic panel, serum and urine immunofixation, as well

as Kappa/Lambda ratio has been unremarkable. Last serum creatinine was 1.8 mg/dL.

The next step would be to perform a Tc-99m PYP scan, as this patient has new onset heart failure with echocardiographic and EKG findings suspicious of amyloidosis. The patient's primary care physician has ruled out the presence of monoclonal proteins and his chronic kidney disease is something to appreciate before considering gadolinium-based contrast. While Cardiac MRI is able to diagnose amyloidosis, based on the presented clinical scenario, 99mTc-PYP scan would likely lead to an appropriate diagnosis without the potential risk of gadolinium based contrast. The patient is not a candidate for defibrillator therapy. Increasing diuretic therapy may improve this patient's symptoms, however it will not lead to diagnosis of the underlying etiology of heart failure.

Case 2

A 55-year-old female with past medical history of hyperlipidemia, atrial fibrillation, and hypertension, presents to clinic after being referred by their primary care physician at the patients request. Upon meeting the patient, she explains that her mother passed away several years ago from complications of heart failure and the treating provider was concerned about cardiac amyloidosis but was unable to confirm this diagnosis. The patient complains of occasional fatigue at the end of the day, dyspnea with significant exertion, as well as generalized lower extremity edema. She reports her exercise tolerance has decreased over the last 1–2 years. Her medications include atorvastatin 20 mg, Amlodipine 10 mg, and Hydrochlorothiazide 25 mg. Her primary care provider obtained a previous workup including electrocardiogram, treadmill exercise stress test, basic metabolic panel, complete blood cell count, as well as thyroid function all of which resulted without any abnormalities. The electrocardiogram showed normal sinus rhythm with low voltage in the pre-cordial leads. On physical examination she has normal heart sounds, clear lungs on auscultation, and grade 1 pitting pedal edema bilaterally. The patient asks what she should do to determine her risks for having cardiac amyloidosis

The next step would be to perform an echocardiogram as well as *serum and urine immunofixation* with *Kappa/Lambda ratio*. The patient's primary care physician has ruled out the most common non-cardiac causes of her generalized complaints. The presence of generalized edema and dyspnea on exertion, could be cardiac in etiology. While Cardiac MRI is able to diagnose amyloidosis and provide an assessment of left ventricular function, echocardiography remains the gold standard for evaluation of not only systolic, but also diastolic dysfunction. Based on the presented clinical scenario, transthoracic echocardiogram would provide the most clinically significant information while avoiding potential radiation and contrast exposure of other imaging modalities. Should the patient have an abnormal trans-thoracic echocardiogram, advanced imaging modality for the diagnosis of amyloidosis can be pursued.

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12 Cardiac Computed Tomography (CT) and Fractional Flow Reserve-Computed Tomography (FFR-CT)

Arieh Fox and Nitin Sabharwal

Cardiac CT has undergone dramatic advances in technology with applications that include the assessment of coronary artery disease (CAD), using coronary computed tomography angiography (CCTA) evaluation of congenital and structural abnormalities, cardiac function, and characterization of anatomy prior to valve and electrophysiology procedures [1, 2]. CT now permits the rapid acquisition of high quality data in the majority of patients using prospective (radiation-sparing) or retrospective ECG gating, with outstanding resolution of the coronary arteries as well as other cardiac structures.

Indications

In 2010, the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR Appropriate Use Criteria for Cardiac Computed Tomography was published with the level of appropriateness to guide physicians. The list is extensive and generally includes usefulness in the acute and chronic setting as well as in the symptomatic and asymptomatic patient. The main appropriate indications are listed below (Table 12.1).

Contraindications

Patients must be able to meet the weight requirements of the scanner, have the ability to lay supine and motionless with arms raised above their shoulders, and follow simple breathing instructions.

Chronic kidney disease (GFR < 60) is a relative contraindication given the potential for contrast-induced nephropathy (CIN); the risk of CIN must be weighed against the potential benefits of the study. However, severe kidney disease (GFR < 30, not on dialysis) is an absolute contraindication and an alternative testing strategy should be pursued. Previous anaphylaxis to iodinated contrast or an allergic reaction to iodinated contrast after premedication is an absolute contraindication.

Atrial fibrillation and frequent ectopy are relative contraindications to CCTA and mandate retrospective gating (acquisition of the entire cardiac cycle). Additionally, heart rates in excess of 70 BPM are usually associated with excessive cardiac motion and efforts to modulate pulse rate must be undertaken. In this regard, an inability to tolerate beta-blockers may be a relative contraindication.

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Table 12.1 Appropriate indications for cardiac computed tomography [1, 2]

1	Detection of CAD in intermediate risk symptomatic patients without known heart disease
2	Detection of CAD in low risk symptomatic patients without known heart disease who are unable to exercise or ECG is uninterpretable
3	Detection of CAD in low and intermediate risk acutely symptomatic patients without known heart disease
4	Detection of CAD/risk assessment in asymptomatic low risk patients with significant family history or intermediate risk patients with coronary calcium score in individuals without known CAD
5	New-onset or newly diagnosed heart failure (HF) and no prior CAD in low & intermediate risk patients
6	Preoperative coronary assessment prior to non-coronary cardiac surgery in intermediate risk patients
7	Normal ECG exercise test and continued symptoms or Duke Treadmill Score-intermediate risk findings
8	Discordant ECG exercise and imaging results or equivocal stress imaging results
9	Evaluation of new or worsening symptoms in the setting of normal past stress imaging study
10	Evaluation of graft patency after CABG in a symptomatic patient
11	Assessment of anomalies of coronary arterial and other thoracic arteriovenous vessels or complex adult congenital heart disease
12	Evaluation of left ventricular function in acute myocardial infarction (MI) or HF when images from other noninvasive methods are inadequate
13	Quantitative evaluation of right ventricular function
14	Assessment of right ventricular morphology in suspected arrhythmogenic right ventricular dysplasia
15	Characterization of native and prosthetic cardiac valves with suspected significant valvular dysfunction and inadequate images from other noninvasive methods
16	Evaluation of cardiac mass (suspected tumor or thrombus) with inadequate images from other noninvasive methods
17	Evaluation of pericardial anatomy
18	Evaluation of pulmonary vein anatomy, coronary vein mapping or localization of coronary bypass grafts prior to intervention

In younger individuals, the risk of potential long-term radiation exposure must be weighed against the potential benefits of the study. Additionally, dense coronary calcification may limit the interpretation and utility of the study, however a specific coronary calcium (Agaston) score that excludes the use of CCTA has not been recommended in the Society of Cardiovascular Computed Tomography (SCCT) guidelines.

Equipment

Cardiac CT imaging equipment must meet the minimal technical capabilities required for the scan indication and the patient's underlying characteristics. According to the ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR Appropriate Use Criteria, cardiac CT generally requires a minimum of 64 multi-detector rows, gantry rotation time no greater than 420 ms, sub millimeter spatial resolution and cardiac imaging software capable of three-dimensional post processing with reconstructed axial data, multiplanar reconstructions, and maximum intensity projections. Additionally, tube potential adjustment must be available for radiation reduction techniques, such as reducing the voltage to 100 mV for non-obese patients. Ideally, prospectively triggered ECG scanning and iterative reconstruction should also be available for further radiation reduction.

FFR-CT requires no special equipment during the acquisition of images but does require high quality data. Once the images are acquired the study, the data is electronically transmitted to a third party vendor, Heartflow Inc. The Heartflow analysis is a commercially available software in the United States, Canada, Europe and Japan. It is anticipated that a similar type of analysis will likely be available on certain manufacturer's workstations in the near future.

Technique

Heart rate control is crucial for obtaining optimal images without significant artifact and therefore the patient should be given oral beta-blockers the night prior and the morning of the procedure. If the patient's heart rate is still elevated (>65 BPM), the patient should be given an additional dose of IV beta-blocker or calcium channel blocker as

needed. Patients should abstain from caffeine or nicotine for at least 12 h prior to procedure for purposes of heart rate control.

Nephrotoxic drugs should be discontinued and the patient should be screened for contrast induced nephropathy risk factors (diabetes mellitus, chronic kidney disease, congestive heart failure, age >75) with an accurate history and a serum creatinine obtained prior to the procedure. Pre-procedural oral and possibly IV hydration may be necessary based on the patient's baseline serum creatinine. Patients with a history of an iodine allergy or an allergic contrast reaction require premedication with corticosteroids and histamine antagonists.

Breath holds are performed during image acquisition and theoretically reduce cardiac motion as well as decrease intrathoracic pressure leading to maximum superior vena cava flow and contrast enhancement.

A coronary scan (CCTA) should begin at the level of the carina or mid-pulmonary artery and end 2 cm below the diaphragm unless the patient has bypass grafts, which would require starting above the arch. A calcium score is often obtained prior to coronary CT for prognosis and estimate of plaque burden, as well as to optimize CCTA image acquisition.

Nitroglycerin 0.4–0.8 mg sublingual should be administered prior to image acquisition to improve image quality by arterial vasodilatation. However, this should be avoided in patients with systolic blood pressures less than 100 mmHg, significant aortic stenosis or hypertrophic cardiomyopathy and patients who are using phosphodiesterase inhibitors.

The appropriate gating technique should be selected based on the study indication and the patient's characteristics. Prospective gating limits the data acquisition period during the cardiac cycle to the points of least coronary movement and is the preferred method for coronary artery assessment given its ability to obtain the necessary data while substantially limiting radiation exposure. Retrospective gating acquires data during the entire cardiac cycle and requires a significantly higher radiation exposure. This may be useful for patients with arrhythmia, rapid heart rates or high calcium scores, where artifacts may be a limiting factor and the additional data acquired throughout the cardiac cycle may be beneficial. ECG pulsed tube current modification is another gating technique used to limit radiation when coronary anatomy and evaluation of left ventricular function is required. Tube voltage and current should also be adjusted according to the patient's size to minimize radiation dose.

Contrast used in cardiac CT is nonionic with high iodine concentration typically dosed according to patient BMI and given through a vein suitable for administration at a flow rate of 4–6 mL/s (usually antecubital). Decreased and increased cardiac output increase and decrease the amount of contrast required.

Once the images are acquired, FFR-CT provides a digital, 3D model of the heart. Subsequently analysis uses computational fluid dynamics to solve millions of complex equations to simulate blood flow and provides FFR values along the coronary arteries. A positive FFR value ($\leq$0.80) indicates a hemodynamically significant lesion, that should be considered for revascularization.

Data Interpretation

CCTA

The Society of Cardiovascular Computed Tomography (SCCT) released updated guidelines in 2014 on the interpretation of coronary CT angiography that are listed in the table below (Table 12.2).

Individual lesions should be graded on a quantitative basis with the recommended SCCT scale listed below. Further, the CAD-RAD classification of the stenosis provides interpretation and further cardiac investigation which is complimentary to the final body of the report (Table 12.3).

Additionally, myocardial chamber cavities and walls should be examined for dilation, hypertrophy, thinning, hypodense enhancement, shunting, masses and congenital anomalies. Reporting of left ventricular and regional function as well as

Table 12.2 SCCT interpretation guidelines [3]

Non-contrast coronary calcium CT	
1.	Agatston score should be calculated for the total study (sum of four vessels)
2.	Presence of calcium in aortic wall, aortic valve, mitral annulus/valve, pericardium, and myocardium should be documented
3.	Noncardiac structures (pleural effusions, pulmonary nodules, mediastinal abnormalities, and so forth) should be documented
Coronary CT	
1.	Interpretation should be made on three-dimensional cardiac-specific interpretation software
2.	Recommended image reconstructions should be viewed
3.	Interpreters should be prepared to customize image reconstructions if necessary
4.	The data set should be previewed for artifacts
5.	Noncontrast studies should be reviewed before contrast studies
6.	The coronary tree should be examined systematically
7.	Lesions should be reviewed in multiple planes and conceptualized in three dimensions
8.	Lesions should be assessed for stenosis severity, quality, and morphology of plaque
9.	Extracoronary cardiac and thoracic anatomy should be examined within the cardiac field of view

valvular pathology may be appropriate depending on the clinical indication.

Reports should include a procedure section with complete details of image acquisition and image reconstruction and a clinical findings section with coronary findings, non-coronary cardiac findings, and non-cardiac findings.

FFR-CT

FFR or fractional flow reserve has been used in invasive angiography for the determination of physiologically significant lesions seen during coronary angiograms. An invasive FFR of ≤0.8 is considered positive for a lesion causing significant compromise of blood flow. FFR-CT has been shown to be clinically useful in assigning clinically significant lesions non-invasively. A FFR-CT value of ≤0.8 is considered significant. However, given its novelty, standardization and optimization of reporting is still lacking. For increased specificity, it has been suggested to measure the FFR value 2 cm distal to the lesion. Given the FFR-CT provides us with values of FFR along the length of the vessel, just considering the lowest value can lead to false positive cases [5].

Table 12.3 CAD-RADS reporting and data system for patient with stable chest pain [4]

CAD-RADS 0	0% no plaque or stenosis	Absence of CAD	No further investigation
CAD-RADS 1[a]	1–24% minimal stenosis or plaque with no stenosis	Plaque with <25% stenosis	No further investigation
CAD-RADS 2	25–49% mild stenosis	Mild non-obstructive CAD	No further investigation
CAD-RADS 3	50–69% stenosis	Moderate stenosis	Consider functional assessment
CAD-RADS 4	A. 70–99% stenosis or B. Left main >50% or three-vessel obstructive (≥70%) disease	Severe stenosis	A. Consider ICA or functional assessment B. ICA recommended
CAD-RADS 5	100% (total occlusion)	Total Coronary occlusion	Consider ICA or viability assessment.
xCAD-RADS N	Non-diagnostic study	Obstructive CAD can't be excluded	Additional or alternative evaluation may be needed

CAD-RADS 1[a]—This category should also include the presence of plaque with positive remodeling and no evidence of stenosis*CAD* coronary artery disease, *ICA* invasive coronary angiography

Complications

Potential complications from cardiac CT include iodinated contrast extravasation, which can rarely lead to ulceration or compartment syndrome, allergic reactions to iodinated contrast, contrast induced nephropathy and radiation exposure. Contrast-induced nephropathy (CIN) is generally defined as a change in serum creatinine of

>0.5 mg/dL or a >25% increase in serum creatinine from baseline within 2–3 days of contrast exposure. Risk factors for CIN include hypotension, congestive heart failure, chronic kidney disease, diabetes, age older than 75, anemia, and volume of contrast. Radiation exposure should always be limited to as low as reasonably achievable while still obtaining the necessary results for an appropriate study. Finally, complications may be due to the medications administered as part of this procedure (beta blockers—bradycardia, bronchospasm, and hypotension; nitroglycerine—hypotension, headache).

Clinical Vignettes

Case 1

Forty-five-year-old police officer, who is active at baseline and has no significant past medical history presents to the emergency department (ED) after experiencing an episode of sharp chest pain earlier in the day. In the ED, the patient was noted to have an ECG without significant abnormalities and an elevated blood pressure of 160/105 mmHg. CCTA was obtained for detection of CAD in this low risk acutely symptomatic patient (Fig. 12.1).

This case shows a CCTA with no significant atherosclerotic lesions of the coronary arteries (CAD-RADS 0). Included below are the curved multiplanar reformation images of the Left Anterior Descending (LAD) artery (Fig. 12.1b), Left Circumflex (LCx) artery (Fig. 12.1c) and the Right Coronary (RCA) artery (Fig. 12.1d) without evidence of significant atherosclerotic disease.

Case 2

Sixty-four-year-old man with a past medical history significant for hyperlipidemia presents requesting a preventive cardiovascular evaluation. Previously, the patient underwent an asymptomatic treadmill stress test with 3 mm ST depressions in the inferolateral leads followed by a nuclear stress test with abnormal ECG findings but normal scintigraphic images without evidence of ischemia. Given discordant ECG exercise and imaging results, a CCTA was obtained for further evaluation.

This case shows a CCTA with severe coronary calcification and significant CAD in two vessels. There is extensive calcification in the proximal portion of the LAD with an elongated non-calcified severely stenotic plaque of approximately 70–99% (CAD-RADS 4A) (Fig. 12.2b). There is also calcification noted in the LCx but without significant obstruction (Fig. 12.2a). The proximal portion of the right coronary artery contains extensive calcification and an area of low density with markedly reduced contrast, which suggests a severe stenosis of 70–99% (Fig. 12.2c).

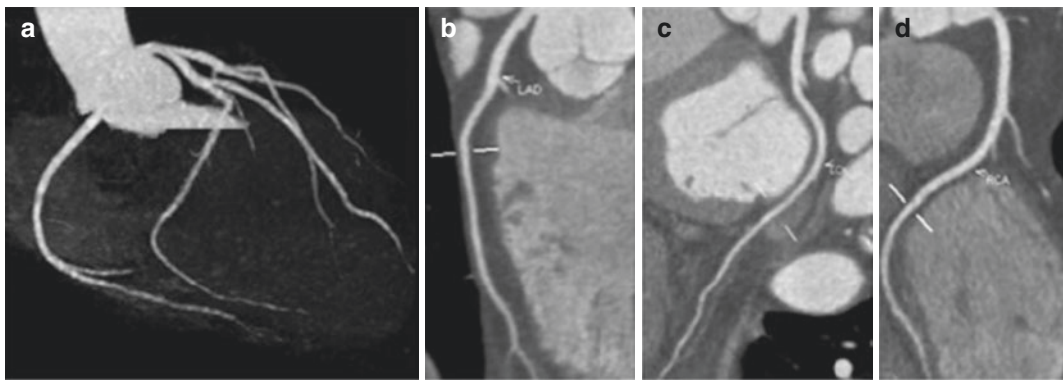

Fig. 12.1 Case #1 (see text for details)

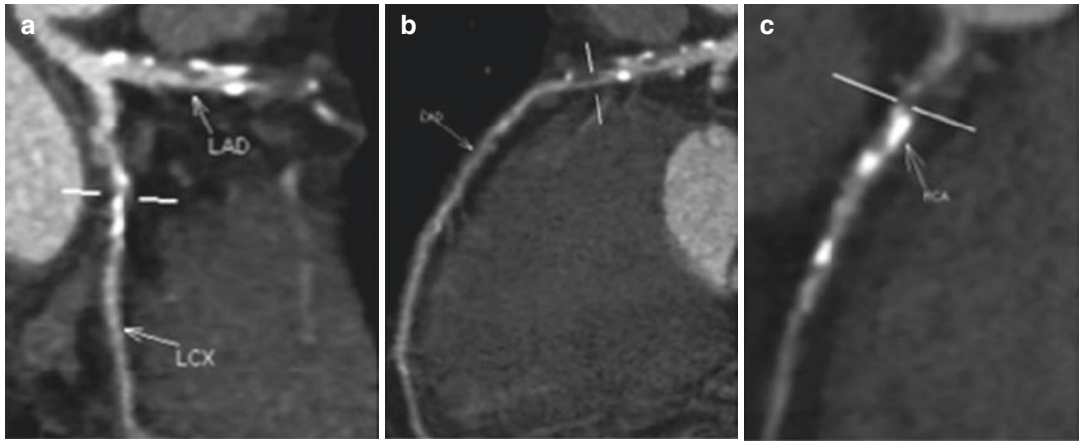

Fig. 12.2 Case #2 (see text for details)

Case 3

A 58-year-old man with a past medical history of diabetes, hypertension and hyperlipidemia presented to the cardiology clinic with atypical chest pain. His last ischemic evaluation was 3 months ago with an exercise treadmill stress test which showed no ischemic ekg changes however patient stopped within 5 min due to ankle pain and did not achieve target heart rate. Given high pretest probability for coronary artery disease and the inability to perform maximum effort, a CCTA with FFR was performed followed by a coronary angiogram and invasive FFR (Fig. 12.3).

This case shows a CCTA with a mid-LAD of approximately 50–69% lesion (CAD-RADS3) as indicated by the white arrows (Fig. 12.3a). The CT-FFR (Fig. 12.3c) was performed which gave a value of 0.85 thereby indicating this was not a functionally significant lesion. Later, a coronary angiogram (Fig. 12.3b) with invasive FFR was performed which confirmed the CCTA and CT-FFR findings.

Case 4

A 58-year-old construction worker with past medical history of hypertension, one pack a day smoking for 20 years comes with chest pain with exertion which resolves with rest. Patient states this chest pain has been occurring for more than year. He is not taking any medications. A CCTA was performed to rule out left main and proximal LAD disease (Fig. 12.4).

This case shows a CCTA with a mid-LAD of approximately 70–99% focal lesion (CAD-RAD 4A) as indicated by the white arrows (Fig. 12.4a). A CT-FFR was performed which showed a FFR of 0.76 across the above-mentioned lesion indicating a functionally significant lesion (Fig. 12.4c). A coronary angiogram later confirmed the above findings (Fig. 12.4b).

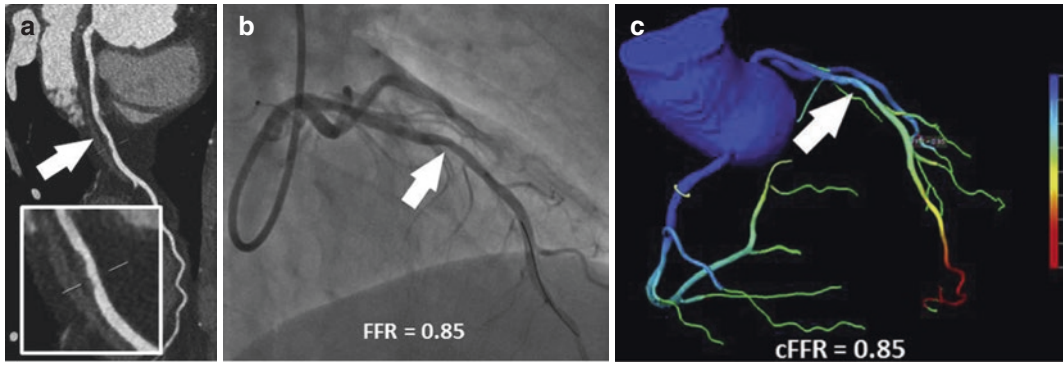

Fig. 12.3 Case #3 (see text for details)

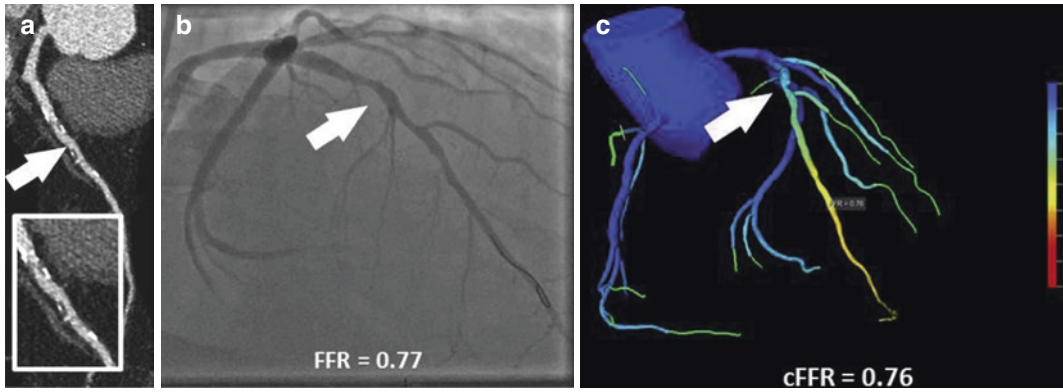

Fig. 12.4 Case #4 (see text for details)

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Cardiac Magnetic Resonance

13

Cesia Gallegos

Cardiac magnetic resonance (CMR) is the imaging modality of choice for the assessment of the heart, providing both anatomic and physiologic information. Its use has increased over the last decade, given the improvement in imaging acquisition, quality, and clinical expertise, with growing evidence from clinical trials supporting its value. The high natural contrast between intracardiac and intravascular blood pool, lack of ionizing radiation, and the three-dimensional nature of this method provide substantial advantages over other methods. It has become an essential tool for the diagnosis and management of cardiomyopathies, both ischemic and nonischemic, and other cardiac pathologies such as myocarditis and pericarditis.

CMR can be used for the assessment of left and right ventricular (LV/RV) volumes and function, wall motion, myocardial and pericardial disease such as inflammation, valvular and congenital heart disease, and perfusion, Though CMR is a safe imaging technique safe, particular caution should be taken in patients with prostheses and implantable devices such as pacemakers, defibrillators, cochlear, and cerebral implants.

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Indications (Table 13.1) [1–3]

Cardiac Anatomy and Ventricular Function

CMR is considered the most reproducible and accurate imaging modality in the study of left ventricular (LV) function. It is the preferred imaging modality as follow-up to echocardiography, as it also allows for assessment of myocardial viability and function. It also allows for stress perfusion testing, as discussed below. Some of the parameters routinely reported in functional CMR include LV end-diastolic volume (LVEDV) and LVEDV index, LV stroke volume, LV ejection fraction (LVEF), LV mass index, and LV end-diastolic and end-systolic diameters. CMR may also be used for qualitative and quantitative assessment of global and regional wall motion of the right ventricle (RV). It is usually the first-line diagnostic test for assessing RV function, and it is indicated in the evaluation of patients for suspected arrhythmogenic RV cardiomyopathy or dysplasia, as well as pulmonary arterial hypertension.

Coronary Artery Disease

CMR is also helpful in the evaluation of suspected coronary artery disease or chronic ischemic heart disease, especially with the delineation of myocardial viability through the use of gadolinium. Vasodilator stress perfusion

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Table 13.1 Class I and II indications for CMR [1]

Indication	Class
Dilated cardiomyopathy	I
Myocarditis	I
Hypertrophic cardiomyopathy	I
Arrhythmogenic right ventricular dysplasia	I
Cardiac amyloidosis	I
Myocardial iron overload	I
LV noncompaction	I
Fabry's Disease	I
Cardiac Sarcoidosis	I
Stress-induced (Takotsubo) cardiomyopathy	I
Endomyocardial fibrosis	I
Restrictive cardiomyopathy	II
Chemotherapy-induced cardiomyopathy	II
Athlete's heart	II

imaging and dobutamine wall motion assessment are CMR techniques for the detection and quantitation of inducible ischemia. This is accomplished by imaging of first pass of gadolinium-based contrast agent after injection of pharmacologic stress. One of the benefits of stress perfusion CMR is that it can be obtained for a wide range of body habitus without ionizing radiation [4]. Table 13.3 lists the appropriate use criteria for the use of CMR in suspected CAD [4].

Myocardial Disease

One of the most valuable uses of CMR is the assessment of myocardial edema and damage through late gadolinium enhancement (LGE) suggestive of necrosis and scar, abnormal function, and wall motion abnormalities, such as seen with myocarditis. For this, an expert consensus proposed the Lake Louise Criteria for CMR diagnosis of myocarditis, which were recently updated [5, 6]. Myocardial changes that can be identified using CMR include interstitial and intracellular edema, myocyte injury with loss of cell membrane integrity, necrosis and capillary leak, and dilatation of the myocardial vascular bed with hyperemia [5]. Table 13.2 shows the CMR criteria for the diagnosis of myocardial inflammation [5].

Valvular and Pericardial Diseases

CMR is more sensitive to changes in volume and structure, therefore, it provides complementary information in the assessment of valvular heart disease particularly in the assessment of flow hemodynamics and cardiac volumes. Through the use of phase-contrast techniques, CMR can also evaluate for valvular stenosis or insufficiency. Furthermore, it characterizes specific tissue configurations of tumors and masses and their relationship to chambers and valves, making it the ideal imaging modality as it allows for the assessment of mediastinal, pericardial, and myocardial involvement in one single study. Lastly, CMR allows for functional and morphologic assessment of pericardial abnormalities and is the test of choice to distinguish between constrictive pericarditis and restrictive cardiomyopathy [7].

Congenital Heart Disease

CMR may be used for the assessment of congenital shunts, precisely to quantify and follow the right and left ventricle volumes and function. CMR is also valuable for some forms of atrial (ASD) or ventriculoseptal (VSD) defects that are challenging for other imaging modalities to identify. The use of CMR along with angiography and flow measurement is also valuable for the assessment of complex congenital anomalies and the determination of chamber size, function, and atrial-ventricular relationships. Other congenital conditions in which CMR has proven to be helpful include pericardial anomalies, as well as valve disease and coronary artery anomalies.

Table 13.2 CMR criteria for the diagnosis of myocardial inflammation [5]

Original Lake Louise Criteria I (Any 2 out of 3)	Updated Lake Louise Criteria II (2 out of 2)	Diagnostic targets
Main criteria		
T2-weighted imaging	T2-based imaging	Myocardial edema
Regional* high T2 SI*or*Global T2 SI ratio ≥2.0† in T2W CMR images	Regional* high T2 SI*or*Global T2 SI ratio ≥2.0† in T2W CMR images*or*Regional or global increase of myocardial T2 relaxation time†	
Early gadolinium enhancement	T1-based imaging	↑ T1—edema (intra or extracellular), hyperemia/capillary leak, necrosis, fibrosisEGE—hyperemia, capillary leakLGE—necrosis, fibrosis, (acute extracellular edema)↑ ECV—edema (extracellular), hyperemia/capillary leak, necrosis, fibrosis
SI ratio myocardium/skeletal muscle (EGE ratio) of ≥4.0† in EGE images	Regional or global increase of native myocardial T1 relaxation time or ECV†‡*or*Areas with high SI in a nonischemic distribution pattern in LGE images	
Late gadolinium enhancement		
Areas with high SI in a nonischemic distribution pattern in LGE images		
Supportive criteria		
Pericardial effusion in cine CMR images	Pericardial effusion in cine CMR images*or*High signal intensity of the pericardium in LGE images, T1-mapping or T2-mapping*or*T1 mapping or T2 mapping	Pericardial inflammation
Systolic LV wall motion abnormality in cine CMR images	Systolic LV wall motion abnormality in cine CMR images	LV dysfunction

*"Regional" refers to an area of at least 10 contiguous pixels.
†Published or local normal values, LV coverage and proper analysis tools must be acknowledged.
‡T1 mapping is highly sensitive to detecting both acute and chronic forms of increased free water content within the myocardium, and thus, the Consensus Group recommends treating it as an alternative criterion to EGE. If paired with LGE to diagnose myocarditis, the areas of T1 abnormality should be beyond that detected by LGE imaging.

Assessment of the Great Vessels

It can frequently demonstrate a lesion directly (stenosis) or indirectly by showing a signal loss resulting from phase incoherence (abnormal communication). CMR angiography is also used to depict the extent, size, and shape of aortic aneurysms dissections, thrombus, vascular wall, and adjacent soft tissues. Its lack of ionizing radiation provides a tool for serial imaging.

Coronary Artery Disease

CMR is also useful in the evaluation of suspected coronary artery disease or chronic ischemic heart disease, especially with the delineation of myocardial viability through the use of gadolinium. Vasodilator stress perfusion imaging and dobutamine wall motion assessment are CMR techniques for the detection and quantitation of inducible ischemia. This is accomplished by imaging of first pass of gadolinium-based contrast agent

Table 13.3 Appropriate use criteria for the use of CMR for detection and risk assessment in suspected CAD [4]

Appropriate	*Symptomatic patients* • With at least medium to high pre-test probability of CAD and/or inability to exercise and/or a noninterpretable ECG
May be appropriate	*Symptomatic patients* • With low pre-test probability of CAD who are unable to exercise or who have an uninterpretable ECG • With intermediate pre-test probability of CAD who are able to exercise and who have an interpretable ECG
	Asymptomatic individuals • With high risk regardless of ECG interpretability and ability to exercise
Rarely appropriate	*Symptomatic patients* • With low or intermediate risk with interpretable ECG and able to exercise
	Asymptomatic individuals • With low or intermediate risk regardless of ECG interpretability and ability to exercise

after injection of pharmacologic stress. One of the benefits of stress perfusion CMR is that it can be obtained for a wide range of body habitus without ionizing radiation [4]. Table 13.3 lists the appropriate use criteria for the use of CMR in suspected CAD [4].

Contraindications

CMR is safe and lacks ionizing radiation, but special caution should still apply. In all cases, a risk/benefit consideration should be performed prior to each test and must be informed to each patient. Most importantly, it is essential to know that all CMR scanners maintain a strong magnetic field that can only be removed in emergency situations [7]. Therefore, physicians should have a thorough knowledge of patient safety, possible neurological effects, tissue heat deposition, the use of contrast as well as other contraindications or special considerations, which include [2, 7]:

Implantable Devices

Common implants, which may present a hazard when undergoing CMR, include pacemakers, ICD's, cochlear implants, neurostimulators, hydrocephalus shunts, metal-containing ocular implants, pacing wires, and metallic cerebral clips [7]. A complete list is available at www.MRIsafety.com. The clinician must be aware that the patient has an implantable device and whether or not it is magnetic resonance (MR) safe, conditional, or not safe. If the decision is made to perform CMR on a patient with a device, knowledge of device programming is necessary. Some of the risks of performing CMR in patients with pacemakers or cardioverter-defibrillators include burns from the generation of an electrical current from the metallic hardware and the "antenna effect," device movement, inappropriate discharging, and sensing. Appropriate emergency equipment and medications to treat possible adverse reactions must be readily available.

Contrast Media

Although more frequent with the use of iodinated contrast, some patients may require pretreatment prior to injection of contrast media even if gadolinium is used for prevention of anaphylactic reaction and/or acute kidney injury. Special caution must be performed in patients with decreased renal function, especially with a GFR <30 mL/min due to the risk for nephrogenic systemic fibrosis, a potentially catastrophic complication of gadolinium exposure.

Additionally, contraindications for pharmacological stress testing are similar to any other stress test modality.

Equipment

The magnetic resonance imaging (MRI) equipment must meet all state and federal requirements and must be accredited by the Academic College

of Radiology (ACR). MRI scanners for CMR must have the following specifications [3]:

1. Field strength ≥1.0 T. Most common is 1.5 T; however, the field strength of up to 3.0 T can be used.
2. Slew rate of at least 70 mT/m/s.
3. MRI scanners should be equipped with ECG gating and multi-channel radiofrequency surface coil.
4. MRI-compatible power injector for myocardial perfusion CMR or any MR angiographic methods.
5. The capability of fast 3D gradient echo imaging, phase-contrast flow quantification, and fast multislice myocardial perfusion imaging, as well as delayed contrast-enhanced myocardial imaging.
6. FDA-approved software for processing data.

Technique

MRI is based on imaging of protons within the hydrogen atoms in the human body that act like tiny magnets. A patient is then placed inside a scanner with a magnetic field, which the resultant vectors are fine-tuned by computer-controlled adjustments of small coils placed within the magnet [7].

Unless impeded by body habitus, a phased array surface coil should be used, as the heart is small, and the visual field should be reduced to maintain adequate spatial resolution. CMR imaging techniques may vary depending on the indication. Nonetheless, most examinations include short and long-axis cine images from the heart obtained for ventricular function.]. For assessment of cardiac morphology, T1-weighted and/or T2 weighted images of the heart are used, and they are usually gated to the R wave of the ECG [3].

For evaluation of mass, tumors, or cysts, pericardial disease, and myocardial inflammation, or perfusion, intravenous (IV) gadolinium is administered. Additionally, in the particular case of myocardial perfusion assessment, gadolinium must be rapidly bolused.

For flow quantification, phase contrast imaging may be used. CMR angiography can be used in addition to other MRI methods as it may provide important information about the great vessels.

CMR tagging is another technique in which bands are applied to the heart in end-diastole. Subsequently, cine images are obtained to observe the movement of the bands, which may provide information about wall motion abnormalities.

Data Interpretation

The CMR imaging planes are oblique to one another and are called "double-obliques" planes as they are at arbitrary angles with respect to the scanner. There are three main planes in which the images are reported: short axis, horizontal long axis or four-chamber view, and vertical long axis or two-chamber view.

Cardiac function is evaluated using cine gradient-echo sequences called "bright blood sequences" used in conjunction with the segmented k-space acquisition. For evaluation of cardiac morphology, "black blood sequences" are also used, for which there are multiple options: half-Fourier, single-shot, fast spin-echo (SS-FSE) being the most common. Ventricular function can then be quantitatively assessed by reviewing the dynamic images. For example, chronic transmural ischemia will be demonstrated by a decrease in the myocardial thickness to less than 6 mm and will also exhibit a lack of wall thickening during systole. Additionally, myocardial tagging is used to track segmental motion and helps to distinguish compromised myocardium from myocardium that may move irregularly because of its proximity to an affected area. However, a more reliable indicator of acute myocardial infarction is delayed contrast enhancement after the administration of IV gadolinium, which demonstrates a good correlation between healthy and infarcted myocardium. In infarcted cells, the gadolinium is retained after a period of washout of other regions (about 5–10 min), resulting in delayed hyperenhancement. This is particularly useful as a greater extent of transmural infarction can predict areas that are unlikely to improve after revascularization.

Complications

1. Ferromagnetic items can possibly be dangerous projectiles in the scanner room and can injury patients and staff
2. Heating of wires of pacemakers and defibrillators resulting in serious burns.
3. Nephrogenic sclerosing fibrosis in patients administered gadolinium that has a reduced GFR.
4. Claustrophobia

Clinical Vignettes

Case 1

Sixty-seven-year-old male with a history of hypertension, diabetes type 2, and chronic obstructive pulmonary disease presented to the hospital with exertional chest pain, cough, hypoxemia, and elevated troponins. As part of his evaluation, he underwent cardiac catheterization, which was non-revealing. A 2D non-contrast echocardiogram demonstrated a normal EF without wall motion abnormalities. Given nondiagnostic work-up, CMR was performed, shown in Fig. 13.1.

The image shown demonstrates an end-diastolic myocardium measuring 18.5 mm at the septum, which was not previously seen on echocardiography, consistent with hypertrophic cardiomyopathy. The patient was found to have COPD exacerbation, and elevation of troponins was likely secondary to demand ischemia in the setting of hypertrophic cardiomyopathy, as they normalized once the infection was controlled. In this case, CMR allowed for the identification of LV hypertrophy in segments not well visualized well with other diagnostic modalities.

Case 2

A 53-year-old man presented to the emergency department following a 45 min episode of chest pain. His ECG revealed deep T wave inversions in the anterior leads, but his symptoms had resolved. Echocardiography revealed anterior akinesis and an LVEF of 27%. He was referred for CMR with LGE to assess for myocardial viability.

Figure 13.2 demonstrates a large area of LGE in the anterior wall, but it is subendocardial, not transmural. Base on this study, with the impression that substantial viability was present, he was referred for cardiac catheterization and underwent PCI of a proximal LAD lesion (90%). Subsequently, an echocardiogram revealed

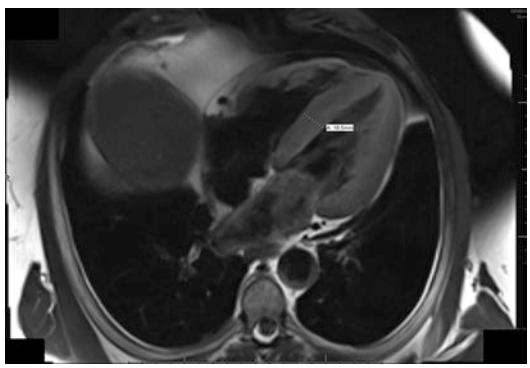

Fig. 13.1 Case #1 (see text for details)

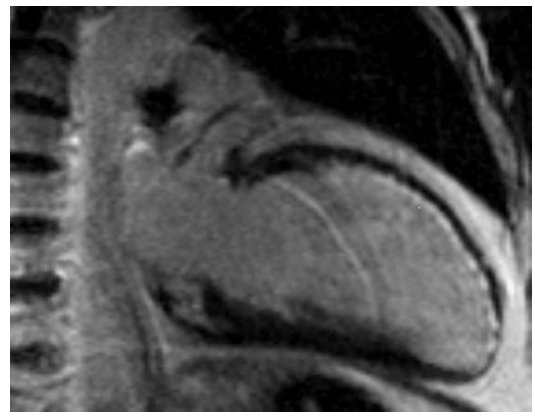

Fig. 13.2 Case #2 (see text for details)

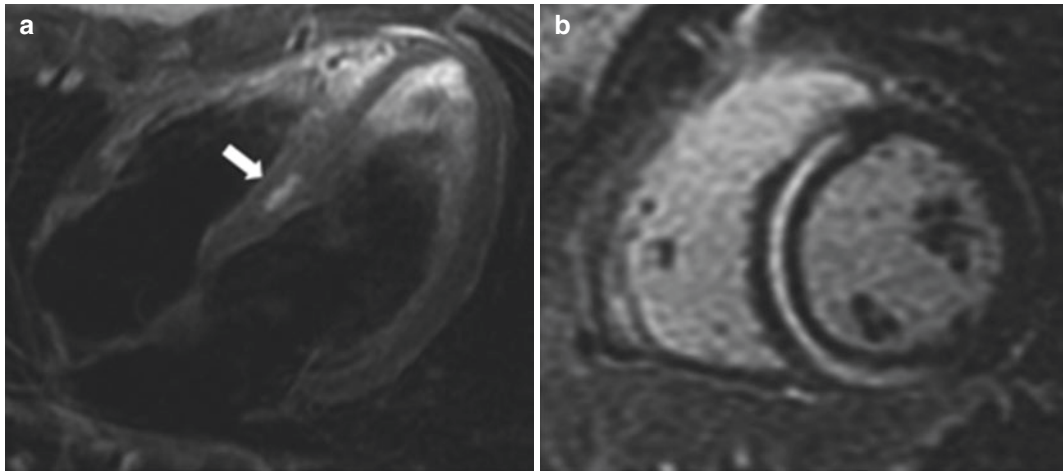

Fig. 13.3 Use of Cardiac Magnetic Resonance in the diagnosis of acute myocarditis. (**a**) Midseptal wall edema on T2 weighted images (*arrow*). (**b**) Prominent late gadolinium enhancement in the mid-wall of the intraventricular septum

marked improvement in anterior wall motion and an LVEF of 45%.

Case 3

A 31-year-old woman presented to her physician's office with severe shortness of breath. She had had an upper respiratory infection approximately 10 days ago, with rhinorrhea and cough, but her symptoms had almost entirely resolved until 1 day before the presentation. She has no pre-existing medical conditions. A chest x-ray was compatible with pulmonary edema, and an echocardiogram revealed severe left ventricular dysfunction. CMR was performed (Fig. 13.3).

These images show mid-septal wall edema on the T2 weighted images (Panel a) and prominent late gadolinium enhancement in the mid-wall of the intraventricular septum (Panel b), consistent with acute myocarditis. After an initially labile hospital course, the patient demonstrated marked clinical improvement over the next week but did have some residual LV dysfunction on discharge.

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Part II

Critical Care

Central Venous Cannulation

14

Saleh Alshalash and Carey Kimmelstiel

Introduction

Central venous cannulation is an essential skill for all cardiovascular specialists and provides a safe and secure route for the administration of parenteral agents. Often performed in an emergent fashion, when intravenous access is required for delivery of potentially life-saving medications, this technique may also be used when limited peripheral options are available.

Indications

Central venous cannulation is required in a variety of clinical scenarios. Current critical care units utilize central venous lines for inotropic and vasopressor medications that require infusion via a central venous catheter. In addition, central access allows for insertion of multi-lumen catheters that can accommodate the infusion of non-compatible medications using a single access point. While peripheral intravenous lines remain the preferred method for large volume resuscitation, central lines are commonly used for this purpose. Hyperalimentation, temporary pacemaker implantation, right heart catheterization for invasive hemodynamic monitoring and right ventricular (RV) biopsy also require central venous access (Table 14.1).

Contraindications

Bleeding is a relative contraindication and benefits should be weighed against risks. Active infection and deep venous thrombosis (DVT) at the site of cannulation are contraindications and if present, a different site should be used. For internal jugular (IJ) and subclavian (SC) venous access, contralateral pneumothorax or high pressure ventilator settings should prompt consideration of an alternative site (Table 14.1).

Equipment

Central venous cannulation requires a sterile field. Methodological full-body draping reduces the incidence of central venous line infections. Local anesthetic, an ultrasound machine with a sterile cover, central line access kit (which includes an 18-gauge needle, syringes, guide wire, scalpel, dilator, and central line—single or multi-lumen), sterile saline flushes, suture, and a dressing are needed to complete the procedure.

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The usual length of central venous catheters is 12–20 cm.

Technique

The site of access should be chosen carefully. The IJ, SC, and femoral veins are among the most widely accessed sites. Peripherally inserted central catheters (PICC) are also an option, particularly when the catheter is needed for a longer period of time (>1 week). Inspection of the site and using ultrasound to identify the target vessel prior to setting up a sterile field increases the odds of a successful procedure and obviates the need to change the site because of anatomical anomalies or DVT. Once the site is identified, meticulous antiseptic technique must be followed while preparing a sterile field and the access site. The use of ultrasound has become the standard of care in accessing the IJ vein as it has been shown to reduce the incidence of carotid puncture, neck hematoma, hemothorax, pneumothorax, number of attempts, access time, and catheter related blood stream infection [1]. The vein is identified using ultrasound; it is compressible and has continuous flow compared to the pulsatile and not-easily compressible artery (Fig. 14.1).

Solely using anatomic landmarks to achieve IJ access, is discouraged as it is associated with a

Table 14.1 Indications for central venous cannulation

Indications	
Infusion of vasoactive medications	Inadequate peripheral access
Right heart catheterization	Administration of medications known to cause phlebitis
Placement of pacing leads	Plasmapheresis
Monitoring of central venous pressure	Hemodialysis
Right ventricular biopsy	
Relative contraindications	
Bleeding diathesis	Active infection at the access site
Deep vein thrombosis	Known distorted anatomy (due to radiation or prior surgery)
Contralateral pneumothorax (for IJ and SC central lines)	High pressure ventilation

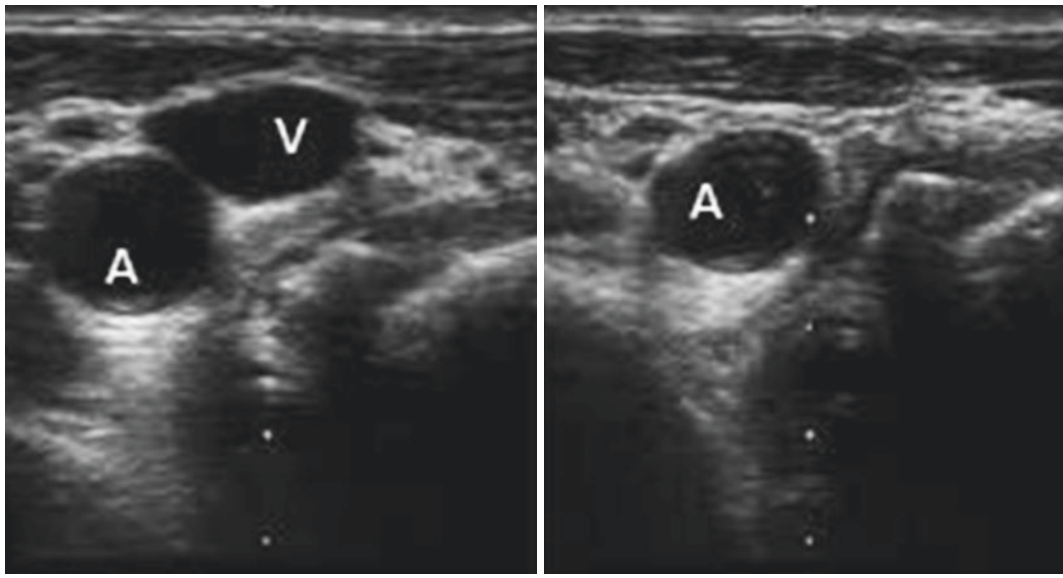

Fig. 14.1 The carotid artery (A) and the right internal jugular vein (V) are seen (*left image*) and after compression, the vein is no longer visible (*right image*)

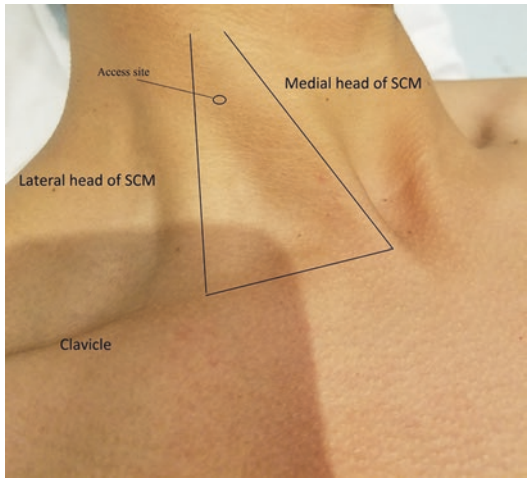

Fig. 14.2 Surface anatomy and landmarks for right IJ access. The apex of the triangle formed by the two heads of the SCM and the clavicle is accessed with the needle pointing towards the ipsilateral nipple (*SCM* sternocleidomastoid muscle)

higher rate of complications [2]. If this approach is ultimately utilized, the patient is placed in a supine or Trendelenburg position, the apex of the triangle formed by the two heads of the sternocleidomastoid and the clavicle is infiltrated with local anesthetic with the needle directed towards the ipsilateral nipple (Fig. 14.2). The use of a 22-gauge "finder" needle to cannulate the vein is sometimes performed to "map the way" for the 18-gauge needle.

For SC vein access, the needle is inserted at the point where the medial third of the clavicle meets the middle third (just medial to the midclavicular line) and the needle is inserted using a shallow angle underneath the clavicle with the needle pointing towards the suprasternal notch. The vein is cannulated underneath the clavicle. It is important to position the patient in a Trendelenburg position to distend the SC vein and increase the odds of venous cannulation. Some operators prefer placing a pillow or rolled-up towel under the patient, between their shoulder blades. In patients with coagulopathy the SC vein should, in general, not be used as it is non-compressible. Aspiration of bright red pulsatile blood indicates arterial puncture and the needle should be withdrawn and pressure is applied. Aspiration of air bubbles may indicate a pneumothorax. The SC vein is associated with less risk of catheter related systemic infection compared to femoral and IJ routes, but a higher risk of pneumothorax [3].

The femoral vein is accessed 1 cm below the inguinal ligament approximately 1 cm medial to the femoral artery. Central venous cannulation using the femoral vein can be done rapidly in unstable patients or during CPR, however, it may be associated with higher rates of catheter-related blood stream infections.

Once the vein being utilized is accessed with the 18-gauge needle, the guide wire is inserted and the dilator is passed over the wire to expand the puncture site to accommodate the catheter. The catheter is inserted over the wire, then aspirated, flushed, and sutured into place. When the IJ or SC veins are used, the tip of the catheter should be in the superior vena cava which is confirmed by a subsequent chest x-ray.

Data Interpretation

The size of the IJ vein when visualized with ultrasound and the respirophasic variation reflects the volume status of the patient as it is commonly a reflection of central venous pressure, except in situations where there is an obstruction caused by DVT, stenosis, or in the presence of moderate to severe tricuspid regurgitation. Once the vein is cannulated and the sheath is introduced, the central venous pressure can be directly measured using a standard fluid-filled transducer. If the operator is uncertain as to whether the vein or artery was cannulated, verification should be made prior to introducing a dilator into the vessel. There are many ways to verify that the vein was cannulated. A widely used method is observing the blood return, which is dark and has continuous flow in the central veins compared to bright red and pulsatile flow in the artery. When uncertainty exists, an oxygen saturation can be performed with a point of care device to assess whether the needle resides within the venous or arterial system. If an oxygen saturation is not immediately avail-

able, fluoroscopy can be utilized, following the course of the guidewire, with skilled operators able to discern the typical course of venous or arterial anatomy. An alternative method involves the infusion of a small amount of contrast which can discriminate between the pulsatile artery from the non-pulsatile vein. In the absence of fluoroscopy, the wire can be visualized in the long and short axes using ultrasound. If the operator is still uncertain that the needle is in a central vein, injection of small amount of agitated saline visualizing the trajectory of the fluid flow will help to confirm the position of the needle. Alternatively, a phased array probe can be used to visualize the agitated saline within the right sided cardiac chambers.

After central venous catheter placement, in the IJ or SC vein, an upright chest x-ray should be obtained to confirm the position of the central line and to exclude the presence of pneumothorax or hemothorax. Figure 14.3 depicts the course and position of a pulmonary artery (PA) catheter. Venous anomalies, such as persistent left superior vena cava (PLSVC) that drains into the coronary sinus, may present a confusing radiographic image when left sided venous access is used (Fig. 14.4) [4]. For central lines the chest x-ray is also helpful in confirming the distal tip of the catheter which should be above the cavo-atrial junction to avoid precipitating atrial arrhythmias and pos-

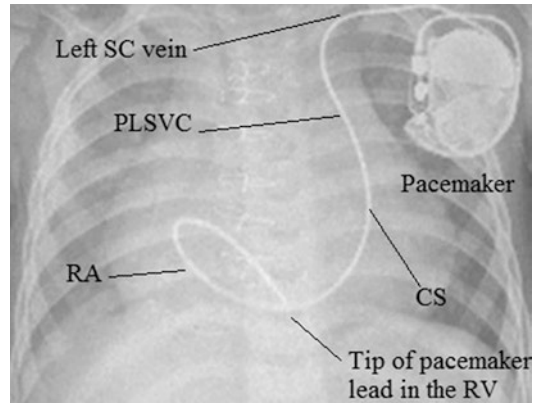

Fig. 14.4 Chest x-ray showing a left sided pacemaker that was implanted in a child with persistent left superior vena cava (*PLSVC*) draining into the coronary sinus (*CS*). The course of the venous drainage is delineated by the pacemaker lead (left SC vein which joins left IJ vein and become left SVC that drains into the coronary sinus which drains into the RA)

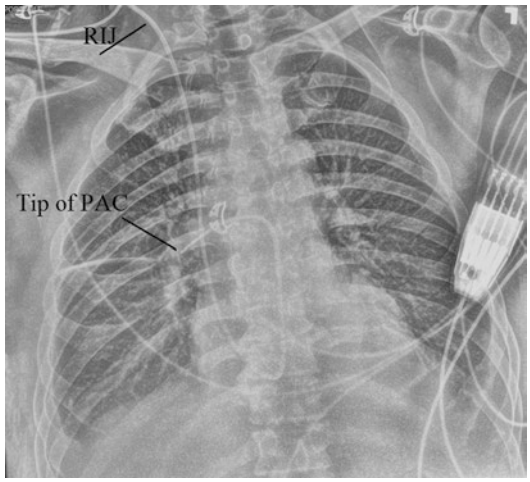

Fig. 14.3 Chest x-ray showing a pulmonary artery catheter (*PAC*) after insertion from the right IJ (*RIJ*) into the right pulmonary artery

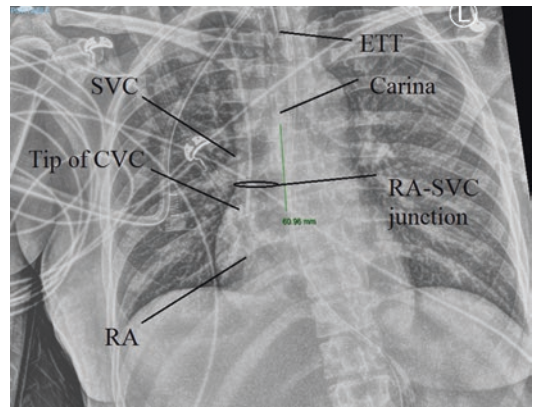

Fig. 14.5 Chest x-ray showing a central venous catheter (*CVC*) inserted into the right IJ passing through the superior vena cava (*SVC*) into the right atrium (*RA*). The tip of the CVC is seen approximately 1 cm below the RA-SVC junction

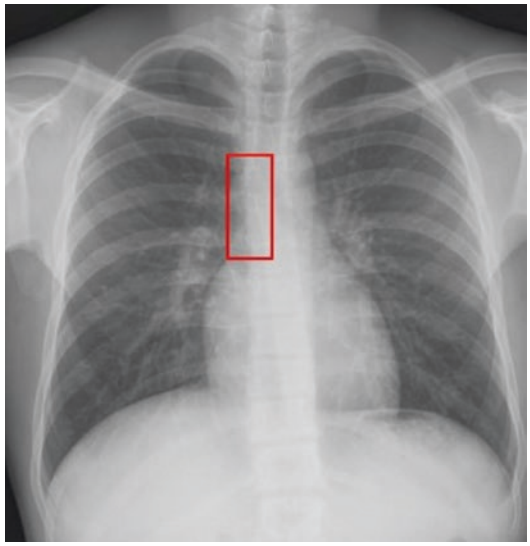

Fig. 14.6 Upright chest x-ray showing the desired position where the tip of the central line can be positioned (*rectangle*). Lower positions risk the possibility of atrial arrhythmias

sible trauma to the right atrium (RA) (Fig. 14.5). The correct position of the tip of the catheter should be in the superior vena cava (SVC) just proximal to the right atrium RA-SVC junction (Figs. 14.5 and 14.6).

Complications

Arterial cannulation, venous dissection, hematoma, catheter associated DVT or infection, pneumothorax, hemothorax, and atrial or ventricular arrhythmias especially during wire insertion are among the most common complications. Constant visualization of the needle tip, confirmation of the needle position after vessel cannulation, and meticulous sterile technique will aid in minimizing complications. Operators should be mindful of the distance between the skin and the anterior wall of the vein and expect blood return after the needle traverses that distance. If blood return is not seen, the operator should pause and identify the needle tip as it is not uncommon for the needle to compress the vein and travel through the posterior wall without blood return. In this instance, slow withdrawal of the needle should result in venous cannulation. Of note, access of left IJ or left SC vein carries a risk of chylothorax.

Clinical Vignettes

Case 1

A 50-year old male with history of DVT and pulmonary embolism, moderate tricuspid regurgitation, pulmonary hypertension, diabetes, hypertension and ischemic cardiomyopathy, presented with dyspnea, a productive cough, leukocytosis, and bilateral infiltrates on chest x-ray. Physical examination reveals heart rate of 115 beats per minute, regular pulse and a blood pressure of 85/50 mmHg. Auscultation of the chest reveals bilateral rhonchi, soft S1, normal S2, and an S4. Extremities are cool and bilateral lower limb swelling is noted. Right heart catheterization is planned to assess filling pressures, calculate cardiac output, and provide central venous access to infuse vasoactive medications.

In situations where the filling pressures are likely to help clinicians resuscitate patients with sepsis and heart failure, the insertion of a pulmonary artery (PA) catheter may be of value. The right IJ provides a direct access point for PA catheter insertion. This can be achieved with a 5–7 French sheath that can accommodate the PA catheter. Once the PA catheter is positioned correctly, vasoactive medications can be given via the lumens of the catheter.

Case 2

A 30-year-old male with acute myeloid leukemia presented with fever and fatigue. Physical examination documented a heart rate of 125 beats per minute, BP 90/60 mmHg, with labs revealing pancytopenia with a profound reduction in the absolute neutrophil and platelet counts and an INR of 1.8. A central line was required for infusion of antibiotics and vasoactive medications and for measurement of CVP.

The risk of bleeding is considerable, therefore, the SC vein should be avoided. Correction of coagulopathy with platelet transfusion prior to the procedure, if feasible, may reduce the risk of bleeding.

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Right Heart Catheterization

15

Youssef Rahban and Carey Kimmelstiel

Introduction

Right heart catheterization is an invasive cardiac procedure that allows accurate measurement of cardiac and pulmonary pressures and calculation of vascular resistance and cardiac output (CO). This is done by inserting a pulmonary artery catheter (PAC), also called Swan-Ganz catheter, into the pulmonary artery in the intensive care unit, cardiac catheterization laboratory or operating room. Although previous studies and trials failed to demonstrate improved outcomes with the use of PAC in high risk surgery, general ICU and heart failure patients, these studies mostly excluded cardiogenic shock patients [1–3]. More recently a large, multicenter cardiogenic shock registry showed that complete hemodynamic assessment using PAC is associated with lower in-hospital mortality compared with incomplete or no assessment [4].

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Indications

In general, there are two main clinical uses for a PAC, either diagnostic, or, to guide therapeutic interventions whether these are pharmacological or mechanical.

From diagnostic standpoint, a PAC is often essential in differentiating the cause of shock when this is not clinically discernible, particularly in patients with a mixed clinical picture. Other diagnostic uses include differentiating constrictive versus restrictive cardiomyopathy, profiling various types of pulmonary hypertension, confirming pericardial tamponade physiology and the evaluation of intracardiac shunts, valvular heart disease or unexplained dyspnea.

From therapeutic standpoint, a PAC can help guide fluid management in addition to titration of inotropes, vasodilators and vasopressors in various clinical situations such as complicated myocardial infarction, cardiac and vascular surgeries, severe pulmonary arterial hypertension, decompensated heart failure or cardiogenic shock. Hemodynamic data obtained from a PAC is often essential in selecting the appropriate mechanical support therapy in patient with cardiogenic shock and screening patients awaiting advanced heart failure therapies such as heart transplantation or left ventricular assist devices.

A consensus statement containing specific recommendations on the use of RHC in various cardiovascular disease states was published by

R. C. Hendel, C. Kimmelstiel (eds.), *Cardiology Procedures*,
https://doi.org/10.1007/978-3-030-95259-4_15

Table 15.1 Indications for right heart catheterization

Differentiation of profound hypotensive states (e.g., cardiogenic shock vs. septic shock vs. hypovolemic shock)
Guidance of therapy in severe left ventricular dysfunction—"hemodynamic tailored therapy"
Assessment of constrictive and restrictive physiology
Cardiac tamponade
Assessment of impaired oxygenation—cardiogenic vs. non-cardiogenic pulmonary edema
Evaluation of pulmonary hypertension
Management of high-risk cardiac patients undergoing non-cardiac procedure or surgery
Assessment of intra-cardiac shunts
Management of complicated myocardial infarction (e.g., cardiogenic shock, mechanical complications)
Management of patients following cardiac surgery
Heart failure with reduced or preserved ejection fraction (diagnosis and management)
Assessment of candidacy for heart transplantation
Left ventricular assist device dysfunction
Acute pulmonary embolism
Assessment of volume status in renal or hepatic failure
Post operative monitoring after cardiac surgery

the American College of Cardiology in 1998. Table 15.1 summarizes some of the commonly accepted indications [5].

Contraindications

The presence of a mechanical prosthetic valve in the tricuspid or pulmonic position, an infection at the insertion site or large saddle pulmonary embolism or clot in transit are generally considered absolute contraindications for RHC. Relative contraindications include coagulopathy or thrombocytopenia (INR > 1.7 or platelet count <50,000), severe electrolyte disturbances, latex allergy (use of non-latex catheters is recommended) and right atrial or ventricular masses The ability to temporary pace the patient with a preexisting left bundle branch block should be available during RHC as flotation of the pulmonary artery (PA) catheter through the right ventricle can induce complete heart block in up to 3% of these patients [6]. Patients with intracardiac devices, such as pacemakers or implantable cardiac defibrillators or a persistent left superior vena cava should have RHC performed under fluoroscopy to avoid the catheter tip getting caught in or dislodging a device lead or misplacing the catheter in the coronary sinus. The presence of severe tricuspid regurgitation, right ventricular dilatation, and pulmonary hypertension might also necessitate the use of fluoroscopic guidance.

Equipment

The Swan Ganz PA catheter is the most widely used catheter for RHC. The balloon tip allows the catheter to follow the flow of venous blood through the right side of the heart to the PA. The catheter has multiple lumens that are accessed by various ports, including a proximal port, a distal port, and a balloon inflation port. These ports allow for the measurement of pressures as well as the sampling of blood oxygen saturation along the right side of the heart and the PA (Fig. 15.1). A thermistor mounted to the distal tip of the catheter allows for temperature measurements [7].

Technique

RHC can be performed via the superior vena cava with percutaneous entry through the internal jugular (IJ) subclavian or basilic veins, or via the inferior vena cava with percutaneous entry through the femoral veins. IJ or subclavian approaches are less susceptible to infection and are less restraining to the patient and thus are preferred for bedside management. When placed at the bed side, the right internal jugular approach is preferred over left as it provides a direct route to the right atrium (RA). The subclavian approach is preferred via the left side, again due to ease of catheter flotation [7].

Central venous access is obtained as described in the previous chapter. Prior to flotation, the system should be appropriately leveled and zeroed. Usually attached to a manifold, the transducer is placed at the level of the mid-axillary line in the fourth intercostal space (also known as the phlebostatic axis which approximates the level of the left atrium) and zeroed by opening the system to room air. It is advisable to use a measuring stick or laser/bubble level to accurately place the

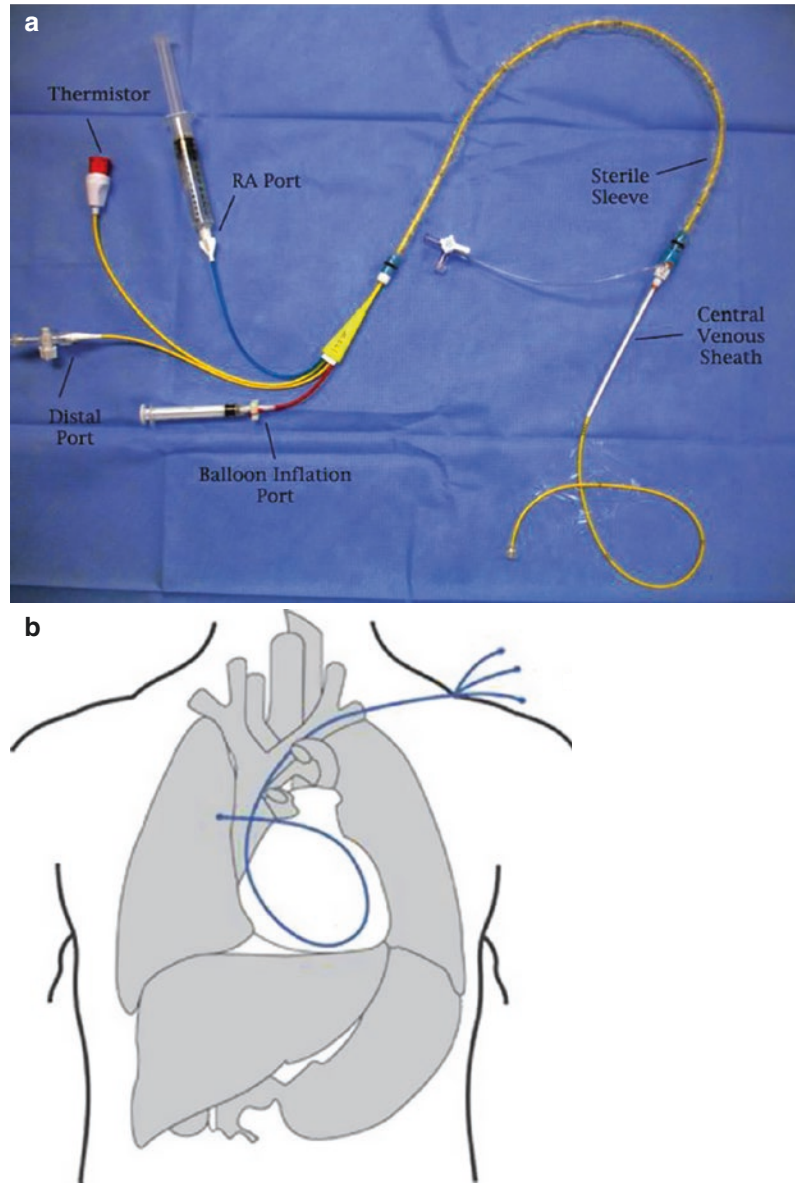

Fig. 15.1 (**a**) The pulmonary artery catheter. (**b**) A schematic showing the proper orientation of the pulmonary artery catheter when inserted through the left subclavian vein

transducer at the midthoracic level. Each port of the PA catheter is then carefully flushed and full inflation of the balloon is confirmed. An air leak should be excluded by dipping the balloon in a sterile bowl of saline. If the PA catheter is to be left in place, it should first be inserted through a protective sterile sleeve. The PA catheter is then inserted through the central venous sheath to approximately 15 cm or until the RA waveforms are observed. The balloon is inflated and advanced gently. Fluoroscopy is used in the catheterization lab to direct placement; however, at the bedside, guidance is provided via the pressure waveforms (Fig. 15.2). Flotation of the PA catheter from the femoral vein is more difficult and usually requires fluoroscopic guidance [6, 8].

To minimize ventricular ectopy, the catheter should be passed rapidly through the right ventricle (RV) into the PA. From the PA the catheter is then advanced slowly to wedge position. In general, the PCWP tracing should be reached within 50–55 cm if the catheter is placed via the internal jugular or subclavian approaches. If the femoral approach is used, it should be reached at

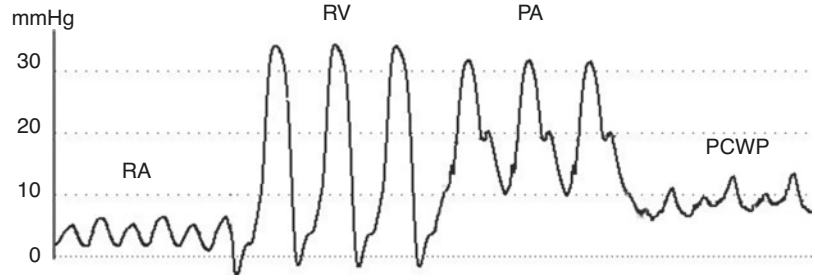

Fig. 15.2 Normal right heart pressure tracings. *RA* right atrium, *RV* right ventricle, *PA* pulmonary artery, *PCWP* pulmonary artery wedge pressure

65–70 cm. In cases of marked respiratory variation, the PCWP should be measured at end expiration. Ideally, when measuring the PCWP, the tip of the catheter should be positioned in the lower lobe where vascular pressure exceeds alveolar pressure to avoid overestimation. Once PCWP is recorded the balloon should be deflated and it should be verified that a clear PA tracing is obtained. The volume of air required to inflate the balloon for obtaining wedge should also be checked. If the volume is less than 1.5 cc, the catheter should be pulled back to avoid "overwedging". Screening blood samples are usually drawn for oximetric analysis from the RA and the PA to evaluate for the presence of intra-cardiac shunts. Oximetric analysis can also be performed to confirm accurate wedge position by obtaining a blood sample with a saturation of ≥95% [6, 8].

The PA catheter can determine CO by two techniques—the thermodilution technique and using the Fick principle to measure oxygen consumption (VO_2). In performing the thermodilution technique, a syringe with 10 cc saline is attached to the proximal port, whose tip is in the RA when the thermistor on the distal tip is in the PA. The entire volume of saline is rapidly injected in a single, smooth effort. The change in temperature as recorded by the distal thermistor is plotted over time and the area under the curve is planimetered to calculate CO (in liters/min). At least three serial thermodilution measurements should be performed and averaged (more if there is substantial variability). Although the TD method is often thought to be less reliable in the setting of tricuspid regurgitation and extremes of CO, studies have shown good correlation with TD and Fick in these situations [9, 10]. With the exception of the presence of a cardiac shunt, the TD is considered by many as the preferred method of measuring CO when a direct Fick is not available.

The direct Fick method, which requires specialized metabolic hood to properly measure oxygen consumption, is considered the "gold standard" for estimating CO. However, this technique is generally not feasible in most catheterization laboratories and is therefore commonly substituted by the indirect Fick method that uses estimated values for oxygen uptake originally derived from the TD method in patient populations that were highly selected. The Fick principle states that the total uptake or release of a substance by an organ is the product of blood flow to the organ and the arteriovenous (AVO_2) concentration difference of the substance [8]. Pulmonary blood flow (which is equal to systemic blood flow in the absence of a significant shunt) is determined by dividing oxygen consumption by the arteriovenous oxygen difference across the lungs. Oxygen consumption can be estimated by three different formulas and is based on body surface area. The AVO_2 concentration difference is calculated from the difference in arterial oxygen content

$$\left(CaO_2\right)\left(1.36\times\text{hemoglobin}\times AO_2\ \text{saturation}\times 10\right)\text{minus the mixed venous}\left(PA\right)$$
$$\text{oxygen content}\left(CvO_2\right)\left(1.36\times\text{hemoglobin}\times VO_2\ \text{saturation}\times 10\right).$$

where 1.36 reflect the amount of oxygen bound to 1g of hemoglobin. When using indirect Fick, Oxygen consumption or VO_2 is estimated as 125 ml O_2/m^2 multiplied by body surface area (BSA).

Thus CO in L/min can then be calculated:

$$CO = VO_2 / \left(CaO_2 - CvO_2\right) = 125\,\text{mL}\,O_2 / \text{m}^2 \times \text{BSA} / \left(1.36 \times \text{hemoglobin} \times \text{arterial}\,O_2\,\text{saturation} \times 10\right) - \left(1.36 \times \text{hemoglobin} \times \text{venous}\,O_2\,\text{saturation} \times 10\right)$$

Dividing the cardiac output in L/min by body surface area (m^2) allows the calculation of cardiac index (CI) in L/min/m^2.

After the measurement of pressures and determination of CO have been completed, the pulmonary and systemic vascular resistance can be calculated using the following formulas:

Systemic vascular resistance (SVR) in Woods Units = MAP–RAP/CO. For conversion to dynes·sec·cm-5, multiply by 80

Pulmonary vascular resistance (PVR) in Woods Units = MPAP–PCWP/CO. For conversion to dynes·sec·cm-5, multiply by 80.

Where MPAP = mean pulmonary artery pressure (mmHg), PCWP = Pulmonary capillary wedge pressure (mmHg), CO = cardiac output (L/min), MAP = mean arterial pressure (mmHg), and RAP = right atrial pressure (mmHg).

Data Interpretation

For accurate interpretation of cardiac and pulmonary pressure waveforms, an electrocardiographic and respirometer tracing should always be present to help identify the corresponding cardiac cycle and respiratory phase.

RA Pressure

The normal RA pressure ranges between 1 and 5 mmHg and under normal conditions decreases with inspiration. The *a wave* reflects atrial contraction and occurs just after the P wave on the surface ECG. Elevations in the *a wave* indicate resistance to RV filling, as can be seen in RV failure/infarction, pulmonic stenosis, or significant pulmonary hypertension. In atrial fibrillation the *a wave* is absent due to the lack of organized atrial contraction. The *x descent* follows and is due to RA relaxation and caudal recoil of the tricuspid valve during RV contraction. The *c wave*, which interrupts the *x descent*, results from bulging of the closed tricuspid valve into the RA during early systole. The *v wave* results from venous inflow into the RA during RV systole. It is prominent in tricuspid regurgitation and in increased flow, such as seen with atrial septal defect. The *v wave* is followed by the *y descent* that reflects the opening of the tricuspid valve. Prominent *y descent* can be seen in constrictive and restrictive states as a result of rapid atrial emptying into the RV [11].

RV Pressure

The normal RV systolic pressure ranges between 15 and 30 mmHg and the RV end-diastolic pressure between 4 and 8 mmHg. The RV systolic pressure can be elevated by pulmonic valve disease or pulmonary hypertension. Abrupt elevation and plateau of the RV pressure in early diastole can indicate the presence of restrictive or constrictive physiology [6, 11].

PA Pressure

The normal PA systolic pressure is 15–30 mmHg and the PA end-diastolic pressure is 4–12 mmHg. Elevations in PA pressures are seen in pulmonary hypertension, left-sided heart failure, mitral valve disease, significant left to right shunt, and pulmonary disease (e.g., pulmonary embolism, chronic obstructive pulmonary disease) [11].

Table 15.2 Normal hemodynamic values

SVO_2 0.6–0.75
CO 4–8 L/min
CI 2.5–4.0 L/min/m^2
RA 1–6 mmHg
RV 25/6 mmHg
PAP 25/10 mmHg
PCWP 8–12 mmHg
SVR 900–1300 dynes-s-cm^{-5}
PVR 40–150 dynes-s-cm^{-5}
MAP 70–110 mmHg

PCWP

The normal mean PCWP is between 4 and 12 mmHg. The PCWP is an accurate measure of the left atrial (LA) pressure in the absence of pulmonary vascular disease. It approximates left ventricular filling pressures except in mitral stenosis and left atrial myxoma, where the LA pressure might be greater than left ventricular end-diastolic pressure (LVEDP). In acute aortic regurgitation, the LVEDP can be higher than the LA pressure. Elevation in mean PCWP is seen in left-sided heart failure, and mitral stenosis or regurgitation. Similar to the RA pressure, the PCWP has *a* and *v waves*, *x* and *y descents*. A prominent *v wave* suggests the presence of mitral regurgitation [11].

Normal hemodynamic values are summarized in Table 15.2.

Complications

Complications of RHC are rare, but can include pneumothorax/hemothorax, arterial puncture, bleeding, infection (including cellulitis at the insertion site, bacteremia, endocarditis and sepsis), venous thrombosis, arrhythmias (including ventricular arrhythmias and heart block/right bundle branch block), pulmonary artery rupture, cardiac perforation, air embolism, pulmonary infarction (if the balloon is left in wedge position too long), and knotting of the catheter. The duration of RHC should be minimized in order to avoid complications [6, 8].

Clinical Vignettes

Case 1

A 69-year-old woman with history of dilated cardiomyopathy is admitted with pulmonary vascular congestion. She is treated with lasix and nitrates. However, further diuresis results in a creatinine rise despite signs of persistent volume overload.

RHC is performed with a BP 88/42 (57) mmHg, RA 14 mmHg, RV 52/7 mmHg, PA 54/25 (39) mmHg, PCWP 26 mmHg CO 2.7 L/min, CI 1.9 L/min/m^2, and SVR 1275 dynes-s-cm^{-5}. The phosphodiesterase inhibitor milrinone is initiated along with further diuresis for treatment of decompensated heart failure.

Case 2

A 54-year-old man with history of ischemic cardiomyopathy and NYHA class III-IV heart failure is transferred to a tertiary care center for cardiac transplant evaluation. Echocardiography from the referring hospital showed diffuse global hypokenesis with an LVEF 15% and was suggestive of pulmonary hypertension with a PA systolic pressure estimated at ≥70 mmHg.

RHC reveals RA 15 mmHg, RV 76/16 mmHg, PA 75/27 (45) mmHg, PCWP 21, CO 3.4 L/min, CI 1.8 L/min/m^2, and PVR 456 dynes-s-cm^{-5} (5.7 wood units). To assess reversibility of pulmonary hypertension and appropriateness of cardiac transplantation, an infusion of nitroprusside is initiated in the cath lab and titrated gradually to 3.0 mcg/kg/min. Hemodynamic assessment is repeated with RA 12 mmHg, RV 62/12 mmHg, PA 60/19 (34) mmHg, PCWP 18 mmHg, CO 5.2 L/min, CI 2.9 L/min/m^2, and PVR 176 dynes-s-cm^{-5} (2.2 wood units). Nitroprusside infusion demonstrates reversible pulmonary hypertension in this patient. Irreversible pulmonary hypertension (>4 wood units) remains an exclusion criteria for cardiac transplant as a normal donor RV will fail in the setting of high recipient PVR.

Case 3

A 75-year-old woman with history of diabetes and hypertension presents to the emergency department more than 10 h after onset of substernal chest pain. ECG reveals ST elevation and q waves in leads II, III, aVF suggestive of an evolving inferior myocardial infarction. Physical exam reveals a harsh holosystolic murmur along the left sternal border. During cardiac catheterization the patient became hypotensive requiring multiple pressors and insertion of an intra-aortic balloon pump. Cardiac catheterization reveals 100% proximal right coronary artery occlusion. Successful percutaneous angioplasty and stent placement of the right coronary artery is performed.

After stent placement, RHC reveals RA 20 mmHg RV 43/21 mmHg PA 45/28 (37) mmHg PCWP 28 mmHg. Oximetric analysis revealed a large step-up in oxygen saturation from RA (47%) to RV (81%) suggestive of ventricular septal rupture. Transesophageal echocardiogram in the cath lab confirms rupture of the basal portion of the inferoposterior ventricular septum with left to right shunt flow. The patient is referred to cardiothoracic surgery.

Case 4

A 73-year-old man with history of hypertension, chronic obstructive pulmonary disease, and atrial fibrillation is admitted for worsening shortness of breath and lower extremity edema. This is his third admission in 6 months for heart failure. Physical exam reveals elevated jugular venous pressure to the mandible, positive Kussmaul's sign (elevation of the jugular venous pressure with inspiration), and 2+ pitting lower extremity edema to the knees. Echocardiogram reveals left ventricular hypertrophy with mild aortic stenosis, normal left ventricular function and a small circumferential pericardial effusion.

RHC is performed with the following hemodynamic findings: RA 18 mmHg, RV 39/5 (18) mmHg, PA 37/18 mmHg, PCWP 18 mmHg, and LVEDP 18 mmHg. Simultaneous recording of right and left heart pressures show elevation and equalization of diastolic pressures and the RV and LV pressure tracings reveal a dip and plateau contour suggestive of constrictive physiology (Fig. 15.3). Subsequent CT of the chest demonstrates a thickened pericardium.

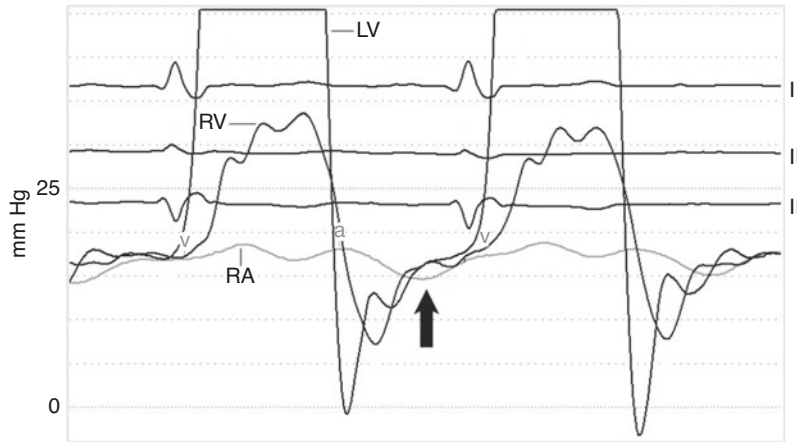

Fig. 15.3 Simultaneous right and left heart pressure tracing in a patient with constrictive pericardial physiology. Note the right atrial, right ventricular, and left ventricular diastolic pressures are elevated and equal (*arrow*). Right and left ventricular tracings show an early diastolic dip followed by a plateau as the non-compliant pericardium hinders ventricular filling in early to mid diastole—the "dip and plateau" sign. *RA* right atrium, *RV* right ventricle, *LV* left ventricle

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Pericardiocentesis

16

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Introduction

Evacuation of pericardial fluid from the pericardial space to treat cardiac tamponade was initially described in 1653 through surgical incision of the sternum [1]. Advancements in the technique were made with percutaneous needle aspiration in the nineteenth century and, currently, the procedure is done in a similar manner using small gauge needles and multimodality imaging (echocardiography, fluoroscopy, or both). Cardiac tamponade is a clinical diagnosis and the size of the pericardial effusion required to cause tamponade depends on the rate of fluid accumulation.

Indications

1. Treatment of cardiac tamponade or prevention of impending cardiac tamponade in patients with moderate to large pericardial effusions and compromised hemodynamics.
2. Diagnostic aspiration to investigate the etiology of a pericardial effusion.
3. Invasive procedures in the pericardial space (epicardial ventricular tachycardia [VT] ablation or left atrial appendage [LAA] closure using the Lariat device)

Contraindications

In a hemodynamically unstable patient there exist no absolute contraindications to pericardiocentesis. Uncorrected bleeding conditions is a relative contraindication to pericardiocentesis. Recurrent pericardial effusion may need surgical treatment with the creation of a pericardial window (communication between the pericardial and pleural spaces).

Equipment

Required equipment includes anti-septic solution, sterile drapes, gown and gloves, local anesthetic, a long small-caliber needle, syringes, alligator clip, guide wire, scalpel, stopcock, pigtail catheter, collection bag, ECG machine, and imaging modality of choice (echocardiography and/or fluoroscopy). Commercially available kits often include all of the needed equipment (Fig. 16.1).

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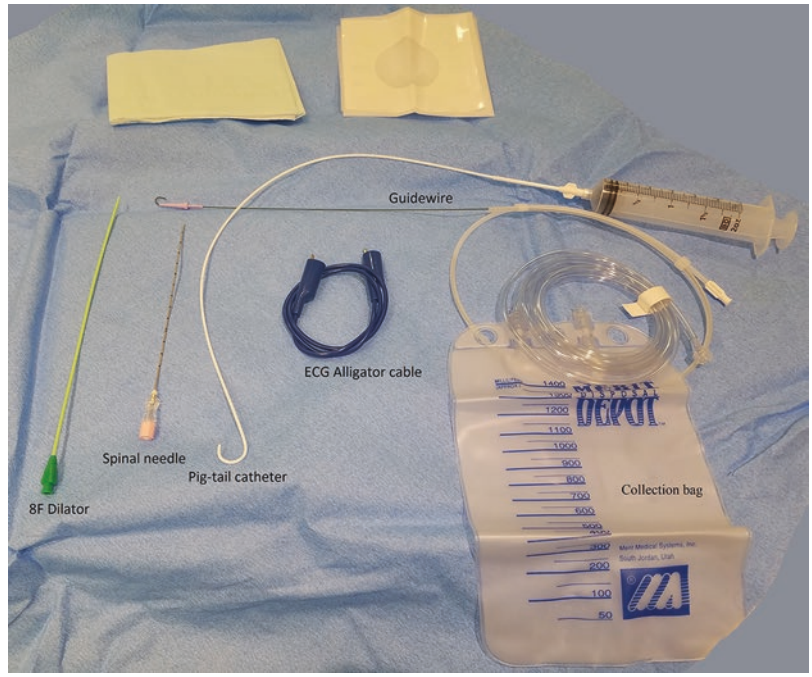

Fig. 16.1 Essential equipment for pericardiocentesis

Technique

There are three established methods to perform pericardiocentesis (Table 16.1). The most widely used is via a subxiphoid approach; other approaches include the apical and left parasternal approaches. The echocardiographic window helps in deciding which approach is most expeditious. Careful examination of the echocardiogram to "map the way" and choose which angle is needed prior to proceeding with pericardiocentesis, is an essential step.

To perform a pericardiocentesis from the subxiphoid approach, the patient is placed in a supine position usually lying on a wedge which elevates the torso to an angle of 30–45° which aids in accumulating the pericardial fluid anteriorly (Fig. 16.2). A sterile field is established. The skin and subcutaneous tissues are infiltrated generously with a local anesthetic. The needle is inserted at a shallow angle just to the left of the xiphoid process immediately inferior to the costal margin (Fig. 16.3). The needle is advanced underneath the ribs, bevel up, while consciously making light contact with the overlying perios-

Table 16.1 Summary of different approaches to pericardiocentesis

Approach	Advantages	Disadvantages
Subxiphoid	Can be done blindly without imaging in cases of emergency. Provides access to the anterior pericardial space. Furthest from pleural space	Possible injury to abdominal structures. Requires the presence of an anterior collection of fluid. Difficult in morbidly obese patients or patients with ascites
Apical	Provides access to the apical/posterior collection. LV wall is thicker than RV, therefore, injury may not result in perforation	Possible access to the pleural space, causing pneumothorax or injury to the LV apex (or LAD)
Left parasternal	Shortest distance from skin to pericardial space, access to the anterior pericardial space, avoids injury to abdominal structures	Possible injury to the internal mammary artery and entry into the pleural space

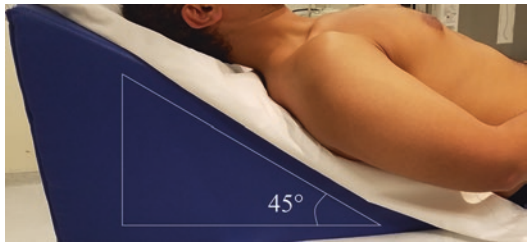

Fig. 16.2 A wedge is positioned underneath the patient to allow the free-flowing fluid to accumulate anteriorly

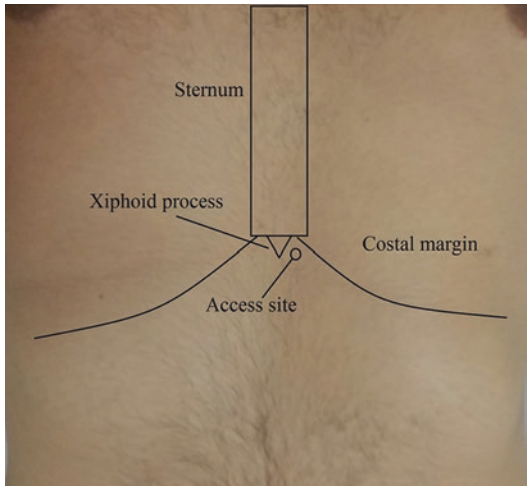

Fig. 16.3 Surface anatomy and landmarks to perform pericardiocentesis. Via the subxiphoid approach

teum of the rib. This is done in an effort to avoid contact with the lung. The needle is directed towards the left shoulder. A "pop" can usually be felt when the pericardium is entered. At this time the trochar is removed and, if in the correct location, pericardial fluid will flow under pressure through the central lumen of the syringe. If no fluid is obtained, the syringe is removed and the process is repeated, usually with a slightly different angulation.

Currently, pericardiocentesis is rarely done with live echocardiographic guidance. However, some operators employ electrocardiographic (ECG) guidance in an effort to avoid ventricular perforation. An alligator clip is connected to an ECG lead. While slowly advancing the needle, the ECG is monitored, watching for ST segment elevation (a current of injury) which is indicative of contact with the thin-walled right ventricle. If seen, obviously the needle is withdrawn, the trochar removed and examination for pericardial fluid flow from the needle lumen is performed. If the operator is using fluoroscopy, then a guidewire is advanced through the needle, into the pericardial space and is visualized into the pericardium. If the operator is not sure that the wire is in the pericardial space, injection of a small amount of contrast may help in defining the position of the needle tip [2]. Using echocardiography to confirm placement involves injecting agitated saline into the pericardial space once the needle enters the pericardium and before the guidewire is inserted into the pericardial space. The agitated saline can be visualized in the pericardial space confirming the position of the tip of the needle (Fig. 16.4). If agitated saline is seen in a cardiac chamber the needle should be withdrawn. After passing the guidewire into the pericardial space, a dilator is advanced over the wire to create a tunnel through the subcutaneous tissues for passage of a pigtail catheter over the guidewire. The guidewire is then removed from the pigtail catheter and a three-way stopcock is attached to the proximal end of the pigtail catheter.

Once the pigtail catheter has been placed, the opening pericardial pressure is recorded, fluid is then aspirated with usually 100 cc sent for laboratory analysis for cellular analysis and chemistries, usually for the determination of a transudate versus an exudate. Aspiration is performed until the operator is no longer able to withdraw any further fluid. At this time the total volume removed is recorded as is the closing pericardial pressure.

The left parasternal approach involves directing the needle almost perpendicularly to the chest (70–80°) often between the fifth and sixth ribs at least 2–3 cm lateral to the edge of the sternum to avoid injury to the internal mammary artery which runs 1–1.5 cm from the edge of the sternum (Fig. 16.5). Care must be taken to go over the rib to avoid injury to the neurovascular bundle which runs in the inferior aspect of the ribs. Echocardiography is used to assess the depth of

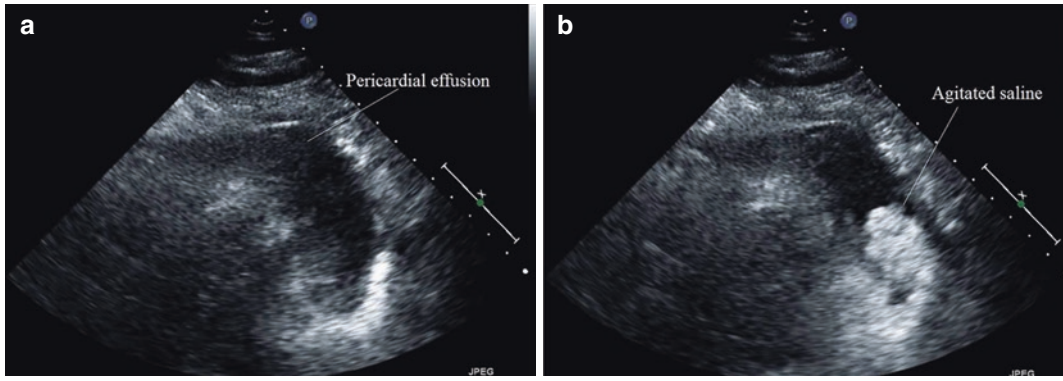

Fig. 16.4 (**a**) Modified apical view showing the pericardial effusion. (**b**) Agitated saline is seen entering into the pericardial space (*arrow*) confirming the correct position of the needle tip

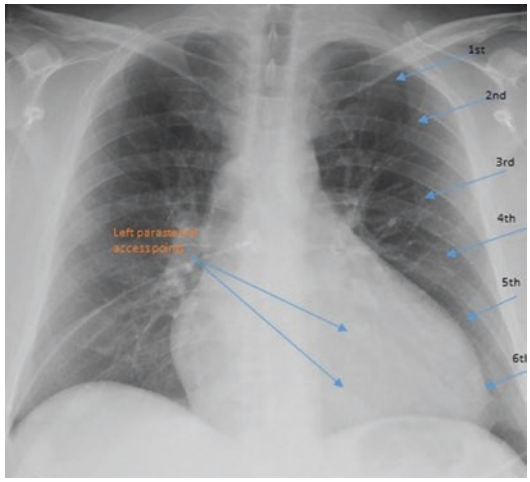

Fig. 16.5 Chest x-ray showing cardiomegaly. The anterior ribs are labeled on the CXR. Left parasternal access is in between the fourth–fifth or fifth–sixth ribs at ≥2 cm away from the edge of the sternum

pockets and to estimate the angle and depth of tissue to enter into the pericardial space.

For the apical approach, the mid-clavicular line is identified in the fifth intercostal space then echocardiographic images are obtained and the point that has the best echocardiographic window is marked. The operator should make note of the angle of the probe as the needle should follow the same angle. The best access point should be the deepest pocket of fluid as well as that closest to the chest wall.

Data Interpretation

Pericardial fluid is sent to the laboratory for fluid analysis; tests are dependent on clinical presentation. The most widely used tests include total protein, glucose, LDH, and culture and sensitivity. Etiology of the effusion can be aided by the determination of whether the aspirated fluid represents a transudate or exudate. Other tests include cytology when there is clinical suspicion of a malignant process and antibody testing (ANA) when the clinical presentation is in keeping with a rheumatological/autoimmune process.

Complications

Possible complications include myocardial injury and puncture or laceration, coronary artery perforation, pneumothorax, laceration of the left lobe of the liver, injury to the phrenic nerve, and inability to access the pericardium requiring a surgical window. The damage resulting from inadvertently injuring structures can be minimized using multi-modality imaging, choosing the access site that has the easiest access to the largest collection of fluid. For example, a posteriorly located pericardial effusion might not be accessible percutaneously even though it is large enough to cause hemodynamic effects. Some have advocated that another way to minimize

complications is to utilize a small caliber needle such as a micropuncture needle which is 21-gauge needle as compared to the standard 18-gauge needle. Using the 21-gauge micropuncture needle allows insertion of a 0.018-in. wire that is exchanged for a 4–5 Fr sheath that can accommodate the standard 0.035–0.038 in. guidewire.

Clinical Vignettes

Case 1 *A 45-year old female with stage IV breast cancer presented with progressive shortness of breath. Her physical examination was remarkable for a heart rate of 110, a blood pressure of 90/60 mmHg, oxygen saturation 99% on room air and a respiratory rate of 22/min. Her heart sounds were muffled and jugular venous distension was present. Lung auscultation was not remarkable. Chest x-ray revealed cardiomegaly and normal lung parenchyma. Echocardiography documented a large pericardial effusion that was circumferential measuring 2.1 cm posteriorly in the parasternal long axis view, 1.8 cm at the apex in the four-chamber window, and 1.9 cm anteriorly using a subcostal window. Fig.* 16.6 depicts the apical five-chamber view showing the large pericardial effusion.

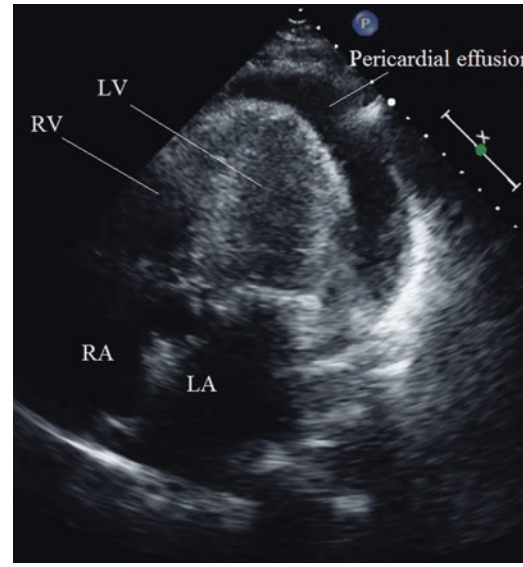

Fig. 16.6 Large circumferential pericardial effusion is seen in this apical four-chamber view. *LA* left atrium, *RA* right atrium, *LV* left ventricle, *RV* right ventricle

This pericardial effusion is most likely to be related to metastatic breast cancer and is accessible percutaneously via apical, left parasternal, or subxiphoid approach. Pericardiocentesis was performed, draining 725 cc of bloody fluid resulting in symptomatic improvement.

Case 2 *A 29-year old female with untreated SLE presented with positional chest pain and shortness of breath. Physical examination showed a heart rate of 115 BPM, blood pressure 100/75 mmHg, oxygen saturation 98% on room air; Jugular venous distention was present. A 16 mmHg pulsus parodoxus was present. ECG showed sinus tachycardia, diffuse ST-segment elevation, and PR depression. Echocardiography documented a moderate-sized circumferential pericardial effusion with right atrial diastolic collapse. Right heart catheterization was performed and revealed the following pressures (mmHg): right atrium: 14, right ventricle: 50/14; pulmonary artery 45/14: pulmonary capillary wedge 14 mmHg; cardiac output 3.4 L/min; cardiac index 2.1 L/min* $\times$ m^2.

The presence of tachycardia, low pulse pressure, echocardiographic evidence of diastolic chamber collapse, and low cardiac index demonstrate the hemodynamic sequelae of cardiac tamponade. Figure 16.4 shows the pericardial effusion with agitated saline injected into the pericardial space to confirm the position of the needle tip.

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Procedural Sedation

17

Grace M. Wu

The American College of Emergency Physicians (ACEP) defines procedural sedation as "a technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function. Procedural sedation and analgesia (PSA) is intended to result in a depressed level of consciousness that allows the patient to maintain oxygenation and airway control independently."

The Joint Commission on Accreditation of Healthcare Organizations in the United States (JCAHO) has defined sedation as a continuum of consciousness: analgesia, minimal sedation, moderate sedation and analgesia (formerly termed conscious sedation), deep sedation and analgesia, general anesthesia, and dissociative sedation. (Table 17.1).

Indications

PSA may be used for any procedure in which a patient's pain or anxiety may be excessive and may impede successful completion of the procedure. Common cardiology procedures include electrical cardioversion, transesophageal echocardiogram, diagnostic and ablation procedures for cardiac arrhythmias, coronary angiography, transcutaneous valve replacements and repair, and insertion of implantable electronic device [1].

Contraindications

There are no absolute contraindications to PSA. Relative contraindications may include older age, significant medical comorbidities and signs of a difficult airway. In older patients, sedating agents should be given at a lower starting dose, using slower rates of administration and repeated dosing of medications at less frequent intervals. Patients with major comorbid medical conditions are at increased risk for adverse events however there is no evidence that alternative approaches (monitored anesthesia care or general anesthesia) are safer. PSA is relatively contraindicated in patients who are likely to be difficult to ventilate or oxygenate. Patients who have eaten recently are not contraindicated to PSA, however if a procedure is not emergent, the American Society of Anesthesiologists (ASA) recommends that the patient fast for 0–2 h after drinking clear liquids and 2–6 h after ingesting solid foods or cow's milk depending on the patient's risk factors [2, 3].

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Table 17.1 Continuum of depth of sedation: definition of general anesthesia and levels of sedation/analgesia

	Minimal Sedation	Moderate Sedation/ Analgesia (Conscious Sedation)	Deep Sedation/ Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response after repeated or painful stimulation	Unarousable, even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

Equipment

Intravenous access should be established. Patients should have constant cardiac and respiratory monitoring, with careful monitoring of blood pressure, heart rate, respiratory rate, oxygen saturation, end-tidal carbon dioxide level and cardiac rhythm. Supplemental oxygen is often recommended to maintain oxygen levels during hypoventilation. In the event of respiratory compromise, equipment for performing endotracheal intubation and managing the airway should be readily available. Resuscitation medications, including medications for advanced life support and reversal agents should be available at bedside [2, 4].

Technique

Ideal pharmacologic agents for PSA will have rapid onset and short duration of action, maintain hemodynamic stability and lack major side effects. (Table 17.2) Some shorter procedures may be performed with the patient awake or only lightly sedated with concomitant local anesthesia. Agents that depress cardiac function may be problematic during ablation of ventricular tachycardia. Pre-oxygenation should usually accompany sedative administration [2, 4].

Benzodiazepines are commonly employed for their ability to produce anxiolysis and amnesia, however they have no analgesic properties. Midazolam is used most often due to its ability to penetrate the blood-brain barrier quickly. It can be used alone or in combination with short acting opioids (eg, fentanyl). With repeat doses, midazolam can accumulate in adipose tissue and can prolong sedation. Care must be taken when using midazolam in the elderly, obese, and patients with renal or hepatic disease [1, 5].

Opioids are often administered alone or in combination with sedatives in procedures requiring PSA. Short acting agents such as fentanyl, alfentanil and remifentanil are used. Fentanyl rarely causes hypotension, however its primary side effect is respiratory depression, which is potentiated by the coadministration of sedatives.

Coadministration of midazolam and fentanyl is useful when ultrashort-acting agents (eg, propofol) are unavailable. The combination of midazolam and fentanyl may cause hypoxia and apnea, and increase the need for airway intervention and medication reversal. It is suggested to administer midazolam first and fentanyl titrated carefully thereafter [1].

Propofol is an ultrashort-acting phenol derivative with highly lipophilic properties allowing it to cross the blood-brain barrier rapidly and therefore must be dosed carefully. It is an effective sedative and amnestic but provides no analgesia. Injecting propofol with lidocaine pretreatment or coadministration can prevent pain when injecting through intravenous catheter. Additional intraprocedural analgesia can be achieved by pretreatment with short acting opioids (eg, fentanyl). Pharmacokinetics of propofol are unchanged in patients with impaired kidney or liver function. In older patients, the dose should be reduced by 20 percent and be given slowly over 3–5 min.

Table 17.2 Intravenous procedural sedation medications for adults

Medication	Initial dose	Onset	Duration	Repeat dose (as necessary
Midazolam	0.02–0.03 mg/kg over 2 min; maximum 2.5 mg (1.5 mg maximum if elderly)	1–2.5 min	10–40 min	May repeat after 2–5 min
Fentanyl	0.5–1 mcg/kg	2–3 min	30–60 min	0.5 mcg/kg every 2 min
Propofol	0.5–1 mg/kg	0.5 min	5 min	0.5 mg/kg every 3–5 min
Etomidate	0.1–0.15 mg/kg	5–15 s	5–15 min	0.05 mg/kg every 3–5 min
Ketamine	1–2 mg/kg over 1–2 min	0.5 min	5–20 min	0.25–0.5 mg/kg every 5–10 min

Propofol is contraindicated in patients with allergy to egg lecithin and soybean oil. Side effects include hypotension and respiratory depression in patients with severe medical problems (such as sepsis, cardiac dysfunction) or hypovolemia [5, 6].

Etomidate is an imidazole derivative that is commonly used for rapid sequence intubation but can be used for PSA as well. Lower doses should be used in patients with renal or hepatic impairment and in elderly individuals. Etomidate also has no analgesic properties and similar strategies to reduce pain can be used as with propofol. Myoclonus is the most frequently reported side effect (reported in up to 80 percent of patients). In the event of severe myoclonus, immediate airway support and treatment with benzodiazepine (midazolam 1–2 mg IV, reduced every 60 s) are indicated. Other side effects include respiratory depression, adrenal suppression and nausea and vomiting [7].

Ketamine is a phencyclidine derivative that acts as a dissociative sedative, producing a trance-like state and provides sedation, analgesia and amnesia while preserving the airway. Ketamine is ideal for brief, painful procedures and for patients who may have a potentially difficult airway or have compromised respiratory function. Ketamine can cause disorientation, dream-like experiences, or hallucinations that can be treated with a small dose of midazolam. Other side effects of ketamine include nausea and vomiting, laryngospasm, tachycardia, hypertension, increased intracranial and intraocular pressure and hypersalivation. Ketamine has been associated with longer median times for return to baseline mental status and increased agitation during recovery [5].

Evaluation

In patients who are at risk of hypotension due to recent illness, dehydration, or cardiac disease, etomidate or ketamine is preferable to propofol. Patients who have potentially difficult airways to manage or have compromised respiratory function can undergo PSA with ketamine. All agents should be given at a lower starting dose with lower rates of administration and less frequent dosing intervals in elderly patients [5, 6].

Discharge Criteria

- Additional monitoring for complications inherent to the procedure is unnecessary
- Vital signs and respiratory and cardiac function should be stable and within acceptable limits
- Mental status and physical function should return to a point where the patient can care for himself or herself with minimal to no assistance
- Symptoms such as pain, lightheadedness and nausea should be well-controlled
- The person should be accompanied home by a reliable person who can provide support and supervision for at least a few hours [4]

Complications

PSA is largely considered safe as serious complications occur rarely. Complications can often be prevented through appropriate selection of patients, proper use of sedative medication and careful monitoring of sedation. The most concerning complication is dose dependent respiratory compromise causing hypoxia or hypercarbia, which develops in less than 1 percent of cases. Naloxone (0.01–0.1 mg/kg IV or IM, max 2 mg) and flumazenil (0.01 mg/kg IV over 20 s, max 1 mg) may be utilized to reverse opioids and benzodiazepines, respectively. Significant hypotension and bradycardia may develop in patients with significant cardiac morbidity and patients receiving beta-blockers. Etomidate may be preferred in these settings. Additional adverse outcomes may include vomiting and aspiration, and inadequate sedation preventing completion of the procedure. Combined adverse event rate (adverse event and failure to perform procedure) occur 15% of the time. Anesthesiology support should be readily available in high-risk patients [4].

Clinical Vignettes

Case 1 *A 61 year old woman with a past medical history of hypertension, hyperlipidemia is diagnosed with new onset atrial fibrillation at her PCP's office. She undergoes DC cardioversion with midazolam and fentanyl without any complications. In the recovery area, the patient awakens, is oriented to person, place and time, and is communicative with nurses and staff. She is eating lunch.*

While serious adverse events such as hypoxia rarely occur after discharge, it is common for patients to experience mild symptoms, such as nausea, lightheadedness, fatigue or unsteadiness for up to 24 h. A reliable person who can provide support and supervision should be present at the patient's home for at least a few hours [2].

Case 2 *A 42 year old male with no past medical history presents after two episodes of syncope. He also reports episodes of lightheadedness that resolve spontaneously. All male members of his family died of sudden cardiac death at an early age. EKG reveals pseudo-right bundle branch block and persistent ST elevation in leads V1 to V2. Echo is unremarkable. The diagnosis of Brugada syndrome is made and patient is scheduled for placement of ICD under PSA with propofol. During the procedure, the patient becomes tachycardic and hypotensive. His SaO_2 drops to 82%.*

There are no reports of endotracheal intubation due to propofol induced respiratory depression during PSA. Mild hypoxia can usually be managed by interruption of the propofol and bag-mask ventilation. Figure 17.1 [6].

Because sedation is a continuum, it is not always possible to predict how an individual patient will respond. Hence, practitioners intending to produce a given level of sedation should be able to rescue patients whose level of sedation becomes deeper than initially intended. Individuals administering *Moderate Sedation/Analgesia (Conscious Sedation)* should be able to rescue patients who enter a state of *Deep Sedation/Analgesia*, while those administering *Deep Sedation/Analgesia* should be able to rescue patients who enter a state of general anesthesia.

Developed by the American society of Anesthesiologists; approved by the ASA House of Delegates October 13, 1999 [4].

Elderly patients are at increased risk of adverse events with these agents and dosing should be adjusted accordingly [5, 7]. See text for details.

Proceed down the intervention sequence as patient condition permits. A. Head-tilt/ chin-lift. B. Jaw thrust maneuver involves thumbs on the maxilla pressing downward and four fingers posterior to the ramus applying upward pressure.

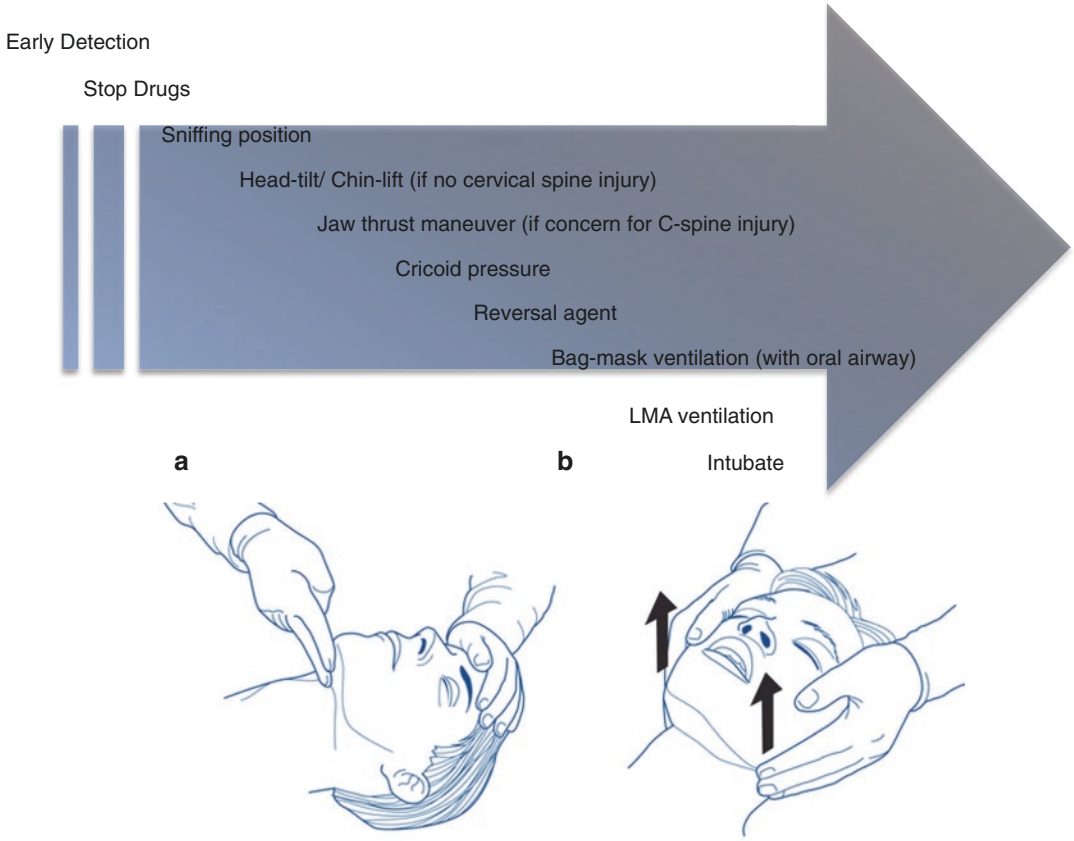

Fig. 17.1 PSA intervention sequence. (**a**) Head-tilt/Chin-lift (**b**) Jaw thrust Maneuver

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Endotracheal Intubation

18

Aaron E. Brice

Indications

Specific indications for planned intubation include patients receiving general anesthesia, surgery in close proximity to the airway, or surgery in an atypical position. Indications for unplanned intubation can be broadly divided into several categories including respiratory failure, acute airway obstruction and loss of protective reflexes (Table 18.1) [1]. Rapid sequence intubation is the standard technique used in unstable patients that require prompt securement of the airway using the concurrent administration of a sedative agent for induction and a neuromuscular blocking agent for paralysis.

Table 18.1 Emergent indications for endotracheal intubation [1]

Respiratory failure	Pulmonary edema, excess secretions, atelectasis, acute respiratory distress syndrome, hypoventilation, neuromuscular failure
Acute airway obstruction	Laryngeal edema, laryngeal spasm, trauma, smoke inhalation, foreign body, hematoma, tumor, retropharyngeal abscess, epiglottitis
Loss of protective reflexes	Drug overdose, stroke, head trauma

Contraindications

Endotracheal intubation may be employed as a life saving measure and in this circumstance there are few absolute contraindications to its use. However, clinicians must be mindful of conditions in which intubation may provoke additional problems. This includes blunt or penetrating trauma to the larynx causing laryngeal fracture or separation of tissue layers. Traction with a laryngoscope, stylet, or endotracheal tube may cannulate a false lumen or tear the airway. When there is significant doubt as to the safety of intubation noninvasive oxygenation and ventilation are preferred until a definitive or surgical airway can be created.

Relative contraindications to intubation include patients with a difficult airway. The mnemonic LEMON (Look, Evaluate, Mallampati Class, Obstruction/Obesity, Neck mobility) can be used to stratify a difficult airway [2]. Look externally for any clear visible evidence of potential problems such as micrognathia. Evaluate using the 3-3-2 rule (Fig. 18.1) to confirm that the mouth can open to fit 3 of the patient's fingers between upper and lower incisors, the submandibular space can fit 3 of the patient's fingers from chin to angle of the neck, and the space between the superior aspect of thyroid cartilage and angle of the neck can fit 2 of the patient's fingers. Mallampati class (Fig. 18.2) rates the

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space for oral intubation based on tongue size and degree of mouth opening from I (most open) to IV (least open). Obstruction and obesity assess any upper airway impediment caused by tumors, swelling, excess adipose tissue, or other masses. Neck mobility assesses the patient's ability to be placed in the sniffing position in which the head is elevated and neck extended forward.

Equipment

Assembly of all necessary equipment prior to starting is essential as unforeseen complications may result in critical delays (Table 18.2).

Fig. 18.1 3-3-2 rule to evaluate the difficult airway. *1* Inter-incisor distance is three fingers. *2* Hyoid mental distance is three fingers. *3* Thyroid to floor of mouth is two fingers

Laryngoscopes are composed of a handle, blade, and light source. The two most frequently used blades are the Macintosh which is curved and the Miller which is straight. The choice of which to use is based on experience and personal preference [4]. These and other images of essential equipment are displayed in Fig. 18.3.

When there is difficulty visualizing the glottis a bougie or tube introducer is placed in the trachea and the endotracheal tube is passed over it. Oral and nasal airways are adjuncts and can be used to prevent the tongue from obstructing the posterior pharynx.

Endotracheal tubes are measured lengthwise in centimeters and by internal diameter in millimeters and French. Assemble tubes one size greater and one size smaller than the estimated tube to be used. Most adults will need at least an 8.0 mm tube but an inappropriately small tube will increase the work of breathing and if a bronchoscopy is to be performed the tube must be sufficiently wide to allow passage of equipment.

Pharmacologic agents for rapid sequence intubation are given IV push and include both a sedative agent for induction and a neuromuscular

Table 18.2 Essential equipment [3]

Face mask with bag valve	Bougie
100% oxygen	Sedative agent
Oral and nasal airways	Neuromuscular blocking agent
Suction device with catheters	Local anesthesia
Laryngoscope with handle and blades	Syringe to inflate endotracheal cuff
Endotracheal tubes with stylet	Tape

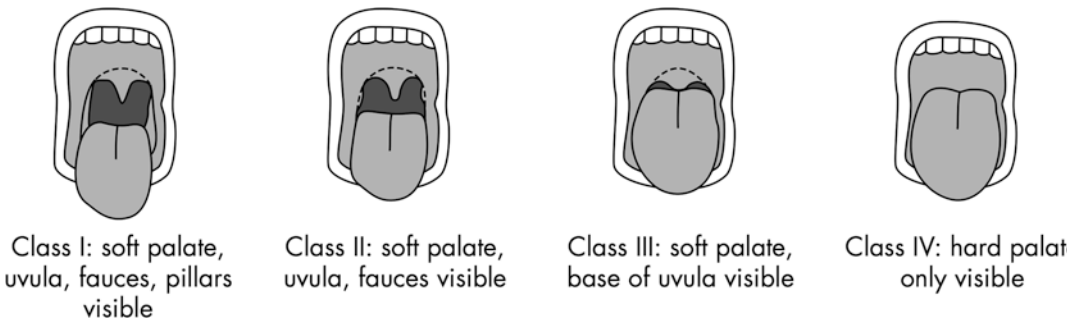

Fig. 18.2 Mallampati class I–IV

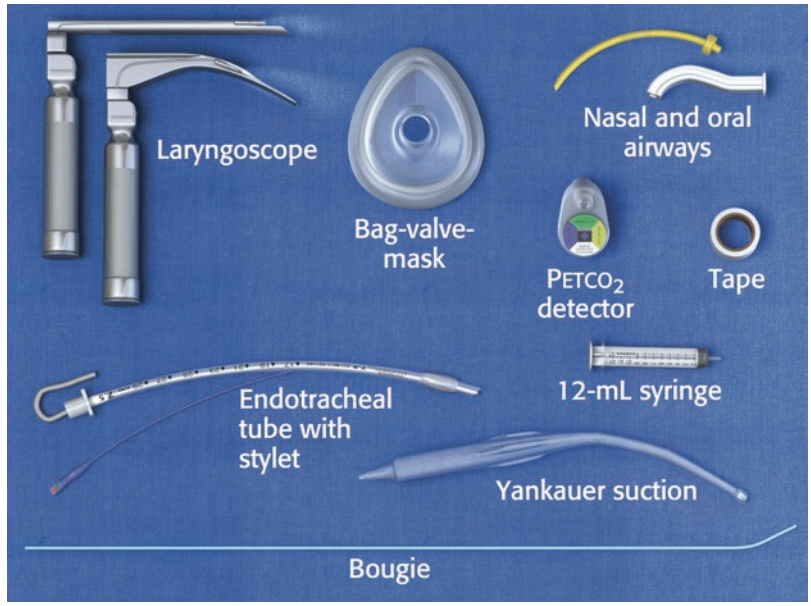

Fig. 18.3 Essential equipment for endotracheal intubation

blocking agent for paralysis. Commonly used sedative agents with dosing listed in mg/kg include midazolam (0.3–0.35), etomidate (0.2–0.6), propofol (2.0–2.5), and ketamine (0.5–2.0). Rapid paralysis with dosing listed in mg/kg is frequently achieved with succinylcholine (1.0–1.5), rocuronium (0.6–1.2), atracurium (0.4–0.5), and vecuronium (0.08–0.1).

Technique

Successful intubation begins with the pre-procedural evaluation but in an emergency some aspects must be omitted. Stepwise technique of rapid sequence intubation can be remembered with the "Seven P's" (Preparation, Preoxygenation, Pretreatment, Paralysis and induction, Protection/Positioning, Placement, and Postintubation management) [5].

Preparation evaluates the airway, gathers supplies, and ensures the patient is connected to required lines and monitors. Preoxygenation with 100% high flow oxygen with saturation monitoring for 3.5–4 min will replace nitrogen in the patient's functional residual capacity with oxygen and increase the time intubation may be attempted during apnea. Pretreatment with lidocaine or fentanyl may be used to decrease natural coughing and gagging reflexes during intubation. Paralysis with induction uses administration of sedative and neuromuscular blocking agents concurrently by IV push to achieve unconsciousness and muscular flaccidity. Protection to prevent aspiration consists of applying cricoid pressure with Sellick's maneuver causing posterior compression of the cricoid cartilage against the vertebral body to lessen the diameter of the hypopharynx. Placement of the tube requires the laryngoscope to be held in the left hand and the gloved right hand opens the mouth by simultaneously pressing the thumb against lower incisors and index finger against upper incisors in a scissor motion. The blade is inserted in the right mouth and in a sweeping motion moves the tongue to the left (Fig. 18.4). The epiglottis is visualized and the blade is advanced to this point and then elevated forward in a straight line at a 45° angle to reveal the vocal cords avoiding contact with teeth to prevent trauma. Direct visualization of the vocal cords is obtained, the tube is passed through them, the cuff inflated, stylet withdrawn, and correct position of the tube is confirmed. Postintubation management involves securing the tube, adjusting ventilator settings, and post-procedure monitoring.

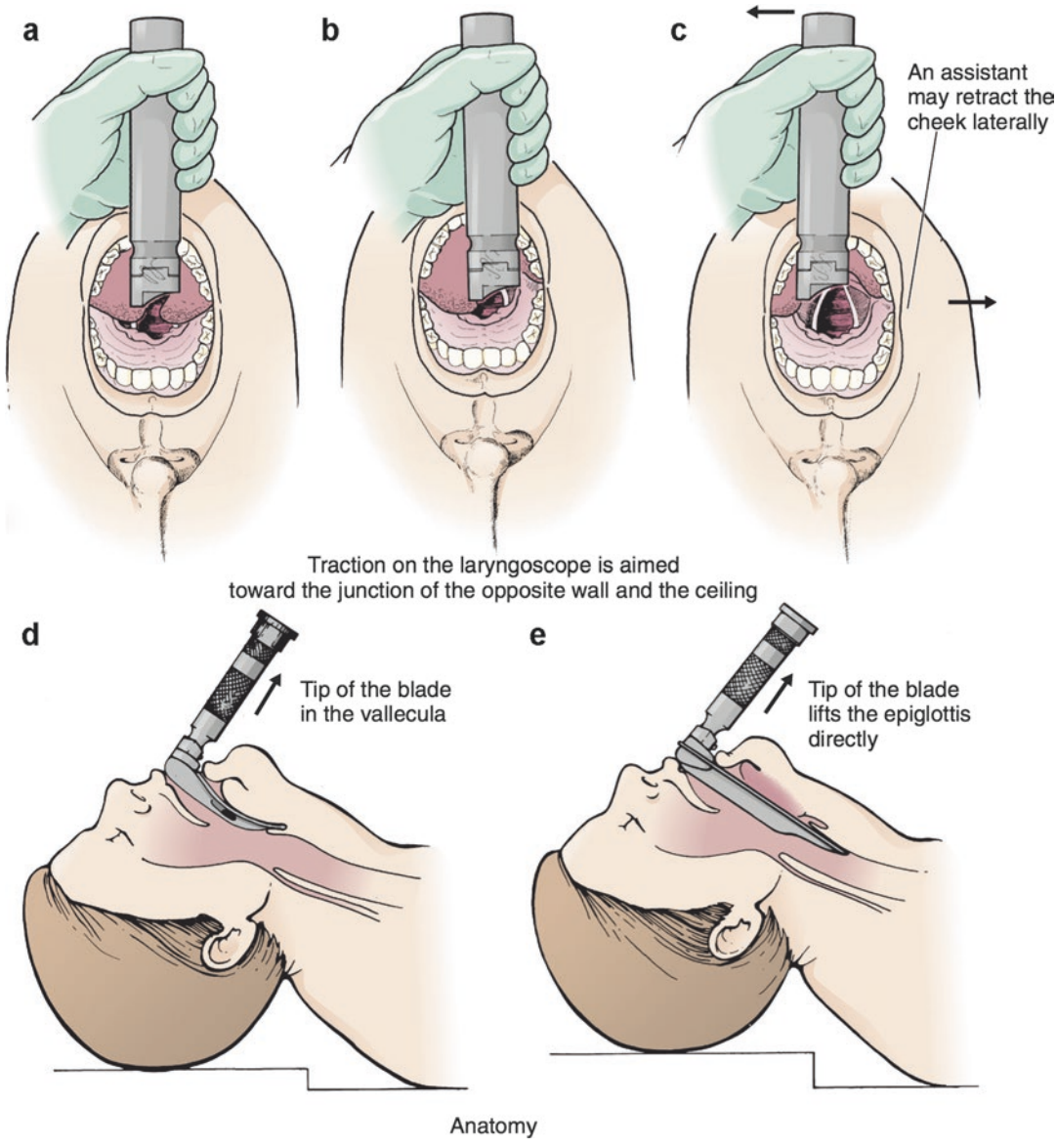

Fig. 18.4 Direct visualization of vocal cords. (**a**) Blade is under middle of tongue and obscuring the glottis. (**b**) Tongue not far enough left and obscuring the glottis. (**c**) Correct blade placement with tongue elevated and to the left. (**d**) Use of curved (Macintosh) blade. (**e**) Use of straight (Miller) blade

Data Interpretation

Potentially difficult mask ventilation may be recognized in patients that are body mass index greater than 26, age 55 or older, edentulous, or with significant facial hair. If these factors are encountered intubation performed while the patient is awake with local anesthesia may be preferred.

During preoxygenation when high flow oxygen is used and saturation cannot be maintained greater than 93% positive pressure ventilation may be employed. If saturation is persistently

less than 91% manual ventilation may be necessary.

Tube placement is measured from lips to distal tube and in average sized adults is at the 23 cm line for males and 21 cm line for females. Correct tube placement is determined by visualizing bilateral symmetric expansion of the chest and checking for breath sounds in both lungs and an absence of sound over the stomach. End-tidal carbon dioxide measured by calorimetric detection or standard capnography can be used to confirm tracheal placement. A chest x-ray shows the degree of tube depth and the distal tube should rest approximately 3 cm above the carina.

Cuff pressure should be 15–30 mmHg and below the approximate capillary pressure of 32 mmHg. The use of a low pressure, high volume endotracheal tube cuff will reduce the chance of ischemic injury caused by tissue compression.

Complications

Trauma from the laryngoscope, stylet, or endotracheal tube may damage the airway or surrounding soft tissue. Nontraumatic complications including bronchospasm, hypoxia, and aspiration of stomach contents can also occur. Significant cardiovascular events including ventricular tachycardia and ventricular fibrillation are not common but may warrant antiarrhythmic prophylaxis in patients with previous arrhythmias or myocardial ischemia. Stimulation of the laryngeal branches of the vagus nerve may cause bradyarrhythmias that are responsive to atropine. Mechanical ventilation may cause hypotension from decreased venous return due to elevated intrathoracic pressure. Initial management consists of bolus intravenous fluids and evaluation of airway pressures but more serious alternative causes of hypotension including myocardial ischemia and pneumothorax must also be considered. When intubation is prolonged patients are predisposed to a number of potential problems including tracheomalacia, tracheal stenosis, and tracheal erosion (Table 18.3) [3].

Table 18.3 Complications from endotracheal intubation [3]

Intraprocedural complications	Aspiration
	Airway perforation
	Laryngospasm
	Trauma to dentition or airway
	Spinal cord injury
	Epistaxis
	Ventricular tachycardia
	Bradycardia
	Endotracheal tube blockage
	Tube dislodgement
	Bronchus intubation
Postprocedural complications	Laryngitis
	Laryngeal edema
	Hypoglossal nerve compression
	Ulceration of airway mucosa
	Vocal cord paralysis
	Tracheal stenosis
	Laryngeal granuloma
	Pneumothorax

Clinical Vignettes

Case 1 *A 68-year-old man is admitted to the hospital for 1 week of worsening shortness of breath. He has a medical history of heart failure with an ejection fraction of 30% and takes metoprolol, enalapril, and spironolactone at home. On physical exam he is afebrile, blood pressure is 94/62, heart rate is 108, respiratory rate is 32 and oxygen saturation is 82% while on a nonrebreather mask. His body mass index is normal. He does not know where he is or the year and attempts multiple times to remove his oxygen mask. His lungs have bilateral rales and cardiac auscultation elicits an S3 heart sound. Arterial blood gas reveals pH 7.48, pCO_2 of 32 mmHg, and pO_2 of 58 mmHg. His chest X-ray shows cardiomegaly, bilateral pleural effusions, and pulmonary edema.*

This patient is severely hypoxic from decompensated heart failure with evidence of impending respiratory failure and requires timely endotracheal intubation and mechanical ventilation. He is confused and in respiratory distress and must be stabilized. There is no role for increasing oxygen flow rate or noninvasive posi-

tive pressure ventilation given his current clinical instability. Other contraindications to noninvasive ventilation include altered mental status, increased risk for aspiration, facial trauma, severe obesity, respiratory arrest, myocardial infarction, and arrhythmias. A surgical airway is also not currently necessary in this patient.

Case 2 *A 42-year-old man is found unresponsive in the street next to an open bag of unmarked white powder. Paramedics intubate him on the scene and transfer him to the emergency department. When he arrives he is unresponsive to verbal stimuli but sternal rub elicits a deep groan. He is afebrile, blood pressure is 98/66, and heart rate is 115. Oxygen saturation is 84% on FiO_2 of 80%. He has reduced expansion of the left side of his chest with reduced breath sounds on the left. The endotracheal tube depth is 29 cm. Cardiac exam is unremarkable. Blood glucose is 94 and his cardiac biomarkers are pending. Electrocardiogram shows nonspecific ST and T wave changes.*

This patient has right mainstem bronchus intubation due to excess endotracheal tube advancement and is likely suffering from drug overdose. His low oxygen saturation can be fixed by withdrawing the tube to a depth of 23 cm in this male patient. Intubations in the field are more difficult and prone to more frequent complications given the uncontrolled environment. Correct tube placement must always be checked by verifying appropriate tube depth, visualizing symmetric chest excursion, auscultating bilateral breath sounds, measuring end-tidal carbon dioxide, and obtaining a chest x-ray showing tube depth. He may have a component of aspiration pneumonia but that would be unlikely to cause persistent hypoxia despite being intubated. A pulmonary embolism can also cause severe hypoxia but his absent left sided breath sounds are not explained by this and he did not have evidence of a lower extremity DVT.

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Part III

Electrophysiology

The Electrocardiogram

19

Alexis Rodriguez

Introduction

The invention of the electrocardiogram (ECG or EKG) dates to the eighteenth century when Luigi Galvani realized that muscular activity could be induced with the exposure to an electric field. However, the term itself was not used until the end of the nineteenth century by Willem Einthoven. Throughout the years, the ECG has continued to evolve, especially in the tracing recording portion, but has never lost its clinical meaning [1].

The physical principle is the recording of electrical activity of the heart using skin electrodes, which detect cardiac myocytes depolarization and repolarization waves. A positive depolarizing wave that travels towards the electrode creates an upward deflection in the paper tracing. Conversely, any wave moving away from the electrode is recorded as a negative deflection. Finally, the amplitude, duration, and direction of any deflection depend on that of the electric vector.

Indications

ECG indications vary between physicians depending on the patient and the clinical presentation. Nonetheless, it is generally accepted that this test aids in the diagnosis of overt or suspected cardiovascular disease with follow up recordings if there is a change in clinical status. It is also generally accepted for the initial evaluation in high-risk individuals, i.e., older than 40, history of dyslipidemia, hypertension, or other risk factors. Additionally, there is an accepted, and widely used, role in the perioperative setting whether for initial evaluation prior to surgery or afterwards to monitor for complications. Selected individuals, albeit healthy otherwise, benefit from routine screening ECGs; these include, athletes, pilots, bus drivers, among others [2].

Equipment and Technique

Cardiac electrical potentials are detected by electrodes placed throughout the torso and limbs in specific arrangements to create the different ECG leads (Fig. 19.1). These leads record the potential difference between two electrodes, the positive and negative. There are three standard limb leads, three augmented limb leads, and six precordial leads for a total of twelve leads. Other systems have expanded to other leads to detect right pre-

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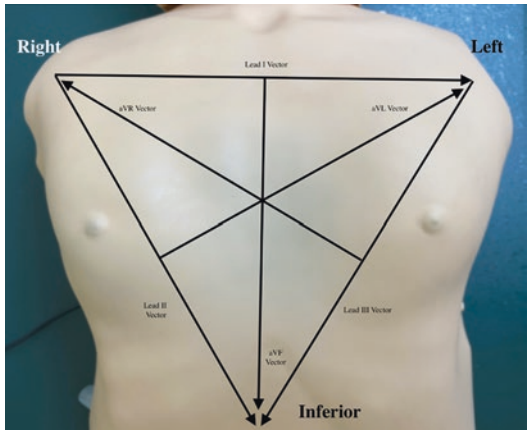

Fig. 19.1 Lead vector for the three standard limb leads, the three augmented limb leads (*left*), and the six unipolar precordial leads

cordial leads to diagnose right ventricular abnormalities, or the left posterior leads to detect acute posterolateral infarctions.

Technique

The patient is initially asked to lie supine and relax as much as possible. The chest is exposed so that there is no interaction with lead placement, but recognizing that patient's privacy should be maintained at all times. Figure 19.2 reveals the anatomic landmarks on a patient on whom an ECG is being recorded. These areas should be identified and cleaned to ensure appropriate electrode placement and contact with the skin. ECG recorders have specific manufacturer's instructions. Beforehand, it is crucial to determine if there are any possible issues that may interfere with the accurate recording, i.e., electrical calibration, signal interference, wandering baseline, among others.

Data Interpretation

Most ECGs are recorded on standard settings at 25 mm/Section (X Axis) and 10 mm/mV (Y axis). Different settings can be obtained depending on the heart rate, or voltage. Before attempting to interpret an ECG, the reader should pay close attention to the standardization. For ease, this can generally be found at either sides of the tracing.

The normal ECG is composed of multiple waves and intervals, which represent the different portions of the cardiac cycle (Fig. 19.3). The P wave, representing atrial activation is best appreciated in lead II or V1. The PR segment is an isoelectric segment, which begins at the end of the P wave and ends with the QRS. Depression of this segment is associated with pericardial disease. Ventricular activation ensues with several complex interactions, which are recorded as a set of deflections giving rise to the QRS.

The T wave represents ventricular repolarization [3]. The QT interval is measured from the last portion of the QRS to the end of the T Wave, and represents a measure how fast the ventricles repolarize. A prolonged QT constitutes a marker for potential ventricular tachyarrhythmias. Since the QT measurements vary with heart rates, a standardized measurement, the QTc, is preferred at times. Different formulas have been derived. The Bazett equation calculates the QTc by dividing the QT by the square root of the RR interval. The Friderecia method uses the cube root.

Different ECG criteria have been developed for the diagnosis of left ventricular hypertrophy. These take into consideration the dimensions of different QRS deflections in specific leads, and their additive values. Overall, the ECG is considered a reliable screening diagnostic tool to

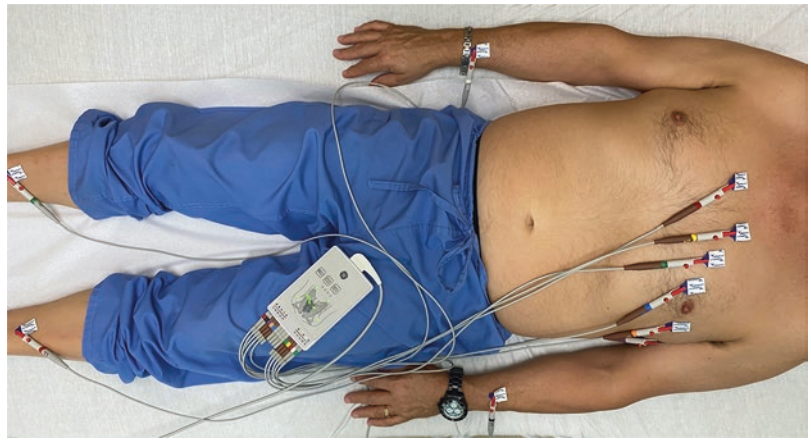

Fig. 19.2 ECG recording

evaluate for LVH. Particularly so, when confirmatory elements are also present; these include a leftward axis, QRS widening, left atrial enlargement, ST-T changes, among others.

Clinical Vignette

Case 1 *50 year-old patient with history of hypertension and dyslipidemia presents to the emergency department referring crushing chest pains for the last 25 min. The ECG is shown in* Fig. 19.4.

Case 2 *74 year old obese man brought to the ED by fire rescue. The patient was initially found tachycardic with a HR at 160 beat per minute. After adenosine and metoprolol IV were administered, his rate slowed and an ECG was performed (*Fig. 19.5).

Case 3 *58 year old man with a family history of ischemic heart disease presents to his primary care physician for an initial evaluation. His father and elder brother developed CAD and underwent CABG and PCI respectively in their early fifties. Unlike his relatives, the patient has never smoked tobacco, and leads an active lifestyle. He runs four times a week 6 miles under 1 h.* Figure 19.6.

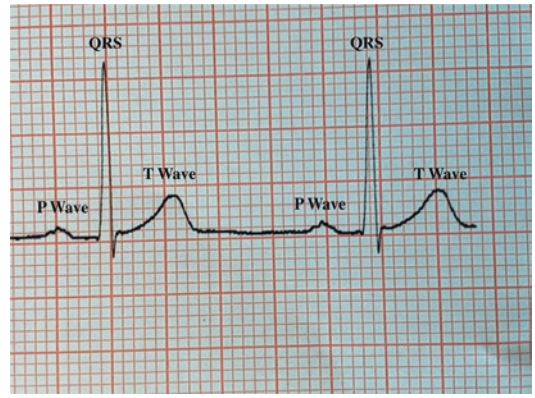

Fig. 19.3 The waves and intervals in a normal electrocardiogram

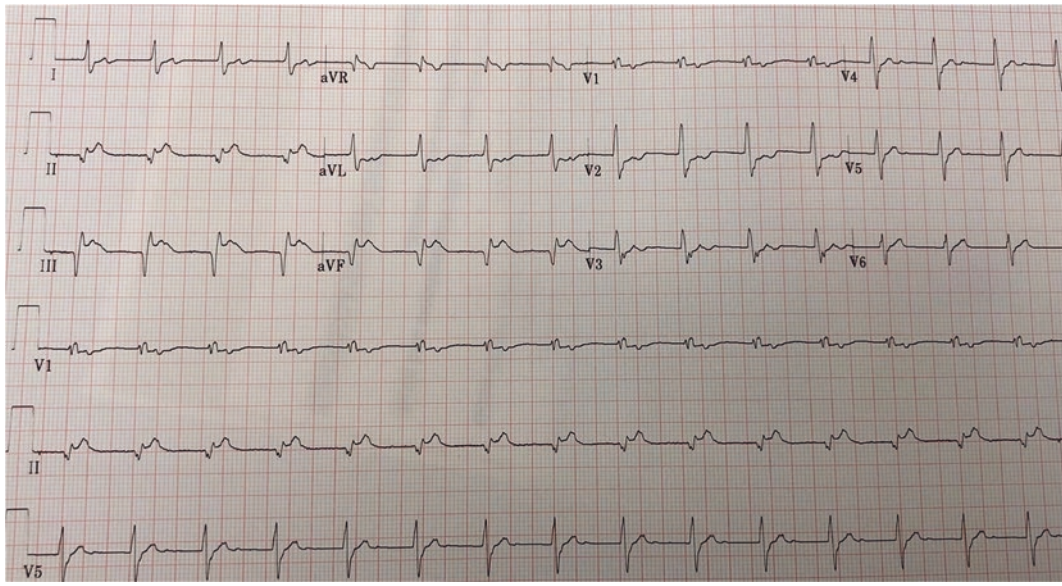

Fig. 19.4 Inferior wall STEMI with ST elevations in the inferior leads and reciprocal ST changes

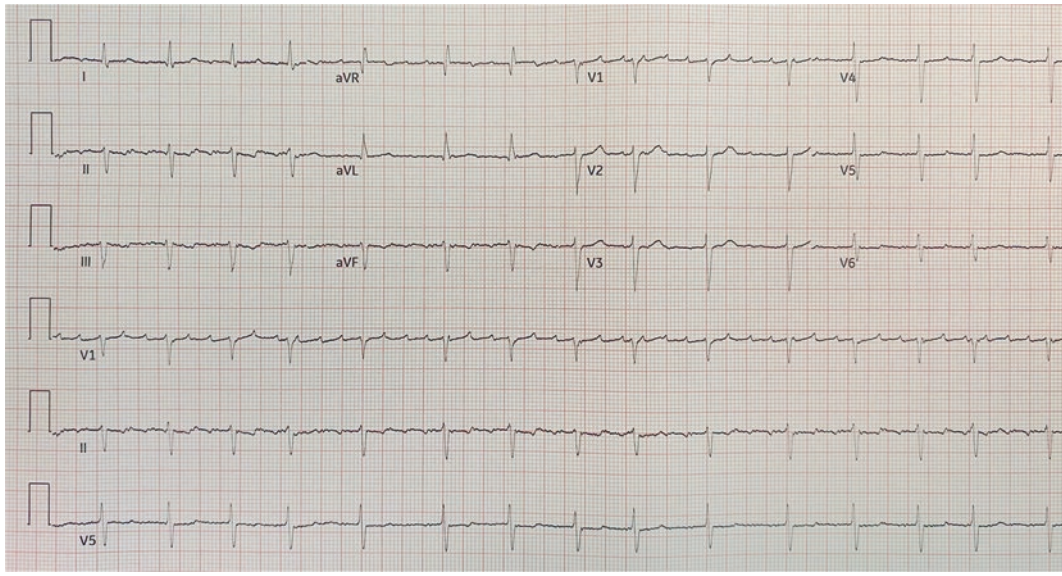

Fig. 19.5 Atrial Flutter

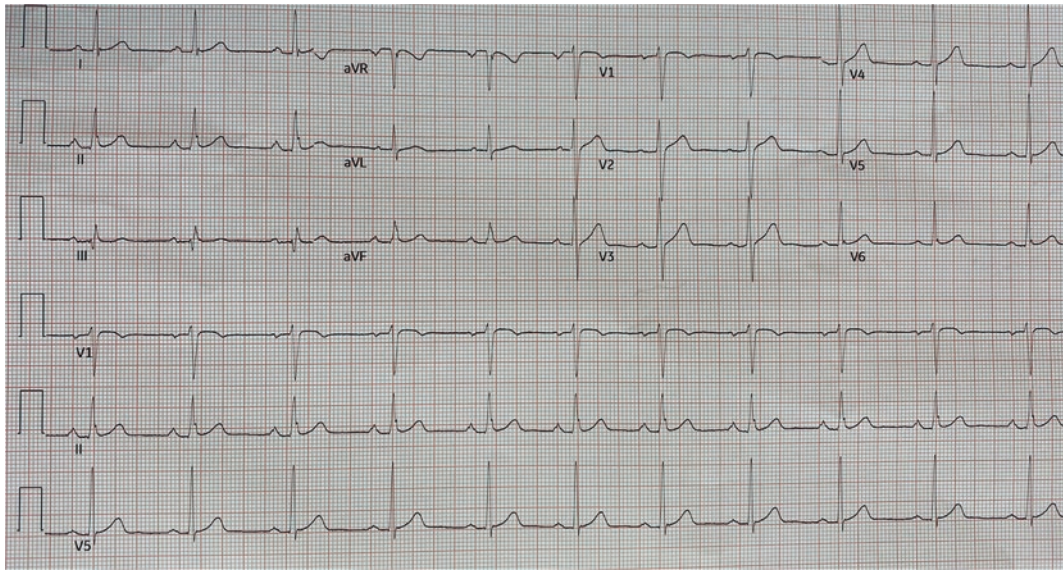

Fig. 19.6 Unremarkable ECG

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Ambulatory Electrocardiography

20

William J. Gionfriddo, Douglas W. Laidlaw, and N. A. Mark Estes III

Introduction

Ambulatory electrocardiography (AECG) refers to outpatient diagnostic techniques used to record the cardiac rhythm from one or more leads for variable durations of time [1–3]. AECG techniques permit evaluation of dynamic cardiac electrical activity that is frequently intermittent, of short duration, and with varying degrees of symptomology. Over the last several years, new technologies have emerged that allow use of multiple types of noninvasive and invasive recorders for AECG.

Holter Monitors

Historically, continuous ambulatory recorders, commonly referred to as Holter monitors, were developed to record the ECG continuously for a period of 24 h. The continuous AECG is most commonly performed in patients with symptoms that occur once daily or more frequently. Contemporary Holter monitoring devices have time markers and patient-activation indicators. Additionally, patch monitors are now available as a leadless form of Holter monitor capable of continuous monitoring for 1–14 days. The recorded digital data are analyzed after monitoring completion by computer software with technical oversight. Current Holter monitoring technology does not allow for remote transmission of data from the patient for analysis. Typically, a Holter monitor report includes information about the total number of heart beats, average heart rate, maximum and minimum heart rate, number of premature atrial and ventricular beats, tachyarrhythmias, pauses, ST segment changes, and patient reported symptoms with the associated ECG recordings of the patient's rhythm.

Event Recorders

Short-term event monitors are small, pocket-sized, recorders that are either worn on the wrist, or carried with the patient. They are useful for patients who experience infrequent symptoms and are applied to the skin with electrodes when symptoms occur. The advantage to event monitors is that they allow the patient to

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be free from continuously wearing inconvenient electrode patches. However, because the device is not constantly recording the ECG, any symptom or arrhythmia must last long enough to permit activation of the recorder by the patient. Current short-term event recorders can transmit digital data, recorded at the time of symptoms, remotely for analysis. Modern advancements in hardware and software technologies have led to the popularization of commercially available wearable cardiac monitoring devices. Common designs include watches and wristbands. Through the sensation of cardiac vibrations (seismocardiography) and photodetection of blood volume variations in the skin (photoplethysmography), the simplest models are capable of trending heart rate variations. More complex devices can be paired with software algorithms to detect arrhythmias such as atrial fibrillation [4]. Furthermore, several smartphone compatible applications utilizing smartphone case-mounted ECG electrodes are available for patient use to detect arrhythmias with more accuracy than external loop recorders over extended timeframes [5].

Loop Monitors

Noninvasive "loop monitors" are a type of event monitor capable of recording the patient's ECG for several days, weeks, or even months. Loop monitors utilize hard-wired electrode patches to record the ECG in a continuous "loop" by recording over any unsaved data for a fixed period of time. This form of AECG monitoring is typically activated by patient triggering during symptoms. The cardiac rhythm is stored prior to, during, and after device activation for 30–60 s. Recordings can then be transmitted remotely for evaluation. More sophisticated versions of this device can be triggered to record automatically based on prespecified parameters of heart rate and irregularity. Most commonly, these devices are programmed to automatically detect bradyarrhythmias, tachyarrhythmias and atrial fibrillation, and are useful for patients with infrequent symptoms [6].

Mobile Cardiac Outpatient Telemetry (MCOT)

To improve diagnostic accuracy of both symptomatic and asymptomatic arrhythmias, the use of mobile cardiac outpatient telemetry (MCOT) has proven to be useful technology [7–8]. These cardiac monitoring systems are an advanced form of event monitor that overcome many limitations of Holter, traditional event monitors and loop monitors. The original version of the MCOT was attached to the patient using 3 chest electrode leads connected to a sensor worn on the waistband. The newest iteration exists as a convenient chest patch, worn continuously. These devices can record all cardiac rhythms for up to 4 weeks, and immediately transmit data remotely to a central location for technical analysis. Like event recorders, transmission can be triggered automatically based on parameters of heart rate and rhythm, or by patients directly for symptoms of interest. MCOT is useful for longer-term continuous monitoring of patients who are asymptomatic, have infrequent arrhythmias, or who require rapid identification and transmission of higher risk arrhythmias [9].

Implantable Loop Recorder

Occasionally, for infrequent and/or asymptomatic arrhythmias, a non-invasive evaluation using cardiac rhythm monitors does not provide a diagnosis. Under these circumstances long-term implantable loop recorders (ILR) are currently available [10]. These devices are typically implanted subcutaneously in the left pectoral region as a simple outpatient procedure under local anesthesia. Similar to the noninvasive loop monitor, the ILR can be activated by the patient at the time of symptoms. Once activated, ILRs record the patient's cardiac rhythm prior to, during, and after a patient triggered event. ILRs will also record the cardiac rhythm automatically when the heart rate or rhythm falls outside a range of predetermined parameters. Recent technology allows more reliable detection of atrial fibrillation, distinguishing it from other rhythms

with a high sensitivity and specificity [11]. Current devices have battery longevity expected to approach 3 years.

Indications

The most common indication for ambulatory monitoring is screening for cardiac arrhythmias or conduction abnormalities as the cause for symptoms such as palpitations, pre-syncope or syncope. Ambulatory monitoring is also indicated for risk stratification of patients with multiple types of cardiovascular disease. It is also used for evaluation of therapy, the detection of asymptomatic arrhythmias, and for identification of silent ischemia. The choice of recording technique depends on the frequency of the arrhythmia of interest, and the patient's symptoms (Table 20.1) [9].

Indications for AECG are summarized in the ACC/AHA Guidelines for Ambulatory Electrocardiography [2]. Common indications for its use include palpitations, unexplained syncope, and ischemia detection in patients with suspected variant angina (Table 20.2). In addition, AECG may be utilized in special circumstances for antiarrhythmic drug monitoring and the assessment of pacemaker and Implantable Cardioverter-Defibrillator (ICD) function (Table 20.3). Other indications for ambulatory monitoring include assessment of the average heart rate and adequacy of rate control in patients with atrial fibrillation. Increasingly, techniques of ambulatory monitoring are being used to evaluate for otherwise undetected atrial fibrillation in patients presenting with cryptogenic stroke or to screen for the asymptomatic recurrence of atrial fibrillation following ablation procedures [6]. Ambulatory monitoring

Table 20.1 Advantages and disadvantages of specific ambulatory ECG recording techniques

Selection of ambulatory ECG recording technique			
Recorder type	Advantages	Disadvantages	Duration of use
Holter monitor	1. Continuous ECG Recording 2. No activation required by patient 3. Preferred method for daily symptoms	1. Less useful for infrequent symptoms 2. Continuous monitoring at times uncomfortable/ inconvenient for patients	24 h–2 weeks
Noninvasive event monitor	1. Intermittent ECG recording with new wearable or handheld designs 2. Downloading of events for immediate assessment 3. Preferred for infrequent symptoms (weekly or monthly)	1. Less useful for brief symptoms 2. Less useful for arrhythmias that cause loss of consciousness	Weeks–Months
Loop monitor	1. Intermittent ECG Recording 2. Transtelephonic downloading of events for immediate assessment 3. Preferred for infrequent or brief symptoms that may cause loss of consciousness	1. Continuous wearing required 2. Recorder must be activated by patient with each event	Weeks–Months
Mobile Cardiac Outpatient Telemetry (MCOT)	1. Continuous ECG Recording 2. Wireless cellular downloading of events for immediate assessment 3. Preferred for infrequent, brief, asymptomatic or high-risk arrhythmias 4. Previously 3 electrodes and a sensor, but now convenient single patch cutaneous application	1. Continuous wearing required 2. Limited to 4 weeks	Weeks–1 Month
Implantable loop recorder (ILR)	1. Long-term continuous monitoring with intermittent ECG recording 2. Preferred for rare symptoms which cause loss of consciousness	1. Must be surgically inserted 2. Risk of infection 3. Higher cost than other noninvasive techniques	Up to 3 years

techniques can also be used to screen patients for asymptomatic premature ventricular contractions and nonsustained ventricular tachycardia for purposes of risk stratification. AECG can provide useful information for risk stratification for sudden cardiac death in select patient populations. These include those patients with hypertrophic cardiomyopathy, long QT syndrome, congenital heart disease, arrhythmogenic right ventricular dysplasia, ischemic heart disease, and dilated cardiomyopathies.

The method of initial ambulatory ECG monitoring for the symptomatic patient depends largely on the frequency and severity of symptoms. Holter monitoring for 24–48 h is most practical as the initial monitor of choice for patients with daily or near daily symptoms. Holter monitoring is also a reasonable approach to assess rate control in patients with atrial fibrillation and for risk stratification for patients with selected types of cardiovascular disease as noted above. By contrast, noninvasive or invasive loop monitoring has a higher diagnostic yield in patients with less frequent symptoms. Such monitoring is appropriate if symptoms occur weekly or monthly but do not prevent the patient from activating the device. MCOT patch monitors provide convenience and accuracy for detecting a wide range of arrhythmias but are limited to 4 weeks of monitoring. Newer commercially available devices have proven useful for long-term intermittent monitoring as detection algorithms improve, and as they gain continued popularity. (Table 20.1).

Contraindications

As a simple, non-invasive technique, there are few absolute contraindications for AECG. However, in patients with previous allergic reactions to the adhesives used in lead/patch attachment, alternative methods should be used, or the patient should be monitored closely for adverse reactions. As a diagnostic test, the ACC/AHA guidelines explicitly discourage the use of AECG for patients with syncope or other symptoms if other causes have been identified [2]. In addition, published guidelines discourage the use of AECG in patients with strokes who are at low risk without other evidence of arrhythmia. These guidelines also do not support the use of AECG for the evaluation of myocardial ischemia, with the exception of suspected variant angina (Table 20.2). Although not contraindicated, AECG also plays a limited role in the assessment of pacemaker and ICD function, and should not be used when data available from device interrogation are sufficient to guide patient management (Table 20.3).

Table 20.2 Indications for AECG to assess symptoms possibly related to rhythm disturbances

A. Indications for AECG to assess symptoms possibly related to rhythm disturbances	
Class I	1. Unexplained syncope, near syncope, or episodic dizziness in whom the cause is not obvious 2. Unexplained recurrent palpitations
Class IIb	1. Episodic shortness of breath, chest pain, or fatigue that is not otherwise explained 2. Neurological events when transient atrial fibrillation of flutter is suspected 3. Syncope, near syncope, episodic dizziness, or palpitations in whom a probable cause other than an arrhythmia has been identified, but in whom symptoms persist despite treatment
Class III	1. Syncope, near syncope, episodic dizziness, or palpitations in whom other causes have been identified 2. Cerebrovascular accidents without other evidence of arrhythmia
B. Indications for AECG for ischemia monitoring	
Class I	None
Class IIa	Patients with suspected variant angina
Class IIb	1. Evaluation of patients with chest pain who cannot exercise 2. Preoperative evaluation for vascular surgery of patients who cannot exercise 3. Patients with known coronary artery disease and atypical chest pain syndrome
Class III	1. Initial evaluation of patients with chest pain who are able to exercise 2. Routine screening of asymptomatic patients

Source: Crawford et al. [2]

Table 20.3 Indications for AECG to assess antiarrhythmic drug and device therapy

A. Indications for AECG to assess antiarrhythmic drug therapy	
Class I	To assess antiarrhythmic drug response in individuals in whom baseline frequency of arrhythmia has been characterized as reproducible and of sufficient frequency to permit analysis
Class IIa	To detect proarrhythmic responses to antiarrhythmic therapy in patients at high risk
Class IIb	1. To assess rate control during atrial fibrillation 2. To document recurrent or asymptomatic nonsustained arrhythmias during therapy in the outpatient setting
B. Indications for AECG to assess pacemaker and ICD function	
Class I	1. Evaluation of frequent symptoms to exclude myopotential inhibition and pacemaker-mediated tachycardia and to assist in the programming of advanced features such as rate responsivity and mode switching 2. Evaluation of suspected component failure or malfunction when device interrogation is not definitive in establishing a diagnosis 3. To assess the response to adjunctive pharmacological therapy in patients receiving frequent ICD therapy
Class IIb	1. Evaluation of immediate postoperative pacemaker function after pacemaker or ICD implantation as an alternative to continuous telemetric monitoring 2. Evaluation of the rate of supraventricular arrhythmias in patients with implantable defibrillators
Class III	1. Assessment of ICD/pacemaker malfunction when device interrogation or other available data are sufficient to establish a cause/diagnosis 2. Routine follow-up in asymptomatic patients

Source: Crawford et al. [2]

Equipment

The original AECG systems utilized a small, lightweight, battery operated electromagnetic tape recorder connected to bipolar electrodes capable of recording in 3 or 12 lead ECG format on a magnetic tape cassette, microcassette, or compact disk. Newer devices now allow for direct recording of the ECG signal in a digital format. This technology avoids potential biases introduced by tape recording as well as problems associated with analog-to-digital conversion before analysis. These recordings allow for extremely accurate reproductions of the ECG signal for more advanced analysis by computer algorithms. Digital recording devices are currently limited by higher costs and smaller storage capacity, although this technology is rapidly advancing. These devices include patient-activated event markers and encoded time markers for simplified data retrieval. Recorded data is converted to a digital format and analyzed using commercially available software that helps identify arrhythmias. Devices that allow trans-telephonic downloading are capable of ECG transmission via telephone by converting the ECG data into an audio signal. Upon receipt at a central location, the audio signal is reconstructed into a conventional ECG recording for printing and analysis. Modern devices also include in-home communicators that utilize wi-fi and cellular technologies to transmit data to a centralized processing center [12].

Techniques of AECG

For wired devices such as Holter monitors and loop recorders, correct patient connection to the device is the single most important step in AECG recording. For traditional wired 24-hour Holter monitors, five, seven, or ten electrodes are placed in standardized lead positions using adhesive gel after the skin sites are shaved and prepped. From these positions, the operator is able to obtain 3 or 12 lead ECG recordings. The number and arrangement of lead wires is determined by the operator at the time of the recording depending on the number of ECG leads that are desired. The operator can then set the desired duration of time for 3 and 12 lead recording to be obtained by the device during the recording period. Patients are instructed to wear the recorder for 24–48 h, performing their daily activities as normal. During

the recording period, patients should avoid any activities that could cause the recorder or the electrodes to become wet. They are also advised to avoid equipment or appliances that may cause electromagnetic interference. All symptoms, activities, and medications taken should be recorded by pressing the Event button on the recorder and entering the event into either the Digital Diary or the paper diary provided.

In comparison to the traditional 24-hour Holter monitor, wired loop monitors utilize two attached ECG leads that can be worn continuously for several weeks. Patients are instructed to detach the device for bathing. At the onset of symptoms, the device is patient-activated for up to 300 s of recording a single ECG lead. Recorded rhythms can be downloaded via telephone to a central location for analysis. In contrast, events monitors do not require ECG lead attachment at the onset of symptoms. Rather, the recorder itself contains ECG electrodes that are held to the skin (either directly to the chest wall, grasped in both hands, or worn on the wrist) for recording during an episode. Recorded rhythms can then be downloaded via various transtelephonic, wireless, or cellular techniques and transferred to a central location for analysis.

Wireless patch monitors and MCOT devices can be worn continuously for weeks of rhythm monitoring. They do not need to be removed for showering. Most devices are still capable of patient-activation single-lead ECG recording during symptomatic episodes in addition to automatic arrhythmia detection algorithms and cellular transmission for centralized analysis by a certified technician.

Data Interpretation

Following the recording period, the saved ECG can then be analyzed using commercially available software which displays and prints selected ECG rhythm strips. In addition, the software provides trend information including ST-segment variation, heart rate (measured R-R interval) and heart rate variability, total ventricular and supraventricular premature beats, and ventricular tachycardia and supraventricular tachycardia beat counts. Accuracy of ECG interpretation varies depending on the amount of background artifact in the recording and with the software system used for analysis. The system is designed to detect all important arrhythmia episodes with high sensitivity, but despite advances in the accuracy of software-based analysis, all recorded rhythms must be over-read by an experienced clinician. When used in combination with a detailed diary of patient symptoms, the diagnostic yield of these devices is high. The ability to temporally correlate ECG abnormalities with patient symptoms is the unique strength of this technique.

Complications

As a simple, non-invasive test, there are few significant complications resulting from this technique. There exists a risk of cutaneous allergic reaction to adhesive patches. Additionally, the risk of misdiagnosis is a potential limitation. If an asymptomatic rhythm abnormality is detected, it may lead to additional unnecessary diagnostic testing. Implantable loop recorders carry the additional risks of bleeding, infection, skin erosion and damage to tissues and surrounding structures because they are subcutaneously inserted. However, the complication rates for these procedures by experienced operators is low [10].

Conclusions

As described above, the clinician has multiple techniques of AECG monitoring available as diagnostic tools for outpatient cardiac monitoring. The indication for the monitoring as well as the frequency and duration of patient symptoms need to be carefully considered in choosing the best monitoring approach. The likelihood of making a diagnosis for patients with intermittent, rare symptoms such as syncope, presyncope or palpitations is increased with extended duration of monitoring. By contrast, when monitoring is being performed to assess the effects of therapy such as rate-controlling drugs in atrial fibrillation or risk stratifica-

tion, Holter monitoring for 24–48 h is sufficient. Holter monitoring has been the appropriate method of AECG monitoring as an initial step in patients with frequent symptoms occurring daily or more frequently. By contrast, noninvasive loop monitoring has been preferred for patients with less frequent symptoms. More recently, patch monitors and MCOT devices have become convenient and efficient modalities for monitoring frequent and infrequent arrhythmias for up to 1 month. When a diagnosis remains absent despite noninvasive cardiac monitoring, it is reasonable to move forward with a more invasive approach using an ILR. Clinicians should remember that the ILR is most useful for patients with extremely infrequent symptoms, including syncope or cryptogenic stroke. However, this invasive approach should generally be reserved for patients in whom noninvasive AECG techniques have failed to yield a diagnosis. Exciting new long-term options are now available in commercial wearable and intermittent handheld monitors, which will likely become more commonly used as arrhythmia detection technology advances and clinician familiarity with these devices improves.

Clinical Vignettes

Case 1 *A 70-year-old male presents with recurrent palpitations every 4–6 days that last for 1–5 minutes. A recent episode lasted 2 h before spontaneously abating, prompting him to seek medical evaluation. He has a history of diabetes, hypertension, and nonobstructive coronary artery disease. ECG at time of visit shows normal sinus rhythm.*

A 2-week patch Holter monitor is performed which documents several episodes of atrial fibrillation with a rapid ventricular response, with the longest episode lasting 12 h (Fig. 20.1). The patient is at increased risk for systemic thromboembolism and is initiated on systemic anticoagulation and options for rhythm and rate management are discussed.

Case 2 *A 65-year-old female presents with frequent palpitation, lightheadedness, and two episodes of syncope. She has a history of paroxysmal atrial fibrillation.*

A 24-h Holter monitor is performed which reveals an episode of atrial fibrillation terminating with a 9.2 s pause and sinus arrest during sleep (Fig. 20.2). She is treated for sick sinus syndrome with a permanent pacemaker.

Case 3 *A 20-year-old male is referred for occasional palpitations. He has no significant past medical or family history, and does not report dizziness, pre-syncope, or syncope.*

A Holter monitor is performed which records an episode of sinus rhythm with second-degree AV block Mobitz I (Wenckebach) in the early morning hours during sleep (Fig. 20.3). No other significant arrhythmias were documented despite several episodes of symptoms. No specific therapy was warranted.

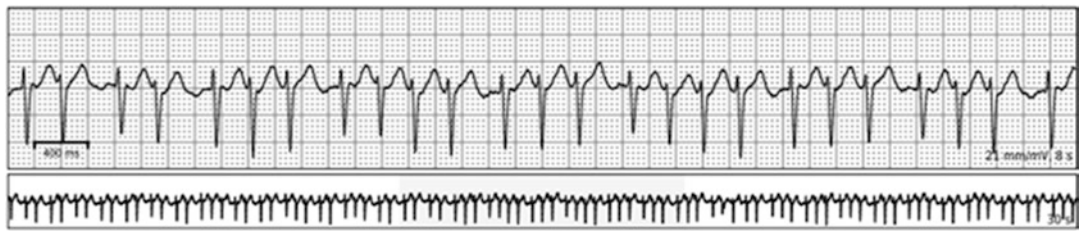

Fig. 20.1 Holter monitor recording of atrial fibrillation with a rapid ventricular response

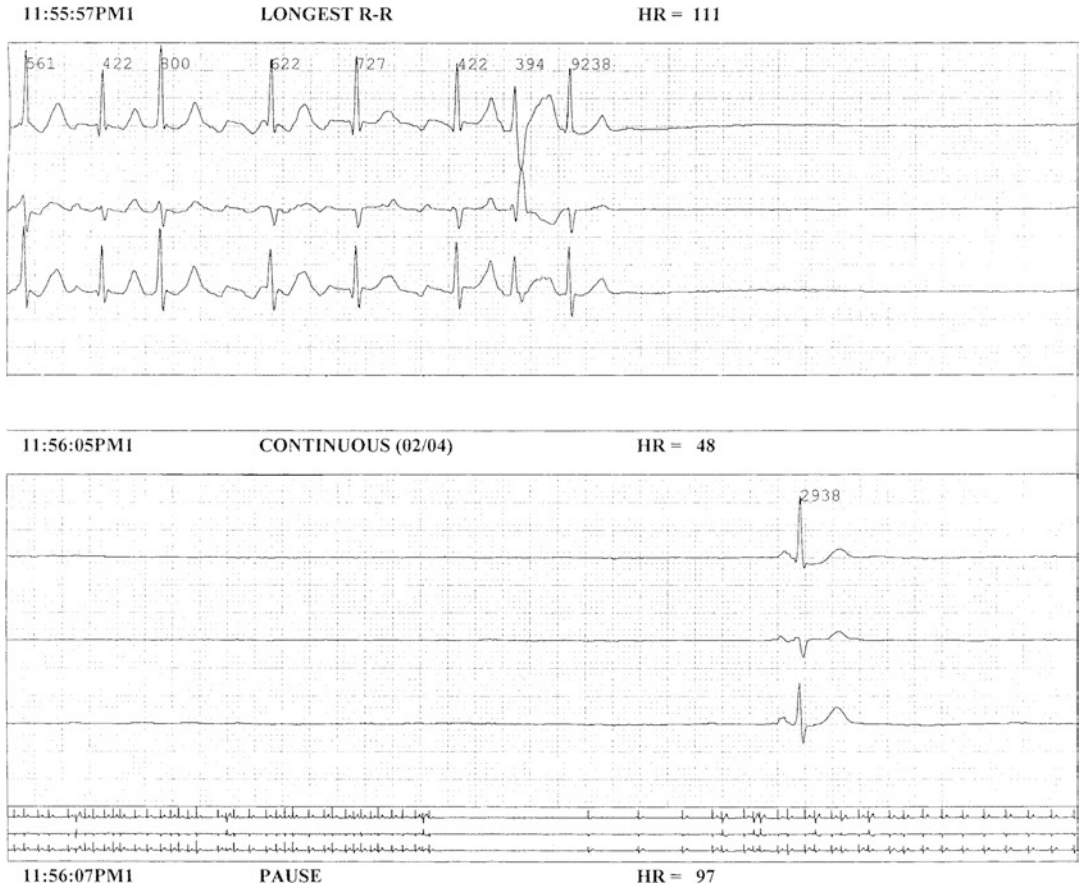

Fig. 20.2 Holter monitor recording of atrial fibrillation with a conversion pause and sinus arrest of 9.2 seconds

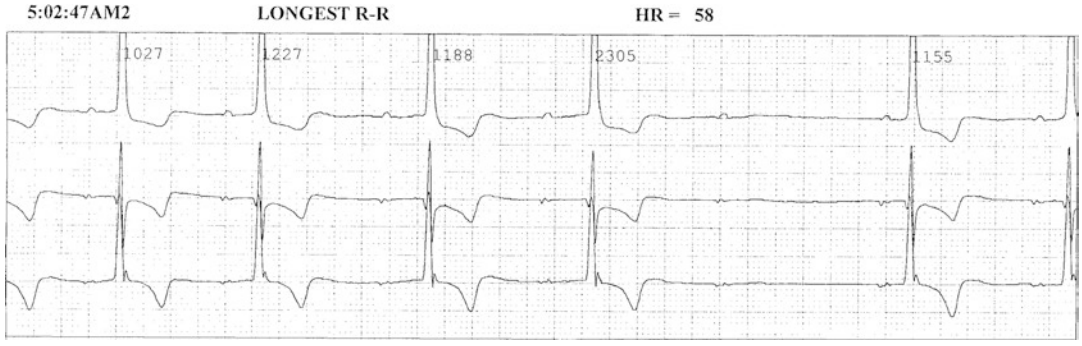

Fig. 20.3 Holter monitor recording of sinus rhythm with Second-degree AV block Mobitz I (Wenckebach)

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Tilt Table Testing

21

Alexis Rodriguez

Introduction

Tilt table testing (TTT) was introduced decades ago for the evaluation of patients with unexplained syncope. Initially, it was welcomed enthusiastically through different medical specialties, but its use has decreased due to the recognition of several limitations when inappropriately employed. Nonetheless, the generalized consensus still stands that TTT remains an important diagnostic tool in the correct patient population.

Indications

TTT has been used for the evaluation of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. It is especially useful in the evaluation of recurrent episodes of syncope in the absence of organic heart disease, or in patients with prior cardiomyopathy diagnosis in whom other syncope etiologies have been excluded. Furthermore, TTT is also a practical option to discriminate between convulsive syncope and epilepsy, to establish a diagnosis of pseudosyncope, and lastly to evaluate patients with hypotension that are less likely to respond to permanent cardiac pacing. Additionally the diagnosis of delayed orthostatic hypotension syndrome can be successfully made through TTT after all other diagnostic studies are negative. Nonetheless, it should not be used when the vasovagal syncope diagnosis is certain; or to guide therapy, its response, or lack thereof [1].

Contraindications

Though a high volume of TTT are performed on a yearly basis, the ordering clinician should be aware of its contraindications. While considered a safe test, complications still may arise from decreased perfusion to the heart, brain, or other organs. Some of the most important contraindications include a history of severe tachyarrhythimas, electrolyte imbalance, end-stage renal disease, left ventricular outflow tract obstruction, severe cerebral or coronary artery disease, hypotensive shock, recent stroke, and lower extremity fracture.

Equipment

The test is performed generally in the electrophysiology laboratory. A tilt table is required, and should be as comfortable as possible (Fig. 21.1). A blood pressure monitor, ECG machine, and oxygen saturation monitor are also needed. Since

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Fig. 21.1 The patient is secured on a padded table with may be placed in a variety of positions, as opposed to position

one of the possible complications is the development of dangerous tachyarrhythmias, a crash cart with defibrillator should be available. During the testing phase, the room should remain quiet comfortable by minimizing disruptive noises, or uncomfortable extreme range of temperatures.

Technique

Multiple protocols have been developed varying the angle tilt, its duration, and the concomitant use of pharmacologic agents. The patient is placed supine and vital signs are closely monitored to obtain a personal baseline. It is recommended that if venous cannulation had been performed prior to the test, the monitoring period should be longer. Another important consideration is to avoid invasive intra-arterial blood pressure monitoring during TTT because catheterization may induce in some individuals a vasovagal reaction.

The patient is positioned in a head-up position. The recommendation is that the tilt angle be between 60° and 70°; however, steeper angles have been described. Heart rate and blood pressures are recorded every 3–5 min and a symptom diary is maintained. Pharmacologic agents can induce symptoms in patients that have remained asymptomatic. Isoproterenol, a non-specific beta agonist, used as an infusion is commonly employed. The infusion is titrated from 1–3 mcg/min to increase the heart rate up to 25% above the recorded baseline, and then the head-up tilt phase of the study begins. Another important consideration is that isoproterenol is contraindicated in patients with ischemic heart disease. Nitrates have also been showed to have some use in tilt table testing, as intravenous or sublingual formulations. Nitrates work by inducing venodilation, and, thus, reducing cardiac preload, stroke volume, and output. Yet, it does not hamper increases in heart rate or arterial constriction. Like isoproterenol, nitrates decrease the exam duration but are better-tolerated and easier to use [2].

Data Interpretation

Test interpretation depends on the clinical setting for indication in the first place. In patients without structural heart disease, TTT is determined to be diagnostic for different outcomes. First, for the evaluation of reflex hypotension or bradycardia that may, or not, be accompanied of spontaneous syncope. Secondly, when the patient develops

progressive orthostatic hypotension even if there are no associated symptoms. In selected patients being assessed for POTS, TTT may play a diagnostic role, but it is still discretionary to the ordering physician. In patients with structural heart disease, arrhythmias should be excluded before considering a test to be diagnostic. Reproduction of a syncopal event even in the absence of hypotension or bradycardia is in turn suggestive of psychogenic pseudosyncope. The rate of false positives and negatives depends on the patient population; however, these are difficult to estimate given that there is no gold standard testing for comparison.

If the patient has remained asymptomatic during TTT, and there is suspicion for false negative results, it is recommended that the test be repeated using isoproterenol. Though relatively safe for most patients, isoproterenol should be avoided in patients with angina and history of arrhythmia. While most make no discriminations regarding test results when isoproterenol is used, some cardiologists make the distinction that a test is positive only if there is loss of consciousness or postural tone. Nonetheless, the most current guidelines do not include separate diagnostic criteria for TTT with concomitant isoproterenol [2]. Nitrates, like isoproterenol, may also increase the rate of false positives. Trials comparing nitroglycerin to isoproterenol have been conducted, thus, showing similar results; however, sublingual nitroglyerine was simpler to administer, much better tolerated, and safer than low-dose isoproterenol [3, 4].

Complications

As previously stated, TTT is rather safe, and severe complications are rare; however, as with any other medical procedure, there are still some intrinsic risks that both patient and practitioner should be aware. Potential complications include, prolonged hypotension, tachyarrhythmias, syncope, and rarely asystole. Most of these complications resolve when the table is turned back to the horizontal position. Nonetheless, precautionary measures should be taken and readily available including cardiopulmonary resuscitation equipment.

Clinical Vignettes

Case 1 *Mrs. Jones is a 40 year- old lady that comes to the office for evaluation of syncope. She has a history of hypertension, hypothyroidism, dyslipidemia, and obesity. She takes synthroid 125 mcg daily, and her primary care physician discontinued hydrochlorothiazide over a year ago as her blood pressure seemed better controlled. She experienced her first syncopal event about 3 months ago while getting up from a chair, and then another one last week after standing for some time. She recalled that the same thing used to happen in her " earlier years." Before both events, she felt her vision darkened and the room spin for some seconds. Both events were witnessed, and the loss of consciousness was transitory and resolved by itself. There was no tongue biting or sphincter incontinence. She had no post- ictal period. However, per her son, there was some lower extremity jerking movements. She has undergone extensive diagnostic studies including brain images; thus far, no clear etiology given. She undergoes TTT with hypotension and reproduction of symptoms.*

Mrs. Jones has had two syncopal episodes that have prompted a medical evaluation. After extensive and thorough evaluation, there is no clear etiology. However, no pertinent positive findings have been noted. While it can be argued, that given the history, this is very likely consistent with vasovagal syncope, there is the confounding factor of lower extremity jerking, which can also be seen in syncope of cardiac nature. The TTT is considered to be positive given her vital signs response and reproduction of symptoms. Mrs. Jones should be advised regarding hydration, prolonged standing, or sudden changes in position. The patient should also be educated on abortive procedures if she experiences an aura.

Case 2 *A 28 year old woman is referred for the evaluation of recurrent fainting episodes. These*

started about 2 years ago, and have consistently recurred. She has no medical history, other than generalized anxiety disorder, and takes no medications or over the counter supplies. The episodes occur without an aura, or clear precipitating event. These last between 5 and 20 min, and the patient just experiences some residual weakness and left lower extremity weakness. She has undergone extensive neurologic evaluation (including MRI and EEG) without a definitive diagnosis. Furthermore, EKG and echocardiography do not show any abnormalities. At the primary care physician' s office her blood pressure was borderline low, but otherwise her vitals were normal. She undergoes TTT, and her vitals remain unchanged but the patient experiences another episode. A psychiatry consultation is placed, and the diagnosis is changed to psychogenic seizures and possibly conversion disorder. With the patient and her family understanding the diagnosis, psychotherapy was started and follow up appointments were provided.

This patient comes with complaints of recurrent syncope without a clear explanation. There is always concern for seizures or syncope of neuro-cardiogenic nature. These seem to have been ruled out. The possibility of vasovagal syncope has to be considered. Her blood pressure was marginally low; however, this is a non-specific finding especially in young healthy individuals. TTTs that reproduce the loss of consciousness without changes in vital signs are suspicious for a psychogenic etiology. The patient and family should be engaged in the therapy, which should remain empathic and consistent throughout. It is crucial to recognize that most of these events are involuntary, legitimate, and disabling to the patient. She should enroll in behavioral and group psychotherapy, and considered for antidepressant or antipsychotic pharmacotherapy.

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Electrophysiologic Testing

22

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Indications

There are a large variety of clinical scenarios in which electrophysiology studies (EPS) are indicated, as a way to diagnose a symptom such as palpitations or syncope, to define the mechanism and possibly treat a documented arrhythmia, or to aid in determining a patient's risk for sudden cardiac death from ventricular arrhythmias. Most EPS are performed via electrode catheters in the heart, but some are with non-invasive programmed stimulation (NIPS) that refers to a limited electrophysiology study performed via an implanted cardiac device, either a pacemaker or a defibrillator.

Invasive EPS can be of use in patients with suspected or known sinus node dysfunction. EPS is helpful in determining a causal relationship between suspected sinus node dysfunction and symptoms in cases where a non-invasive evaluation (event recording) has failed to establish the link. Indications for EPS in patients with known or suspected AV block, include those in whom His-Purkinje block is suspected as the cause of symptoms such as syncope or near syncope, but has not been definitively established, most notably in those with pre-existing conduction abnormalities (bundle branch block) on a surface electrocardiogram.

EPS are indicated in patients with recurrent supraventricular tachycardia (narrow QRS complex <120 milliseconds), to better define the mechanism of the arrhythmia and for selection of the appropriate therapy- medical or ablative. Wide complex tachycardias (wide QRS > 120 milliseconds) may be a result of either supraventricular arrhythmias with intraventricular conduction delay (aberration), pre-excitation in the Wolff-Parkinson-White syndrome, or ventricular tachycardia. When the mechanism of documented arrhythmias is not clear on a surface ECG or telemetry, EPS are indicated to define the mechanism and guide therapy. Non-invasive programmed stimulation-NIPS- via an ICD may be indicated in patients who have ventricular arrhythmias, in whom prescription of new antiarrhythmic medications may alter the characteristics of the tachycardia affecting the ICD programmed settings.

Indications for EPS in patients with Wolff-Parkinson-White syndrome (WPW) include patients in whom ablation of an accessory pathway is planned, and patients with WPW manifest on a surface ECG who suffer a cardiac arrest or syncope. Asymptomatic patients with WPW who have a family history of sudden cardiac death, or

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who engage in high risk occupations, may require EPS, for risk stratification, and to determine the best therapy if required, including pharmacologic or ablation therapies.

Non-sustained ventricular tachycardia can be a risk factor for sudden cardiac death in patients with left ventricular dysfunction. EPS with ventricular stimulation is indicated in patients with non-sustained ventricular tachycardia, coronary artery disease, and left ventricular dysfunction for risk stratification; where, if inducible for ventricular arrhythmias, patients may benefit from implantation of a cardiac defibrillator. In patients with non-ischemic cardiomyopathy, the results of ventricular stimulation are not predictive of risk. Patients with highly symptomatic, drug resistant, uniform premature ventricular contractions; or non-sustained ventricular tachycardia (with or without structural heart disease) may undergo and EPS to localize the arrhythmia as a target for ablation. PVC ablation is also indicated for patients who suffer from cardiomyopathy due to high density PVC's from identifiable foci.

EPS are indicated in patients with syncope and structural heart disease in whom the cause of syncope is unknown after routine evaluation. Additionally, patients without structural heart disease who have recurrent unexplained syncope despite an appropriate non-invasive workup (eg: EKG, echo, Holter and event recording, stress testing) may require EPS to assist in the diagnosis. EPS are indicated in patients with recurrent palpitations in whom repeated efforts to obtain electrocardiographic recordings have failed, or in patients in whom palpitations preceded a syncopal event.

Contraindications

As with most intravascular cardiac procedures, EPS are contraindicated in the presence of significant coaguloapathies or known obstruction to venous access. EPS should not be performed in the setting of hemodynamic instability, acute exacerbations of heart failure, systemic infection, and respiratory distress. Additionally, EPS is contraindicated in patients with left main coronary disease, a large burden of cardiac ischemia, severe aortic stenosis, acute myocardial infarction, or unstable angina. Extra caution is advised for those patients with known DVT/ pulmonary embolism and intra-atrial communication (ASD/ PFO) where a clot on the catheter could result in a thrombotic or embolic event.

Equipment

Equipment required to perform EPS, is like other cardiac catheterization equipment and includes a fluoroscopic unit, a patient table suitable for radiography, a physiologic recorder and display for hemodynamic, surface electrocardiography and intracardiac recordings, and equipment for intravascular access. Equipment for emergencies such as an external defibrillator, tools for airway support, and emergency medications should be easily available in the room in which the procedure is performed.

Unique to EPS are a programmable stimulator, a junction box, and electrode catheters. The stimulator is a device that can deliver accurately timed (within 1 millisecond) stimuli via intracardiac catheters triggered either by previously paced beats or intrinsic beats. Multiple stimuli (S) can be delivered with complex timing sequences (S1-S4). The junction box is where catheters connect to the recording and pacing equipment. Specialized catheters are used which have a variable number of electrodes on their ends (4–20), to both record intracardiac electrical activity and to deliver pacing stimuli to the heart. Most electrophysiology laboratories are equipped with additional equipment such as 3-D imaging/ mapping systems that assist in the diagnosis and localization of arrhythmias, and specialized ablation catheters and generators (radiofrequency and cryo-thermal energies) for delivery of catheter directed energy that destroys the arrhythmia focus. Electro-anatomic mapping systems have become an integral part of ablation procedures. The use of haptic assisted robotic navigation systems has been used in some labs.

Technique

The patient is brought to the electrophysiology laboratory in the fasting state and the sites of venous access are sterilized with either betadine or chlorhexadine, after which the patient is draped. General anesthesia is rarely used for diagnostic EPS, as most procedures can be achieved by conscious sedation. General anesthesia may be employed for longer procedures such as AF or VT ablations for airway protection and more ventilatory support. The sites of access are almost always the femoral veins, with only the rare need for arterial access. Upper extremity veins (subclavian and internal jugular veins) are often used for placement of a coronary sinus catheter that records from the left atrium and ventricle.

Venous access is gained via the Seldinger technique. A series of sheaths are placed intravenously. Through those sheaths the appropriate number of multipolar electrode catheters are positioned under fluoroscopy in standard locations in the heart. Between 2 and 4 catheters can be used for an EPS, depending on the clinical scenario. Standard catheter positions include the high lateral right atrium, the His bundle position, and right ventricular apex (Fig. 22.1). A complete ventricular stimulation protocol also includes the repositioning of the right ventricular catheter in the right ventricular outflow tract- below the pulmonic valve. If the EPS is designed to specifically diagnose or induce supraventricular arrhythmias, an additional multipolar catheter is usually positioned within the coronary sinus-accessed from the right atrium. Access to the left atrium and left ventricle, when required, may be achieved via a transseptal puncture of the intra-atrial septum from the venous approach and right atrium, or retrograde across the aortic valve via the femoral artery and aorta.

A basic EPS consists of a standard protocol that assesses baseline characteristics of the conduction system followed by attempted induction of arrhythmias. EPS begins with the measurement of baseline conduction intervals beginning with those on the surface electrocardiogram such as PR interval, and QRS width, and includes the intra-cardiac intervals measuring the time for conduction from the atrium to the His bundle deflection (AH interval), and from the His bundle deflection to the ventricular activation deflection (HV interval) (Fig. 22.2).

Pacing maneuvers are employed to assess sinoatrial (SA) node function and conduction properties from the atrium to ventricle (AV con-

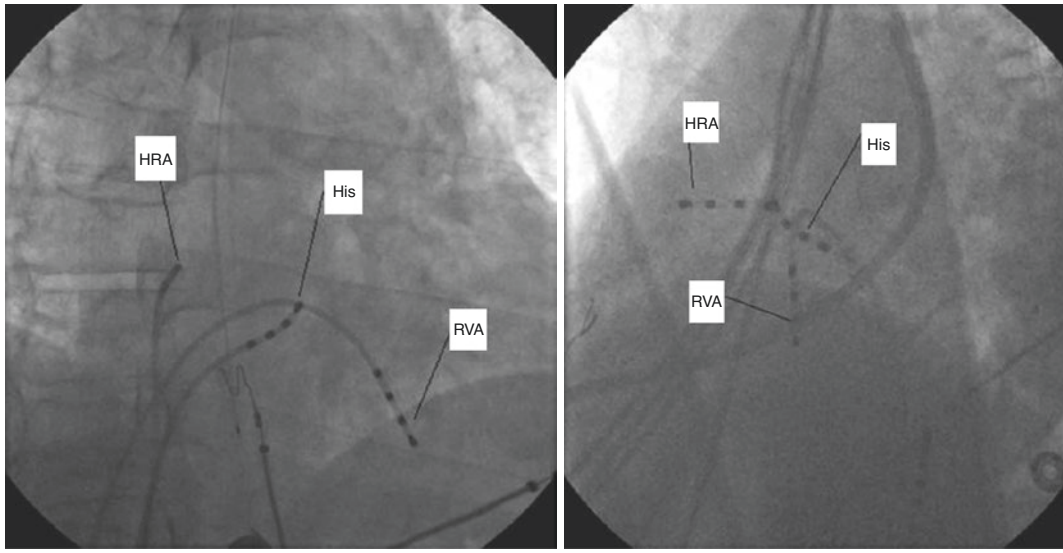

Fig. 22.1 AP and Lateral views of cardiac silhouette with 3 diagnostic (quadripolar) catheters placed in the high right atrium (HRA), across the tricuspid annulus for His bundle recording (His), and in the right ventricular apex (RVA)

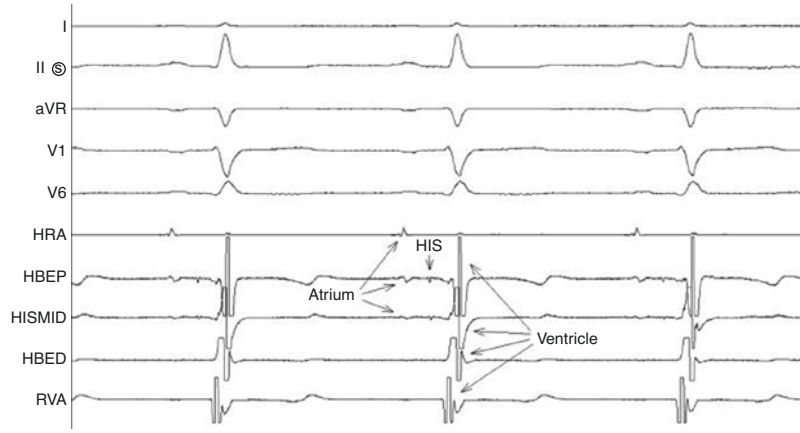

Fig. 22.2 Recording of sinus rhythm during an electrophysiology study. The top 6 tracing are from the surface electrocardiogram, the next 5 lines are intra-cardiac recordings from the high right atrium (HRA), proximal His bundle (HBEP), mid His bundle (HISMID), distal His bundle (HBED) and right ventricular apex (RVA). The recording speed is 50 mm/sec. The deflections on the individual catheters are labeled as atrium, His bundle, and ventricle, corresponding to sensed depolarization of each structure

duction), from the ventricle back to the atrium (VA conduction), and of the atrio-ventricular node (AVN) including the rate at which the AVN displays both antegrade and retrograde Wenkebach and 2:1 conduction block. Introduction of premature atrial stimuli is performed in a standard fashion (S1–S4) to further define the arrhythmogenic substrate (dual AVN pathways; accessory pathways), and to expose various forms of SVT's (AV nodal reentry, AV reentry, atrial arrhythmias). These pacing maneuvers also help to define the refractoriness of the AV node, and to characterize the antegrade conduction properties of an existing accessory pathway. Similar maneuvers are performed from the ventricle(s) to characterize ventricular conduction and detect ventricular arrhythmias (VT, VF)).

Various pacing maneuvers are performed in a variety of locations to induce supraventricular or ventricular tachycardia. Extra-stimuli are delivered in increasing numbers (S2–S4) and prematurity after a drive train of 8 beats (S1) from multiple sites (RA, RVA, RVOT, +/− CS/LA) in an attempt to induce an arrhythmia. The administration of drugs such as epinephrine, isoproterenol, atropine or Pronestyl is often added to standard induction protocols to increase the chance of induction or block. Optimal therapy (drug, ablation, or device) can be planned based on the arrythmia or conduction block identified. Hemostasis is achieved with manual pressure at the end of the procedure after the catheters and sheaths are removed.

Data Interpretation

An electrophysiology study provides a wealth of data to guide diagnosis and treatment of patients with arrhythmias. For example:

– Abnormal sinus node function indicated by a long sinus node recovery time (the interval

following atrial pacing after which the sinus node fires) in combination with unexplained syncope is an indication for a permanent pacemaker.
- A prolonged HV interval (≥100 msec), or easily induced block in the His-Purkinje system (infra-Hisian) is a relative indication for a permanent pacemaker as it predicts a high likelihood of progressing to high degree AV block.
- The presence of two AV nodal pathways with atrial pacing maneuvers suggests AV nodal reentry tachycardia as the etiology of a supraventricular arrhythmia in symptomatic patients.
- Induction of monomorphic VT in a patient with unexplained syncope identifies a cause for the syncope, and an indication for an ICD.

The reproducible induction of a supraventricular tachycardia in the electrophysiology laboratory allows for a variety of pacing maneuvers to be performed during the tachycardia. These maneuvers in combination with the initiation and termination characteristics of the arrhythmia allow for an exact diagnosis of the arrhythmia by careful analysis of the intracardiac recordings. Most supraventricular tachycardias are amenable to relatively safe and effective ablation procedures, which can be performed in the same session. Atrial flutter, AV nodal reentry tachycardia, atrioventricular reciprocating tachycardia (WPW), and atrial tachycardia are examples of supraventricular tachycardias that can be cured with ablation.

Ventricular tachycardias may be characterized and identified by their location, morphology, rate, and induction characteristics. Sustained monomorphic ventricular tachycardia is a more specific finding than polymorphic ventricular tachycardia or ventricular fibrillation. Specificity is greatest with induction at the right ventricular apex with low number of slower extrastimuli. The specificity decreases as the number and rapidity of extrastimuli increase. Localization of the tachycardia via 3-D mapping techniques allows for the ablation of stable VT's in appropriate ablation candidates.

Complications

Bleeding and hematoma formation either superficially or in deep tissue (retroperitoneum) is a potential complication of EPS. Venous thromboembolism (DVT/PE) occurs in approximately 0.05% of EPS procedures. The risk of arterial thromboembolism (peripheral arterial embolus, CVA) increases when catheters are placed in the left atrium or left ventricle making anticoagulation necessary during the procedure. Cardiac tamponade as a result of cardiac perforation by electrode catheters occurs in approximately 0.08% of studies but is higher if ablation is performed. The risk of death from EPS is rare despite the routine induction of life-threatening arrhythmias, as the response to such events in such a controlled setting results in a rapid effective response.

Clinical Vignettes

Case 1 *A 76-year-old man presented with recurrent syncope, and a left bundle branch block on ECG. EPS revealed block below the bundle of His (Fig. 22.3). A permanent pacemaker was implanted, and his syncope did not recur.*

Case 2 *A 62-year-old man with a remote myocardial infarction, reduced left ventricular ejection fraction (40%), presented with recurrent syncope. Ventricular tachycardia was induced during an electrophysiology study (Fig. 22.4). An ICD was implanted, and he subsequently received appropriate shocks for ventricular arrhythmias.*

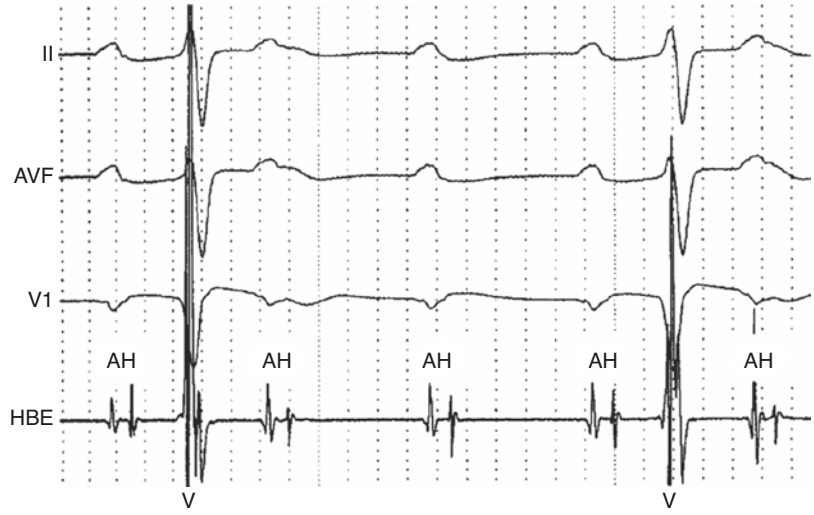

Fig. 22.3 Electrophysiology study recording of a patient with syncope and infra-Hisian heart block. The first three tracings are surface leads, HBE is the electrogram recorded at the His bundle. An A (atrial) deflection is followed on each occasion by an H (His) deflection. Only the first and fourth atrial impulse conduct to the ventricle signified by V. The remainder of the atrial impulses block at the infra-Hisian level

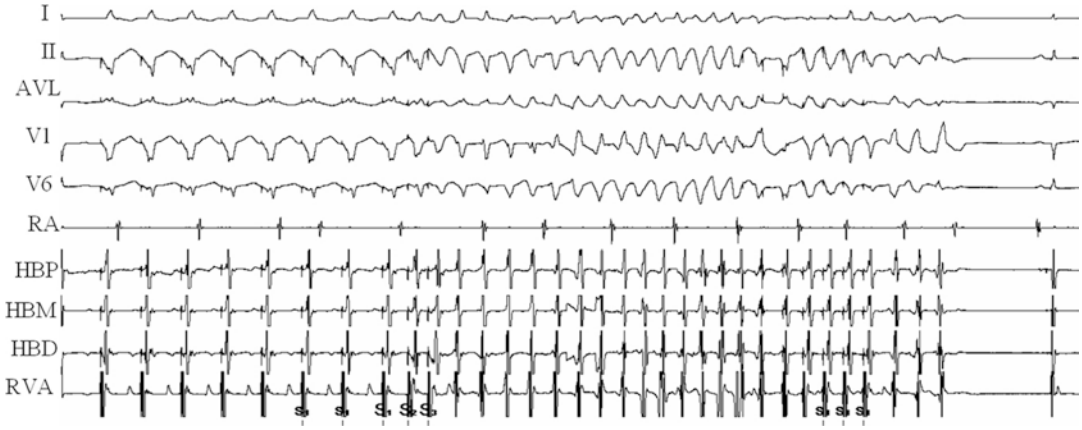

Fig. 22.4 Tracing from an electrophysiology study during induction of ventricular tachycardia with double extra-stimuli (S1, S2, S3). The first 5 recordings are surface ECG, followed by RA (right atrium), HBP (His bundle proximal), HBM (His bundle mid), HBD (His bundle distal) and RVA (RV apex). The first 8 QRS complexes result from ventricular pacing (S1), followed by 2 premature stimuli (S2, S3), which induced ventricular tachycardia. Rapid ventricular pacing (S1- S1) terminates the tachycardia

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Temporary Transvenous Pacing

23

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Indications

Temporary cardiac pacing is generally indicated for the acute management of serious and often symptomatic bradyarrhythmias, that are refractory to medical therapy [1]. Several approaches to temporary pacing are available, including transvensous, transcutaneous, epicardial, or transesophageal. Compared to the other modalities, the transvenous approach is the most stable and readily available option, with the unique ability for selective atrial or ventricular pacing. Conversely, this approach is associated with a variety of complications, and its safe and effective use requires considerable knowledge and technical skill.

Conduction disturbances may be observed in acute myocardial infarction (AMI) and are usually related to the extent of myocardial ischemia/infarction, location of infarction, the degree of vagal tone and coronary perfusion to the atrioventricular/sinus node. Generally, temporary pacing should be performed in any patient with AMI and a bradycardia (either related to sinus node disease (SND) or atrioventricular block) associated with symptoms or hemodynamic compromise (class I). Second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, alternating bundle branch block, or third-degree atrioventricular block (persistent or infranodal) is also an indication for pacing during AMI regardless of symptoms (class I). If any of the above indications persists, permanent pacing is needed. In the absence of AMI, temporary transvenous pacing is reasonable in patients with SND, second-degree/third-degree atrioventricular block who have symptoms or hemodynamic instability refractory to medical therapy (class IIa) until a permanent pacemaker is available.

Temporary transvenous pacing is also indicated in any patient presenting with acute symptomatic bradyarrhythmia refractory to medical therapy when there is a possibility of reversible/transient atrioventricular block until the resolution of the offending agent (Drug toxicity in case of beta-blocker, non-dihydropyridine calcium channel blocker or digoxin and infection such as in Lyme carditis) (class I) [1]. Temporary transvenous pacing is also used after the removal of an infected permanent pacemaker in patients who are deemed pacemaker dependent. A temporary pacemaker is placed until the infection is treated with intravenous antibiotics, after which it is replaced with a new permanent pacemaker [2]. Similarly, temporary transvenous pacing may be indicated in patients with acute endocarditis

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(especially with aortic valve involvement) who show signs of conduction disturbance (advanced AV block or new bundle branch block). In addition, prophylactic transvenous pacing may be considered during right heart catheterization or right ventricular endomyocardial biopsy in patients with existing left bundle branch block, given the associated risk of traumatic right bundle branch block during the procedure leading to complete heart block. Moreover, in patients undergoing transcatheter valve procedures, routine use of temporary pacing wire is recommended due to the high risk of conduction disturbance in the periprocedural period.

Transvenous overdrive pacing may also be useful in the management of ventricular arrhythmias. It is classified as a class IIa recommendation for recurrent ventricular tachycardia in the context of acute coronary syndrome that is resistant to antiarrhythmic medications when catheter ablation is not possible, as well as for increasing the heart rate to suppress recurrent torsades de points in the setting of acquired QT prolongation and bradycardia (Class I) [3, 4].

Contraindications

The only absolute contraindication to temporary transvenous pacing is refusal by a competent patient. Relative contraindications include a bleeding diathesis that cannot be corrected for safe placement of a temporary transvenous pacer. A decision regarding temporary transvenous pacing depends on the specific clinical situation including the nature of the underlying arrhythmia and availability of other temporary pacing modalities (e.g., transcutaneous or transesophageal). The presence of a mechanical tricuspid valve also precludes the safe placement of a right ventricular temporary pacer although in these situations left ventricular pacing via the coronary sinus may be considered.

Equipment

Temporary transvenous pacing is usually performed in the cardiac catheterization laboratory. It is done through intravenously placed catheter electrodes (leads) that are in direct contact with the endocardium. Pacing leads are connected to an external generator providing electrical current pulses to stimulate the myocardium. Pacing leads are most commonly bipolar in configuration in which both the cathode (negative pole) and anode (positive pole) are intracardiac near the tip of the lead. Unipolar configuration can also be used, in which one pole, typically the anode, is extracardiac. Pacing leads are either flexible with an inflatable balloon near the tip to direct flow, or semi-rigid without a flow-directing balloon. Semi-rigid catheters are easier to manipulate and can have preformed distal curvatures for easier manipulation and positioning. Once positioned, the lead is connected to an external generator through which pacing rate and mode, sensitivity, and current output can be adjusted. Alternatively, a permanent screw-in pacing lead can be introduced and then attached to a permanent pacing generator that is securely positioned outside the body. This temporary arrangement provides the most lead stability, and allows for prolonged pacing and safe patient ambulation. For any patient in which temporary pacing may be needed for a prolonged period of time (i.e., while treating an infected pacemaker) a permanent screw-in lead is a reasonable option to pursue. This arrangement is also preferable for atrial pacing.

Technique

As with any procedure involving transvenous insertion of a foreign body, standard sterile techniques should be followed. An external defibrillator with pacing capabilities should be present in the room during lead insertion or manipulation. The right internal jugular vein provides the most rapid and direct route for proper transvenous pacing lead positioning. Subclavian venous access can be used, but carries the added risk of a pneumothorax and injury to the subclavian artery, and is typically saved for a future permanent pacemaker should the patient need one. Femoral vein access can also be used, but carries the added risk of venous thrombosis and a potentially higher infection rate. For positioning in the right atrium, a J-curve configuration is typically used, and the

lead is typically advanced to the level of the tricuspid valve, and then withdrawn back gently until it hooks on the right atrial appendage. For right ventricular positioning, the lead is advanced through the tricuspid valve either directly with the tip first, or after formation of a loop in the right atrium under fluoroscopy, which is then advanced through. Once in the right ventricle, gentle advancement and torque is required to reach the apex (counter-clockwise torque if coming in from the superior vena cava, or clockwise if from the inferior vena cava). Once the lead is positioned, appropriate sensitivity and output are confirmed (see below), then the lead is sutured to the skin, and covered with sterile dressing.

Ideally, lead advancement is performed under fluoroscopic guidance to ensure appropriate positioning and minimize risk of cardiac perforation. However, electrocardiographic guidance can be used, whereby the lead is connected to an ECG while being advanced. A large ventricular electrogram indicates presence in the ventricle, while development of ST segment elevation indicates contact with ventricular endocardium. Pacing leads can also be advanced under echocardiographic guidance utilizing the apical or subxiphoid windows for best visualization of the right atrium and ventricle. Under emergency conditions, a pacing lead can be advanced blindly while connected to a generator set to highest output until ventricular capture (paced QRS) is seen. Electrocardiographically, a paced QRS originating from the right ventricular apex should have a left bundle branch block morphology with superior axis. A right bundle branch morphology most commonly indicates pacing from the coronary sinus or left ventricle (i.e., perforation into the left side). Regardless of the guidance modality used, a chest x-ray should be obtained in all patients after a temporary transvenous pacer to ensure appropriate positioning.

Data Interpretation

The term "sensitivity" as used for cardiac pacing relates to the amplitude (often in millivolts, mV) of the P wave or R wave as seen by the intracardiac electrode in the atrium or ventricle respectively. Sensing threshold (the amplitude above which intrinsic activity is not detected) can be determined by setting the pacemaker to a rate lower than the intrinsic rate, and then lowering the sensitivity (increasing the amplitude on the mV scale) until pacing occurs. Pacing occurs at the sensing threshold because the pacemaker does not "see" the intrinsic beat. Sensitivity is then set at 25–50% of the sensing threshold. High amplitude is desired (>1 mV for P wave, and >5 mV for R wave), to allow for a comfortable sensitivity safety margin at which the pacemaker can reliably sense intrinsic activity without running the risk of sensing low amplitude "noise" (i.e., oversensing). Pacing (output) threshold can be determined by setting the pacemaker to a rate higher than the intrinsic rate at low output, and then increasing the output current gradually until myocardial capture (pacing spike followed by a QRS complex) occurs. Optimal pacing threshold is less than 1 milliampere (mA). Output is typically set at 3–5 times the pacing threshold to allow for any temporal changes in pacing threshold. Both sensing and pacing thresholds should be checked daily and sensitivity and output changed accordingly.

Complications

Complications are common in patients undergoing temporary pacing though their rate has decreased since the introduction of this modality [5]. These complications are often related to obtaining and maintaining venous access, intracardiac catheter manipulation and retaining an intravascular foreign body [6]. In addition, these leads can perforate the myocardium at any time after insertion. Risks specific to venous access include bleeding, vascular arterial injury, pneumothorax (with subclavian or internal jugular access), air embolism, cardiac perforation including tamponade, pericarditis, and venous thrombosis/thrombophlebitis (more common with femoral vein approach). Using balloon floating electrode catheters and fluoroscopy can reduce such complications. Intracardiac catheter manipulation carries the risk of inducing atrial or ventricular tachyarrhythmias. While bacteremia can

be demonstrated in many patients with temporary transvenous pacers, clinical infection (including sepsis) is much less common occurring in <5% of patients. The most common complication is related to the catheter itself with loss of capture estimated in 10–37% of cases [1, 5].

Clinical Vignettes

Case 1 *A 50 year old woman with diabetes mellitus and hypertension was noted to be bradycardic with a heart rate of 40 beats per minute during a routine colonoscopy. An electrocardiogram demonstrated complete heart block. She reported an episode of syncope 1 week prior. Given her risk factor profile, work up for coronary disease and structural heart disease was ordered.*

While awaiting the ordered workup and given her recent syncope, a temporary transvenous pacer with a screw in lead was placed through a right internal jugular venous approach (Fig. 23.1). A dipyridamole myocardial perfusion scan was normal, and a transthoracic echocardiogram revealed no structural heart disease with a left ventricular ejection fraction of 60%. A new left sided permanent dual chamber pacemaker system was placed through a left subclavian venous approach (Fig. 23.2a, b) and the temporary pacer was removed.

Case 2 *An 84 year old female with hypertension and dyslipidemia presented with acute pulmonary edema and respiratory distress requiring intubation. Her electrocardiogram showed anterior Q waves in leads V1–V5. A transthoracic echocardiogram showed a left ventricular ejection fraction of 30%. The patient was noted to have intermittent episodes of complete heart*

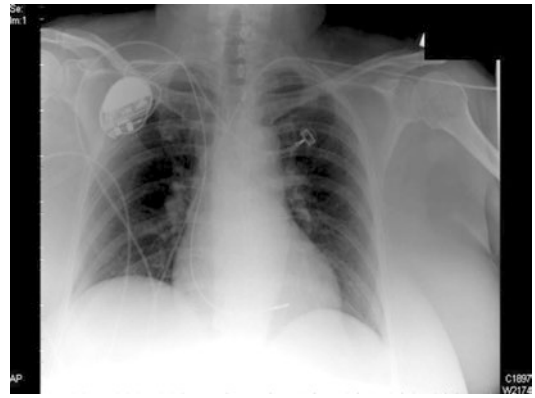

Fig. 23.1 Temporary transvenous screw-in pacing lead is seen placed through right internal jugular vein. The generator (outside the body) is seen next to the right shoulder

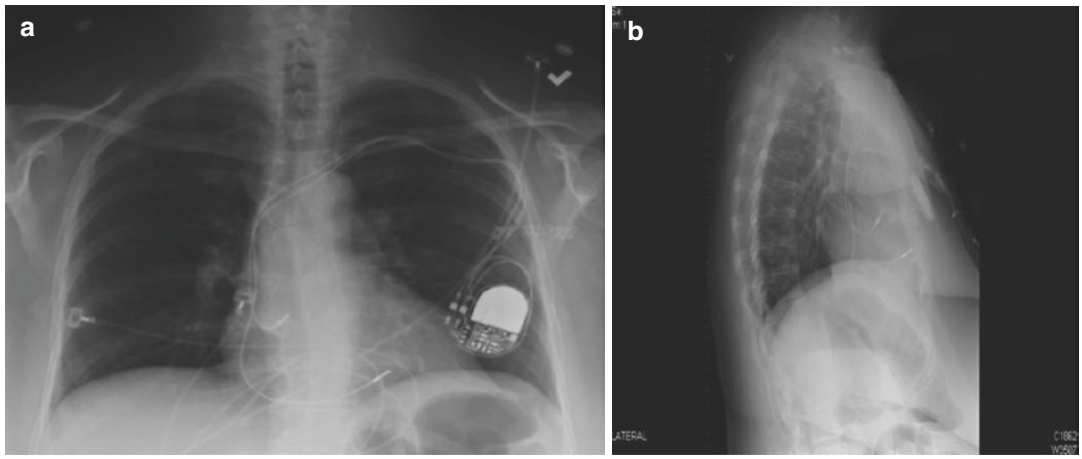

Fig. 23.2 (**a, b**) PA (2A) and lateral (2B) chest radiographs. The temporary pacer has been removed and a new permanent dual chamber pacemaker through the left subclavian vein is in place. Note the anterior orientation of both pacing leads indicating appropriate positioning. A posterior orientation of the ventricular lead would indicate placement in the coronary sinus

block with a wide QRS complex escape rhythm around 30 beats per minute.

A temporary non-screw in pacing lead was placed urgently through a left subclavian approach (Fig. 23.3). Because of recurrent fevers, and in anticipation of a prolonged hospitalization, a new temporary screw-in lead connected to an external generator was placed through the right internal jugular vein, and the old non-screw in lead removed (Fig. 23.4). Once her infection was treated, a permanent pacemaker was placed and the temporary one removed.

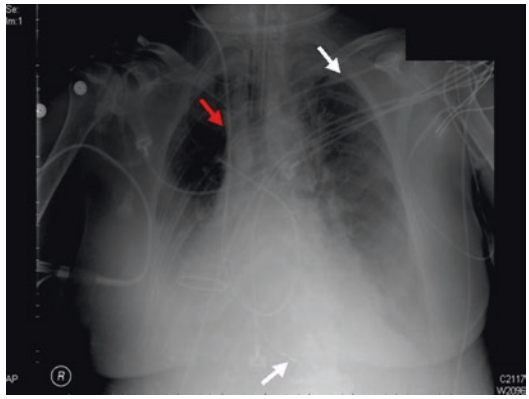

Fig. 23.3 Temporary transvenous non-screw-in pacing lead is seen placed through the left subclavian vein (*white arrow*). A pulmonary artery catheter is also seen placed through the right internal jugular vein (*red arrow*)

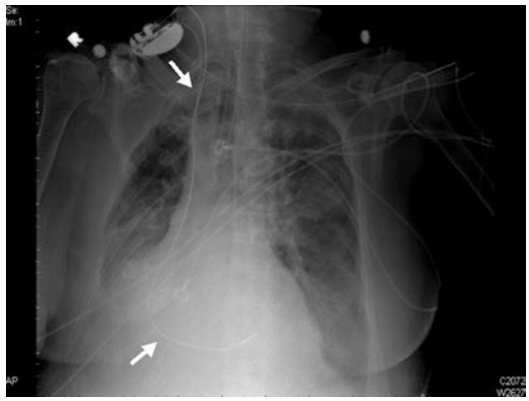

Fig. 23.4 The temporary non-screw in pacer has been removed and a new screw-in lead is seen (*white arrows*) placed through the right internal jugular vein and attached to an external generator

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Cardiac Pacemakers

24

Constancia F. C. Macatangay

Introduction

A single chamber pacemaker is a device wherein one pacing lead is implanted in either the right atrium or right ventricle. Recently, there has been a type of single chamber right ventricular pacemaker which does not involve any lead and is directly implanted into the heart, called leadless pacemaker. A dual chamber pacemaker has two pacing leads, one in the right atrium and one in the right ventricle, this is the most commonly used type of pacemaker. The right ventricular pacing component of the dual chamber pacemaker is further subdivided into three different types: the traditional right ventricular myocardial (apex or septal location) pacing, and the other two involve pacing of the conduction system (His bundle and left bundle branch). Biventricular pacemaker or cardiac resynchronization therapy (CRT) is a device wherein in addition to single- or dual-chamber right heart pacing leads, a third lead is advanced to the coronary sinus for left ventricular epicardial pacing. In patients with left ventricular ejection fraction between 36 and 50% and atrioventricular block, who have an indication for permanent pacing and are expected to require ventricular pacing >40% of the time, techniques that provide more physiologic ventricular activation (e.g. CRT therapy or His bundle pacing) are preferred to right ventricular pacing to prevent heart failure.

Indications

It is mandatory to assess the association of symptoms with the bradyarrhythmia. Direct correlation between the two will increase the likelihood that the pacemaker therapy would result in clinical improvement. A careful history taking and documentation of cardiac rhythm, with either an electrocardiogram or ambulatory monitoring, should be done. There is a wide range of symptoms that may accompany bradyarrhythmia, it may be dizziness, lightheadedness, syncope or presyncope, fatigue, or poor exercise tolerance.

The most common indications for permanent pacemaker implantation are sinus node dysfunction (SND) and high-grade or symptomatic atrioventricular (AV) block. SND refers to abnormalities in sinus node and atrial impulse formation and propagation. It is primarily a disease of the elderly and is thought to be due to senescence of the sinus node and atrial muscle. SND encompasses a wide array of abnormalities which include: persistent sinus bradycardia and chronotropic incompetence (defined as failure to achieve 80% of age-

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predicted maximal heart rate), paroxysmal or persistent sinus arrest with replacement by subsidiary escape rhythms in the atrium, AV junction, or ventricular myocardium, and "tachy-brady syndrome". In SND, there is no established minimum heart rate or pause duration where permanent pacing is recommended. The current recommendation still lies on the mandatory establishment of temporal correlation between symptoms and bradycardia as the key to determine whether permanent pacing is needed.

Type II second-degree AV block is characterized by fixed PR intervals before and after blocked beats and is usually associated with a wide QRS complex. The level of conduction block is usually infranodal (either intra- or infra-His), especially when the QRS is wide, and typically indicates diffuse conduction system disease. Prognosis is compromised and progression to third-degree AV block is common and sudden. Third-degree AV block (complete heart block) is defined as absence of AV conduction. In patients with acquired second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block not caused by reversible or physiologic cause, permanent pacing is recommended regardless of symptoms.

The 2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac conduction delay has subcategorized pacing indications into those who have SND, AV block, and conduction disorders with 1:1 atrioventricular conduction and normal PR interval (bundle branch block or fascicular block). Please refer to Tables 24.1, 24.2, and 24.3 for a full listing of all the indications. Please refer to Table 24.4 for the different types of cardiac pacemakers for a specific type of conduction abnormality.

Table 24.1 Recommendations for Permanent Pacing for Management of Bradycardia Attributable to SND [1]

Indication	Strength of indication
In patients with symptoms that are directly attributable to SND, permanent pacing is indicated to increase heart rate and improve symptoms	Class I
In patients who develop symptomatic sinus bradycardia as a consequence of guideline-directed management and therapy for which there is no alternative treatment and continued treatment is clinically necessary, permanent pacing is recommended to increase heart rate and improve symptoms	Class I
In patients with tachy-brady syndrome and symptoms attributable to bradycardia, permanent pacing is reasonable to increase heart rate and reduce symptoms attributable to hypoperfusion	Class IIa
In patient with symptomatic chronotropic incompetence, permanent pacing with rate-responsive programming is reasonable to increase exertional heart rates and improve symptoms	Class IIa
In patients with symptoms that are likely attributable to SND, a trial of oral theophylline may be considered to increase heart rate, improve symptoms, and help determine the potential effects of permanent pacing	Class IIb

Table 24.2 Recommendations for Permanent Pacing for Management of Atrioventricular Block [1]

Indication	Strength of indication
In patients with acquired second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, or third-degree atrioventricular block not attributable to reversible or physiologic causes, permanent pacing is recommended regardless of symptoms	Class I
In patients with neuromuscular diseases associated with conduction disorders, including muscular dystrophy (eg, myotonic dystrophy type 1) or Kearns-Sayre syndrome, who have evidence of second-degree atrioventricular block, or an HV interval of 70 ms or greater, regardless of symptoms, permanent pacing, with additional defibrillator capability if needed and meaningful survival of greater than 1 year is expected,is recommended	Class I
In patients with permanent AF and symptomatic bradycardia, permanent pacing is recommended	Class I
In patients who develop symptomatic atrioventricular block as a consequence of guideline-directed management and therapy for which there is no alternative treatment and continued treatment is clinically necessary, permanent pacing is recommended to increase heart rate and improve symptoms	Class I
In patients with an infiltrative cardiomyopathy, such as cardiac sarcoidosis or amyloidosis, and second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, permanent pacing, with additional defibrillator capability if needed and meaningful survival of greater than 1 year is expected is reasonable	Class IIa
In patients with lamin A/C gene mutations, including limb-girdle and Emery-Dreifuss muscular dystrophies, with a PR interval greater than 240 ms and LBBB, permanent pacing, with additional defibrillator capability if needed and meaningful survival of greater than 1 year is expected, is reasonable	Class IIa
In patients with marked first-degree or second-degree Mobitz type I (Wenckebach) atrioventricular block with symptoms that are clearly attributable to the atrioventricular block, permanent pacing is reasonable	Class IIa
In patients with neuromuscular diseases, such as myotonic dystrophy type 1, with a PR interval greater than 240 ms, a QRS duration greater than 120 ms, or fascicular block, permanent pacing, with additional defibrillator capability if needed and meaningful survival of greater than 1 year is expected, may be considered	Class IIb

Table 24.3 Recommendations for Permanent Pacing for Management of Conduction Disorders (With 1:1 Atrioventricular Conduction and Normal PR Intervals) [1]

Indication	Strength of indication
In patients with syncope and bundle branch block who are found to have an HV interval 70 ms or greater or evidence of infranodal block at EPS, permanent pacing is recommended	Class I
In patients with alternating bundle branch block, permanent pacing is recommended	Class I
In patients with Kearns-Sayre syndrome and conduction disorders, permanent pacing is reasonable, with additional defibrillator capacity if appropriate and meaningful survival of greater than 1 year is expected	Class IIa
In patients with Anderson-Fabry disease and QRS prolongation greater than 110 ms, permanent pacing, with additional defibrillator capability if needed and meaningful survival of greater than 1 year is expected, may be considered	Class IIb
In patients with heart failure, a mildly to moderately reduced left ventricular ejection fraction (36–50%), and LBBB (QRS > =150 ms), CRT therapy may be considered	Class IIb
In asymptomatic patients with isolated conduction disease and 1:1 atrioventricular conduction, permanent pacing is not indicated (in the absence of other indications for pacing)	Class III

Table 24.4 Permanent Pacing Techniques and Methods for Management of Bradycardia Attributable to Atrioventricular Block [1]

Indication	Strength of indication
In patients with SND and atrioventricular block who require permanent pacing, dual chamber pacing is recommended over single chamber ventricular pacing	Class I
In select patients with atrioventricular block who require permanent pacing in whom frequent ventricular pacing is not expected, or who have significant comorbidities that are likely to determine clinical outcomes and that may limit the benefit of dual chamber pacing, single chamber ventricular pacing is effective	Class I
For patients in sinus rhythm with a single chamber ventricular pacemaker who develop pacemaker syndrome, revising to a dual chamber pacemaker is recommended	Class I
In patients with atrioventricular block who have an indication for permanent pacing with a left ventricular ejection fraction between 36 and 50% and are expected to require ventricular pacing more than 40% of the time, it is reasonable to choose pacing methods that maintain physiologic ventricular activation (eg, cardiac resynchronization therapy/CRT or His bundle pacing) over right ventricular pacing	Class IIa
In patients with atrioventricular block who have an indication for permanent pacing with a left ventricular ejection fraction between 36 and 50% are expected to require ventricular pacing less than 40% of the time, it is reasonable to choose right ventricular pacing over pacing methods that maintain physiologic ventricular activation (eg, CRT or His bundle pacing)	Class IIa
In patients with permanent or persistent AF in whom a rhythm control strategy is not planned, implantation of an atrial lead should not be performed.	Class III

Contraindications

Once it has been established that the bradycardia or a conduction disorder warrants permanent pacing, there are a few contraindications for the actual permanent pacemaker insertion. These include local infection at implantation site and/or active systemic infection with bacteremia.

In general, pacemakers are not indicated for asymptomatic patients. Symptoms due to sinus node dysfunction have to occur during the documented episodes of bradycardia. It is of utmost importance to assess for the etiology of the bradycardia: bradyarrhythmia due to a non-essential drug therapy would require drug therapy cessation, and if due to reversible cause (e.g., Lyme disease, increased vagal tone, hypoxia in sleep apnea syndrome in absence of symptoms), would require treatment of underlying cause. Finally, an appropriate diagnosis of the type or level of block is mandatory. Asymptomatic first degree, type I second degree AV block at the supra-His (AV node) level, and fascicular block without AV block, do not need a pacemaker.

Equipment

The basic equipment required for a permanent pacemaker insertion includes: fluoroscope, topical anesthesia (1–2% lidocaine or bupivacaine), instrument tray, pacing system analyzer, introducer kit, suture material, electric cautery, external pacemaker, antimicrobial flush and saline for pocket irrigation. A single-plane fluoroscopy using anteroposterior, right anterior oblique, and left anterior oblique views is used. A pacemaker system consists of two major components: a pulse generator and one or more electrodes (Fig. 24.1). The pulse generator is the "battery" component of the pacemaker and it provides the electrical impulse for the myocardial stimulation. The electrodes, also known as "leads" (Fig. 24.2), deliver the electrical impulse from the generator to the myocardium. Currently, the most common cardiac pacing system utilizes transvenous electrodes (leads). However, there are certain clinical situations wherein transvenous leads are not possible (i.e., infection, venous thrombosis/stenosis). In these situations, the epicardial or leadless pacing systems (Fig. 24.3) may be considered. A full discussion of these types of pacing system is beyond the scope of this chapter.

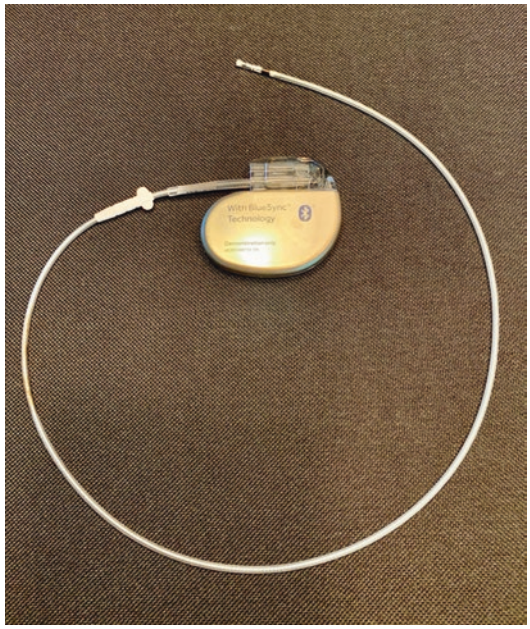

Fig. 24.1 Example of a pacemaker generator and lead

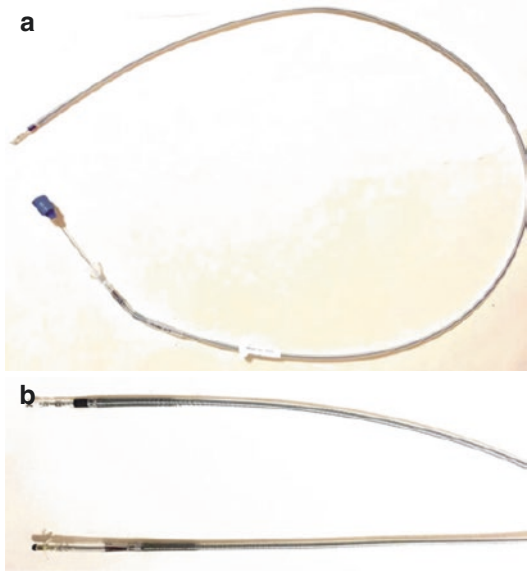

Fig. 24.2 (**a**) Example of an intravenous lead. (**b**) Two types of lead tips: helical screw (*above*) and grappling hook (*below*)

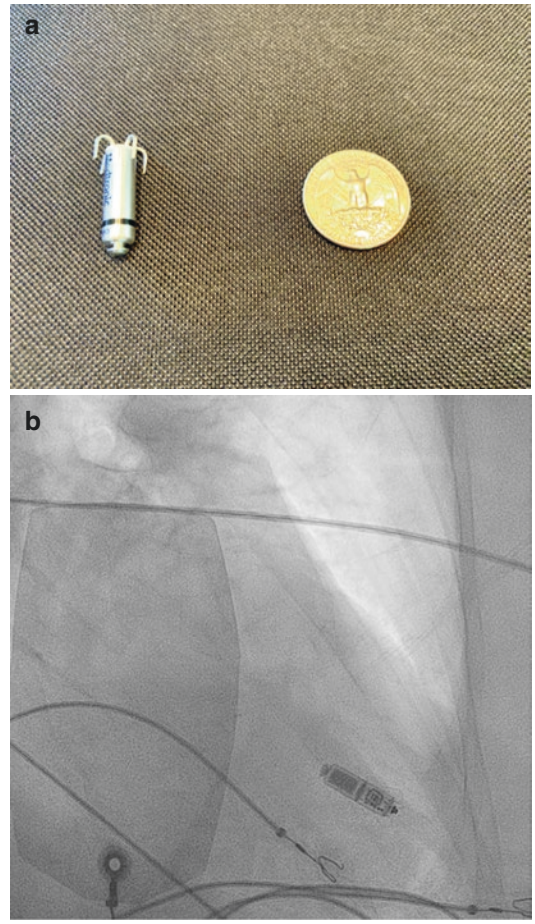

Fig. 24.3 (**a**) Example of a leadless pacemaker (*pictured in reference to size of a quarter coin)* (**b**) Fluoroscopic RAO view of an implanted leadless pacemaker

Technique

Pacemaker implantation usually involves a combination of local anesthesia and conscious sedation. The pacing generator is typically placed subcutaneously, superficial to the pectoralis, however, under certain conditions, it may also be placed subpectoral/infra-mammary, or intra-abdominal (i.e., surgically via thoracotomy).

Antibiotic prophylaxis, either with cefazolin or vancomycin, is a standard for device implantation. A central vein: subclavian, internal jugular, or axillary vein, is access via percutaneous approach. A venous cut down of the cephalic vein may also be done. After venous access is obtained, a guidewire is advanced and subsequently, a sheath and dilator are advanced. The pacemaker lead is then advanced to the chamber of interest (i.e., right atrium, right ventricle). Usually, the ventricular lead is positioned before the atrial lead to prevent its dislodgment.

Once the correct lead positioning is confirmed, lead is affixed to the endocardium either passively with tines (grappling hook) or actively via a helical screw located at the tip (Fig. 24.2). Pacing and sensing thresholds and lead impedances are measured with the pacing system analyzer. Pacing is also performed at 10 V to assess for diaphragmatic stimulation. After confirmation of lead position and threshold, the proximal end of the lead (s) is then secured to the underlying tissue and connected securely to the pulse generator. The pacemaker pocket is usually irrigated with antimicrobial solution. The incision is closed in layers with absorbable sutures and skin with either adhesive strips or skin glue. An arm sling is applied to the unilateral arm for 12–24 h to limit movement. A post-procedure chest radiograph is usually done for lead position confirmation and to rule out pneumothorax (Fig. 24.4). On the following day, postero-anterior (PA) and lateral chest radiographs will again be done to confirm lead positions and exclude any delayed pneumothorax.

Leadless pacemaker insertion, however, is usually performed under general anesthesia or monitored anesthesia care (MAC). The pacemaker is deployed into the right ventricle via catheter through a long sheath inserted into the femoral vein.

Data Interpretation

A universal pacing code system, also known as NBG pacemaker code, is used to facilitate the understanding of pacemakers. It describes the five-letter code for operation of implantable pacemakers and defibrillators.

- **Position I** reflects the chamber (s) paced. "**A**" indicates the atrium, "**V**" indicates the ventricle, and "**D**" means dual chamber (i.e., both atrium and ventricle).
- **Position II** refers to the chamber (s) sensed. The letters are the same as those for the first position: "**A**", "**V**",or "**D**". An addition option "**O**" indicates an absence of sensing. If a device is programmed in this mode, it will pace automatically at a specific rate, ignoring any intrinsic rhythm.
- **Position III** refers to how the pacemaker responds to a sensed event. "**I**" indicates that a sensed event inhibits the output pulse and causes the pacemaker to recycle for one or more timing cycles. "**T**" indicates that the output pulse is triggered in response to a sensed event. "**D**" indicates dual modes of response and is restricted to dual chamber systems.
- **Position IV** reflects rate modulation, also known as rate adaptive or rate responsive pac-

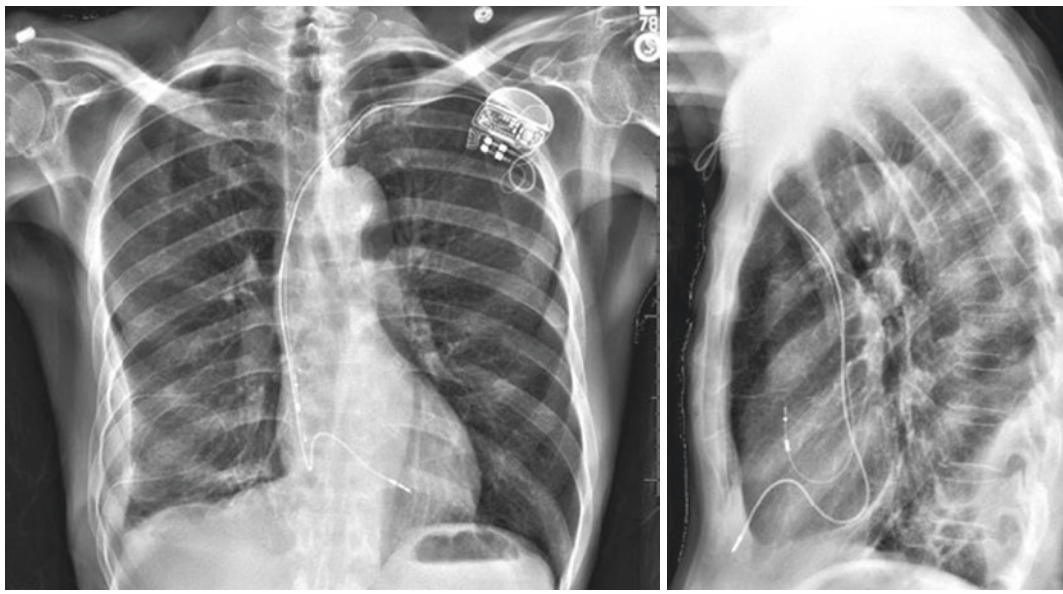

Fig. 24.4 Chest radiograph PA and lateral of a patient with dual chamber pacemaker

ing. "**R**" indicates that the pacemaker has rate modulation and incorporates a sensor to adjust its programmed paced heart rate in response to patient's activity. "**O**" indicates that rate modulation is either unavailable or disable.

– **Position V** is rarely used and specifies only the location of multisite pacing or absence thereof. Multisite pacing is defined as stimulation sites in both atria, both ventricles, more than one stimulation site in any single chamber, or a combination of these. "**O**" indicates no multisite pacing. "**A**" means multisite pacing in the atria. "**V**" means multisite pacing in the ventricles, and "**D**" for both atrium and ventricle. The most common application of multisite pacing is biventricular pacing.

Complications

Although considered a minimally invasive procedure, the incidence of complications in modern pacing therapy is still substantial. Permanent pacemaker placement poses various risks ranging from minor to serious life-threatening complications. These complications may be classified according to severity (minor or major), component of pacing system involved (lead, generator/pocket, patient), or to timing of occurrence: in-hospital or acute, sub-acute, or late.

Acute complications occur peri-procedural or in-hospital. Pneumothorax may occur in 1–3% in patients undergoing pacemaker implantation. Due to this known complication, chest radiographs are performed immediately after, and often, the day after the procedure. Vascular access complications may also occur. Direct subclavian vein punctures are associated with a higher incidence of pneumothorax and lead damage from subclavian crush syndrome. The axillary venous puncture approach and cephalic venous cut down, on the other hand, are associated with lower incidence of pneumothorax and lead damage. Myocardial perforation has been reported to occur in 1% of patients, with the asymptomatic subclinical perforation occurring to as much as 15%. Device pocket hematoma is also a common complication. It has an incidence of approximately 5%, with a higher incidence in patients on anticoagulation or antithrombotic medications. Finally, in-hospital death generally occurs in less than 1% of pacemaker implantations [2].

Subacute post-implantation complications occur after hospital discharge and less than 30 days after placement. During this period, several types of pacemaker and lead function/failures have been reported: failure to capture, failure to output, undersensing, and inappropriate pacemaker rate [2].

Late complications occur more than 30 days after placement. The most common complications include infection, device/lead advisories, lead function problems/failures, venous thrombosis or stenosis. Localized infection involving the device pocket may occur up to 60% of the patients, with the rest presenting as endovascular infection. Device malfunction leading to device explantation occurs in <1% of patients. A rise in capture threshold may occur beyond 6 weeks of implantation. As this threshold rises, it may exceed the maximum output of pulse generator. This phenomenon is called "exit block". Venous stenosis, less commonly thrombosis, has also been reported after implantation of pacing leads [2].

Clinical Vignettes

Case 1 *A 56 year old man with hypertension and dyslipidemia comes in for an annual check- up. He is feeling well, is active, denies any complaints, and runs marathon twice a year. His medications include lisinopril and atorvastatin. His resting heart rate was found to be 43 beats/min with a blood pressure of 120/75. His documented heart rate the previous year was 45 beats/min. ECG was done which shows sinus bradycardia 44 beats per minute, with normal PR and QRS intervals.*

The most important feature in this patient's history is the absence of any symptom. It is a Class III recommendation to implant a permanent pacemaker for sinus bradycardia in asymptomatic patients. ECG monitoring may be done should any symptom arise and if there is a need to

correlate it with bradyarrhythmia. Given the lack of symptoms and patient's high level of activity, pacemaker is not indicated.

Case 2 *A 75 year old woman with hypertension and coronary artery disease presented to the hospital after two episodes of syncope. She has been having palpitations and several pre- syncopal episodes for the past 3 months. Upon arrival, patient is awake and alert but complaining of shortness of breath. A rhythm strip was obtained which showed atrial fibrillation with a rapid ventricular rate of 175 beats/min. Her BP was 115/70. metoprolol 2.5 mg IV was given and patient became pre- syncopal with a heart rate of 30 beats/min and a BP of 90/60. EKG done showed sinus bradycardia 35 beats/min, with normal PR and QRS intervals. An hour later, she was again in atrial fibrillation with a ventricular rate of 170 beats/min.*

This association of paroxysmal atrial fibrillation with rapid ventricular response and sinus bradycardia, accompanied by symptom, is worrisome for a "tachy-brady syndrome", a type of sinus node dysfunction. Individuals with tachy-brady syndrome have diseased SA nodes and often display exaggerated overdrive suppression. Given the patient's symptoms and sinus node dysfunction, a pacemaker is recommended.

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Biventricular Pacing

25

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Introduction

As left ventricular (LV) systolic dysfunction progresses to clinical heart failure, it is frequently accompanied by impaired electromechanical coupling which may further impair ventricular contractility [1]. Prolonged interventricular and intraventricular conduction results in regional mechanical delay within the LV and can cause reduced ventricular systolic function, functional mitral regurgitation, and ventricular remodeling/dilation. Modification of ventricular electromechanical delay with multisite ventricular pacing (commonly referred to as biventricular [BiV] pacing or cardiac resynchronization therapy [CRT]) can improve ventricular systolic function, promote favorable ventricular remodeling, decrease heart failure hospitalizations, reduce mitral regurgitation, and reduce mortality [2, 3]. Currently, CRT is indicated for mortality reduction and symptom improvement in patients with systolic heart failure and LV dyssynchrony, as evidenced by a wide QRS complex (QRS > 150 ms) on electrocardiogram (EKG). Numerous markers of LV dyssynchrony have been described, including several echocardiographic measurements. However, the marker which best predicts outcomes following CRT is the width/morphology of the QRS complex. As such, the strength of the indication of CRT is dependent on the patient's QRS duration and morphology, as well as New York Heart Association (NYHA) heart failure classification [4].

Indications

Currently, per the most recent ACC/AHA guidelines as of 2013, the only Class I indication for CRT is for patients in sinus rhythm with a LV ejection fraction (LVEF) ≤35%, a QRS duration ≥150 ms, left bundle-branch (LBBB) morphology, and NYHA class II, III, or ambulatory IV heart failure. All patients who are being considered for CRT should undergo careful pre-implant screening which includes: evaluating comorbidities, routine labs, functional assessment, quality-of-life measurement, echocardiogram for quantification of LVEF and cardiac size, and ECG to document QRS duration and morphology. It is important to note that all these recommendations refer to patients who are already on guideline directed medical therapy [4]. Please refer to Table 25.1 for a full listing of the all the indications for CRT.

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Table 25.1 Indications for Cardiac Resynchronization Therapy

Indication	Class	Level of Evidence
Sinus rhythm, LVEF ≤35%, LBBB with a QRS duration ≥150 ms, and NYHA class II, III, or ambulatory IV symptoms, on GDMT	I	A
Sinus rhythm, LVEF ≤35%, LBBB with a QRS duration 120-149 ms, and NYHA class II, III, or ambulatory IV symptoms, on GDMT	IIa	B
Sinus rhythm, LVEF ≤35%, non-LBBB pattern with a QRS duration ≥150 ms, and NYHA class III or ambulatory IV symptoms, on GDMT	IIa	A
Atrial fibrillation, LVEF ≤35% on GDMT, 1) patient requires ventricular pacing or otherwise meets CRT criteria, and 2) AV nodal ablation or pharmacologic rate control will allow near 100% ventricular pacing with CRT	IIa	B
LVEF ≤35% and undergoing new or replacement device placement with anticipated requirement for significant (great than 40%) ventricular pacing	IIa	C
Sinus rhythm, LVEF ≤35%, non-LBBB pattern with 120-149 ms, and NYHA class III or ambulatory IV symptoms, on GDMT	IIb	B
Sinus rhythm, LVEF ≤35%, non-LBBB pattern with a QRS duration ≥150 ms, and NYHA class II symptoms, on GDMT	IIb	B
Sinus rhythm, LVEF ≤30%, ischemic etiology of heart failure, LBBB with a QRS duration of ≥150 ms, NYHA class I symptoms, on GDMT	IIb	C
CRT is not indicated for patients with comorbidities and/or frailty that limit survival to less than 1 year	III	C
CRT is not recommended for non-LBBB pattern with a QRS duration less than 150 ms, NYHA class I or II symptoms	III	B

GDMT goal directed medical therapy, *LVEF* left ventricular ejection fraction, *LBBB* left bundle branch block, *NYHA* New York Heart Association

Contraindications

There are two circumstances under which CRT carries a Class III recommendation (no benefit and may cause harm). These are patients who do not fulfill implant criteria (NYHA class I or II symptoms, non-LBBB pattern, and QRS duration <150 ms) and patients with an estimated survival of <1 year based on comorbidities and/or frailty [4].

Equipment

CRT devices, like the majority of cardiac implantable electronic devices (ICD), consist of two basic components, the pulse generator and the leads (Fig. 25.1). There are two main categories of CRT devices, BiV pacemakers and BiV ICDs. Most devices implanted are BiV ICDs, as the majority of patients who are candidates for CRT also have an indication for an ICD for primary prevention of sudden cardiac death.

CRT devices are typically larger in size when compared to standard pacemaker or ICDs. However, even the largest devices are smaller than an average deck of playing cards. The device contains two main components, the electronics that control the device function and the compact battery.

All CRT devices have at least two leads, although most have three leads. Typically, there is an atrial lead to facilitate AV synchrony, though in some circumstances this may not be necessary (chronic atrial fibrillation). By definition, these devices must have two ventricular leads. Usually, one lead is placed the right ventricular (RV) apex or elsewhere in the RV along the interventricular septum. Unique to BiV devices, is the presence of a pacing lead in the coronary sinus. The coronary sinus lead can have as many as four pacing electrodes along the lead (Fig. 25.2). This allows for multiple possible pacing vectors, to produce the most synchronous contraction of the LV.

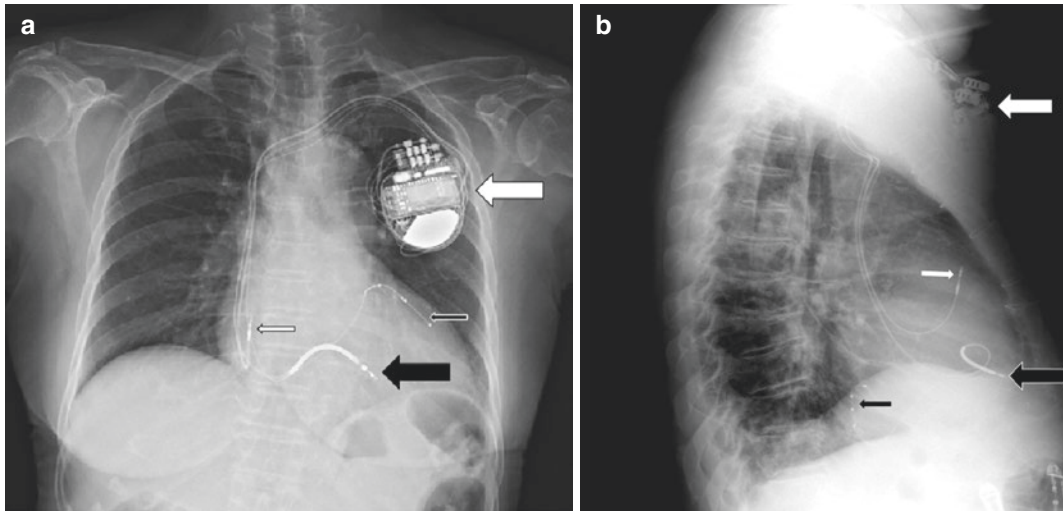

Fig. 25.1 PA and lateral radiographic images of a biventricular implantable cardioverter defibrillator. PA (Picture **a**) and lateral (Picture **b**) chest x-rays showing a biventricular implantable cardioverter defibrillator. Both images show the device (*thick white arrow*) implanted in the left chest, the atrial lead (*thin white arrow*) positioned in the right atrial appendage, the right ventricular lead (*thick black arrow*) positioned in the right ventricular apex, and the left ventricular lead (*thin black arrow*) positioned in a lateral branch of the coronary sinus

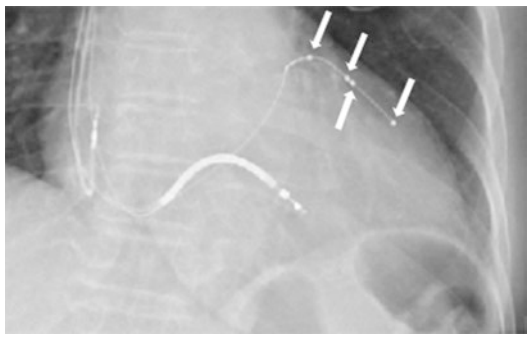

Fig. 25.2 Radiographic image of coronary sinus lead. PA chest x-ray showing a quadripolar lead implanted in a lateral branch of the coronary sinus. Note the four pacing poles marked by the *white arrows*. This allows for numerous possible pacing configurations

Technique

Placement of a CRT device involves two procedural components, creation of the pocket where the pulse generator will sit and placement of the leads. The procedure is performed in a sterile environment (either an electrophysiology laboratory or an operating room). The most common locations of the device pocket are the left and right chest. The device is typically placed prepectorally however, the device can also be placed below the pectoralis muscle if necessary (desire for better cosmetic result, etc.). Placement of the device below the pectoralis muscle results in a relative increase in the risk of post-procedure bleeding. The device can be placed in the abdomen instead of the chest wall when necessary, although this is uncommon.

Whenever possible, all leads are placed via the transvenous route. Typically, access is obtained via the axillary or subclavian vein, and the right atrial (RA) and RV leads are passed via the superior vena cava to their ultimate locations. The coronary sinus lead is typically the most challenging lead to place. First, a guiding catheter is placed via the RA into the coronary sinus. Then, a balloon-tipped catheter is advanced through the guiding catheter into the coronary sinus. With the balloon inflated in the proximal coronary sinus, a venogram of the coronary sinus is obtained. This provides anatomical information, so that the most ideal branch of the coronary sinus can be deter-

mined for lead placement. The branch which allows the most lateral location of the lead is commonly chosen. Next, a wire is advanced through the guiding catheter and positioned in the chosen coronary sinus branch. The coronary sinus lead is then advanced over the wire to its ultimate location. As with any pacing system, all leads must be tested after placement for adequate sensing, impedance, and pacing thresholds.

Occasionally, the leads cannot be placed in adequate locations for various reasons (central venous stenosis, unfavorable coronary sinus anatomy, etc.). In these circumstances, patients may require epicardial lead placement via an open, surgical approach [5].

When all the leads have been placed, they are connected to the device which is secured in the pocket and the incision is closed.

Data Interpretation

The most important response to placement of a CRT device is the patient's functional capacity. Many coronary sinus leads have multiple electrodes, and if a patient has a suboptimal response to CRT, a different pacing vector for the coronary sinus lead can be chosen. Different protocols exist for echocardiographic or SPECT guided CRT optimization. However, data on these approaches is currently limited (Fig. 25.3).

Complications

Placement of a CRT device is an invasive procedure that carries the risk of serious and possibly life-threatening complications. The most common complications include device infection and bleeding at the incision site or in the pocket. Bleeding can typically be control with the use of a pressure dressing, but occasionally large pocket hematomas require drainage. Infection is a more serious complication and compete extraction of all device components is recommended whenever possible, in addition to antibiotic therapy.

Less common complications include injury to the SVC or other major blood vessels; perforation of the RA, RV, interventricular septum, or coronary sinus; pericardial effusion; cardiac tamponade; arrhythmia; and death. Pericardial effusions can usually be treated conservatively with observation. However, if there is evidence of cardiac tamponade, percutaneous drainage is

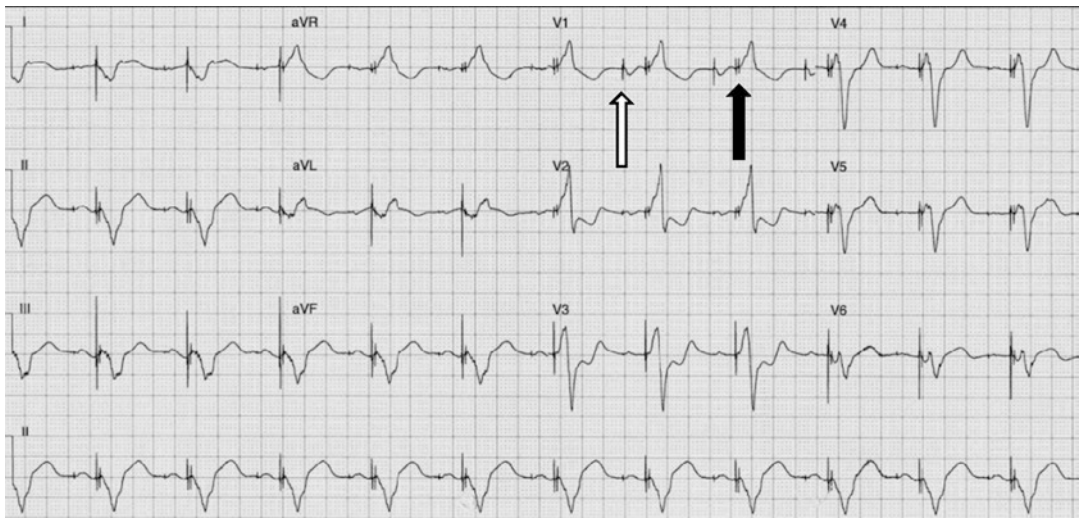

Fig. 25.3 Electrocardiography (ECG) illustrating Bi-V pacing. Atrial pacing spikes can be seen prior to the P-wave (*White arrow*). Two separate pacing spikes (*Black arrow*) can be seen prior to the QRS complex indicating pacing of both the left and right ventricle. ECG shows a monophasic negative Q-wave in Lead I and dominant R wave in V1

required. In rare cases, emergent surgery may be necessary.

Clinical Vignettes

Case 1 *A 69-year-old female with coronary artery disease, ischemic cardiomyopathy, and hypertension presents to clinic for dyspnea on exertion after one block. Her medications include daily aspirin 81 mg, atorvastatin 40 mg, furosemide 40 mg, metoprolol succinate 100 mg, spironolactone 25 mg, and sacubitril/valsartan 49/51 mg twice daily. An echocardiogram is obtained and shows an LVEF of 30%, global hypokinesis, a mildly dilated left ventricle, and moderate mitral regurgitation. Her EKG showed sinus rhythm with a LBBB and a QRS duration of 153 ms. What would be the most appropriate next step in the management of this patient?*

Cardiac resynchronization therapy (CRT) would be the next step as this patient has a Class I indication for CRT (systolic heart failure, NYHA class II or III, sinus rhythm, LBBB, QRS ≥150 ms, and EF ≤35%). In this case, the patient has NYHA class II/III symptoms in the setting of a chronic cardiomyopathy being treated with GDMT. In these patients, CRT has been shown to improve ventricular contractile function, reverse ventricular remodeling, improve LVEF, and reduce secondary mitral regurgitation. Given her reduced LVEF of <35%, she would receive a CRT with defibrillator.

Case 2 *A 45-year-old male with non-ischemic cardiomyopathy (with an ejection fraction of 40-45%) presents to the hospital with dizziness, palpitations and near syncope. During his admission, an EKG is obtained showing complete heart block. Electrophysiology is consulted for possible dual-chamber pacemaker implantation for newly diagnosed complete heart block. Would this patient benefit from CRT?*

Yes, this patient already has evidence of cardiomyopathy (EF 40-45%) and he would be expected to pace nearly 100% of the time due to complete heart block. He would be at risk of deterioration in his EF from chronic RV pacing, and this would be reasonable to consider a CRT device.

Case 3 *A 77-year-old female with nonischemic cardiomyopathy presents for evaluation with 3 months of dyspnea on exertion. She normally walks without any issues but recently noticed that she has been more short of breath when going uphill. This has slowly progressed and she now occasionally notices dyspnea when walking on flat ground. The patient denies chest discomfort, recent weight gain, orthopnea, or edema. Previous echocardiogram 1 year earlier showed a left ventricular ejection fraction (LVEF) of 35% with diffuse hypokinesis. A cardiac catheterization at that time revealed mild diffuse, nonobstructive coronary disease. She is currently on maximally tolerated goal-directed medical therapy. A repeat echocardiogram reveals an LVEF of 30%, a mildly dilated left ventricle (LV), and mild mitral regurgitation. Otherwise, there are no significant changes when compared with the prior study from 1 year earlier. An EKG is performed showing normal sinus rhythm with a left bundle branch block and a QRS duration of 167 ms.*

Cardiac resynchronization therapy (CRT) is indicated for patients who have an LVEF ≤35%, sinus rhythm, left bundle branch block (LBBB) with a QRS duration of ≥150 ms, and New York Heart Association (NYHA) class II or III symptoms or ambulatory class IV symptoms on guideline-directed medical therapy. There is echocardiographic evidence of LV dilation along with chronic cardiomyopathy. The ECG confirms an LBBB with a QRS duration of >150 ms. CRT has been shown to improve ventricular contractile function, reverse ventricular remodeling, improve LVEF, and reduce secondary mitral regurgitation. It can also improve blood pressure, allowing titration of neurohormonal antagonists that may have additional benefits.

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Pacemaker Interrogation and Programming

26

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Introduction

Pacemaker programming and interrogation is essential not only in the immediate post-implantation period, but also at regular follow-up visits throughout the life of the pacemaker. The implantation of a pacemaker follows a clinical event and it is incumbent upon the physician implanting the device to ensure that the device has met its clinical goals. Current pacemakers are endowed with a variety of features to help meet the aforementioned requirement. Hence, patients with pacemakers should be seen regularly and their pacemakers should be interrogated with each visit, at least once every 6–12 months.

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Indications

Pacemaker function post-implant should be observed on cardiac telemetry prior to discharge. In patients who are not pacemaker dependent, an electrocardiogram performed with a magnet applied against the pacemaker will elicit a pacing spike from the chamber being paced.

Following discharge, patients are often seen 1–2 weeks after the implant to assess the site of the incision. The patient will then follow-up in an outpatient setting for pacemaker interrogation in 6–12 weeks. This follow-up is important because it assesses the rise and subsequent decline in pacing thresholds. The pacemaker generator outputs can then be programmed to outputs lower than those programmed at implant. This process preserves generator battery life while providing an adequate safety margin for expected fluctuations in the pacing thresholds.

After this initial outpatient interrogation is performed, Medicare and Medicaid guidelines allow for dual chamber devices to be followed up every 6 months. Patients with single chamber pacemakers who are not pacemaker dependent may follow-up on an annual basis. During these visits, the original indications for pacemaker implant, as well as the need for modification of the existing pacemaker system should be assessed. Modifications may include the need to adjust the lower pacing rate, the upper tracking rate, or the AV interval. The activity sensor may

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need to be turned on if the patient is complaining of fatigue. The sensor parameters should be tested in the pacemaker clinic by observing the patients' heart rate response to graded activity. The development of new clinical events such as heart failure or the recovery from an acute myocardial infarction may prompt an upgrade of the pacemaker to an implantable cardioverter defibrillator (ICD) or a pacemaker capable of biventricular pacing.

Beyond routine follow up, certain events warrant interrogation of a pacemaker. Pacemaker interrogation should be performed when a clinical event has occurred that could have been cause by pacemaker malfunction, e.g. syncope, or when a clinical event can be further delineated by intracardiac electrograms that can be retrieved during pacemaker interrogation. Intra-cardiac electrograms retrieved from pacemakers can be useful in differentiating supraventricular tachycardias from ventricular tachycardias, as well as excluding arrhythmias as a source of syncope in patients with a pre-existing pacemaker.

A variety of procedures performed in the hospital may interfere with the pacemaker's normal function or may damage a pacemaker. The pacemaker should be interrogated before and after certain types of procedures are completed. Examples of such procedures include radiofrequency ablation, cardioversion, diathermy, electroconvulsive therapy (ECT) and lithotripsy. Patients scheduled for surgery who are pacemaker dependent should have their pacemakers programmed to an asynchronous mode if the use of diathermy is anticipated. This would eliminate the fear that diathermy would inhibit pacing. The patient should be continuously monitored in case asynchronous pacing induces an arrhythmia. At the time of this writing, MRI scanning in patients with pacemakers should be restricted to patients who have received pacemakers and leads that have been approved for conditional use in the MR environment. It is important for the provider ordering the MRI to confirm that the patient does not have an older, non-MRI compatible lead before proceeding with the study. If a patient with a pacemaker lacking conditional approval inadvertently has an MRI performed, the pacemaker should be promptly interrogated to determine its status.

Contraindications

Contraindications to permanent pacemaker insertion include local infection at the site of device implant and active severe infection with bacteremia. Relative contraindications include active anticoagulation therapy and severe bleeding diathesis (such as severe coagulopathy).

Equipment

Pacemaker interrogation requires company-specific device programmers. Pacemaker interrogation and programming cannot occur between products from two different device companies. Although there are several pacemaker companies (Medtronic®, Boston Scientific®, Biotronik® and Abbott/St. Jude Medical®) widely used in the US, the techniques for pacemaker interrogation and concepts for pacemaker data interpretation are similar. Each programmer is equipped with a programming head, surface ECG leads, power cord, printer, and touch-screen programmer (Fig. 26.1). Clinics where pacemaker interrogation is performed must be equipped with an external defibrillator in the rare event the patient develops a life-threatening arrhythmia.

Technique

Pacemaker interrogation can be performed in either the sitting or supine position. ECG surface leads should be connected to the patient and the programmer using the device specific electrodes. The pacemaker programming head should be placed over the patient's pacemaker. The pacemaker is usually located in either pectoral region, or rarely in the abdomen. The programming head

Fig. 26.1 Pacemaker interrogation

should be positioned in a stable manner, such that constant telemetry can be maintained between the device and programmer. Once the programmer is turned on, interrogation can then proceed. Many newer programmers have automated follow up algorithms that proceed once prompted by the operator.

Complications

Early complications related to pacemaker implantation include bleeding at the pocket site, hematoma, infection, pneumothorax (from axillary or subclavian vein access), thrombophlebitis, hemothorax, air embolism, lead dislodgement, pectoral muscle or diaphragm stimulation, and vascular and myocardial perforation. Poor lead placement may also lead to failure to sense and capture appropriately. More delayed complications include device infection, device or lead erosion, venous thrombosis, lead dislodgement, lead fracture, and device malfunction resulting in inappropriate device therapy.

Data Interpretation

Once device interrogation has occurred, baseline data should be ascertained and lead testing should be performed. This data and testing results are essential in evaluating a variety of pacemaker malfunctions. All available data should be systematically retrieved and evaluated during each pacemaker interrogation. The core of this evaluation includes battery life, lead impedances, as well as capture and sensing thresholds. The underlying rhythm of the patient, as well as lead configuration (unipolar or bipolar) should also be determined. In addition, most pacemakers have stored electrogram events that need to be retrieved and evaluated at each interrogation.

Battery Status

Pacemaker battery status should be evaluated with each interrogation. At the beginning of life (BOL) the battery voltage is approximately 2.8 V (specific values vary from manufacturer to manufacturer), and pacemaker behavior is as programmed. Over the life of the pacemaker, the battery reaches elective replacement indicators (ERI). At ERI, the battery voltage is reduced, but still able to support most if not all of the pacemaker functions. At this point, generator replacement should be scheduled in weeks to months depending upon the degree of dependence upon the pacemaker. As voltage reduces further, battery end of life (EOL) is reached. At this junction, the voltage is unable to support basic pacer function, and immediate generator change is required. It usually takes 3–6 months for the pacemaker battery to reach EOL status after the battery reaches ERI. Another parameter used to determine the pacemaker's battery status is the battery's impedance. As the battery voltage declines, the battery impedance rises.

Lead Impedance

While different leads offer different impedances, once a lead is implanted, the fluctuation of impedance is very narrow. The lead impedance of each implanted lead should also be measured during each interrogation. Lead impedance is the sum of all factors that retard current flow. Very high lead impedances suggest the existence of lead fractures or a loose connection in the device header (between the lead pin and the set screw). Very low lead impedances suggest insulation failure. The change in impedance from a previous recording is more important than the absolute value of the lead impedance. Changes greater than 300 Ω are abnormal and should prompt further evaluation.

Sensing and Pacing Thresholds

Although many devices have automated evaluations of pacing and sensing thresholds, many require manual pacing and sensing threshold determinations. Sensing is the ability of the pacemaker to detect and respond to intrinsic atrial and ventricular activity. Sensing thresholds are unable to be assessed without the presence of native atrial and/or ventricular activity. Most current programmers will automatically check the amplitude of the underlying atrial or ventricular electrograms by transiently inhibiting pacing or lowering the pacing rate in the respective chambers. This would allow the emergence of the underlying rhythm and measurement of its amplitude as sensed by the pacemaker in its respective chamber. Two other techniques can be used to evaluate sensing thresholds if the programmer lacks the automated mode. One technique involves recording telemetered electrograms and measuring peak-to-peak amplitudes of the resulting signal. The more common technique, utilized in both automated and semi-automated fashions, is to progressively reduce the sensitivity setting of the pacemaker until an inappropriate spike is delivered indicating that the pacemaker no longer senses an intrinsic electrical activity in the chamber being tested. To use this method to assess ventricular sensing manually, the pacing rate needs to be programmed to a rate below the patient's intrinsic heart rate. The patient's dependency upon the pacemaker can also be assessed during this maneuver. By programming the ventricular chamber to a less sensitive mode (increasing the millivolt values) in the VVI mode the sensitivity value (in mV) at which an inappropriate pacer output is displayed corresponds to the sensing threshold of the ventricle. Atrial sensing thresholds can be manually determined in a similar fashion.

The capture threshold is the lowest pacing output that results in consistent capture of myocardium. This capture threshold is a measurement of the least amount of energy that is required to consistently cause myocardial depolarization. This energy is a function of current, voltage and pulse duration or width. Capture is reported in both voltage and pulse duration. Both of these parameters can be independently programmed. When determining capture threshold, it is most commonly reported as voltage threshold at a given pulse duration. It can also be reported as pulse duration threshold at a given voltage. The relationship between these two parameters is defined as the strength-duration curve. The curve is automatically created after threshold testing with some Medtronic devices. Manually, capture threshold is determined by pacing the desired chamber at a rate higher than the intrinsic rate while progressively decreasing the output (amplitude or pulse duration) until capture is lost (Fig. 26.2). The lowest voltage at which capture consistently occurs is the capture threshold. Conversely, capture threshold can be tested by progressively decreasing pulse duration. In most patients, especially those who are pacemaker dependent, programming should provide a 2:1 safety margin in voltage threshold. Some pacemaker systems automatically monitor capture thresholds and automatically adjust the output based on detected changes.

The basics of pacemaker interrogation are the assessment of battery voltage, lead impedances, sensing thresholds, and capture thresholds.

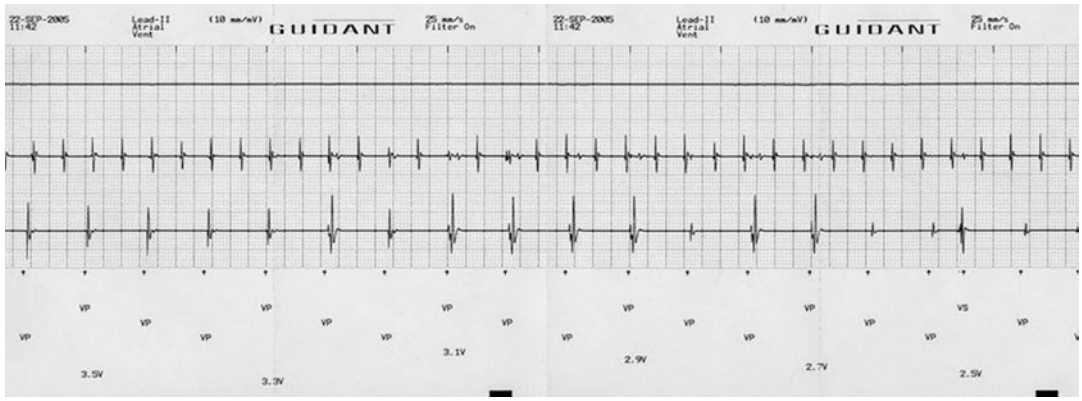

Fig. 26.2 Capture threshold determination. With decreasing output voltage, capture is lost at 2.7 V, noted by absence of ventricular capture at the right side of the electrogram

During each pacemaker evaluation it is also important to evaluate all baseline programmed parameters. These parameters include pacing mode, lower rate limit, upper rate limit, AV delay, voltage output, and sensitivity. The inadvertent exposure to eletromechanical interference may result in inadvertent programming of various pacing parameters.

Event Markers and Electrograms

Current devices all have the capability for electrogram storage. Event markers are displayed on the programmer screens and intracardiac electrograms. These event markers report behavior of the pacemaker in regards to paced and sensed events using alphanumeric labeling. The interpretation of these markers during real-time evaluation as well as in the assessment in the evaluation of stored events is crucial in the pacemaker interrogation.

Rate-Adaptive Pacing and Mode Switching

Two additional basic concepts are important to evaluate during pacemaker programming. The DDDR or VVIR modes are rate-adaptive pacing modes. Rate adaptive-pacing provides a heart rate response to meet the increased metabolic requirements for those patients with chronotropic incompetence during physical activity. Commercially available sensors include accelerometers that respond to upper body movement or minute ventilation that responds to changes in transthoracic impedance. They attempt to provide input to the pacemaker modulating the heart rate to meet the body's metabolic requirements. Specific algorithms then convert this data to a heart rate response in attempt to simulate the heart's normal response. Programming the DDDR or VVIR mode to DDD or VVI, respectively, can turn off these sensors.

Most patients known to have supraventricular tachycardias, especially atrial fibrillation, have mode switching programmed on. Without mode-switching algorithms, inappropriate tracking of rapid atrial activity would cause pacing at the upper rate limit. When rapid atrial activity occurs, as in atrial fibrillation, the pacing mode is switched from the DDDR to VVIR or DDIR mode depending on pre-programmed parameters.

Remote Monitoring

Transtelephonic monitoring has been available for years and provides basic information on battery status and capture thresholds. More recently,

home transmitters (now available from most major device companies) are able to interrogate the device, either manually by the patient using a telemetry wand or automatically using wireless technology. The data (including battery status, lead impedances, and sensing and capture thresholds) downloaded from the device by the transmitter is then sent to the physician on a pre-specified schedule. Unscheduled transmissions of alerts (for instance, device integrity) may also be sent to the physician as necessary. Thus, remote monitoring avoids unnecessary clinic visits for pacemaker patients. However, it is important to note that remote device programming is currently not possible for safety reasons, therefore any programming changes necessitates an in-person visit. Several studies have demonstrated the superiority of remote monitoring compared with in-person pacemaker interrogation in the detection and management of actionable events.

Troubleshooting

The two following clinical vignettes give two examples of how pacemaker interrogation can be useful in clinical diagnosis. Figure 26.3 is a real time intra-cardiac electrogram with event markers from an 82-year-old patient with permanent pacemaker who presented to pacemaker clinic for routine follow-up. The intracardiac electrograms reveal atrial undersensing as clearly indicated by the absence of atrial channel markers when native activity is present. By decreasing the sensing millivolt value, the sensitivity is increased and normal pacing function resumed.

Figure 26.4 is a real time intracardiac electrogram from a patient with a single chamber device who was found to have pauses on telemetry while being hospitalized for an episode acute renal failure. Event markers revealed evidence of failure to capture. Voltage output was subsequently increased. This maneuver coupled with the reso-

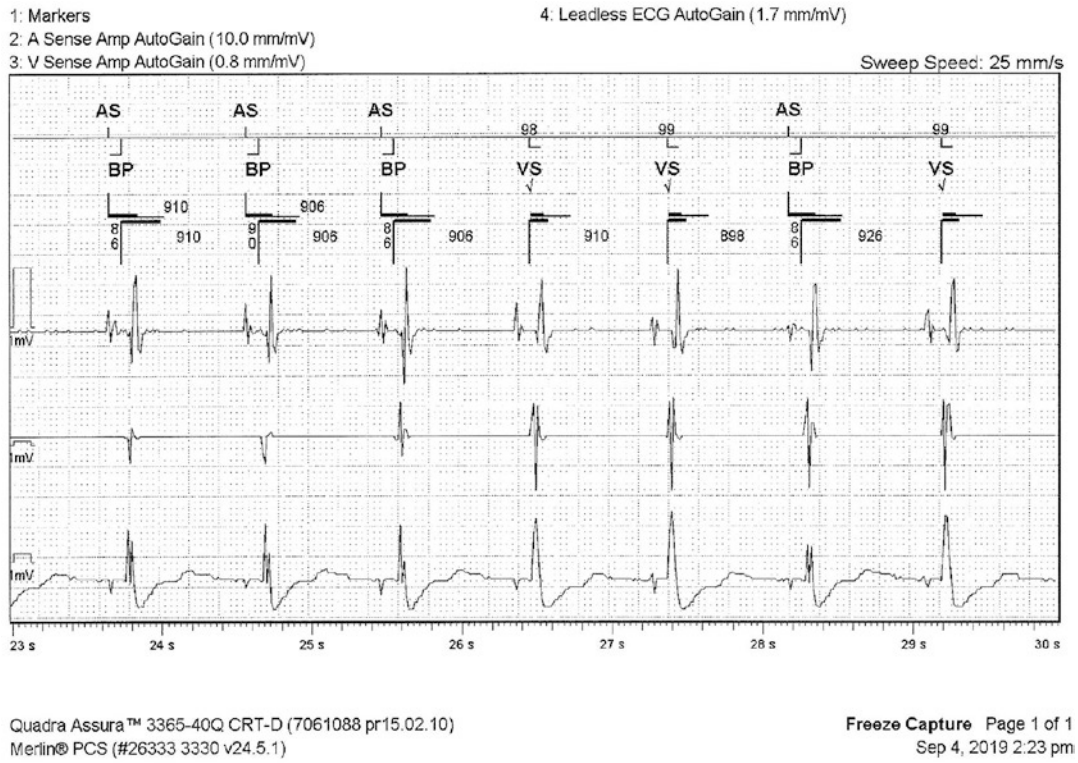

Fig. 26.3 Atrial undersensing: atrial activity is present, but is intermittent on the channel markers at bottom

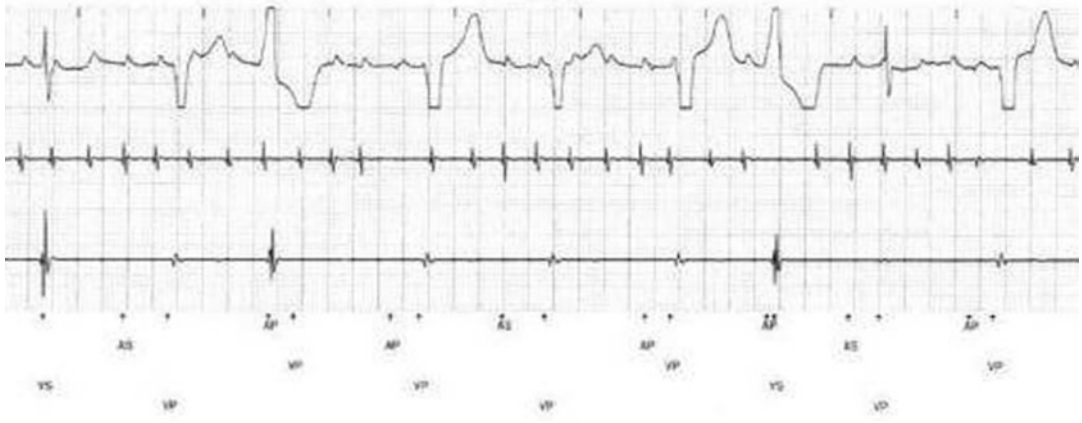

Fig. 26.4 Intermittent ventricular capture

lution of electrolyte abnormalities restored normal pacemaker activity.

Clinical Vignettes

Case 1

A 35-year-old man with complete AV block, pacemaker dependency, contacts the pacemaker clinic to inform them that earlier in the day he had an unheralded syncopal episode. This resulted in a laceration on his forehead. The day before, he reported two presyncopal spells. He had never had any prior episodes. He is known to have had obstructive hypertrophic cardiomyopathy and left bundle branch block and had undergone alcohol septal ablation 5 years ago. The procedure was followed by the development of complete AV block requiring the implantation of a pacemaker.

Upon interrogation of his pacemaker, the RV pacing threshold was seen to have climbed from 0.7 volts at 0.4 ms. measured 4 weeks ago to 5.2 volts at 0.4 ms. Furthermore, pacemaker interrogation intermittently registered high right ventricular lead impedances. Pacemaker interrogation does not show that he has had any ventricular arrhythmias. His underlying rhythm is sinus with complete AV block and no escape greater than the lowest pacing rate the pacemaker could be programmed to. Elevation of pacing impedance when coupled with elevation of pacing threshold in a lead that has not been recently implanted, raises the concern for a fractured lead. The unheralded syncopal episode and the two preceding presyncopal spells point to a recent fracture. The patient is pacemaker dependent, and was admitted so that a new lead could be implanted. While awaiting lead implantation, the impedance and pacing threshold of the RV lead can be tested in unipolar mode. If the pacing threshold and impedance are within normal in the unipolar mode, a temporary pacemaker can be avoided. This observation points to fracture of the outer coil. In this patient, a chest X-ray demonstrated the fracture.

Case 2

Seven years after a 78-year old hypertensive male patient receives a dual chamber pacemaker for complete AV block he contacts the pacemaker clinic complaining of a 1-week history of fatigue and shortness of breath. Examination reveals an otherwise healthy man with a BP 110/70 mmHg and a pulse 65 bpm. An electrocardiogram demonstrates sinus rhythm, complete AV block and ventricular pacing at 65 bpm in a VVI mode. Given the age of this pacemaker, the battery most likely crossed ERI. Pacemakers are programmed to revert to a mode that would consume less energy, slowing down impending battery depletion, thus resulting in the shift to the VVI mode. However, upon losing atrioventricular synchrony, symptoms not unlike those of heart failure can be provoked. Once a new, dual chamber PM was implanted, the patient's symptoms were completely relieved.

Suggested Reading

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27 Implantable Cardioverter Defibrillators (ICD)

Harold Rivner and Camilo A. Gomez

Indications

Implantable cardiac defibrillators (ICD) are currently indicated for the prevention of sudden cardiac death (SCD). In survivors of ventricular tachycardia (VT) or ventricular fibrillation (VF) cardiac arrest, ICDs are the optimal treatment for secondary prevention of patients. This has been supported by multiple randomized controlled trials that compared ICD to medical therapy.

ICDs are also used as primary prevention in patients with marked reduction of left ventricular function (ejection fraction [EF] ≤ 35%) who are considered to be at high risk for VT/VF. The use of ICDs for primary prevention currently represents more than 80% of total implantations. Current guidelines assign a Class I indication for ischemic cardiomyopathy (ICM) with EF ≤ 35% and NYHA II/III or EF ≤ 30% and NYHA I. There is a class I indication for nonischemic cardiomyopathy with EF ≤ 35% and NYHA II/III. There are other high risk conditions that are known to be associated with SCD, such as in patients with other forms of structural heart disease or inherited channelopathies. Consideration of ICD therapy, particularly those for primary prevention, apply only to patients who are receiving optimal medical therapy, have a reasonable expectation of survival with good functional status for more than 1 year, and after independent risk assessment, including patient preference (See Table 27.1) [1, 2].

Contraindications

Major ICD implantation contraindications are included in the ACC/AHA/HRS guidelines (See Table 27.2). Other contraindications include: in hemodynamically unstable patients, in the setting of acute myocardial ischemia or hypoxia, post coronary artery bypass surgery, in the setting of active infection in the chest wall or bloodstream infections, with electrolyte imbalances, and with drug toxicities [1, 2].

Equipment

The physical components of the implanted system consist of:

1. ICD generator: consist of a battery, capacitor, DC-DC converter, a microprocessor, and telemetry communication coils with their connections (Fig. 27.1).

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Table 27.1 ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities

CLASS I INDICATIONS evidence and/or general agreement that ICDs are useful and effective
1. Survivors of cardiac arrest due to ventricular fibrillation or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes
2. Structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable
3. Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or ventricular fibrillation induced at electrophysiological study
4. LVEF less than or equal to 35% due to prior myocardial infarction who are at least 40 days post–myocardial infarction and are in NYHA functional Class II or III
5. Nonischemic dilated Cardiomyopathy who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III
6. LV dysfunction due to prior myocardial infarction who are at least 40 days post–myocardial infarction, have an LVEF less than or equal to 30%, and are in NYHA functional Class I
7. Nonsustained VT due to prior myocardial infarction, LVEF less than or equal to 40%, and inducible ventricular fibrillation or sustained VT at electrophysiological study
CLASS IIa INDICATIONS conflicting evidence about the usefulness of ICD therapy, with the weight of evidence/opinion in favor of usefulness/efficacy
1. Reasonable for patients with unexplained syncope, significant LV dysfunction, and nonischemic cardiomyopathy
2. Reasonable for patients with sustained VT and normal or near-normal ventricular function
3. Reasonable for patients with hypertrophic cardiomyopathy who have 1 or more major risk factor for SCD
4. Reasonable for the prevention of SCD in patients with arrhythmogenic RV dysplasia who have 1 or more risk factors for SCD
5. Reasonable to reduce SCD in patients with long-QT syndrome who are experiencing syncope and/or VT while receiving beta blockers
6. Reasonable for non hospitalized patients awaiting for transplantation
7. Reasonable for patients with Brugada syndrome with syncope or who have documented VT that has not resulted in cardiac arrest
8. Reasonable for patients with catecholaminergic polymorphic VT who have syncope and/or documented sustained VT while receiving beta blockers
9. Reasonable for patients cardiac sarcoidosis, giant cell myocarditis, or Chagas disease
CLASS IIb INDICATIONS usefulness/efficacy is less well established by evidence/opinion
1. Considered in patients with nonischemic heart disease who have an LVEF of less than or equal to 35% and who are in NYHA functional class I
2. Considered for patients with long-QT syndrome and risk factors for SCD
3. Considered in patients with syncope and advanced structural heart disease in whom through invasive and noninvasive investigations have failed to define a cause
4. Considered in patients with a familial cardiomyopathy associated with SCD
5. Considered in patients with LV noncompaction

From Ref. [1]

Table 27.2 CLASS III conditions for which there is a general agreement that ICDs are not useful and possibly harmful

1. Not indicated for patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria
2. Not indicated for patients with incessant VT or VF
3. Not indicated in patients with significant psychiatric illnesses that may be aggravated by device implantation or that may preclude systematic follow-up
4. Not indicated for NYHA class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation or CRT-D
5. Not indicated for syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease
6. Not indicated when VF or VT is amenable to surgical or catheter ablation (e.g., atrial arrhythmias associated with the Wolff-Parkinson-White syndrome, RV or LV outflow tract VT, idiopathic VT, or fascicular VT in the absence of structural heart disease)
7. Not indicated for patients with ventricular tachyarrhythmias due to a completely reversible disorder in the absence of structural heart disease (e.g., electrolyte imbalance, drugs, or trauma)

From Ref. [1]

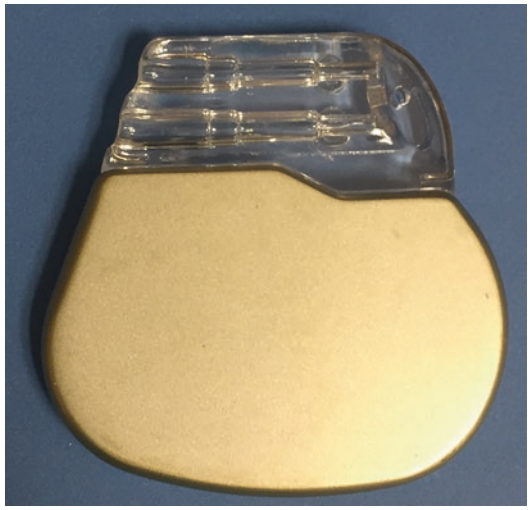

Fig. 27.1 ICD generator that is implanted subcutaneously in the prepectoral region. It is replaced when the battery reaches end of life. The leads are connected in the upper portion of the device

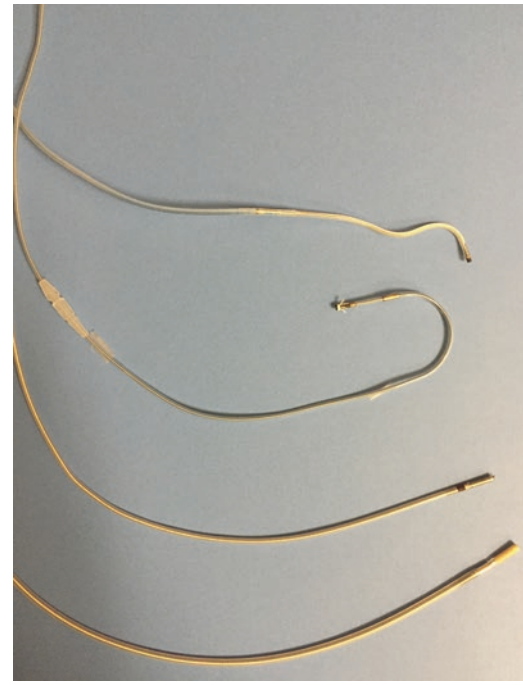

Fig. 27.2 Different examples of leads that has pacing and sensing capabilities, which exist in different shapes according the chamber were they are placed (atrium or ventricles) and distal portions with different end tip electrodes for active or passive fixation

2. Leads: The older DF-1 lead consisted of a bifurcated or trifurcator connected header pin with a pace-sense IS-1 connector and either one or two DF-1 high voltage connectors. These connectors were integrated into a single lead body. The newer D4-4 standard combines the high voltage and pace-sense into one connector. In addition to being smaller, it allows for only a single distal screw into the generator without requiring any additional connectors or yoke [3]. The lead delivers the three essential functions of the ICD: detection, tachycardia therapy and bradycardia pacing (Fig. 27.2) [2, 4].

Technique

Implantation of the ICDs system involves its subcutaneous insertion, positioning of the leads, and finally testing the sensing and pacing functions. Usually, the generator is implanted in the left prepectoral area with the purpose to create a left-to-right vector for defibrillator shocks. Alternatively, the right pectoral area may be used in selected left-handed patients, when left venous access is impeded, or in cases of infection or other abnormalities.

Initially with an standard sterile technique, an incision is made in the left pre-pectoral area to create a pocket. The leads are inserted into the subclavian, cephalic, or axillary veins. Cephalic or axillary vein access is preferred over subclavian because they carry a smaller risk of arterial puncture, pneumothorax and subclavian crush injury (when the inserted leads are trapped within the subclavius muscle or the costoclavicular complex). The leads are advanced under fluoroscopic guidance into the right heart until reaching the pulmonary artery. then the lead is pulled back and fixed in the right ventricle (RV) apex. Subsequently lead positioning, electrocardiogram stability, and adequate sensing and pacing parameters are confirmed. When a dual-chamber ICD is implanted with the insertion of an additional atrial lead, the atrial lead is placed following the insertion of the ventricular lead. It should be placed in the high right atrium or in the superior aspect of the atrial appendage to avoid crosstalk between atrial stimuli and the ventricular

detection circuits. The sleeve of the lead is anchored using silk sutures to the surrounding muscular fascia.

Either before or after vascular access, a pocket is created where the generator will be seated. It should be of adequate size for the device to avoid device erosion, migration, or seroma formation. It is usually placed on the medial aspect anterior to the plane of the pectoral fascia. Additionally, it should be inferior to the clavicle and in a medial position to avoid restriction of movement of the shoulder and the arm. The leads are then connected to the generator header with verification of secure insertion into the correct ports. The pocket is then cleaned for tissue, secretions, and blood that may be interposed. An antibiotic solution is used to irrigate the port, and the generator is placed in the pocket. The device is then tested to confirm adequate pacing and sensing. While once routine, defibrillation threshold testing is no longer commonly performed.[5] Once adequate device function is confirmed the pocket is closed with sterile suture.

The patient's arm is placed into a sling, and the lead position is confirmed by immediate post-operative chest x-ray. This is also performed to rule out complications as pneumothorax. Before discharge, a definitive postero-anterior and lateral chest-x ray are performed to once again confirm position (Fig. 27.3) [4, 6]

In addition to the traditional ICD as discussed above, there is a completely subcutaneous ICD system. This system may avoid complications associated with long term transvenous leads such as infections or venous stenosis. However, long term outcomes are still being studied. The generator is implanted in a subcutaneous pocket in the left lateral, midaxillary thoracic position between the anterior and midaxillary line. The lead is then tunneled subcutaneously until the distal electrode is just below the sternal notch. The subcutaneous ICD can sense and deliver shocks, however, it cannot pace [7, 8].

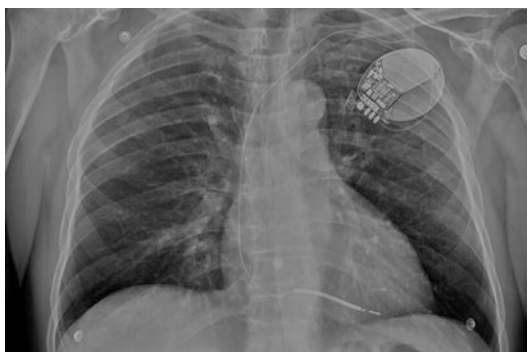

Fig. 27.3 X-ray of a patient post single chamber ICD implantation. All parts of the ICD system can be appreciated, the generator with a single lead directed and attached in position at the apex of the right ventricle

Data Interpretation

Patients are followed with routine clinical visits usually at quarterly intervals which can be performed both in person or remotely. Devices are interrogated to evaluate its function, battery depletion, alarms and events. It also allows for monitoring of arrhythmias and volume status.

Complications

- Surgical related: Ranges between 3 and 5% for single or dual-chamber ICDs. Complications are similar to those of pacemaker implantation: cardiac perforation, tamponade, vascular perforation, pneumothorax, hematoma, infection and lead dislodgement. Pulse generator changes add a 1–4% risk of infection, and complications can increase up to 15% when a new transvenous lead is added at the time of replacement.
- Late complications: less than 4% and include lead fracture, generator migration/erosion, generator failure, thrombosis, and complications related to defibrillation testing as myocardial or cerebral ischemia, electromechanical dissociation and refractory VF [4, 9].

Clinical Vignettes

Case 1

A 55 year old male was admitted with substernal chest pain that radiated to the left arm for 30 min.

Vitals on admission were blood pressure of 88/50, heart rate of 98 and respiratory rate of 22. The electrocardiogram showed ST elevation in anterior leads (V1–V4), and the troponin level was found elevated. Emergent cardiac catheterization was performed with percutaneous intervention of a completely occluded left anterior descending artery by a thrombus. Post myocardial infarction (MI) echocardiogram showed an ejection fraction of 15–20% with severe akinesis of the anterior wall. The patient was discharged with dual antiplatelet agents, beta blocker, statin and ace-inhibitor. Forty days post MI was seen in the clinic, echocardiogram was performed and showed an ejection fraction (EF) of 20–25%.

The patient has ischemic cardiomyopathy with an EF less than 35%, is 40 days post MI, and is functional class II. Therefore, he should receive an ICD for primary prevention of SCD.

Case 2

A 30 year old male with no known medical conditions suddenly collapsed at home, CPR was started by one of his family members. When EMS arrived at the scene, he was found with ventricular fibrillation and was shocked 2 times before the return of spontaneous circulation. He was taken to the hospital, and admitted to the cardiac intensive care unit. Initial echocardiogram showed and EF of 10% with global hypokinesis post cardiac arrest. He progressively recovered over the following 2 weeks without neurological deficits, but the cause of cardiac arrest could not be clarified after extensive cardiac workup. Repeat echocardiogram showed an EF of 55% with a normal ventricular wall motion.

An ICD is indicated in patients such as this, who are survivors of cardiac arrest due to VF. It is also indicated in hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes.

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Cardioversion and Defibrillation

28

Aaron E. Brice

Indications

Cardioversion is effective in eliminating arrhythmias caused by a reentrant circuit by depolarizing all tissue in the circuit and inducing a refractory period which breaks the circuit. Cardioversion is therefore only indicated for specific arrhythmias (Table 28.1). Defibrillation may be employed in cardiopulmonary resuscitation and is indicated for VF, pulseless ventricular tachycardia (VT), and polymorphic VT. In cases of hemodynamic instability, angina, or heart failure caused by tachyarrhythmias immediate shocks are indicated. In the absence of such features cardioversion may be done electively. Appropriate timing of cardioversion, use of vagal maneuvers, and medications including antiarrhythmics are specific for each arrhythmia.

Table 28.1 Type of arrhythmia and response to cardioversion/defibrillation [1]

Reentrant (shockable)	Ventricular fibrillation Most ventricular tachycardias Atrial fibrillation Atrial flutter AV reentrant tachycardia (AVRT) AV nodal reentrant tachycardia (AVNRT) SA nodal reentrant tachycardia
Automatic (typically not shockable)	Sinus tachycardia Junctional tachycardia Atrial tachycardia Accelerated idioventricular rhythm

Contraindications

There are few absolute contraindications to cardioversion and defibrillation. Patients with digitalis overdose or electrolyte abnormalities including hypokalemia are at increased risk of developing VF or VT with cardioversion. The procedure should be deferred if possible until these are corrected. Atrial fibrillation of unknown or prolonged duration should not be cardioverted without first taking appropriate steps to reduce risk of thromboembolism. Caution must be taken in patients with severe disease of the cardiac conduction system as a shock may precipitate bradyarrhythmia and temporary pacing capabilities should be on hand. Sinus tachycardia may be a physiologic response to a specific cause such as hypotension and should not be confused with a rhythm treatable with cardioversion.

Patients with implantable cardioverter/defibrillators (ICD) or pacemakers can undergo DC cardioversion but the electric charge may disrupt computer programming or damage the device. If cardioversion is performed interrogation must be completed afterward. Pregnancy also is not a contraindication to cardioversion or defibrillation

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but fetal heart rate should be monitored during the procedure.

Equipment

External cardioversion and defibrillation normally employ pads or paddles that are pressed to the skin and connected by cables to a case which houses the computer, energy source, and cardiac monitor (Fig. 28.1). Devices manufactured prior to the year 2000 normally use monophasic waveforms and those made after generally use biphasic waveforms. Electrode types include handheld paddles that use electrically conductive gel and self-adhesive pads which stick to the patient's skin [2].

Equipment for monitoring heart rhythm and vital signs should be available along with supplies needed for an emergency response including a code cart for advanced cardiac life support, temporary pacing, and airway equipment. Supplemental oxygen should also be present. Clippers for removing excess hair may be necessary for application of adhesive pads and to reduce electrical impedance. If procedural sedation is to be performed the appropriate sedative and analgesic agents must be available.

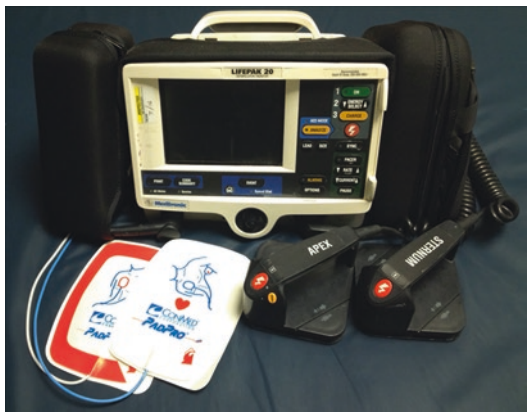

Fig. 28.1 Portable cardioverter/defibrillator

Technique

Intravenous access, cardiac telemetry, and vital signs monitoring must be present throughout the procedure. A 12-lead electrocardiogram should be done prior to and following cardioversion. To reduce the risk of aspiration patients should not eat or drink for at least 6 hours before elective cardioversion. Supplemental oxygen should ideally be removed prior to discharge of any electrical energy due to the potential risk of fire.

Procedural sedation is commonly performed as cardioversion may cause pain, anxiety, and unpleasant memories. Commonly used agents with initial dose in mg/kg include midazolam (0.02–0.03), fentanyl (0.5–1.0), etomidate (0.1–0.15), ketamine (1.0–2.0), and propofol (0.5–1.0).

Proper electrode placement is important for successful cardioversion as this determines the pathway of current [3]. Pads are primarily placed in two positions, antero-lateral and antero-posterior (Fig. 28.2). If an ICD or pacemaker is present pads or paddles should not be placed directly over the device and the antero-posterior position may be favored. Pad placement should also avoid breast tissue.

The initial amount of energy selected will depend on the arrhythmia being treated (Table 28.2). Higher energy levels have greater effectiveness in terminating the arrhythmia but are more likely to result in complications. The lowest energy should be used that is effective in eliminating the abnormal rhythm.

The synchronization function should be selected for cardioversion and the cardiac monitor should be checked to verify the arrhythmia is still present. The capacitor may then be charged and all personnel should be cleared and avoid contact with the patient or bed. The clinician may then manually press the button to discharge a shock. The monitor should be checked after shock delivery to verify termination of the arrhythmia. If the arrhythmia is still present the energy level should be escalated in a stepwise

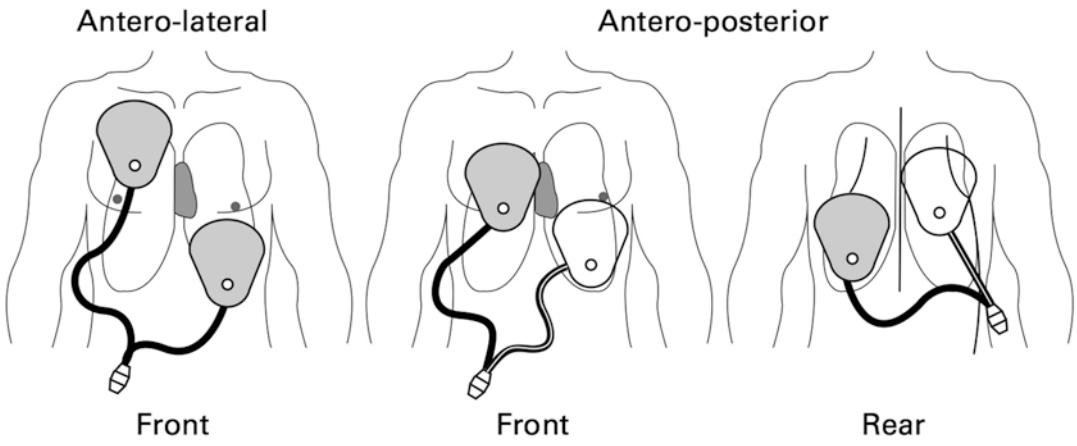

Fig. 28.2 Correct pad placement

Table 28.2 Suggested initial energy for cardioversion/defibrillation [1]

Arrhythmia	Biphasic	Monophasic
Atrial fibrillation	120–200 J	200 J
Atrial flutter	50–100 J	50–100 J
AVNRT, AVRT	50–100 J	50–100 J
Monomorphic VT with pulse	100 J	100 J
Polymorphic VT and pulseless VT	120–200 J	360 J
Ventricular fibrillation	120–200 J	360 J

fashion and repeat shock delivered with a minimum of 1 minute between shocks.

Data Interpretation

If the device cannot synchronize with the QRS complex the electrical deflections may be too small to capture and the clinician should reposition the pads placing them closer to the patient's heart. Selecting the programmed lead with the largest QRS complex can also significantly help with proper synchronization.

When evaluating the post cardioversion electrocardiogram temporary ST elevations and depressions or T wave changes may be noted. This usually occurs in the absence of cardiac biomarker elevation and is a non-specific finding rarely due to myocardial injury [4].

Cardiac monitoring commonly displays arrhythmias after cardioversion. Malignant arrhythmias such as VF and sustained VT must be quickly recognized and treated with defibrillation. Sinus arrest and other bradyarrhythmias may occur but are usually of short duration; if persistent, cardiac pacing may be required.

Complications

Transcutaneous discharge of electrical energy may result in pain and first-degree burns at the site of shock delivery and is related to the amount of energy used. Good contact with the defibrillator pad/paddle and skin is essential. Improper pad placement and use of monophasic waves increase this risk. Cutaneous burns may be best treated with a cream, such as silver sulfadiazine. Myocardial necrosis may manifest as a small elevation in cardiac biomarkers which is usually due to high energy discharge.

Thromboembolism is a risk in patients with atrial fibrillation or atrial flutter treated with cardioversion. Risk is reduced with 4 weeks of anticoagulation or transesophageal echocardiogram confirming absence of clot in the left atrium.

Hypotension may be seen after cardioversion and is usually brief and responsive to IV fluids. Pulmonary edema is infrequently encountered and may be due to left ventricular dysfunction or decreased atrial mechanical activity after shock.

Clinical Vignettes

Case 1

A 67-year-old man is brought to the emergency department by his wife for worsening weakness, shortness of breath, and palpitations. He believes his palpitations began about 2 days ago but is not certain. He has a history of a DVT and heart failure with an ejection fraction of 45% measured 4 months ago. He reports taking his medications which are carvedilol, lisinopril, and rivaroxaban. On physical exam he is afebrile, blood pressure is 74/52, heart rate is 142, respiratory rate is 32, and oxygen saturation is 82% on face mask. Cardiac exam discloses an irregularly irregular rhythm and on lung auscultation rales can be heard bilaterally. Laboratory studies are pending. Electrocardiogram shows an irregularly irregular narrow complex tachycardia.

This patient has atrial fibrillation with rapid ventricular response that is hemodynamically unstable. Synchronized cardioversion should be promptly delivered. He is hypotensive and although vasopressors may be helpful, his hemodynamics may improve with restoration of sinus rhythm alone. Further delays including establishing central venous access should not take precedence over treatment of his unstable arrythmia. Ventricular rate control with a nondihydropyridine calcium channel blocker or beta blocker should not be attempted in an acutely decompensated patient. Immediate synchronized cardioversion is indicated in this unstable patient. He has been on anticoagulation for his DVT and therefore his risk of thromboembolism is low.

Case 2

A 52-year-old woman undergoes cardiac catheterization for evaluation of coronary artery disease after an episode of chest pain and syncope. She is found to have normal coronary arteries on angiography. After the procedure while in the periopertive area she develops chest pain, palpitations, and severe anxiety. On physical exam she is afebrile, blood pressure is 95/72, heart rate is 180, respiratory rate is 22, and oxygen saturation is 96% on room air. She appears nervous and cardiopulmonary exam reveals a rapid heartbeat but is otherwise unremarkable. Serum chemistry

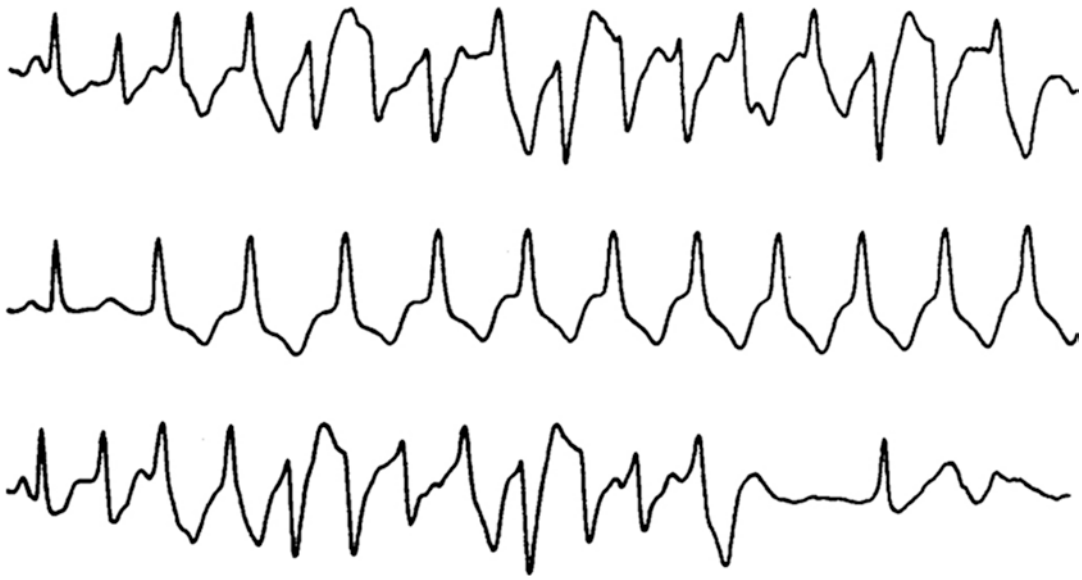

Fig. 28.3 Case 2 cardiac monitor display

panel prior to the procedure was normal. Her cardiac monitor is examined and is shown in Fig. 28.3. *Electrocardiogram prior to catheterization showed normal sinus rhythm with QTc interval of 410 ms.*

This patient has spontaneous polymorphic VT with a normal QT interval. This may be seen in the setting of structural heart disease, familial syndromes, or coronary artery disease. She currently has stable blood pressure but may decompensate and should be shocked with defibrillation energy level of 120–200 J. The use of antiarrhythmics including amiodarone would be too slow in this patient with acute and symptomatic polymorphic VT. Although this arrythmia is often seen in patients with ischemic heart disease or an acute coronary syndrome, it can be seen in other clinical settings as well. Cardiac MRI is useful for diagnosis and quantification in structural heart disease, but it is time consuming and should not delay prompt treatment in this case. Polymorphic VT is classified according to presence or absence of QT prolongation. Of note she does not have polymorphic VT with prolonged QT interval or torsades de pointes which is responsive to magnesium.

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Pulmonary Vein Isolation

29

Gursukhman Deep Singh Sidhu

Introduction

Atrial fibrillation (AF) is an abnormal rhythm increasing in prevalence. It is highly symptomatic, resulting in palpitations, dyspnea on exertion, chest pain, and alteration of mood and affect [1]. The cornerstone of the management of AF is pulmonary vein isolation (PVI). The rapid atrial rate in AF is initiated by foci of abnormal activity, most commonly near the pulmonary vein ostia. It is maintained by multiple micro and macro reentrant circuits in the atria. Over time, secondary to consistent depolarization, calcium overload, and abhorrent signaling, the atria dilate, develop focal fibrosis, secondary to indolent inflammation (Fig. 29.1). This atrial tissue can sustain AF and is unable to self-terminate [2]. Ventricular response to atrial episodes varies, a high burden of ventricular response over time can lead to heart failure (HF).

Indications

The primary indication for a PVI is symptomatic AF which is refractory to electrical or chemical cardioversion. The patient has to document failure or intolerance of at least one Class I or class III antiarrhythmic medication. Furthermore, PVI may be considered appropriate in certain symptomatic patients with heart failure, especially those with a reduced ejection fraction. (Table 29.1) [3].

Contraindications

The absolute contraindication to AF PVI is a preexisting left atrial or left atrial appendage thrombus. The patient who wishes to undergo a PVI needs to tolerate anticoagulation perioperatively and postoperatively safely. Other contraindications include the inability to tolerate anesthesia, presence of a septal-occluder device. While not a contraindication, severe LA dilatation, valvular AF has a poor outcome with a high rate of AF recurrence after PVI. In this subgroup, it should not be attempted before other options are exhausted.

Equipment

The PVI ablation uses standard electrophysiology lab equipment: A mapping system, long sheath catheters, an intracardiac ultrasound probe, transeptal puncture needle, mapping catheter, and an ablation catheter. There is commonly hemodynamic fluctuation seen during the procedure, secondary to tachy/bradyarrhythmias and

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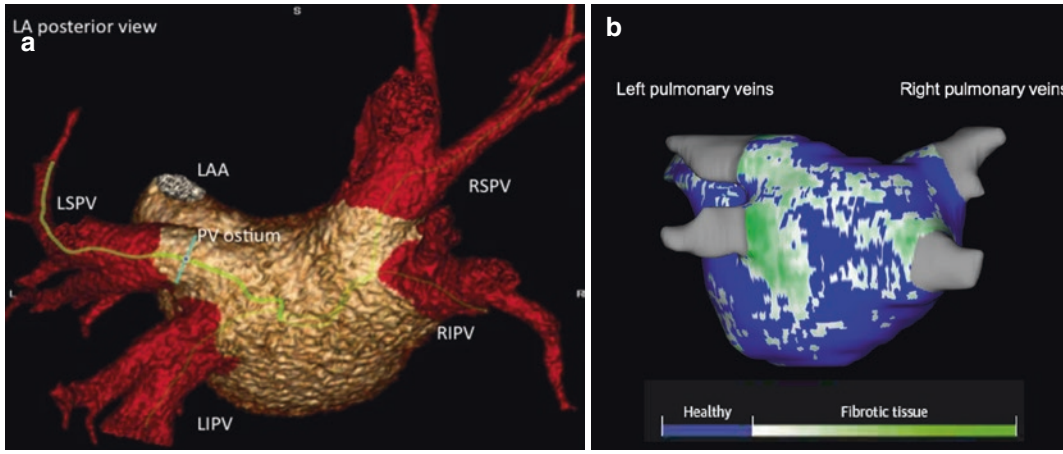

Fig. 29.1 (**a**) Computed tomography pulmonary vein assessment. LIPV: Left Inferior Pulmonary Vein; LSPV: Left Superior Pulmonary Vein; RIPV: Right Inferior Pulmonary Vein; RSPV: Right Superior Pulmonary Vein; LAA: Left Atrial Appendage. (**b**) Late gadolinium enhancement Magnetic resonance image of the posterior surface of the left atrium. The pulmonary veins and the fibrotic tissue are demarcated

Table 29.1 AF catheter ablation to maintain sinus rhythm: recommendations

Class I
AF catheter ablation is useful for symptomatic paroxysmal AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired. (*Level of Evidence: A*)
Before consideration of AF catheter ablation, assessment of the procedural risks and outcomes relevant to the individual patient is recommended. (*Level of Evidence: C*)
Class IIa
AF catheter ablation is reasonable for some patients with symptomatic persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication. (*Level of Evidence: A*)
In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm-control strategy before therapeutic trials of antiarrhythmic drug therapy, after weighing the risks and outcomes of drug and ablation therapy. (*Level of Evidence: B*)
Class IIb
AF catheter ablation may be considered for symptomatic long-standing (>12 months) persistent AF refractory or intolerant to at least 1 class I or III antiarrhythmic medication when a rhythm-control strategy is desired. (*Level of Evidence: B*)
AF catheter ablation may be considered before initiation of antiarrhythmic drug therapy with a class I or III antiarrhythmic medication for symptomatic persistent AF when a rhythm-control strategy is desired. (*Level of Evidence: C*)
AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF. (*Level of Evidence: B*)
Class III: Harm
AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and after the procedure. (*Level of Evidence: C*)
AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation. (*Level of Evidence: C*)

pacing, which require careful monitoring and treatment by trained medical personnel. AF during the procedure may require direct current cardioversion. Furthermore, a pericardiocentesis set and an echocardiography machine should be present in case of urgent need. Adequately trained support staff and anesthesiology staff should be able to monitor the case.

Technique

Patients are instructed to start/continue anticoagulation before the procedure. All antiarrhythmic medications are withheld in certain cases. It can help to locate/map the abnormal areas of atrial activity accurately. During procedure day, the patient is brought to the electrophysiology laboratory and intubated. A pre-ablation transesophageal echocardiogram is often done to rule out a thrombus in the left atrium or appendage although a CT pulmonary vein study may also be adequate to detect a thrombus. Sometimes, the procedure maybe deferred if the patient is in sustained sinus rhythm or is compliant with his antiarrhythmic/anticoagulation regimen. The patient is draped in a sterile fashion. Bilateral femoral venous access is obtained using local anesthesia to ensure maximum comfort. Frequently, the left common femoral vein access is used to guide the intracardiac echocardiography catheter. A long sheath catheter is advanced viz the right common femoral vein to obtain transseptal access. The interatrial septum is accessed once or twice to access the left atrium (Fig. 29.2). That is a critical juncture, as the access requires significant skill, given there is a risk of perforation of the aortic inlet with devastating consequences. Once transseptal access is available, it becomes necessary to maintain the activated clotting time preferably over three hundred and fifty to reduce the risk of thromboembolism due to catheter manipulation and from the heat of ablation. Catheters advanced typically in the LA include the multipolar mapping catheters and ablation catheters. Electroanatomic mapping is performed to create a virtual voltage/impedence-based structure of the left atrium and the pulmonary veins to guide ablation. Once an appropriate image map has been created, circumferential ablation lines are drawn around the antrum of the pulmonary veins (Fig. 29.3). The goal is to achieve electrical isolation of the veins, which correlates with the procedure's success. It is achieved either using a radiofrequency catheter, which delivers thermal energy, or a cryoablation catheter, which delivers a refrigerant through an inflatable balloon. Post PVI ablation, certain operators also attempt ablation of arrhythmogenic foci in the LA posterior wall. It is essential to visualize the esophagus and monitor the amount of energy delivered near this structure. Usually, it is done via temperature probes in the esophagus. To monitor for success of isolation, intravenous adenosine is administered to unmask dormant pulmonary vein conduction, reversible injury, and identify any vein reconnection. Stimulation of the phrenic nerve is conducted to ensure no injury during ablation of the right superior pulmonary vein.

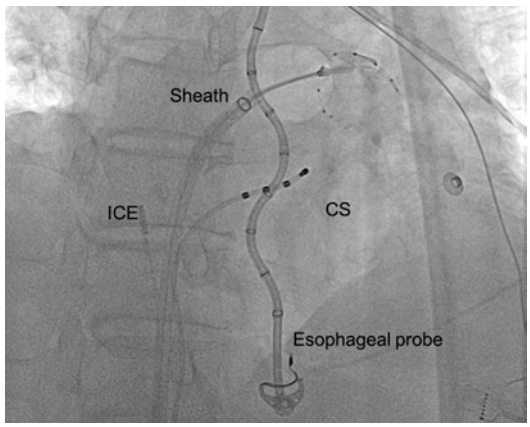

Fig. 29.2 Right anterior oblique view of the long sheath advanced through the septum. The intracardiac catheter, the circular ablation catheter, and the esophageal probe are visualized in the background

Data Interpretation

The success of PVI depends on the type and pattern of AF (i.e., paroxysmal vs. persistent), degree of remodeling of the heart, and operator expertise. Usually, it ranges between 60–80% over two years of follow-up. Two recent trials, CASTLE-AF [4], and STOP-AF [5] have invigorated interest in PVI for symptomatic relief of AF symptoms in heart failure. CASTLE—AF study documented a reduction in unplanned hospitalization and death over three years in patients with heart failure and AF who underwent catheter ablation compared to medical therapy. In the STOP-AF trial, Initial therapy with cryoablation was superior to initial therapy with antiarrhythmic medication to maintain sinus rhythm and

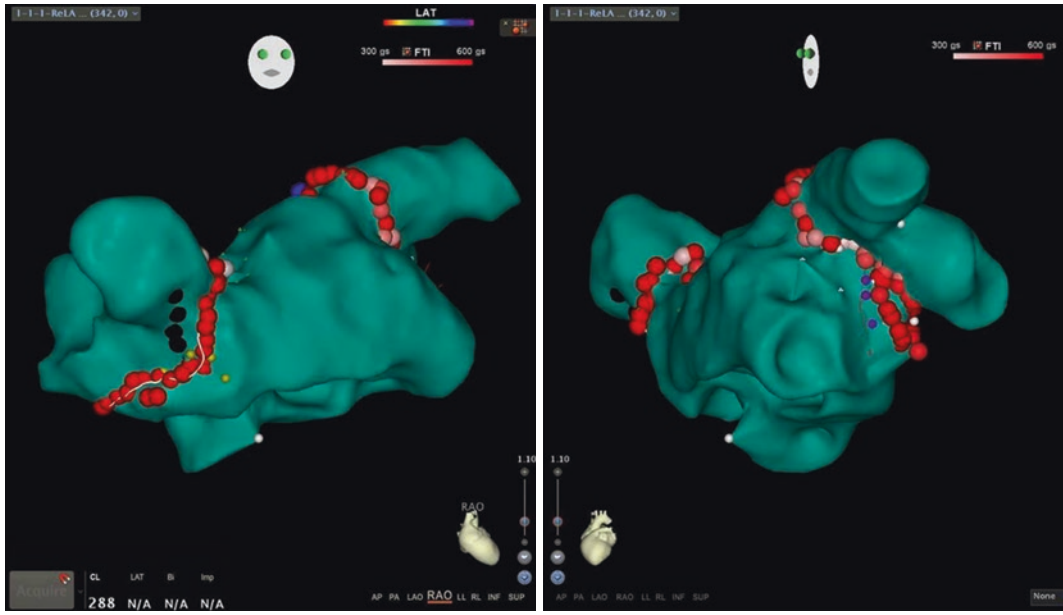

Fig. 29.3 Right anterior oblique and left anterior oblique electroanatomical map of the ablation spots marked in red dots encircling the pulmonary veins

associated with improved quality of life and less health care utilization.

While the role of PVI in reducing major cardiovascular events remains to be clearly established, it has shown safety and efficacy to reduce symptoms and AF burden when medication and lifestyle measures fail. Eventually, AF recurs for most patients after undergoing any rhythm control strategy.

Complications

Single-center and meta-analysis data report the range of acute complications after PVI between 1–4% [6, 7]. Overall, complications have reduced over the years due to improved operator skills and advancement in procedural equipment. The most feared intraoperative complication is cardiac tamponade as a result of perforation. It manifests by sudden hemodynamic instability, and demonstration of pericardial blood on ultrasonography. The management is urgent pericardiocentesis, and critical care. In the past, there was a very high incidence of thromboembolism/stroke/transient ischemic attack during ablation procedures which has abated secondary to aggressive anticoagulation in patients. Other complications include phrenic nerve injury, especially during cryoablation procedures, which occur secondary to the approximation of the phrenic nerve towards the superior vena cava and the right superior pulmonary vein. Catheters may rarely damage the mitral valve apparatus as well during manipulation leading to valvular regurgitation. Vascular complications such as hematoma, pseudoaneurysm, arteriovenous fistula, retroperitoneal bleeding are also commonly encountered as a side product of vascular access.

Finally, esophageal perforation is a dreaded complication of PVI. The esophagus is susceptible to injury during the ablation of atrial tissue closest to its proximity. Local inflammation can lead to the development of an esophageal ulcer, which may precede an atrial-esophageal fistula, it has a mortality of over 80%. Post PVI endoscopy may diagnose esophageal ulceration, placing patients at high risk for atrial esophageal fistula. Lastly, pulmonary vein stenosis is a delayed presentation of PVI, presenting with signs of volume overload, and requires a high index of suspicion for diagnosis. Multiple ablations may lead to a

stiff left atrial syndrome, characterized by large V waves on hemodynamic monitoring in the setting of minimal mitral regurgitation.

Clinical Vignette

Case 1

A 65 year old male with a history of hypertension, hyperlipidemia, with persistent atrial fibrillation for over twenty-five years, presented with a one-year history of progressive dyspnea on exertion NYHA Class III, orthopnea, occasional episodes of palpitations, and an inability to perform activities of daily living. He had failed trials of antiarrhythmic medications. Physical exam documented an irregular rhythm at a rate of 87. Electrocardiogram demonstrated atrial fibrillation at a rate of 94 with right bundle branch block. Cardiac magnetic resonance imaging revealed a moderately enlarged left atrium with an ejection fraction of 37%. He had a recent normal coronary angiogram.

Given persistent symptoms, heart failure with reduced ejection fraction, and patient preference, PVI was decided. Electroanatomic map of the left atrium confirmed four pulmonary vein ostia. Direct current cardioversion was performed to set the patient into sinus rhythm. The mapping catheter was advanced into pulmonary ostia to determine the source of triggers of atrial fibrillation. A radiofrequency catheter was advanced and electrical isolation was achieved covering the antrum of the four pulmonary vein Ostia. Post-ablation adenosine infusion determined no pulmonary venous reconnections present. The patient had an uneventful postoperative recovery. Endoscopy the next day revealed a normal esophagus. On a three-month follow-up, the patient reported a marked improvement with NYHA I symptoms. A four-week cardiac event monitor showed only sinus rhythm. Cardiac MRI demonstrated a normal-sized left atrium, with an ejection fraction of 56%.

Case 2

A 43-year-old female with a history of hypertension, obstructive sleep apnea on therapy presented with worsening palpitations over 5 years. She was diagnosed with paroxysmal atrial fibrillation nine months ago documented on her loop recorder. She is symptomatic despite a trial of flecainide and sotalol. She was intolerant to metoprolol. Physical exam documented an obese female, with regular rhythm at a rate of 60. Electrocardiogram demonstrated normal sinus rhythm, left ventricular hypertrophy and frequent premature atrial complexes. Computed tomography pulmonary vein study demonstrated normal four pulmonary vein ostia without stenosis entering appropriately into the left atrium, and a left atrial appendage without clot. She had an ejection fraction of 65% with absence of perfusion defects on nuclear stress imaging.

Patient agreed to undergo a PVI for symptomatic relief. She was brought to the procedure suit. The computed tomography study and the electroanatomic map were superimposed to provide accurate visualization. The mapping catheter was advanced into pulmonary ostia to determine the source of triggers of atrial fibrillation. A cryoablation balloon catheter was advanced into each pulmonary vein ostia with complete occlusion of the ostial-antral zone and frozen. Post-ablation adenosine infusion determined no pulmonary venous reconnections present. The patient had an uneventful postoperative recovery. On a three-month follow-up, the patient reported a marked improvement in symptoms and required no medications. The loop recorder showed only sinus rhythm with rare premature atrial complexes.

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Left Atrial Appendage Closure

30

Michael Crawford

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in adults across the world affecting more than 33 million individuals. As a result, it imposes a large burden on the health care system, in particularly, by increasing the risk of stroke. Patients with AF are often prescribed oral anticoagulant (OAC) drugs which have proven to minimize the risk of cardioembolic stroke and mortality. Despite the benefit, OAC therapy does not completely mitigate stroke risk and there are several barriers to their use including increased bleeding risk, high costs, and medication noncompliance [1]. The left atrial appendage (LAA) is (a particularly low flow area) a remnant of the embryonic left atrium where more than 90% of thrombi form in patients with non-valvular AF. This observation has led to the development of different techniques of LAA closure [2]. While surgical ligation of the LAA has been performed for many years, it is only suitable for those that have another indication for cardiac surgery. More recently, percutaneous closure of the LAA has become a popular, non-pharmacological strategy to prevent thromboembolism in those with AF and contraindications to long-term OAC use. The WATCHMAN device is the only percutaneous LAA closure device studied in randomized clinical trials, to this date. It is a self-expanding nitinol cage that is deployed in the LAA via transseptal approach. The device is covered by a permeable polyethylene terephthalate membrane which is endothelialized within 45 days [1].

Indications

Percutaneous LAA closure is appropriate for patients with non-valvular AF and an increased risk for stroke (CHADS2 $\geq$ 1 or CHA2DS2-VASc $\geq$ 2) that have a relative or absolute contraindication to OAC therapy [2]. Patients with recurrent bleeding, prior severe bleeding, high risk of falling, or a coagulation defect, such as thrombocytopenia, are typical candidates for LAA closure. While mainly indicated for those that are intolerant of long-term OAC, it may also be considered for those that have suffered a stroke despite their use.

Contraindications

There are several contraindications to the use of percutaneous LAA closure devices. First and foremost, the LAA anatomy must be accommodating for device placement. The appendage must measure at an appropriate size and there should be no evidence of thrombus. Other contraindica-

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tions include the presence of an atrial septal defect or patent foramen ovale repair or closure device. Patients must also be able to tolerate warfarin for at least six weeks and dual antiplatelet therapy for six months after device implantation, allowing for endothelial tissue to grow over the device.

Equipment

Percutaneous LAA closure uses standard equipment for intravascular access, a transseptal puncture access system, specialized access and delivery sheaths, and a LAA closure device, such as Watchman. Other necessary equipment includes a fluoroscopic unit, intracardiac echocardiography (ICE), and transesophageal echocardiography (TEE) to assist with catheter placement and device deployment [3].

Technique

Percutaneous LAA closure is performed in the electrophysiology laboratory under general anesthesia. Heparin is administered throughout the procedure to prevent device-related thrombus formation. TEE is performed prior to the procedure to evaluate the size and anatomy of the LAA and rule out the presence of a thrombus. A venous sheath is then placed into the femoral vein using the Seldinger technique. Through that sheath, a catheter is advanced over a wire into the right atrium under fluoroscopy. Under TEE guidance, the interatrial septum is crossed with a guidewire at the posterior and inferior location using a standard transseptal access system. A specialized access sheath is then advanced over the transseptal guidewire into the left atrium. A pigtail catheter is advanced through the sheath into the distal portion of the LAA under fluoroscopic guidance. Contrast is injected at this time to visualize the LAA and the access sheath is then advanced over the pigtail catheter into the LAA. The appropriately sized LAA closure device is selected based on the LAA ostium width and depth. The device is delivered through the sheath and subsequently deployed into the LAA. Certain criteria must be met prior to the final release of the device. The position and degree of compression of the device is assessed by TEE in multiple imaging planes. It should be at or just distal to the LAA ostium with compression to 10–30% of its original size. Next, the stability of the device is tested by applying gentle traction. Lastly, the seal of the device is assessed with TEE using color doppler. There should be minimal to no residual flow surrounding the device. Once all criteria are met, the device may be released. TEE is again utilized to assess for any pericardial effusion and all sheaths and catheters are removed [3] (Figs. 30.1, 30.2, 30.3, and 30.4).

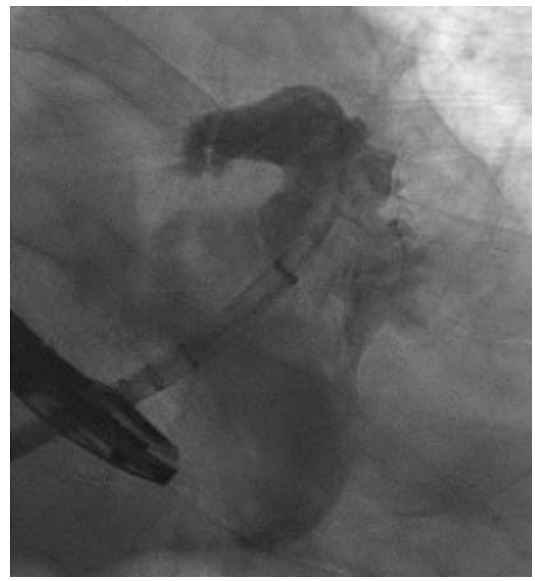

Fig. 30.1 Angiographic visualization of the left atrial appendage prior to placement of an occlusion device

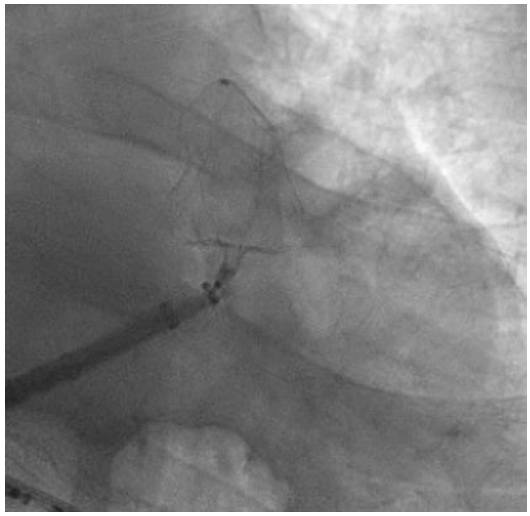

Fig. 30.2 Fluoroscopic visualization of an occlusion device within the left atrial appendage following deployment

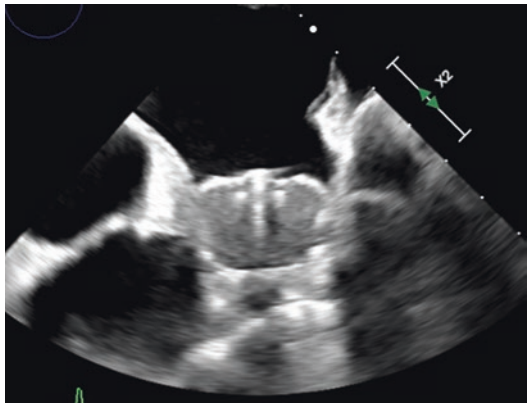

Fig. 30.3 Visualization of an occlusion device within the left atrial appendage by transesophageal echocardiography

Data Interpretation

Following placement of a LAA closure device, patients must continue OAC with warfarin (INR goal 2–3) along with aspirin for 45 days post-implantation to allow for adequate endothelialization. Repeat TEE is then performed to assess for any peri-device leakage. If there is adequate seal, warfarin therapy is discontinued and dual antiplatelet therapy with clopidogrel 75 mg daily and an increased aspirin dose to 300–325 mg daily is continued for six months post-implantation. Aspirin therapy should be continued indefinitely [3].

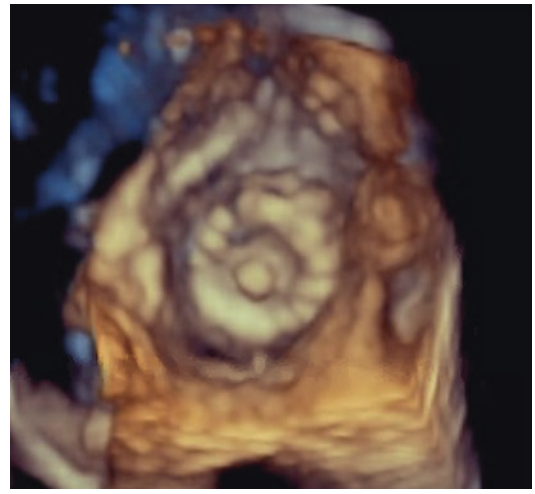

Fig. 30.4 Another view of the occlusion device by 3D echocardiography

The WATCHMAN device has been evaluated in randomized trials. Based on the results of these studies, the device was approved by the United States Food and Drug Administration for patients with nonvalvular AF and an indication for long-term OAC but an adequate reason to avoid such therapy.

Complications

Percutaneous LAA closure is an invasive procedure that carries a risk of minor to life-threatening complications. The most common complication is bleeding at the access site. Pericardial effusion with cardiac tamponade is one of the most seri-

ous complications as the LAA is a thin-walled structure that is susceptible to injury. Air embolism into systemic circulation is another serious complication that may result in myocardial infarction or stroke. Device-related thrombus formation may occur prior to endothelialization of the device, hence the need for intraprocedural and postprocedural anticoagulation therapy. Another rare complication is device embolization. This is avoided by ensuring adequate sizing and placement of the device [3].

Clinical Vignettes

Case 1

A 65-year-old man with a history of hypertension and diabetes mellitus type 2 presented to clinic after a recent hospital admission for an upper gastrointestinal bleeding due to bleeding gastric ulcers requiring transfusion of packed red blood cells. This was his third admission for the same issue. During the admission, he was diagnosed with non-valvular atrial fibrillation. Upon discharge, he was referred to cardiology clinic to assess the use of oral anticoagulation therapy for stroke prophylaxis. He denied any further bleeding symptoms. Vital signs were within normal range and repeat lab work revealed a stable hemoglobin level since discharge.

This patient is a good candidate for percutaneous left atrial appendage (LAA) closure. He carries a high stroke risk given his elevated CHADS2 and CHA2DS2-VASc scores but is also at increased risk for bleeding given recurrent admissions for bleeding gastric ulcers. Transesophageal echocardiography should be performed to ensure favorable LAA anatomy and absence of thrombus. Once a LAA closure device is placed, he would need to continue anticoagulation therapy for a 45-day period followed by dual antiplatelet therapy until 6 months post-implantation.

Case 2

A 70-year-old woman with a history of nonvalvular atrial fibrillation and prior cardioembolic ischemic stroke was admitted to the hospital for an episode of intracranial hemorrhage in the setting of warfarin use. Following stabilization, she was discharged with close follow up in cardiology clinic to discuss restarting warfarin for stroke prophylaxis. In clinic, she was doing well and denied any further neurologic events. While she was reluctant to restart warfarin therapy given her recent intracranial hemorrhage, she was also very fearful of having another ischemic stroke and inquired about alternative therapies.

In these situations, it is important to have an in-depth risk-benefit discussion with the patient. While she is hesitant to restart warfarin therapy due to her recent bleeding event, she is also at high risk of having a recurrent cardioembolic stroke if she were to forgo oral anticoagulation therapy. In this situation, percutaneous LAA closure should be discussed with the patient. While she would need to resume warfarin therapy following device placement, it would only be for a 45-day period. After this, she may discontinue warfarin without an increasing her risk of cardioembolic stroke.

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Part IV

Interventional Cardiology

Coronary Angiography

31

Nima Aghili, Edouard Daher,
and Carey Kimmelstiel

Introduction

Coronary angiography remains the gold standard for evaluation of ischemic heart disease. For more than 50 years, cardiac catheterization and the invasive evaluation of coronary arteries has defined the role of a cardiologist and serves as the diagnostic backdrop for coronary intervention and myocardial revascularization.

Indications

Coronary angiography is performed most commonly after non-invasive tests have shown the presence of coronary artery disease (CAD) in patients presenting with symptoms of chest pain, despite medical therapy. These noninvasive tests could be conclusive as to the presence of CAD, and in that case, angiography is performed to accurately define the coronary arterial anatomy and whether any defined stenoses are suitable for revascularization to achieve symptom relief. In the case of indeterminate non-invasive tests results, coronary angiography is frequently performed when the index of suspicion for CAD remains high. Occasionally, patients are referred for coronary angiography in the setting of an emergency such as acute coronary syndromes such as myocardial infarction or unstable angina. Coronary angiography is performed in patients with newly diagnosed cardiomyopathy and in cases of valvular or congenital heart diseases to evaluate for concomitant CAD that might affect the therapeutic management of these patients, especially when surgical correction is planned. Coronary angiography is also indicated in recipients of heart transplant to evaluate for "cardiac allograft vasculopathy" (CAV) which can affect up to 50% of patients during the first 10 years following transplantation [1].

Contraindications

The only absolute contraindication for performing coronary angiography, is a mentally competent patient that refuses to consent for the procedure. More commonly, there are relative contraindications for this procedure when the risk of coronary angiography outweighs the benefit. These include, but are not limited to uncontrolled hypertension, uncontrolled ventricular arrhythmias, severe electrolyte abnormalities,

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severe bleeding diathesis, history of contrast intolerance, renal insufficiency, a non-cooperative patient, or one with a febrile condition that has not been treated. These conditions should be assessed carefully against the potential benefit of cardiac catheterization. These issues can mostly be addressed and coronary angiography then performed safely once they are corrected or adequately treated. Of note, a patient that has renal insufficiency but is already contemplating or undergoing dialysis does not have contraindications for proceeding with coronary angiography. Moreover, in cases where coronary angiography is urgent, such as in patients presenting with an acute coronary syndrome, coronary angiography should not be delayed. Instead, efforts should be concentrated on minimizing the risks associated with the relative contraindications, therefore decreasing the risk of complications.

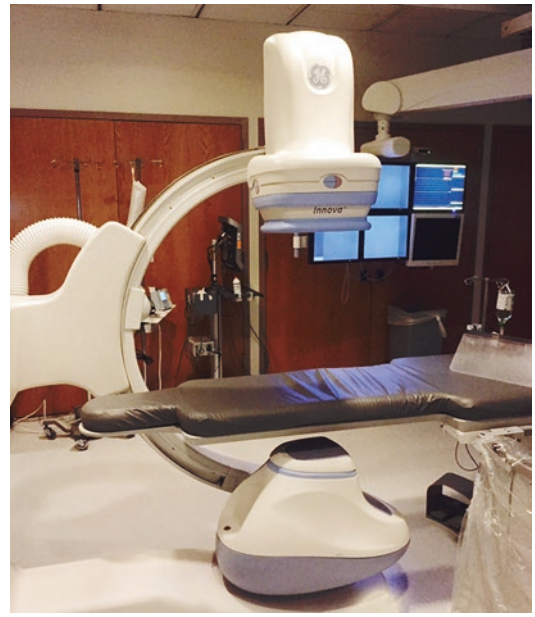


Fig. 31.1 Fluoroscopic unit

Equipment

The fluoroscope and the hemodynamic monitor are the basic components required to perform a coronary angiogram. Hemodynamic monitoring is performed continuously during the procedure to monitor central and peripheral aortic pressure as well as heart rate and rhythm. The fluoroscope includes an x-ray tube and generator, and the image intensifier (Fig. 31.1). The fluoroscope is mounted on a C-arm that rotates around the patient in a half circle of 180° while the patient is lying supine on the table. Some labs are equipped with dual x-ray tubes and image intensifiers at a 90° angle, so that orthogonal views of the coronary arteries can be imaged simultaneously, thus reducing procedural time as well as minimizing contrast and radiation exposure to the patient. A contrast power injector is utilized for ventriculography and aortography when these procedures are performed.

Images are captured using equipment that store images in a digital format where they can be displayed off line for further viewing and analysis and where reports are generated. The hemodynamic data acquired during the case are also digitally stored (Fig. 31.2). Disposable equipment come in sterile packaging. These include

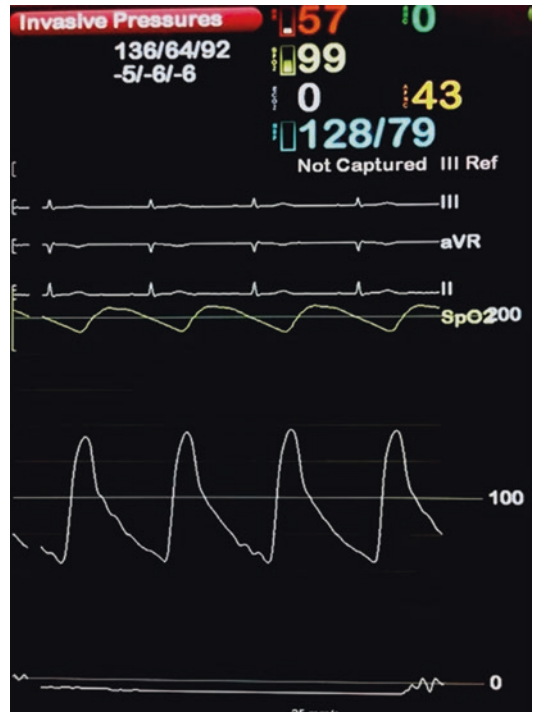


Fig. 31.2 Example of an aortic pressure tracing during a cardiac catheterization

various supplies such as syringes, needles, wires, manifolds, sutures, clamps, bowls, gauze, drapes, towels, and catheters (Fig. 31.3). A code cart

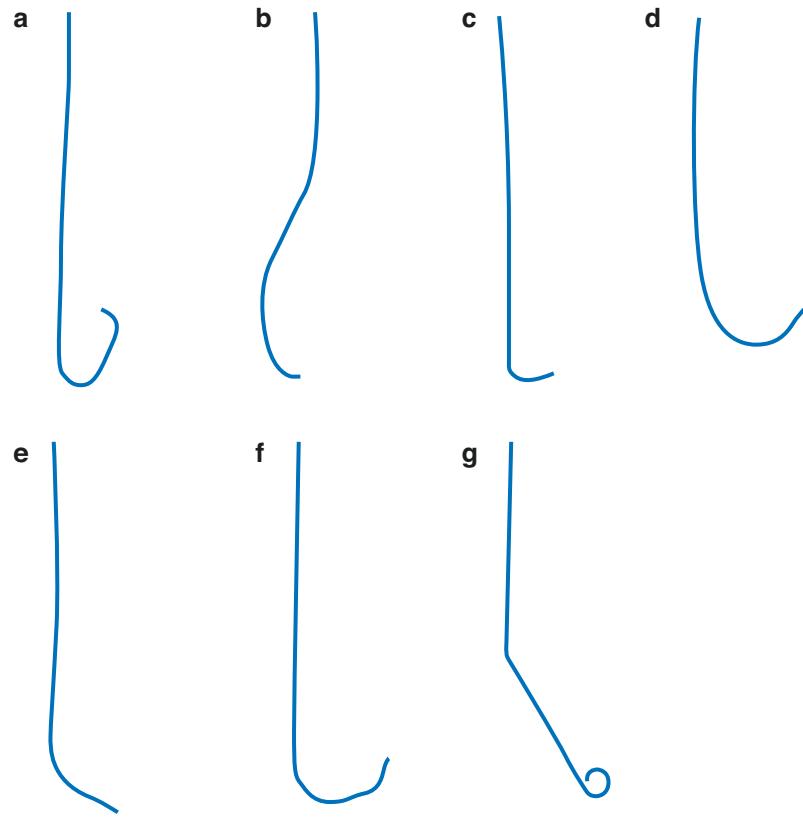


Fig. 31.3 Example of different coronary (**a**–**f**) and left ventricular (**g**) catheters. (**a**) Judkins left, (**b**) Judkins right, (**c**) Modified Amplatz Right, (**d**) Amplatz Left, (**e**) Multi-purpose, (**f**) Jacky, (**g**) Pigtail

needs to always be present in the angiography suite in the event of an emergency such as a cardiac arrest or a cardiac arrhythmia that requires resuscitation of the patient.

Technique

Coronary angiography is performed via access to the femoral, radial or brachial artery. For the femoral approach, which is still the dominant route utilized in the United States, under sterile conditions, the groin is prepped and local anesthesia is applied. A needle is used to access the femoral artery through which a wire is advanced into the aorta. Fluoroscopy is used briefly to confirm the position of the wire in the aorta and the needle is exchanged over the wire for a sheath, usually 5 or 6 F, which is inserted into the femoral artery where catheter exchanges can then be made. The radial approach requires testing the patency of ulnar artery by performing an Allens's test [2] prior to the procedure. This is done, because placement a catheter can result in thrombosis or rarely injury to the radial artery. Therefore the test is used to reduce the risk of hand ischemia ensuring adequate collateral flow from the ulnar artery. The Allen's test is performed by having the patient clench their fist. The, physician then applies occlusive pressure to both the ulnar and radial arteries, to obstruct blood flow to the hand. The patient then opens their hand, and the patient's fingers are observed to ensure that they have blanched. The physician then releases the occlusive pressure on the ulnar artery to determine its patency and adequate perfusion to the hand in the event of radial artery occlusion. Reversal of blanching and return of normal hand coloration or flushing the hand within 5–15 s indicates adequate perfusion of the hand by the ulnar artery allowing for use of the radial approach. Once the radial sheath is inserted a wire is advanced through the sheath to ascending aorta.

Irrespective of the route of arterial access, once the sheath is placed, a preformed catheter

(Fig. 31.3) is then advanced over the wire, with fluoroscopy guidance through the sheath into the ascending aorta. A number of different catheters are used to selectively engage the left and right coronary arteries. Once selectively engaged, iodinated contrast is injected at a rate of 5–7 cc/s and cineangiography is performed in multiple angulated views with different obliquities to capture the major coronary arteries and their branches in orthogonal views for the detection of coronary stenoses. Frequently, a pigtail catheter is used to perform left ventriculography as well as aortography to assess left ventricular systolic function, the presence and severity of mitral and aortic regurgitation. If a right heart catheterization is being performed at the same time, the assessment of mitral and aortic stenosis can be performed as well. The pigtail catheter is positioned in the proximal aorta, above the coronary arteries when performing aortography and is otherwise advanced across the aortic valve into the left ventricle to perform left ventriculography or perform the hemodynamic assessment of stenotic left sided heart valves. For imaging, the pigtail catheter is connected to a power injector that is programmed to deliver contrast at a specific rate and volume into the aorta or left ventricle. The catheter has several sideholes and the distal end of the catheter is curved—both properties lend themselves to atraumatic contrast delivery while minimizing trauma to the area where it resides. After all views are obtained, the catheters are withdrawn from the body through the access sheath.

Upon completion of the cardiac catheterization the access sheath is removed. In the case of femoral access cases, frequently, vascular closure devices are used to aid in achieving hemostasis. The totality of the data suggests that these devices might reduce the incidence of bleeding, albeit at a greater financial cost as opposed to not using them. If these devices cannot be deployed, then manual compression is applied for approximately 20 min to provide hemostasis. Patients are then asked to remain supine at bed rest for a period of approximately 4 h. Radial sheaths are removed with the use of compression bands. These bands proved pneumatic compression of the radial artery and are deflated after 1–2 h. Vital signs should be done routinely as part of standard post-procedural care. Special attention should be given to the distal lower extremity pulses where the access was obtained.

Data Interpretation

There are three main coronary arteries (Fig. 31.4). The left main coronary artery takes its origin from the superior portion of the left coronary sinus and then divides into two main branches that usually supply blood to the left ventricle: the left anterior descending artery (LAD) along with its diagonal and septal branches supply the anterior, anterior septal, apical and anterolateral left ventricular (LV) walls, The left circumflex artery (LCX) along with its obtuse marginal branches supply the lateral LV wall. In 10–15% of patients, the LCX gives rise to the posterior descending artery (PDA) which supplies blood to the inferior LV wall. The right coronary artery takes its origin from the right aortic sinus and supplies the right ventricle through its RV branches, and usually the inferior and the posterior walls of the LV through the PDA and posterior LV branches respectively.

Coronary angiograms are performed to determine the percent diameter stenosis of coronary arteries. This is done by measuring the diameter of the stenosed vessel and dividing it by diameter of the normal reference reference vessel. Coronary arteries should be imaged in at least two orthogonal views to most accurately gauge stenosis severity. Visual assessment of a stenosis is most commonly done in the laboratory in daily

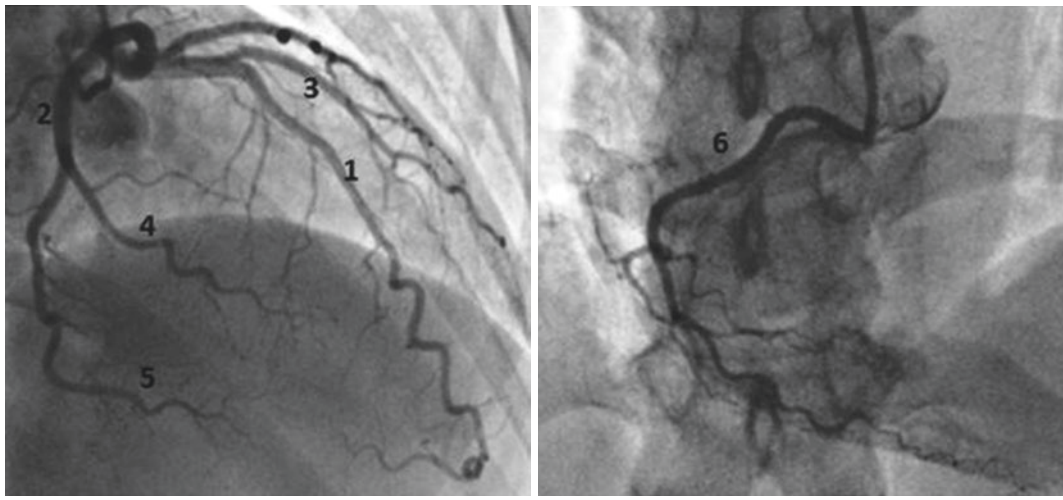


Fig. 31.4 Normal coronary anatomy: *Left image*: Left main bifurcates into Left Anterior Descending artery (1) and Left Circumflex (2). The LAD gives rise to diagonal branches (3) and the LCx gives rise to the obtuse marginal branch (4). In approximately 10% of the population, the posterior descending artery (5) arises from the left circumflex artery as opposed to the RCA. *Right image*: Right Coronary Artery (6)

practice and stenoses greater than 70% are considered significant [3]. However, the decision of which coronary lesion is responsible for a patient's ischemia is not always certain. Therefore, there are other modalities that can be used as adjuncts to coronary angiography which aid in establishing which coronary lesion is significant. These include imaging techniques such as intravascular ultrasound (IVUS) [4] and optical coherence tomography (OCT) [5] or functional assessment with fractional flow reserve (FFR) [6]. FFR measures the pressure ratio across a coronary artery stenosis at maximal hyperemia to determine the likelihood that the stenosis is responsible for an ischemic syndrome.

In the presence of totally occluded vessels or highly stenotic coronary arteries, evaluation of the supply of the distal coronary bed by collaterals (Fig. 31.5) should be done when performing cineangiography. The vessel of origin and degree of collateralization can be used to guide decision making regarding possible revascularization strategies.

The coronary microvasculature is assessed semi-quantitatively by assessing the 'Thrombolysis In Myocardial Infarction' (TIMI) flow in the respective coronary artery. TIMI flow is graded from 0 which is defined as no perfusion to 3 which indicates normal flow which fills the distal coronary bed briskly and completely [7].

Finally, left ventricular function can be quantified visually and quantitatively through power injection of contrast media into the LV on average at 12–15 cc/s for a total of 35–45 cc of contrast media with the pigtail catheter in the LV. Left ventriculography (Fig. 31.6) can be done in two views simultaneously in angiographic suites equipped with biplane capacity. Assessment of the degree of mitral regurgitation is feasible during left ventriculography with its severity graded visually from 1+ to 4+. Similarly, aortography (Fig. 31.7) can be performed to evaluate the severity of aortic insufficiency and for the assessment of structural and congenital heart disease that involves the aorta. Aortography

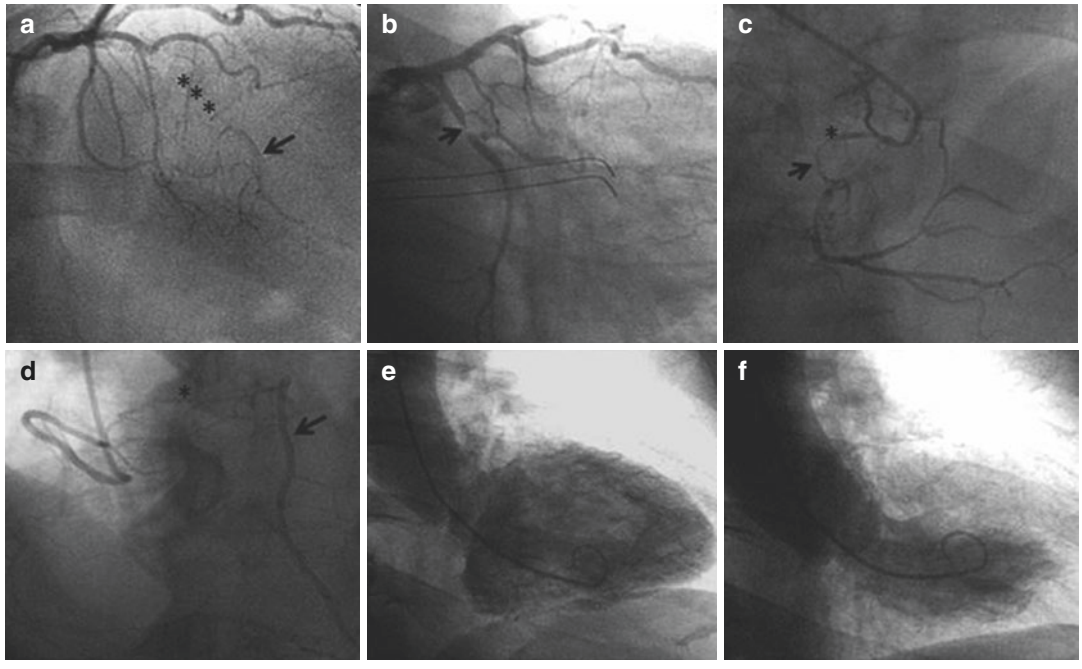
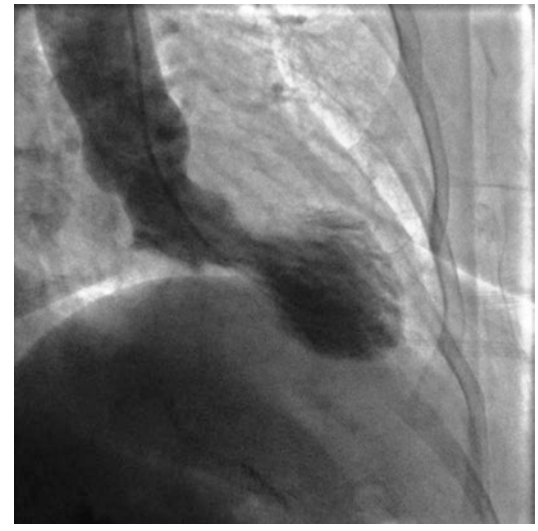


Fig. 31.5 The importance of coronary collateral vessels. (**a**) Site of total occlusion of the LAD (***) which reconstitutes distally (*arrow*) from left-sided collateral vessels. (**b**) The same patient has a significant stenosis of the left circumflex artery (*arrow*). (**c**) The RCA of the same patient is occluded proximally (*star*) and reconstitutes through bridging collaterals (*arrow*). (**d**) The conus branch of the RCA gives rise to collaterals (*) to the occluded LAD (*arrow*). This patient's ventriculography is depicted in diastole (**e**) and systole (**f**) showing an overall normal ejection fraction which is most likely due to the maintenance of myocardial perfusion from collateral blood flow

Fig. 31.6 Left ventriculogram in an RAO projection in a patient with stress induced cardiomyopathy showing apical ballooning



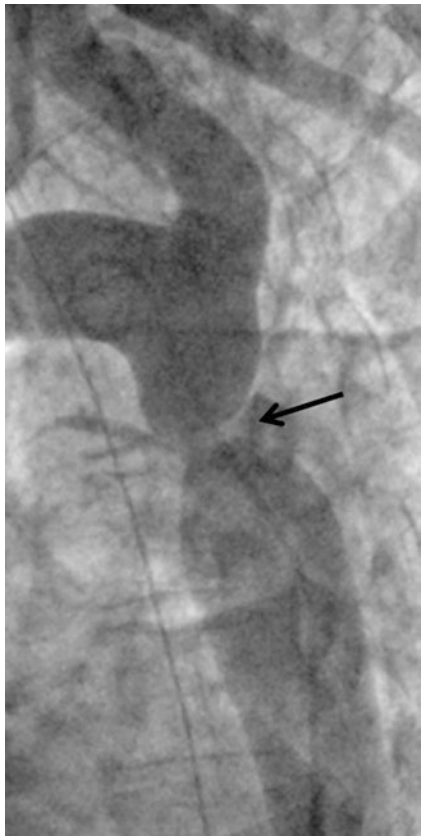


Fig. 31.7 Aortography in a patient with a descending aortic coarctation (*arrow*)

can also be used to locate coronary bypass grafts that have not been seen by selective injection techniques.

Complications

Coronary angiography is for the most part a relatively safe procedure with a low risk of complications in the average population, however they still do occur. Fortunately, the risk of major complications in current practice is <1%. The risk varies according to patient characteristics. Patients with an acute coronary syndrome, congestive heart failure, severe vascular disease, left ventricular dysfunction, severe three vessel coronary artery disease, critical valvular heart disease, prior stroke, and history of renal insufficiency are at higher risk for complications compared to other patients. Major complications include the risk of death, myocardial infarction, and stroke which typically occur in <0.5% of the cases. Other vascular complications including major thrombosis, bleeding requiring transfusion, pseudoaneurysm or arteriovenous fistula occur in <1% of cases. Minor complications including transient supraventricular arrhythmias, minor bleeding at access sites, fever, and hypotension occur in <3% of cases. Transient increase in creatinine is believed to occur in at approximately 5% of patients. Allergic reactions to dye occur in about 1% of patients. A morbid complication of coronary angiography and heart catheterization is systemic cholesterol embolization that occurs in <0.2% of cases but has severe consequences such as renal failure and bowel ischemia/infarction.

Clinical Vignettes

Case 1

A 44 year old male with a history of diabetes, hypertension and smoking presented with chest pain at rest. His electrocardiogram revealed ST elevation in the lateral leads. He was emergently referred to the cardiac catheterization laboratory.

Coronary angiography was performed through a radial approach and documented proximal thrombotic occlusion of the LCX (Fig. 31.8). The patient underwent uneventful primary angioplasty and stenting of the occluded LCX and made an uneventful recovery.

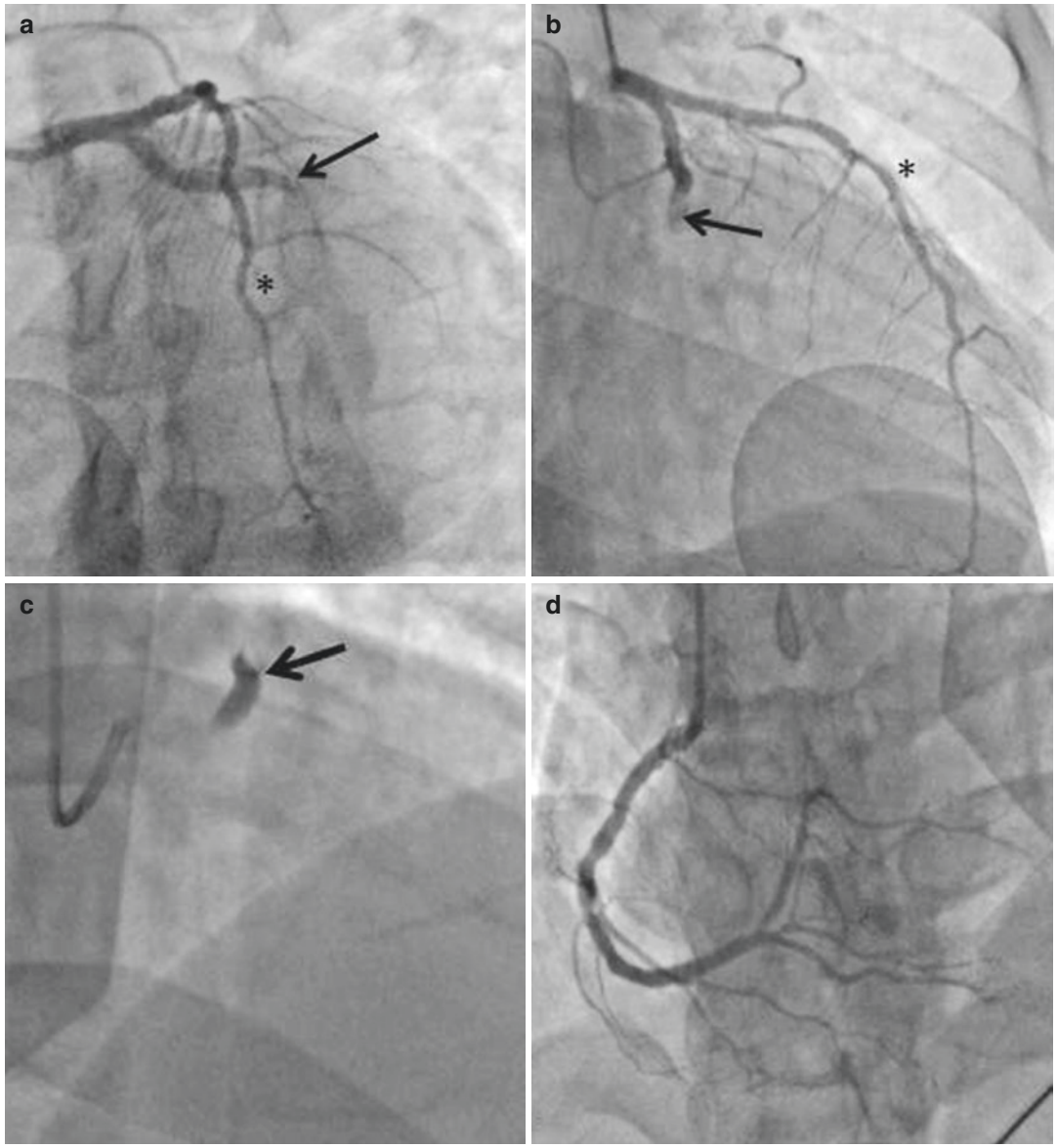


Fig. 31.8 Case 1 catheterization images. (**a**) LAO caudal view shows the LAD (*) and thrombotic occlusion of the LCX (*arrow*); (**b**) AP caudal view also shows the LAD (*) and thrombotic occlusion of the LCX; (**c**) RAO cranial view before injecting contrast depicts residual staining from prior injection in the LCX due to thrombus; (**d**) LAO cranial view of the RCA

Case 2

A 64 year old man with multiple cardiac risk factors including hypertension, hyperlipidemia, known coronary artery disease, and a previous history of smoking presented with increasing angina which was unsuccessfully treated with multiple anti-anginal medications. He was referred for a stress test that revealed a large infero-lateral ischemic defect.

The coronary angiogram documented a critical stenosis in the mid LCX (Fig. 31.9). The mid LCX lesion was stented with a single drug-eluting stent and the patient was afforded complete relief of his angina.

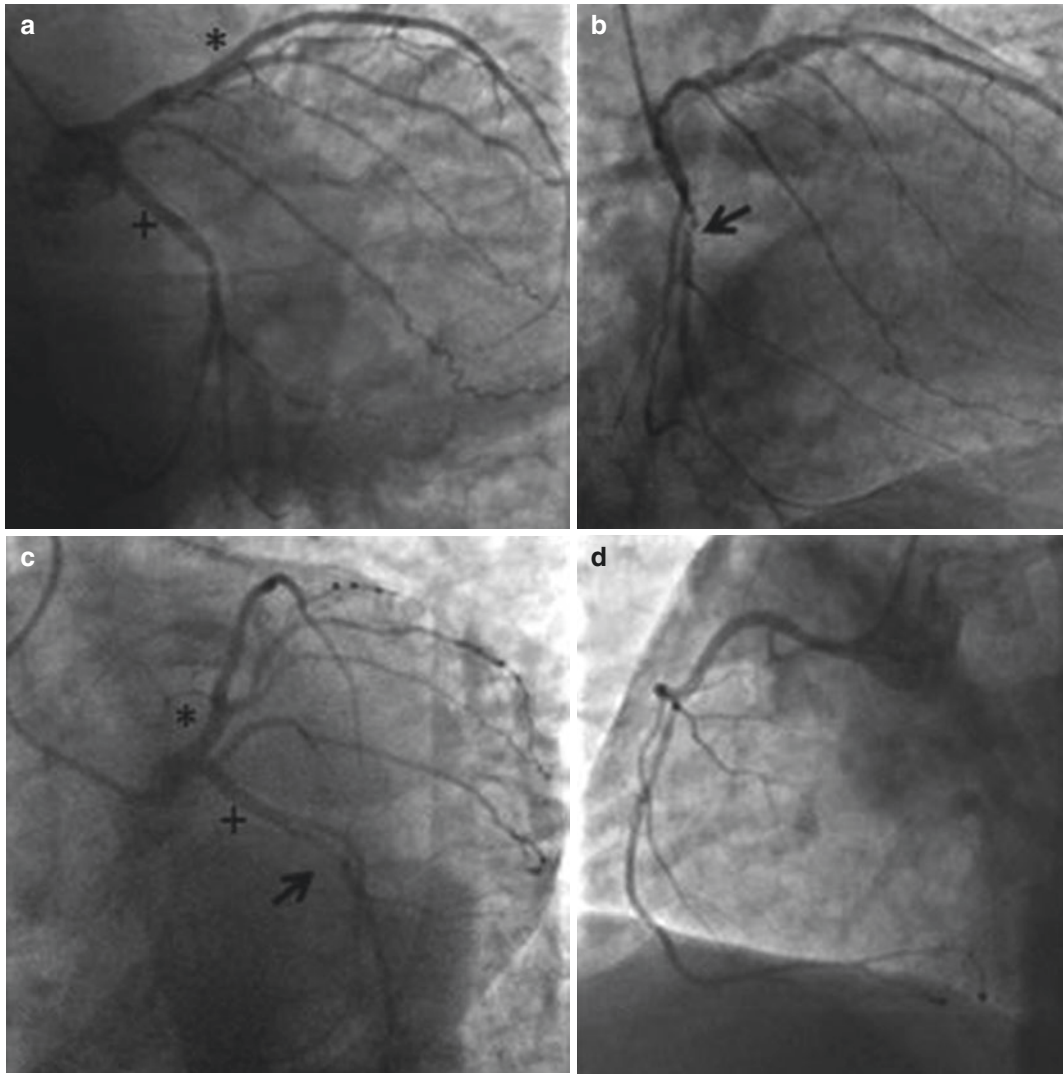


Fig. 31.9 Case 2 angiography. (**a**) AP caudal view showing the LAD (*) and the LCX (+); (**b**) RAO caudal view showing the stenosis in the LCX (*arrow*); (**c**) LAO caudal view also shows the proximal LAD (*) and the LCX (+) with the critically stenotic segment (*arrow*); (**d**) LAO Cranial view of the RCA in this patient

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Coronary Blood Flow and Pressure Measurements

32

Travis J. Cohoon and Morton J. Kern

Introduction

Measuring coronary blood flow and pressure complements the angiographic evaluation of coronary artery disease and facilitates decision-making regarding therapy. Both the macrocirculation (i.e. epicardial arteries >400 mc) and the microcirculation (i.e. small arteries, arterioles, and capillaries, <400 mc) are assessed by different means, both invasively and noninvasively (Fig. 32.1) [1]. The focus of this chapter will be on wire-based, invasive hemodynamic assessments in the cardiac catheterization laboratory.

Precise quantification of stenosis severity by angiography is inherently limited, as coronary "luminograms" are two dimensional representations of complex three-dimensional structures, resulting in confounding angiographic assessment made from different radiographic projections. Moreover, lesions of similar reported diameter narrowing can have drastically different effects on coronary blood flow due to a variety of morphologic factors not quantitated by angiography (Fig. 32.2) [2].

Without investigation into the hemodynamic significance of an angiographically intermediate lesion, operators are at risk of over- or under-treating a stenosis. Although not yet routinely incorporated into angiography, direct measurement of translesional coronary hemodynamics provides the interventional cardiologist with a complete assessment of both coronary anatomy and its ischemic potential (i.e. pathophysiology). Moreover, in patients with chest pain syndromes who undergo elective angiography after an abnormal stress test who are found to have no obstructive coronary artery disease, measurements of coronary blood flow, reserve, and myocardial resistance by various techniques can illuminate the clinical prognosis and be used to diagnose coronary microvascular disease (CMD).

Translesional pressure ratios can be measured at rest or during hyperemia. Fractional flow reserve (FFR) is the ratio of distal coronary artery pressure (Pd) over aortic pressure (Pa) measured during maximal pharmacologically induced hyperemia. Pd/Pa at rest, taken over the entire cardiac cycle or from portions during the diastolic period are called nonhyperemic pressure ratios (NHPR). Both FFR and NHPR been demonstrated to effectively determine the hemodynamic significance of coronary stenoses and the clinical outcomes of patients with treatment guided by the findings.

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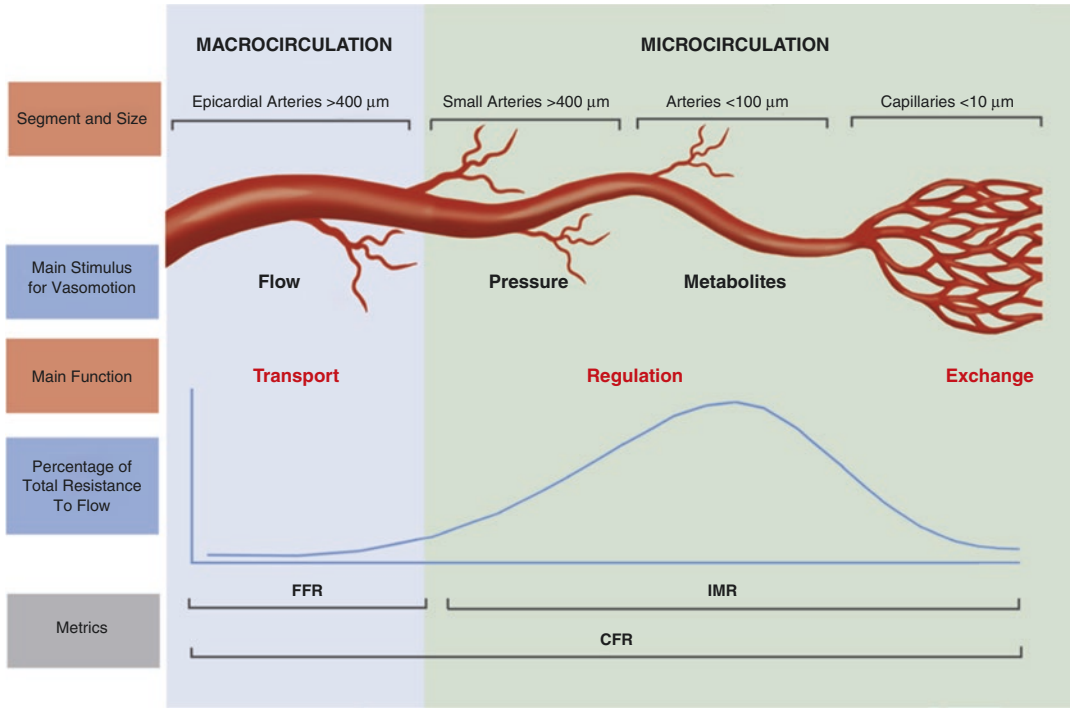

Fig. 32.1 Coronary macro- and microcirculation. The epicardial conduit is >400 μm and offers no resistance to flow. Epicardial stenoses can be measured by hyperemic and nonhyperemic pressure ratios. Small arteries (<400 μm) and arterioles (<100 μm) regulate, and this create resistance to flow. Capillaries are less than 10 μm. The microcirculation is measured by IMR. CFR is a measurement of both the macro -and microcirculation. From De Bruyne B, Oldroyd KG, Pijls NHJ. J Am Coll Cardiol. 2016;67(10):1170–1172

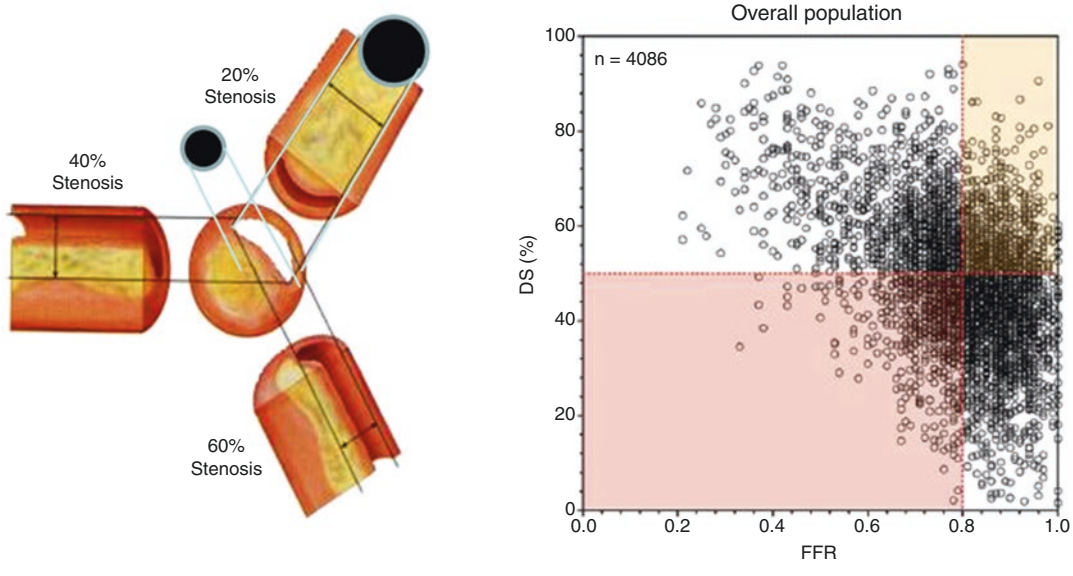

Fig. 32.2 The rationale for the use of coronary physiology is the intrinsic limitation of angiography. Angiographic assessment of epicardial stenosis is limited by differential appearance depending on view. A significant portion of angiographically significant stenoses are not hemodynamically significant by FFR (*yellow shaded area*), and conversely, angiographically insignificant stenoses can be hemodynamically significant (*red shaded area*). From Toth G, Hamilos M, Pyxaras S, et al. Eur Heart J. 2014;35(40):2831–2838

The first principle of translesional pressure measurements is that in normal coronary arteries, the aortic pressure, Pa, is transmitted completely down the vessel with negligible resistance to pressure or flow. Pa is thus the same along the entire length of an epicardial vessel in the absence of atherosclerosis. As developed by Dr. Nico Pijls and colleagues, fractional flow reserve represents the percentage of flow across a stenosis compared to the hypothetical normal flow through the artery in the absence of a stenosis (Fig. 32.3) [3]. The full derivation of FFR initially included venous pressure but for daily clinical practice, venous or RA pressure is considered negligible and can be ignored from the calculation in most circumstances.

$$\text{FFR} = \text{Pd / Pa at maximal hyperemia}\left(\text{i.e.,the lowest Pd / Pa during hyperemic stimulation}\right)$$

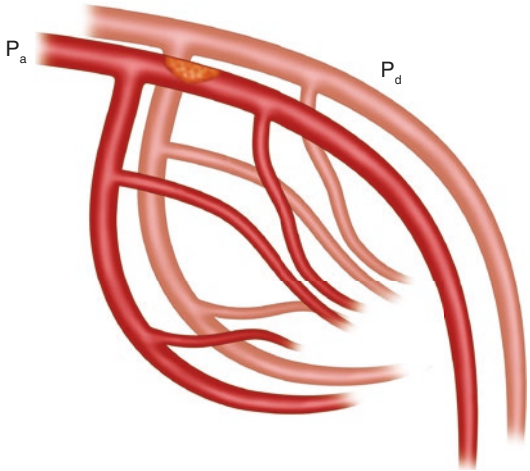

Fig. 32.3 Derivation of Fractional Flow Reserve (% of normal flow across a lesion) = Myocardial flow (Qs) across stenosis/myocardial flow (Qn) without stenosis = FFR. Fractional flow reserve is the ratio of maximal myocardial perfusion in the stenotic territory divided by maximal hyperemic flow in that same region but in the hypothetical case if the lesion were absent. Stated another way, FFR represents that very fraction of hyperemic flow that still persists despite the presence of the stenosis. It has been demonstrated that this ratio of two flows could be calculated solely from the ratio of mean coronary pressure divided by mean aortic pressure provided both pressures are recorded under conditions of maximal hyperemia. In brief, the derivation begins with the fact that aortic pressure, Pa, is the same along the length of the normal vessel. Resistance = P/Q, where Q is Flow. Hence, Q = P/R where R is resistance of the LAD myocardial bed, and that the ratio of stenosis vessel flow, Qs, to flow in the theoretically normal vessel, Qn, equals (Pd/Rs)/(Pa/Rn). If Rstenosis = Rnormal, then Qs/Qn = Pd/Pa; hence, FFR = Pd/Pa, at maximal hyperemia. Courstey of Dr. Bernard De Bryune

The most widely available NHPR is the full cycle mean Pd/P ratio. The first diastolic subcycle Pd/Pa was the instantaneous wave free ratio, the iFR (Philips), which had a good correspondence (about 80%) to FFR. Subsequently, other proprietary NHPR algorithms by various manufacturers [RFR (Abbott), dPR (Opsens), and DFR (Boston Scientific) (Fig. 32.4)] were found to be identical in their correspondence to one another. Using FFR or NHPR, investigators found that stable ischemic heart disease patients benefit both from intervening on hemodynamically significant lesions and deferring intervention on non-hemodynamically significant lesions [4].

Prior to the application of translesional pressure ratios, translesional measurement of coronary flow and flow velocity reserve (CFVR) with intracoronary Doppler sensor guidewires were thought to be able to assess for hemodynamic significance of lesions. This was only true if the microcirculation was known to be normal, which unfortunately cannot be done. True CFVR is valid in the absence of epicardial resistance. Translesional pressure ratios were found to be independent of the microcirculation and became the gold-standard for hemodynamic lesion assessment. Doppler or thermodilution flow measurement of coronary flow reserve (CFR) and index of microcirculatory resistance (IMR, see below) are reserved for assessment of coronary microvascular disease (CMD).

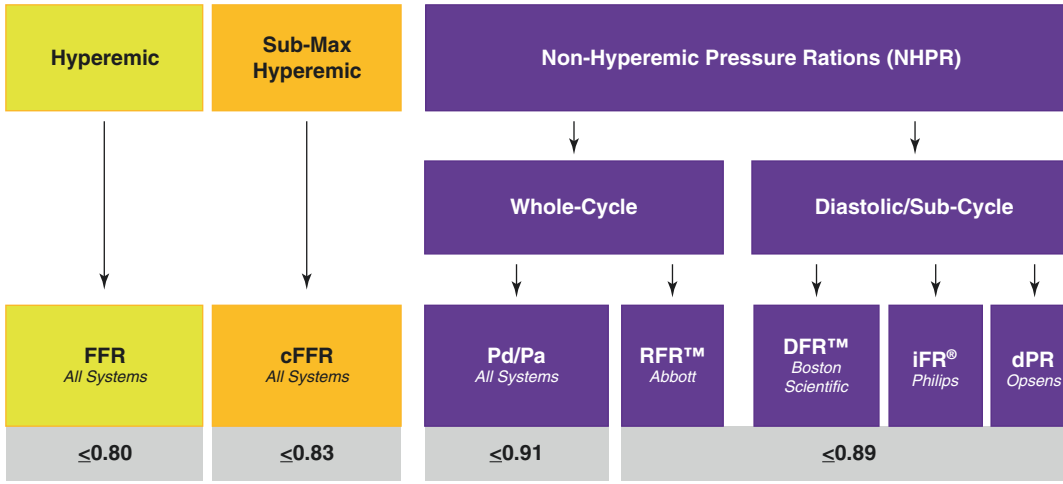

Fig. 32.4 Hyperemic, submaximal hyperemic, and non-hyperemic pressure ratios. FFR is available on all hemodynamic systems with a threshold of ≤0.80. cFFR, contrast FFR, is also available on all systems with a threshold of <0.83. NHPRs: Pd/Pa (all) with a threshold of <0.91. RFR, resting flow reserve ratio (Abbott); DFR, diastolic flow ratio (Boston Scientific); instantenous flow ratio, iFR (Philips); dPR, diastolic pressure ratio (Opsens) have a threshold of ≤0.89. Modified from Kogame Norihiro, Ono Masafumi, Kawashima Hideyuki, et al. *JACC Cardiovasc Interv*. 2020;13(14):1617–1638

Indications and Contraindications for Physiologic Lesion Assessment

Indications for performing translesional coronary physiologic measurements are shown on Table 32.1. The contraindications to physiologic measurements are few. According to current guidelines, no physiologic measurement is warranted for clinical decisions when the clinical, angiographic, and objective ischemia markers are concordant with the diagnosis [5, 6]. Other contraindications include the inability to use anticoagulation for angioplasty sensor wire placement or unstable clinical syndromes.

Table 32.1 Indications for physiologic measurements in the catheterization laboratory

Prior to Intervention
• Establish hemodynamic significance of angiographically intermediate lesions
• Assess diffuse disease
• Evaluate ostia and bifurcation lesions
• Guide therapy with tandem lesions
• Assess culprit and non-culprit lesion in multivessel coronary artery disease or ACS
• Assess collateral circulation
After Intervention
• Estimate prognosis with post PCI FFR/NHPR
• Assess for residual lesions or diffuse disease not amenable to stenting (Stent optimization is anatomically determined)
In the Setting of Nonobstructive Disease
• Assess for structural changes in the microcirculation
• Assess for vasomotor disorders

PCI percutaneous coronary intervention, *FFR* fractional flow reserve, *NHPR*, non-hyperemic pressure ratio

Equipment and Technique

Intracoronary physiologic measurements are made with special sensor tipped guidewires with standard angioplasty equipment and techniques. Several companies make pressure wire/microcatheter products, and in recent years, combination wires that combine multiple diagnostic modalities, such as FFR and CFR, and some that are also workhorse wires have been developed (Fig. 32.5). Unique handling characteristics arise from the special construction of the devices, as they must incorporate the thin wires or optical fibers to transmit the pressure, temperature, or Doppler signals.

For any coronary pressure or flow measurement, the initial procedural steps are the same.

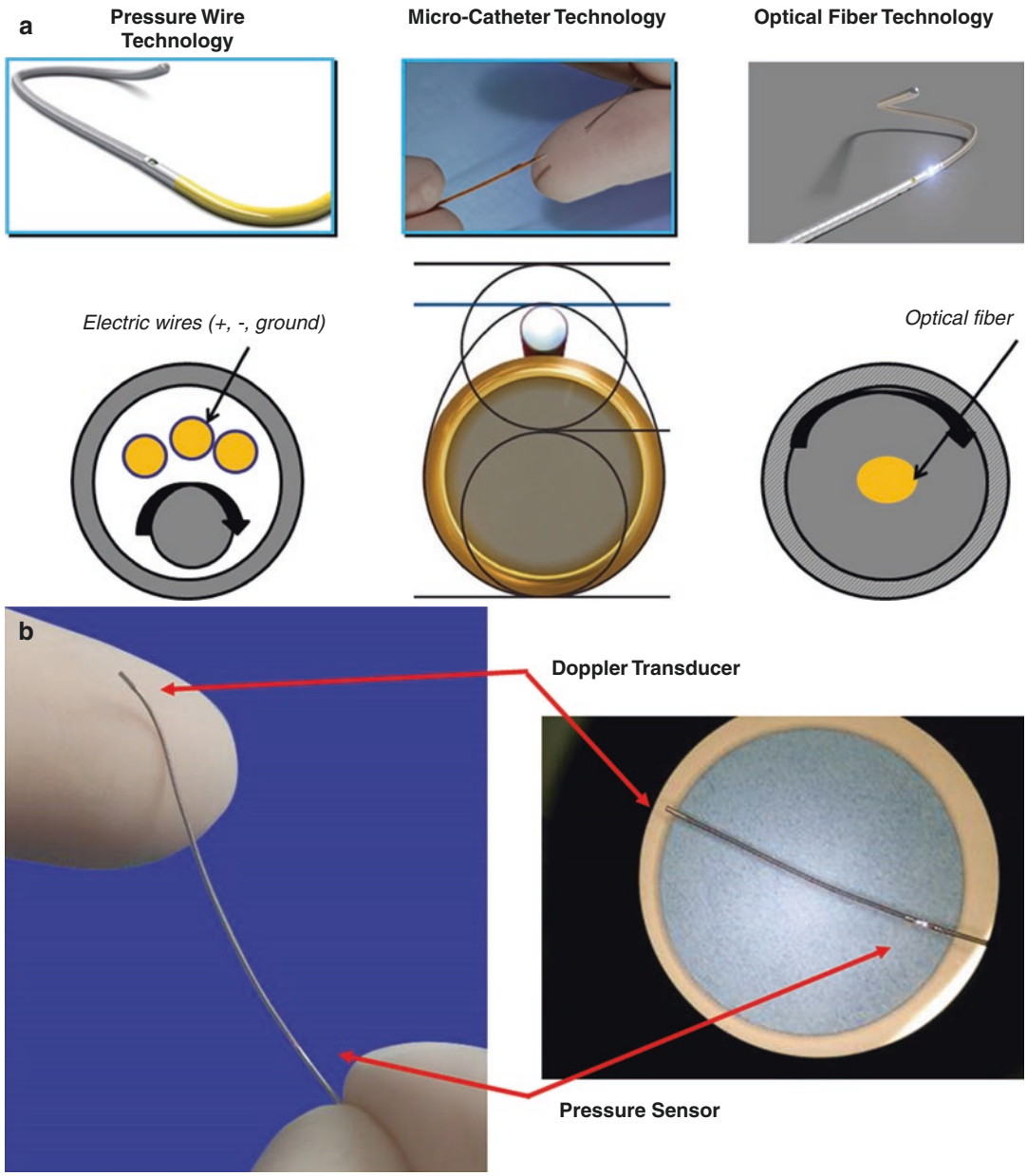

Fig. 32.5 (**a**) Comparisons of available pressure wires. Sensor Wire/Catheter Construction and special features of current pressure wire and microcatheters systems for FFR. *Left*, standard wire core surrounded by thin transmission and ground wires for piezo-resistive transducer signal. *Center,* shape of Rxi microcatheter. *Right*, nitinol or cobalt chromium wire core around central optical fiber to transmit pressure signal. Increase in core dimension and concentricity produces increased torque. Piezoelectric wires have a core wire (steel, thin, low torque) compared to optical wires with a hollow wire (nitinol or cobalt chromium, larger, high torque). From Kern MJ. Cath Lab Digest, May 2016. (**b**) Combination pressure and flow wire from Philips. Pressure sensor is 3 cm proximal to the tip where the Doppler transducer is located

After diagnostic angiography or during angioplasty (and appropriate heparin anticoagulation), the sensor guidewire is zeroed to atmosphere on the cath table and introduced into the guide to the central position. Intravenous (IV) heparin 40–70 units/kg and IC nitroglycerin (100–200 μg) are given several minutes before the guidewire is advanced into the artery. The sensor wire is then passed through an angioplasty Y-connector attached to a diagnostic or guiding catheter. After matching the guide catheter and sensor wire pressure signals, the wire is then passed beyond the stenosis to measure distal translesional pressure.

Hyperemic and Nonhyperemic Pressure Ratios

After the wire is situated at least 10 artery diameters (about 2 cm) beyond the stenosis (to minimize turbulence and optimize laminar flow), the resting translesional pressure ratio, [pick your NHPR] is measured. It is important to accept the NHPR value only during a period of stable resting flow as minimal hyperemia from contrast or saline will alter the resting values. Next, coronary hyperemia is then induced by one of multiple agents (Table 32.2), and the Pd/Pa is continuously recorded over the hyperemic period [8]. FFR is accepted as the lowest Pd/Pa during the hyperemic period. It is worth noting that the injection of radiographic contrast media itself results in submaximal hyperemia and can be used to assess lesions in certain circumstances. Side hole guiding catheter use is discouraged during hemodynamic assessments.

A common algorithm for lesion assessment is noted below:

Begin with NHPR. If deemed reliable proceed with PCI. If NHPR questionable (ie, borderline), perform contrast FFR (cFFR); if cFFR<0.83, proceed with intervention. If cFFR borderline, perform FFR. If FFR < 0.80, proceed with intervention.

FFR is computed as minimum Pd/Pa at maximal hyperemia (Fig. 32.6). Confounding technical factors for physiologic measurement are listed in Table 32.3. The most common errors impacting physiologic measurements are listed in Fig. 32.7.

For NHPRs, operators must ensure that any residual hyperemia from contrast or saline injection has subsided before accepting the resting NHPR as accurate. Some of the NHPR algorithms utilize pressures throughout the entire cardiac cycle (whole cycle) and some measure pressure only during a portion of diastole (Diastolic sub-cycle) (Fig. 32.8) [8]. To distinguish between a focal stenosis and diffuse disease, a continuous pressure pullback can be performed, as described in Fig. 32.9.

Table 32.2 Pharmacologic agents used to induce maximal coronary hyperemia in the cath lab

	Adenosine	Adenosine	Papaverine	NTP	Regadenoson
Route	IV	IC	IC	IC	IV
Dosage	140 mcg/kg/min	100–200 mcg LCA, 50–100 mcg RCA	15 mg LCA, 10 mg RCA	50–100 mcg	0.4 mg
Half-life	1–2 min	30–60 s	2 min	1–2 min	2–4 min (up to 30 min)
Time to max hyperemia	<1–2 min	5–10 s	20–60 s	10–20 s	1–4 min
Advantage	Gold standard	Short action	Short action	Short action	IV bolus
Disadvantage	↓BP, chest burning	AV block, ↓BP	Torsades, ↓BP	↓bp	↑HR,? Redose, long action

Modified from Fearon [7]
FFR indicates fractional flow reserve, *IC* intracoronary, *IV* intravenous, and *VT* ventricular tachycardia *NTP* nitroprusside, *BP* blood pressure, *AV* atrioventricular node

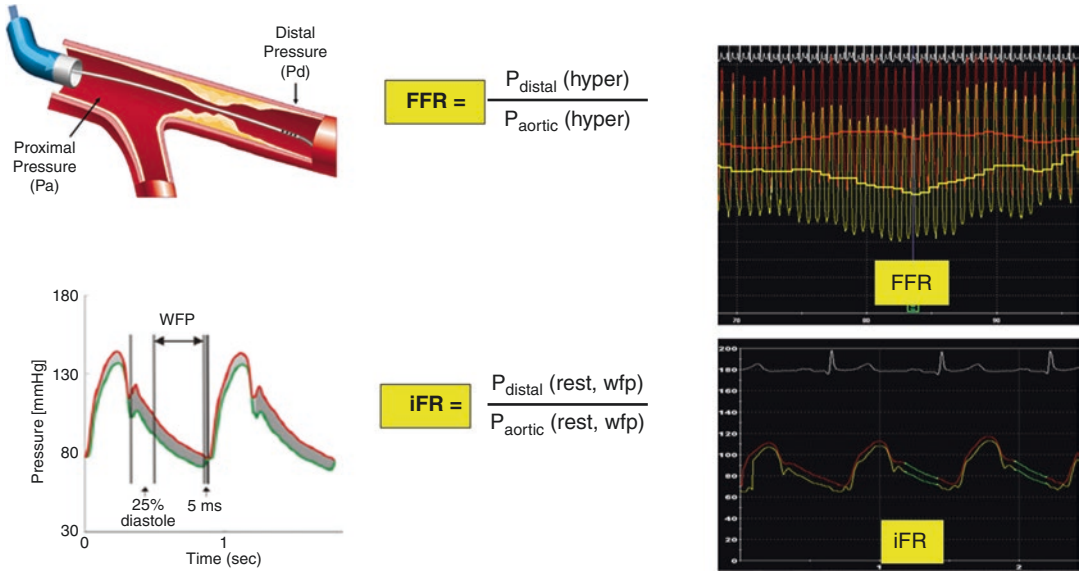

Fig. 32.6 Invasive Translesional Pressure Measurements. *Top*, diagram of pressure wire across a stenosis with guide catheter in place at the coronary ostium. Formula for FFR, fractional flow reserve, is Pdistal (where P is pressure) during hyperemia (hyper). The upper right tracing demonstrates the FFR value taken at the lowest Pd/Pa during hyperemia. *Bottom*, graphic demonstrating the wave free period of diastole (WFP) where the iFR, instantaneous wave free ratio is computed. Right lower is a tracing of the iFR signal (in *green*). From Sen S, et al. J Am Coll Cardiol Intv. 2012;59(15):1392–1402

Table 32.3 Technical factors for translesional pressure measurement accuracy

1. Equipment factors
Erroneous zero
Incomplete pressure transmission (tubing/connector leaks)
Faulty electric wire connection
Pressure signal drift
Hemodynamics recorder miscalibration
2. Procedural factors
Guide catheter damping
Incorrect placement of pressure sensor
Inadequate hyperemia (FFR, CFR only)
3. Physiologic factors
Serial lesion
Reduced myocardial bed
Acute myocardial infarction
4. Theoretical conditions that might influence FFR
Severe left ventricular hypertrophy
Exuberant collateral supply
Adenosine insensitivity (FFR, CFR only)

FFR fractional flow reserve, *CFR* coronary flow reserve

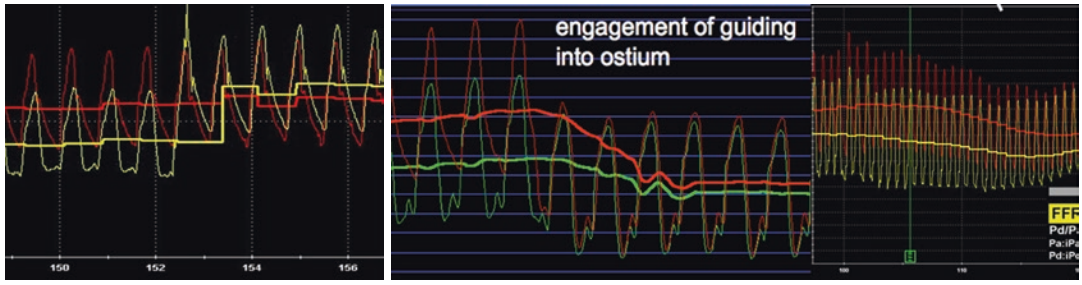

Fig. 32.7 Most common errors of translesional physiologic measurements. *Left*, signal drift. Note the *yellow* tracing of the wire pressure exceeds the *red* pressure of the guide catheter on the far-right side. *Middle*, damping of the pressure signals of both the aortic guide catheter and the guidewire pressure. The left side of the tracing is the baseline before damping and right side shows deep engagement and damping of both signs. *Right*, variance of FFR during IV adenosine infusion shows the correct location to accept the FFR value (*green marker line*). This point is called the smart minimum FFR value

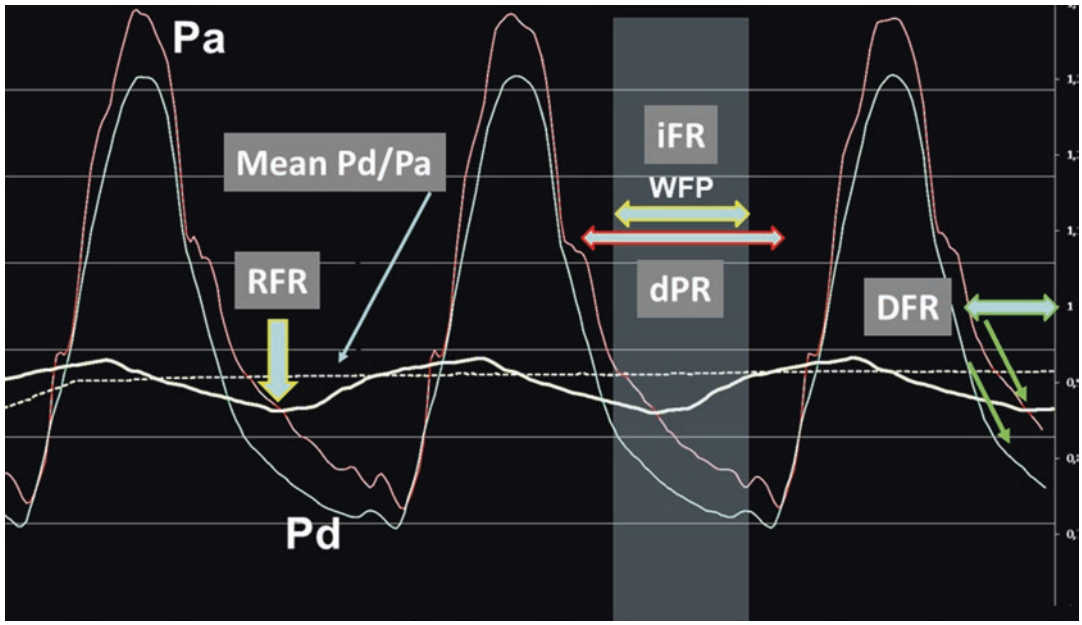

Fig. 32.8 Non-hyperemic pressure ratios. *Pd* distal pressure, *Pa* aortic pressure, *Mean Pd/Pa* whole cycle distal to aortic pressure ratio, *RFR* relative flow reserve, lowest absolute mean Pd/Pa, *WFP* wave free period, *iFR* instantaneous wave free pressure ratio, *DPR* full diastolic pressure ratio, *dPR* Pd/Pa during flat period of the dP/dt of aortic pressure

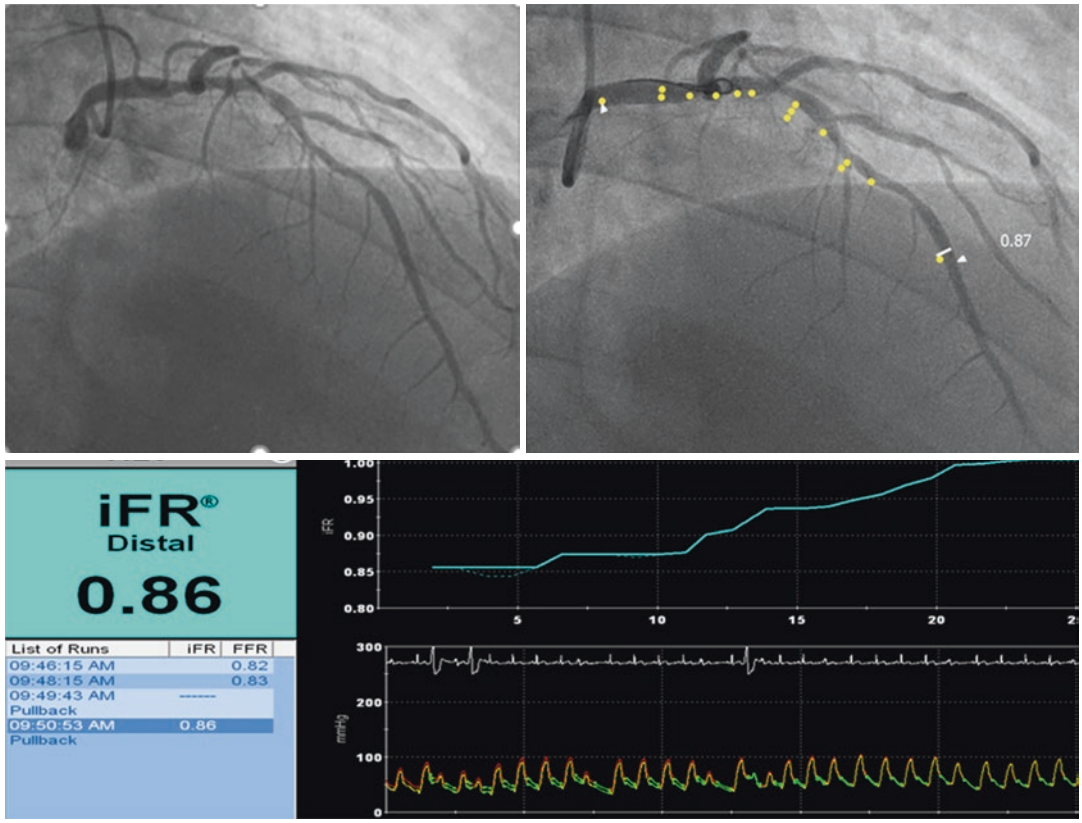

Fig. 32.9 LAD Assessment using iFR pullback showing diffuse disease. Note the gradual increase in iFR measurement during the pullback (lower right), which is the indicator of diffuse disease. FFR = 0.82; iFR = 0.86 but no focal lesion which would be indicated by a sharp step up in iFR

Doppler and Thermodilution Evaluation of Coronary Blood Flow

For Doppler flow velocity evaluation, the sensor tip is advanced at least 5–10 artery-diameter lengths (>2 cm) beyond any luminal narrowings to measure velocity in a region of re-established laminar flow. Resting flow velocity data are recorded. Induction of coronary hyperemia by IC or IV adenosine is performed, continuously recording through peak hyperemic flow velocity (Fig. 32.10). Coronary flow reserve, CFR, is computed as maximal hyperemic to basal average peak velocity (APV) (Fig. 32.11).

Poor Doppler signal acquisition may occur in 10–15% of patients even within normal arteries. Like transthoracic echo Doppler studies, the operator must adjust the guidewire position (sample volume) to optimize the velocity signal [9]. In the absence of hemodynamically significant epicardial coronary artery disease, coronary flow reserve reflects the function of the microvasculature, and is used in testing for endothelial function with an endothelin-independent vasodi-

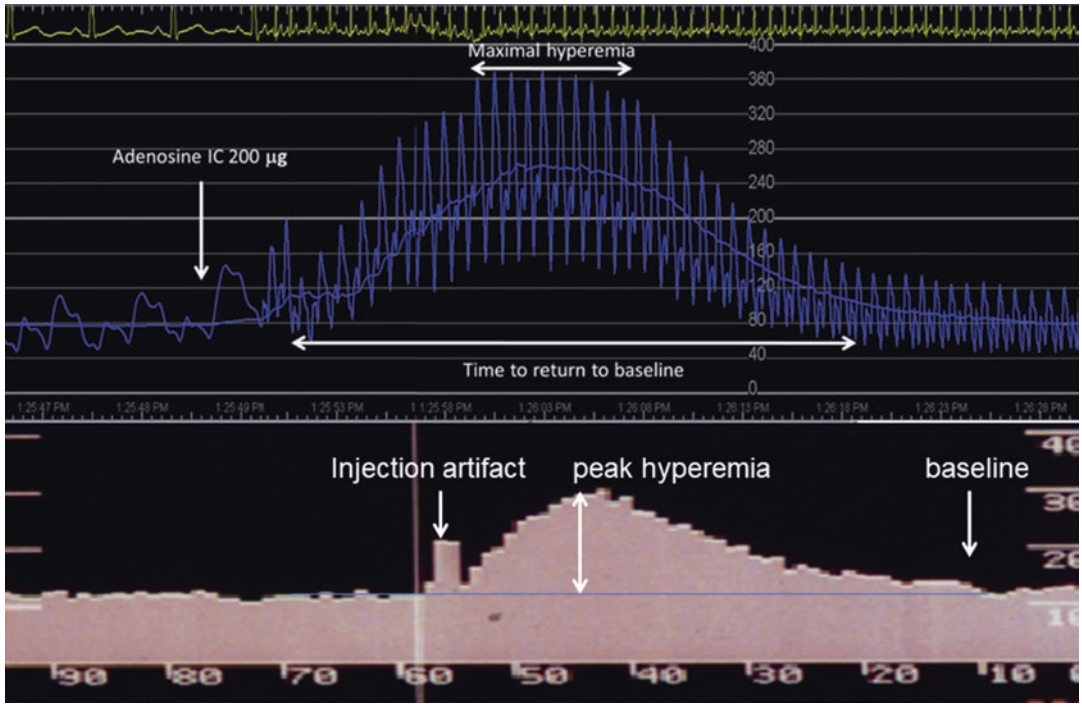

Fig. 32.10 Intracoronary Doppler flow velocity with intracoronary adenosine. *Top*, zero cross Doppler signal showing the maximal hyperemic response after 200mcg adenosine injected intracoronary (IC). Adapted from Adjedj et al. J Am Coll Cardiol Intv. 2015;8(11):1422–1430. *Bottom* shows trend plot of average peak velocity (APV) from Doppler wire with spectral signal during injection of 30mcg IC adenosine. From Kern MJ, 1991

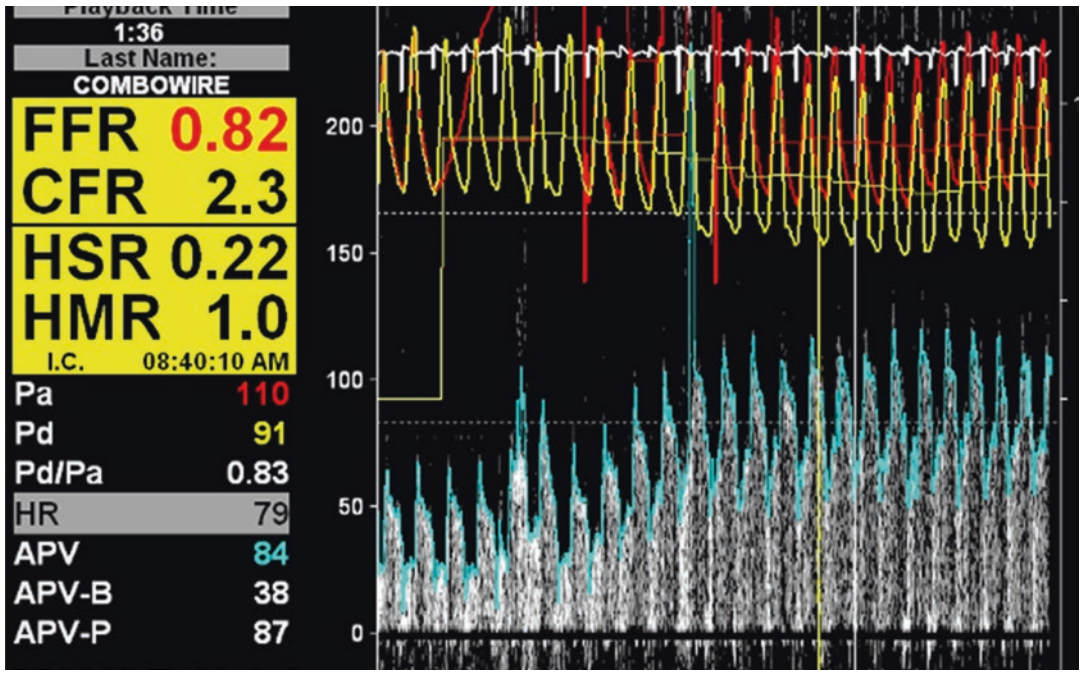

Fig. 32.11 Combination FFR and CFR assessment with combination pressure and Doppler flow wire. *HSR* hyperemic stenosis resistance, *HMP* hyperemic myocardial resistance, *APV-B* average peak velocity at baseline, *APV-H* average peak velocity at hyperemia

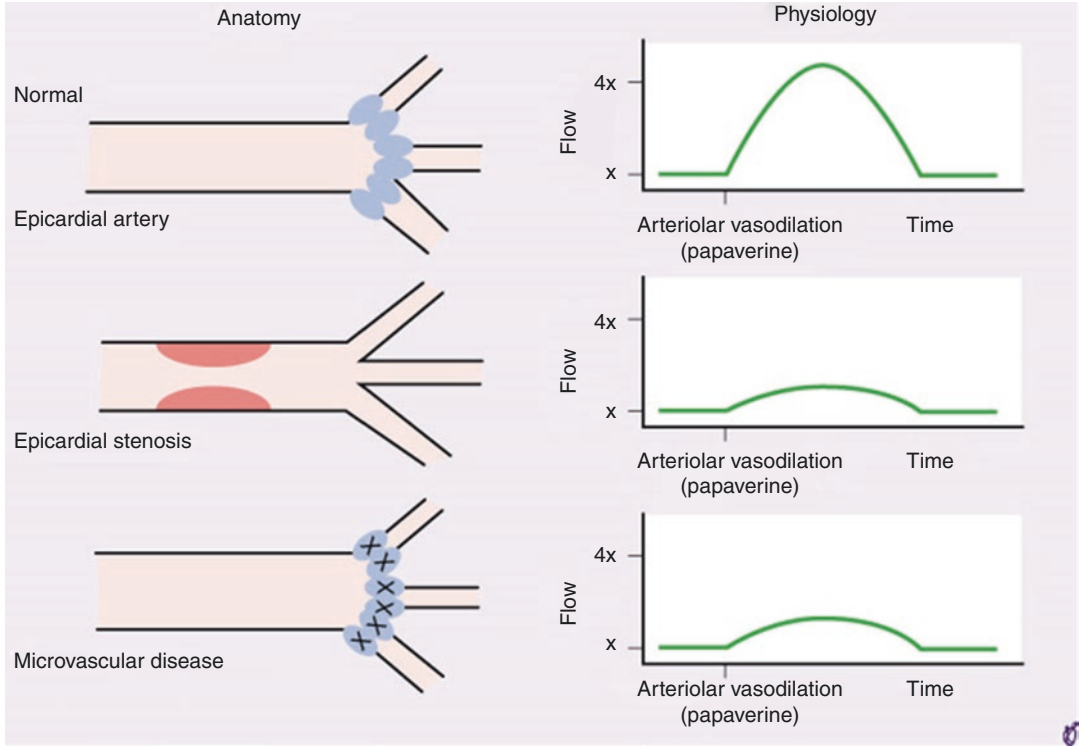

Fig. 32.12 CFR measures the sum of flow through the epicardial arteries and the microvasculature, and it cannot distinguish between a focal epicardial stenosis and microvascular disease. As such, it should only be used in the setting of normal epicardial arteries when measuring the microcirculation. Modified from Wilson R et al., Circulation 1980

lator such as adenosine (for structural changes in the microcirculation) or with an endothelin-dependent vasodilator challenge such as acetylcholine to assess for vasomotor disorders [10]. Of note, CFR cannot distinguish between a stenosis obstructing hyperemia or an impaired microcirculation (Fig. 32.12).

For thermodilution CFR, the method is similar to that of cardiac output using a thermodilution balloon tipped pulmonary artery catheter. Using a proprietary pressure/temperature sensing guidewire (Abbott Vascular), aortic pressure, distal coronary pressure (Pd), the Pd/Pa, (Fig. 32.13) and intracoronary temperature are recorded after consecutive injections of 3 boluses at rest and 3 boluses during steady-state hyperemia. Hyperemia can be induced by intravenous adenosine or intracoronary papaverine. Coronary flow is directly related to the inverse of the time to minimal temperature (Tmn) and is used to compute CFR as (1/Tmn at base)/(1/Tmn at hyperemia). Measurement of fractional flow reserve (FFR), coronary flow reserve (CFR), and the index of microvascular resistance (IMR) are computed. The index of microcirculatory resistance (IMR) is the distal pressure divided by the inverse of the mean transit time during maximal hyperemia [10].

Fig. 32.13 Thermodilution method of measuring CFR. Simultaneous recordings of aortic pressure (Pa; *red tracing*), distal coronary pressure (Pd; *green tracing*), their ratio (Pd/Pa; *yellow tracing*), and intracoronary temperature after consecutive injections of 3 boluses at rest (*blue tracings*) and 3 boluses during steady-state hyperemia (orange tracings). Hyperemia can be induced by intravenous adenosine or intracoronary papaverine. These recordings allow simultaneous measurement of fractional flow reserve (FFR), coronary flow reserve (CFR), and the index of microvascular resistance (IMR). The *yellow arrows* point to the average values of resting and hyperemic mean transient time (Tmn) as well as to the average distal coronary pressure (Pd) during hyperemia. These values are needed to derive CFR and IMR. From Alessandro Candreva et al. J Am Coll Cardiol Cardiovasc Interv 2021; 14:595–605

Complications

The complications of invasive coronary physiologic measurements are the same as those related to diagnostic coronary angiography and with those associated with coronary angioplasty guidewire insertion and lesion transit. The major safety considerations involve guiding catheter/wire vessel trauma (the same as occurs with regular angioplasty wires), thrombus, or coronary vasospasm. The incidence of such complications is <0.01%. The use of vasodilators, such as adenosine, may be associated with bradycardia and hypotension. IC papaverine has been associated with rare occurrences of torsade de pointe ventricular fibrillation. Overall, the clinical practice using sensor wire measurements with pharmacologically induced hyperemia is very safe with the benefit of providing valuable information offsetting the small risk of the invasive approach.

Data Interpretation

Ischemic Thresholds of Coronary Physiologic Measurements

A hemodynamically significant coronary lesion is associated with one or more of the following parameters which have been correlated to provokable myocardial ischemia (Table 32.4). In addition, diffuse versus focal disease can be assessed by pullback as discussed earlier (Fig. 32.8). Outcome studies have demonstrated that lower FFR values portend increased cardiovascular risk, and FFR guided intervention improves outcomes (Fig. 32.14) [4, 11]. Further studies of NHPRs, such as DEFINE FLAIR and SwedeHeart for iFR have demonstrated noninferiority to FFR (Fig. 32.15) [7, 12].

Table 32.4 Ischemic thresholds for intracoronary physiologic measurements

Hyperemic Pressure Ratios	Threshold
Adenosine FFR:	≤0.80
Contrast FFR:	≈0.83
Nonhyperemic Pressure Ratios	
Distal coronary pressure/proximal coronary pressure (Pd/Pa):	≤0.91
Resting full-cycle ratio (RFR):	≤0.89
Diastolic hyperemia-free ratio (DFR):	≤0.89
Instantaneous wave-free ratio (iFR):	≤0.89
Diastolic pressure ratio (dPR):	≤0.89
Diastolic pressure ratio (DPR):	≤0.89
Coronary Doppler	
Coronary flow reserve (CFR):	<2.0
Proximal to distal flow velocity ratio (P/D):	<1.7
Diastolic to systolic velocity ratio (DSVR):	<1.8

Multivessel Coronary Artery Disease

Data from multiple prospective clinical trials strongly support the concept that patients with multivessel CAD benefit from physiologic guided compared to only angiographically guided revascularization [13–17]. FFR >0.80 is associated with exceptionally good prognosis when treated with optimal medical therapy alone. FFR in and around the 'gray zone' (0.75–0.80) still has important prognostic value, especially in proximal lesions, and confirms that FFR ≤0.80 is valid to guide clinical decision making [17].

Left Main Coronary Artery Assessment

Numerous studies support FFR use for assessment of left main (LM) coronary stenoses (Table 32.5) [18]. For complex LM disease with downstream significant LAD or CFX stenosis, the data from in vitro, animal, and human studies of LM stenosis demonstrate that in most cases, downstream disease does not have a clinically significant impact on the assessment of FFR across an intermediate LM stenosis. Downstream stenoses in the LAD or LCx must be severe (i.e., FFR < 0.60) and proximal to have a marked effect on the LM FFR measured in the remaining uninvolved branch. Should both branches have significant stenoses, then IVUS assessment of the LM with a threshold minimal luminal area of <6.0 mm^2 is recommended [8, 19].

Acute Myocardial Infarction

Acute myocardial injury produces transient microvascular dysfunction to various degrees and impairs maximal coronary hyperemia depending on the size of the injured myocardial mass. Reducing the flow across a stenosis will yield an artificially high FFR which, days later during recovery of flow may then drop to a significant level. After the patient recuperates, myocardial recovery may increase coronary flow, and higher flow would lower the FFR, perhaps below the ischemic threshold thus changing a treatment decision from that made during the acute event. As a result, FFR of a culprit vessel that is involved in a ST-elevation myocardial infarction or large non-NSTEMI can result in a false-negative result. Nonetheless, for a culprit vessel, FFR has been demonstrated to be accurate after 4–6 days of recovery from the index event or immediately for most unstable angina patients and small NSTEMI patients. FFR of most non-culprit lesions at a distance from the infarct related artery has also been shown to be accurate.

Microvascular Dysfunction

Microvascular dysfunction is the impairment of coronary flow reserve or elevated myocardial resistance thought to be due to either structural or function abnormalities of the intramyocardial vasculature (i.e. precapillary and capillary vessels, <400mc). Coronary microvascular dysfunction (CMD) has been examined using a number of invasive coronary physiologic parameters (Table 32.6). Patients with low CFR and high IMR have a poor prognosis [20]. Indeed, it has been proposed to algorithmically assess microcirculatory dysfunction in the setting of ischemia without obstructive coronary artery disease [21].

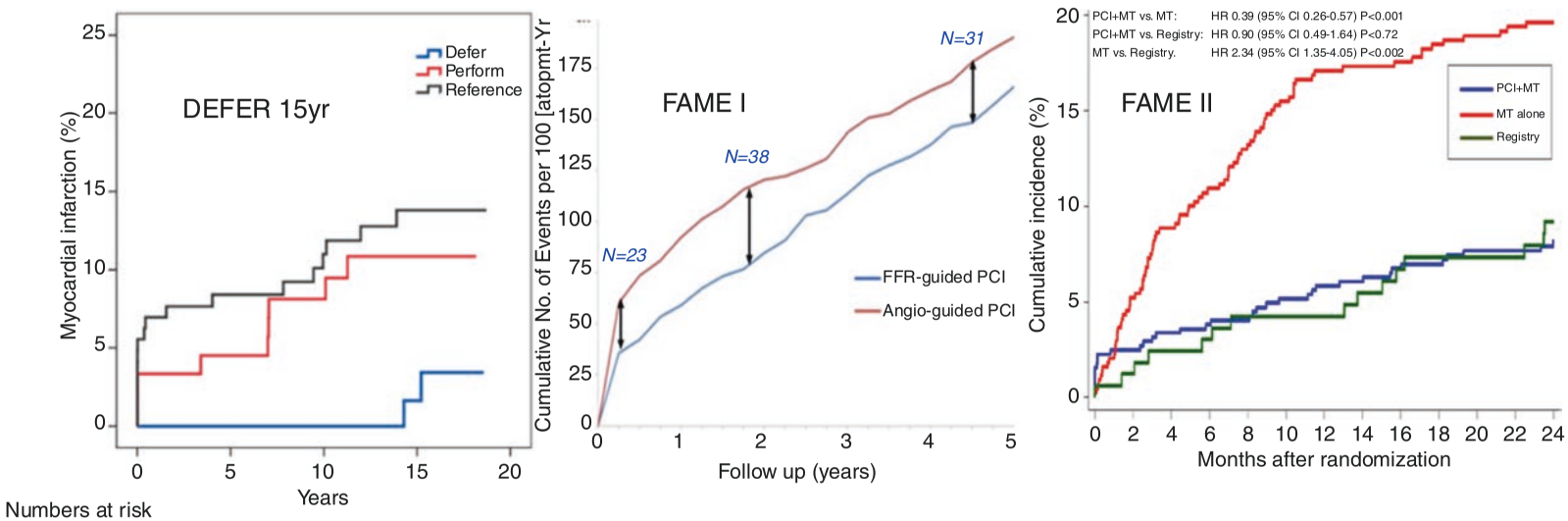

Fig. 32.14 Three major FFR outcome studies: DEFER 15 yr., FAME I, and FAME II. In the DEFER study (*left panel*), FFR was 0.86 + 0.06 in the Defer treatment group, 0.87 + 0.07 in the Perform group, and 0.57 + 0.16 in the Reference group. The rate of MI was significantly lower in the Defer group (2.2%) compared with the Perform group (10.0%), $P < 0.03$. This was almost exclusively due to less target vessel-related infarctions. Patients with a baseline FFR ≥ 0.75 had a significantly lower rate of MI compared with patients with an FFR < 0.75 (6.1 vs. 12.5%, RR 0.49, 95% CI: 0.24–1.00, $P < 0.044$). From Zimmerman EHJ 2015; 36, 3182–3188. In the FAME study (middle panel), FFR guided PCI was superior to only angiographically guided PCI with fewer MACE over 5 years. From van Nunen LX, et al. Lancet. 2015 Nov 7;386(10006):1853-60. In the FAME 2 study (right panel), patients with significant low FFR treated medically without revascularization (*red group*) had significantly more MACE over the first 2 years than either the FFR guided revascularized group (*blue*) or the multivessel FFR negative reference group (*green*). From Xaplanteris P, et al. NEJM. 2018; 19;379(3):250–259

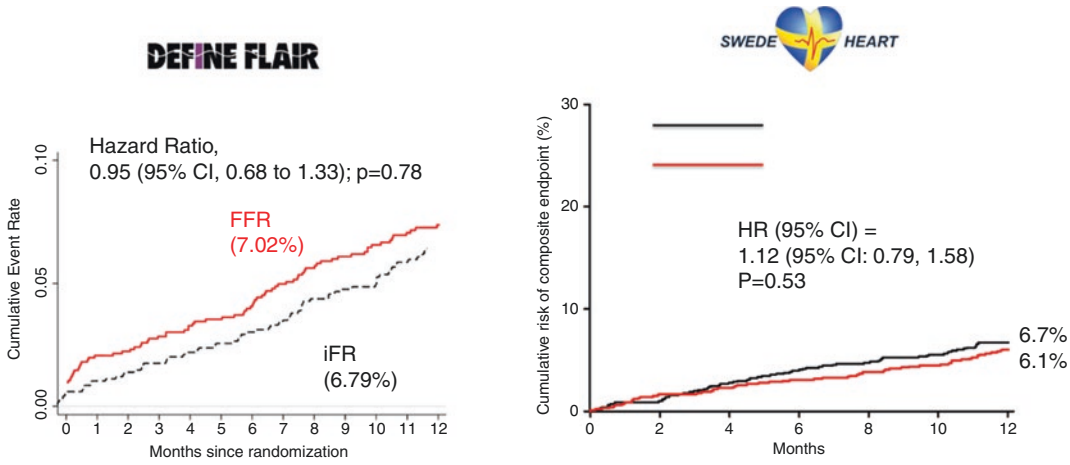

Fig. 32.15 *Left* Define Flair Study using iFR and FFR demonstrated the cumulative risk of the composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization at 1 year. *Right* The Swede heart iFR Study demonstrated the cumulative risk of the composite of death from any cause, nonfatal myocardial infarction, or unplanned revascularization within 12 months after the index procedure. Both studies demonstrated iFR was non-inferior to FFR in these stable ischemic heart disease patients. From Davies J et al., Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI. N Engl J Med 2017;376:1824–34 and Gotberg M et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. N Engl J Med 2017;376:1813–23

Table 32.5 Fractional flow reserve (FFR) studies assessing intermediate left main stenosis

			Medical Therapy			Surgical Therapy			
Study	FFR Threshold	Total N	N (%)	MACE	Death	*n* (%)	MACE	Death	Follow-Up Time
Hamilos (2009)	0.8	213	136 (65%)	26%	9 (6.5%)	73 (35%)	17%	7 (9.6%)	35 ± 25
Courtis (2009)	0.75 surg; >0.80 med	142	82 (58%)	13%	3 (3.6%)	60 (42%)	7%	3 (5%)	14 ± 11
Lindstaedt (2006)	0.75 surg; >0.80 med	51	24 (47%)	31%	0	27 (53%)	34%	5 (19%)	29 ± 16
Suemaru (2005)	0.75	15	8 (53%)	0	0	7 (47%)	29%	0	33 ± 10
Legutko (2005)	0.75	38	20 (53%)	10%	0	18 (46%)	11%	2	24 mean
Jimenez-Navarro (2004)	0.75	27	20 (74%)	10%	0	7 (26%)	29%	2	2 ± 12
Bech (2001)	0.75	54	24 (44%)	24%	0	30 (56%)	17%	1	29 ± 15

From Lokhandwala J, Hodgson J. Assessing intermediate left main lesions with IVUS or FFR. *Cardiac Interventions Today*. October 2009

Table 32.6 Definitions of CMD

Indices of Coronary Microvascular Disease	Threshold
CFR, coronary flow reserve (Doppler or Thermodilution):	<2.0 ≥23 U
IMR, index of microvascular resistance (Distal pressure/(1/mean transit time) at maximal hyperemia):	

Post PCI Physiology

Use of translesional physiology after the implantation of the stent will provide better optimization and prognosis. As shown in the DEFINE-PCI study, 25% percentage of angio-

graphically adequate interventions have residual hemodynamic impairment due to diffuse CAD, unsuspected new narrowing, edge stent dissection, proximal vessel narrowing or vasospasm [22]. Post-intervention FFR can be utilized to assess for residual disease, amenable to further stenting or manage with medical therapy alone (Fig. 32.16). Moreover, the post PCI FFR provides valuable prognostic information (Fig. 32.17) [22].

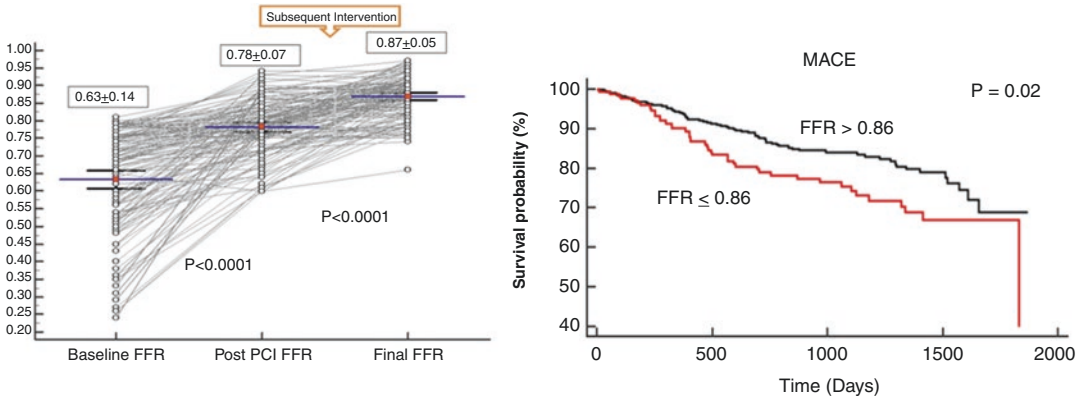

Fig. 32.16 Utilizing Post-Intervention FFR to Optimize Acute Results and the Relationship to Long-Term Outcomes. *Left* Impact of interventions on post-PCI FFR. Despite angiographic optimal results, 20% of all lesions (n = 137) had a persistently ischemic FFR necessitating subsequent intervention. The FFR prior to reintervention was 0.78 ± 0.07 and after intervention was 0.87 ± 0.05. *Right* Kaplan–Meier curve showing significantly higher survival free of major adverse cardiovascular events (MACE) in the patients with final fractional flow reserve (FFR) > 0.86 in comparison with the final FFR ≤0.86 group. From Agarwal SK. JACC Cardiovasc Interv. 2016 May 23;9(10):1022–31

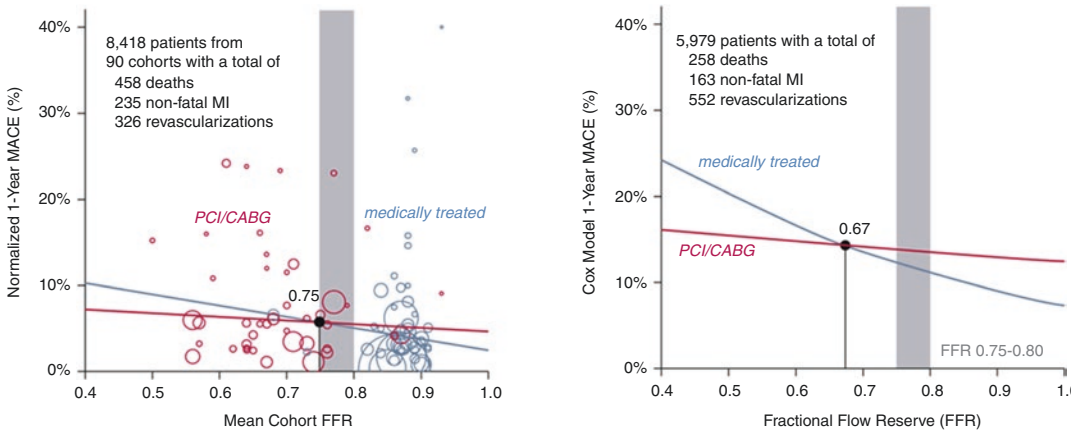

Fig. 32.17 Prognostic Value of Post-Stent FFR. *Left*, normalized 1-year major adverse cardiac event (MACE) rate for study-level analysis. Meta-regression for the study-level data fits the normalized 1-year MACE rate (circles whose size reflects the number of patients) for cohorts treated with either revascularization (*red*) or medical therapy (slate) as a function of mean lesion FFR. Colored lines depict the meta-regression fit. These curves cross at the optimal FFR threshold, shown here for a univariate model with random effects. *Right*, cox model 1-year MACE rate for patient-level analysis. Patient-level analysis fits the outcomes data to a Cox proportional hazards model of survival, shown here with the best-fit 1-year MACE rate as a function of individual lesion FFR. Colored lines depict the model fit for revascularization (*red*) or medical therapy (slate) treatment. These curves cross at the optimal FFR threshold, here shown for the unadjusted model. From Johnson N, et al. J Am Coll Cardiol. 2014 Oct 21;64(16):1641–54

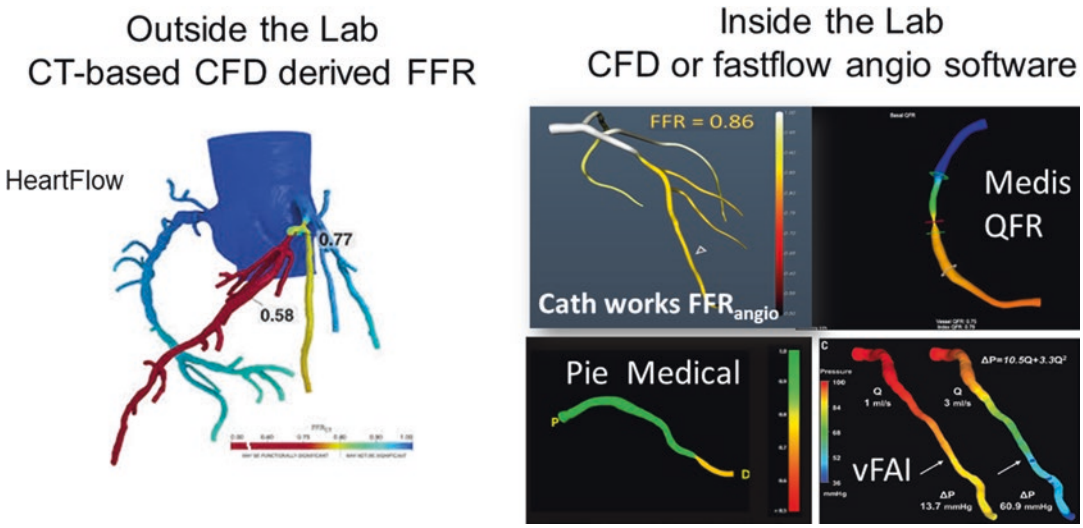

Fig. 32.18 Methodologies for Angiographic derived FFR. *Left*, FFRCT image provides a color coded FFRCT map. Adapted from Taylor C et al. *Right*, 4 commercial approaches to angiographically derived FFR from 2 orthogonal coronary angiographic projects. Upper left, the CathWorks FFR_{angio} processes the data, reconstructs a qualitative 3D model of the coronary tree and calculates FFR of a culprit lesion. A color mapped mesh is then generated that represents the FFR values at every location, as long as vessel diameter is not limited by image resolution. The results are displayed on the Cath Lab's integrated monitors and can be observed and manipulated as required. From Ran Kornowski, MD, FACC, FESC, Rabin Medical Center, Petach Tikva, Israel. Upper right, Angiograms and corresponding FFRangio Maps. From Pelicano et al. courtesy of Medis QFR. Lower left, 3-D QCA & TIMI Frame Count from Tu S et al., JACC *Interv* 2014. Lower right, Virtual Functional Assessment Index (vFAI) From Papafaklis MI et al., EuroIntervention 2014

Future Directions—Angiographically Derived FFR

Currently, angiographic systems are available to compute FFR from 3D reconstructed angiograms with accuracy for invasive FFR of around 80%. Continued research and clinical studies for the application and validation of angiographically-derived FFR based on computational fluid dynamics is ongoing for both CT-derived (CT-FFR) and angiography-derived images (e.g., quantitative flow ratio, QFR) to assess for hemodynamic significance of lesions without wires (Fig. 32.18).

Clinical Vignette

A 56-year-old man with exertional angina while mountain biking presents for evaluation. Chest pain was substernal, stopped with rest, and restarted on exertion. The patient was admitted and started on medical therapy with beta-blockade, aspirin, and heparin. ECG demonstrated deep T-wave inversions in the inferolateral leads. Serial troponins were negative. The patient was taken to the cardiac catheterization laboratory, revealing a moderate, focal stenosis in the left circumflex artery and a moderate, focal stenosis as well as diffuse disease in the right coronary artery (Fig. 32.19).

At rest, the Pd/Pa of the left circumflex artery was 0.63, well below the cutoff for hemodynamic significance, and percutaneous coronary intervention in the proximal left circumflex resulted in a Pd/Pa of 1.0 (Fig. 32.20). Next, the Pd/Pa of the RCA was measured at 0.97, and contrast FFR was 0.87, well above the cutoff for hemodynamic significance, and no intervention was performed (Fig. 32.21). This case illustrated the value of translesional physiology changing 2 vessel CAD into functional 1 V CAD with reduced chances of stent related events going forward.

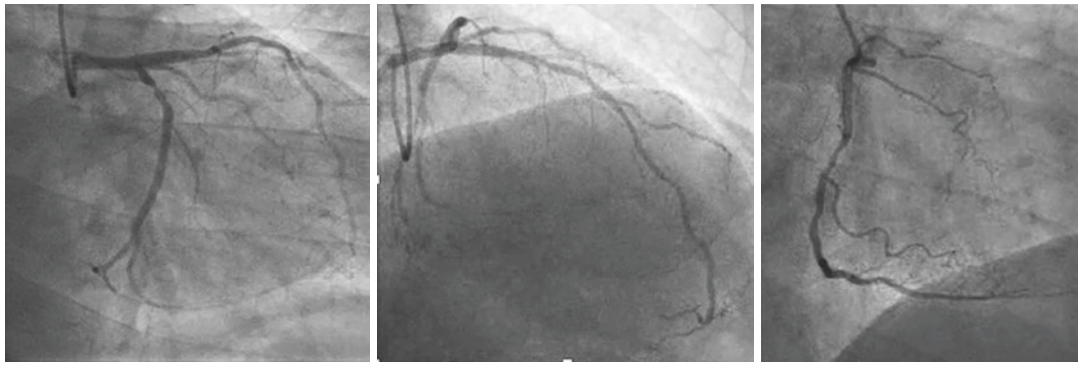

Fig. 32.19 56-year-old man with exertional angina of recent onset. Coronary angiography shows luminal irregularities of the LAD and significant narrowing in the circumflex artery (left and center panels, RAO caudal and cranial projections) with diffuse mid RCA narrowing (right panel, RAO view)

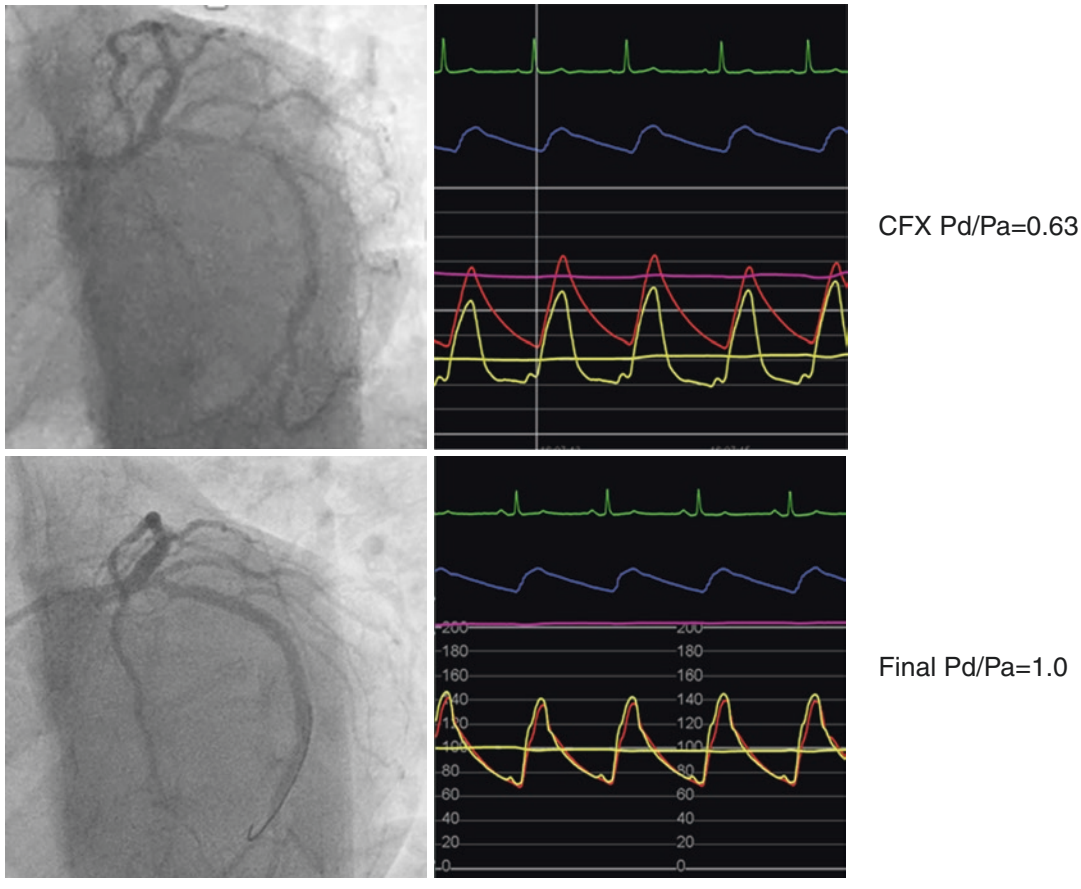

Fig. 32.20 *Top* pre-PCI with LAO caudal view showing significant circumflex lesion and corresponding resting Pd/Pa = 0.63, a significant ischemic value. *Bottom* Left panel shows CFX after stenting and corresponding Pd/Pa of 1.0 on the right, a completely normal value. No further intervention was deemed necessary

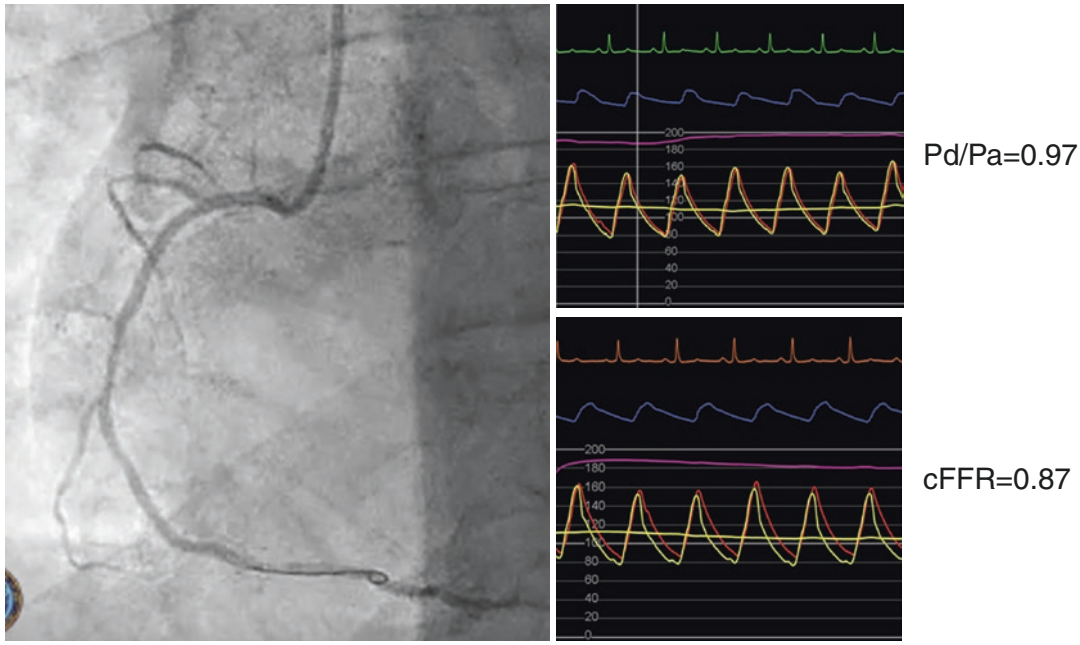

Fig. 32.21 Coronary angiography and resting Pd/Pa (0.97) and contrast FFR (cFFR = 0.87) both near normal values. No intervention was deemed necessary on the RCA

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Percutaneous Coronary Intervention

33

Yousef Bader, Fahim H. Jafary, and Carey Kimmelstiel

Introduction

There are over one million percutaneous coronary interventions (PCI) performed each year in the United States. PCI refers to catheter- based procedures that allow for improved perfusion through epicardial coronary arteries to the myocardium. PCI originally referred to percutaneous transluminal coronary angioplasty, a solely balloon-based procedure, which was limited by high rates of abrupt closure as well as restenosis ("re-narrowing") largely due to recoil of the vessel following balloon dilatation. PCI has since expanded to include coronary plaque modification techniques like directional, rotational, orbital and extraction atherectomy, excimer laser angioplasty and intravascular lithotripsy, followed most commonly by stent deployment. The devices used for PCI are meant to relieve coronary stenoses by several mechanisms including fracturing or debulking the atherosclerotic plaque and stretching the target arterial segment. PCI is effective in reducing fatal and nonfatal ischemic complications in patients with acute myocardial infarction and high-risk acute coronary syndromes. In stable coronary artery disease PCI significantly improves symptoms and reduces ischemic burden.

Indications

PCI is indicated in patients whose clinical presentation is an acute coronary syndrome including ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction, and unstable angina. It is also indicated in those patients with angina pectoris and objective evidence of ischemia with one or more high-grade coronary artery lesions who have failed medical therapy. PCI is also indicated in patients who have a high burden of ischemia on stress testing with favorable anatomy [1]. Several invasive tools are available to further assess angiographically moderate stenoses. Fractional flow reserve (FFR) is a measurement that can be obtained using a coronary pressure wire comparing pressure distal and proximal to a stenosis during maximal hyperemia with an agent such as adenosine. An FFR value less than 0.8 would be an indication to intervene. More recently, non-hyperemic pressure ratios such as the instant wave-free ratio (iFR) allow invasive assessment of lesion significance without the need for inducing hyperemia,

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with a cut-point of ≤ 0.89 an indication to intervene [2]. Intravascular ultrasound is useful in further defining coronary anatomy and characterizing the plaque burden and morphology, e.g. the vessel size for appropriate stent sizing, the luminal area to infer hemodynamic significance and the presence and extent of calcification. These parameters can be useful in selecting which devices and which size devices to be used in PCI. A luminal area of less than 4 mm^2 in the left anterior descending, left circumflex or right coronary arteries is one indication to perform PCI. In the left main coronary artery, a luminal area of less than 6 mm^2 is considered indicative of significant disease.

Contraindications

Contraindications to PCI can be divided into those related to patient characteristics and those related to coronary anatomy. Patient factors such as a history of recent gastrointestinal bleeding, intracranial hemorrhage, recent surgery or bleeding diathesis are relative contraindications as anticoagulants are required intraprocedurally and antiplatelet agents must be taken for weeks to months after the procedure. Active life threatening bleeding is an absolute contraindication to PCI. The inability to ensure compliance with oral antiplatelet therapy is almost an absolute contraindication to stent implantation as the risks of stent thrombosis will outweigh any potential benefit. Coronary revascularization should not be performed in asymptomatic patients with <50% stenosis severity and/or without evidence of ischemia on either non-invasive stress testing or invasive physiology (FFR, iFR). Coronary artery anatomy significantly influences feasibility of PCI in an individual patient. In general, the more complex the anatomy is, the more appropriate surgical (rather than percutaneous) revascularization becomes for long-term benefit. Coronary calcification, severe tortuosity, multiple chronic total occlusions, complex bifurcation disease, small reference vessel diameter (<1.5 mm), diffuse disease and low ejection fraction are all characteristics that may predict relatively poorer outcomes with PCI. Left main coronary artery disease was once an absolute contraindication for PCI, is now considered a reasonable target for PCI provided overall disease complexity is moderate. Irrespective of these relative contraindications, patients presenting to the cardiac catheterization laboratory are increasingly older, sicker, with more frailty and comorbidities as they are often either unwilling or unsuitable for surgical revascularization. Thus, it is common to see patients with extensive disease present to the interventionalist for PCI. In recent years advances in PCI techniques have significantly improved our ability to successfully treat patients with complex coronary artery disease. Consequently, a careful evaluation of lesion and patient characteristics and in complex cases, a multidisciplinary team approach are indicated to determine the best management strategy for the patient (PCI versus coronary artery bypass grafting versus medical therapy) [1, 3].

Equipment

Access

PCI is performed after obtaining arterial access, through which guide-catheters are advanced towards the ascending aorta and coronary ostia over a guide-wire. Femoral, brachial and radial arteries are all potential access points for intervention based on the operator's preference and the patient characteristics. Typically, a 6F sheath is introduced into the radial or femoral artery (most commonly the right although left sided access is equally effective), following which the guide catheter is advanced. The radial route is often preferred on account of a lower bleeding risk and earlier ambulation compared to femoral with the trade-off being a slight increase in procedural complexity and lesser guide catheter support. However, complex anatomy such as bifurcation or, heavily calcified lesions or chronic total occlusions may require a 7 French sheath

and/or femoral access for better guide catheter support to more easily perform PCI with potentially higher-profile devices. In the vast majority of cases, the access sheath is removed immediately after successful PCI and hemostasis is secured using some sort of compression device (radial) or vascular closure devices for femoral arteriotomies.

Guiding Catheter & Guide Catheter Extensions

Guiding catheters have larger inner lumen diameters than diagnostic catheters and allow for the passage of guidewires, balloon catheters, and stents into the coronary artery and across the lesion. These catheters are selected based on the size of the ascending aorta, coaxial engagement of the coronary artery and the amount of backup support required to perform the case safely and effectively. The most commonly used catheters are the Judkins left and right coronary guiding catheters. Guiding catheters can be divided into active or passive manipulation catheters. The Judkins left, right and Ikari left are active-type catheters, meaning a "power position" can be employed by the operator to provide backup support. The Extra back up (EBU) and Xtra backup (XB) guiding catheters are passive-type guides which provide support without the need for operator manipulation. These may be easier to use but are associated with a somewhat higher risk of left main dissection. For the right coronary artery, the Ikari left can be used from the radial approach as an active-type guiding catheter. The Amplatz left is a passive-type guiding catheter (Fig. 33.1) that can be used for PCI of both the left and right coronary arteries. In general, guide catheter support increases progressively with French size (but at the increased risk of ostial dissections). In recent years, the use of guide-catheter extensions (GCE) has enabled operators to exponentially increase guide catheter support by "extending" the guide to well beyond the proximal portion of the coronary artery (and in extreme cases, all the way down to the distal vessel) (Fig. 33.2). This enables both delivery of devices, such as stents to distal parts of the coronary tree across barriers like tortuosity and calcification, and provides the "push" force to help facilitate balloon and stent delivery across distal lesions.

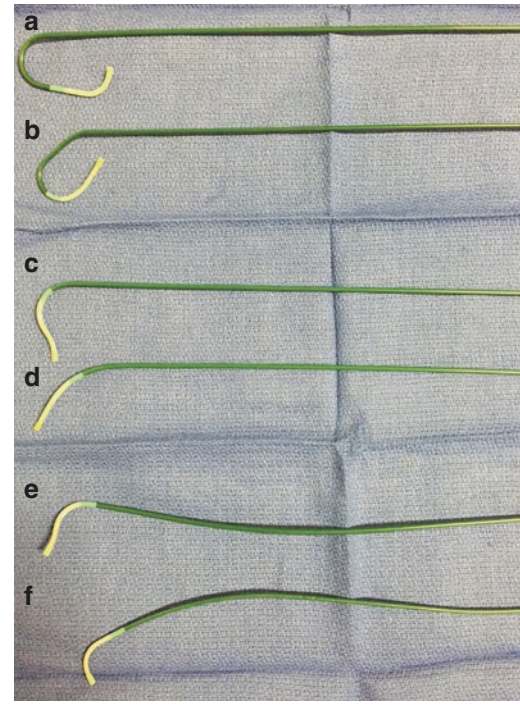

Fig. 33.1 This image shows six guiding catheters. (**a**) A JL-4 guiding catheter is used to engage the left coronary artery and obtain images of the left coronary system in different projections. (**b**) A Voda Left-3 catheter is used to engage the left coronary artery. It is particularly useful for providing enhanced support for LCx coronary interventions. (**c**) An Amplatz Left-1 catheter is a supportive guide which can be used to engage the left coronary arteries and bypass grafts and occasionally, the native right coronary artery. (**d**) A multipurpose-1 catheter can be shaped in the body and used to engage any coronary or bypass graft. It is particularly useful for anomalous coronary arteries. (**e**) An Amplatz Right 2 guiding catheter is useful in engaging the native right coronary artery as well as anomalous right coronary arteries with an inferior take-off. (**f**) A JR-4 diagnostic catheter is used to engage the right coronary artery and obtain images of the right coronary artery in different projections. This catheter can also be used to engage bypass grafts

Guidewires & Microcatheters

Guidewires are usually 0.014 inch-thickness wires that are advanced across a lesion in the coronary artery and used as a rail to support the passage of devices. Crossing the lesion in question with a guidewire is the first and most essential step of PCI and failure to cross effectively ends the procedure. The guidewires are selected based on coronary anatomy and lesion morphology. Each guidewire must be flexible, steerable, as well as stiff enough to support advancing devices beyond the lesion. Guidewires are characterized by their coating, their stiffness, and tip load. When compared to hydrophobic wires, hydrophilic wires allow for easier passage across lesions but with less tactile feedback leading to an increased risk of entering the subintimal space and/or small branches (where a perforation may occur). An operator usually has a "workhorse" wire, which is a safe wire that is used routinely. A workhorse wire should be safe, durable, retain its tip shape, have 1:1 torquability, and offer moderate support for the delivery of devices. If the operator is unable to succeed using the workhorse wire, a different wire is used. The next choice of wire depends on the specific barrier to success with the workhorse. If more support is needed, upgrading to a wire with extra support such as a Choice Extra Support, Grand Slam or HT Iron Man is recommended. If there is difficulty in crossing the lesion, one may consider using a hydrophilic wire but these wires are more likely to enter the subintimal space and are associated with a somewhat higher risk of perforation. If the difficulty is crossing the lesion because of insufficient tip load, as in the case of a chronic total occlusion, one may move to a specialty wire such as a Miraclebros 3–12, Gaia series or a Confianza Pro 9–12 (Fig. 33.3). These stiff guidewires are associated with a higher risk of causing a perforation,hence, after the lesion is crossed (at which point the stiff wire has served its purpose) operators may exchange them for a workhorse wire with the help of a microcatheter.

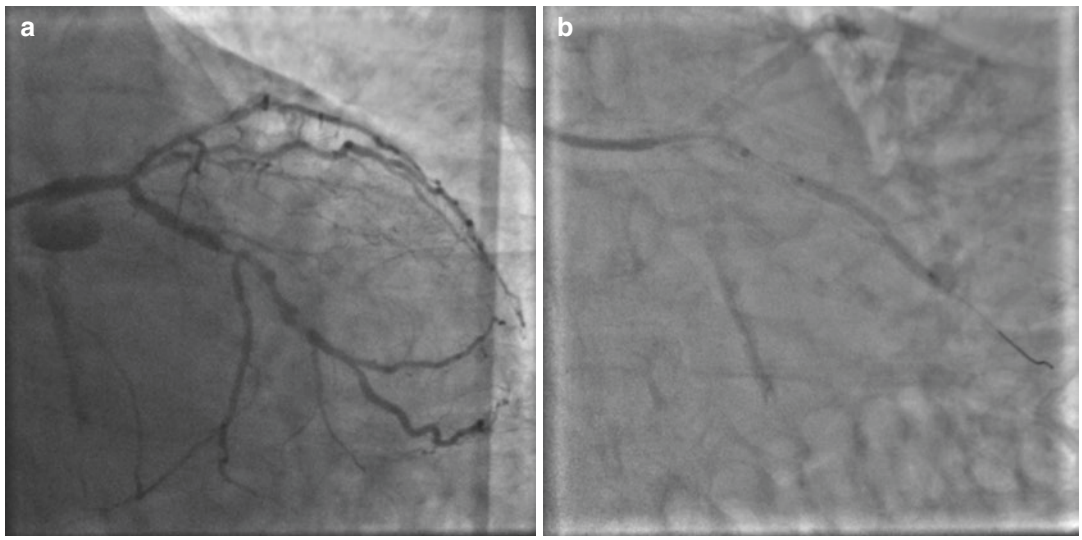

Fig. 33.2 Utility of guide catheter extensions. Panel **a**. This is a severe and very calcific mid left circumflex lesion where even a small compliant balloon would not cross the lesion. Panel **b**. A guide catheter extension was positioned beyond the guide tip into the proximal left circumflex artery, increasing support. Subsequently balloons and stents were delivered easily

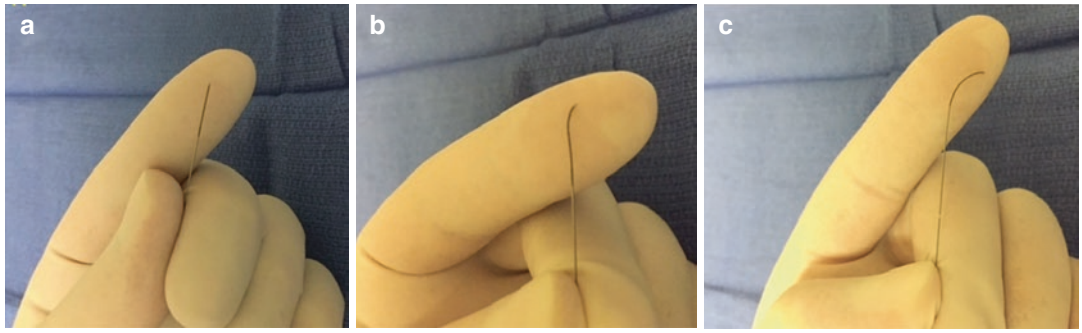

Fig. 33.3 This is an image of a coronary wire. In (**a**–**c**) one can visualize different curves on the wire to allow for access to the desired vessel. Wires are shaped based on the size and tortuosity of the vessel and the angle at which the target vessel comes off the main branch

Balloon Catheters

Balloon catheters are designed to perform lesion dilatation. Each balloon catheter is essentially a plastic hypotube that culminates in a balloon that is filled with diluted contrast under pressure with a device called an indeflator. The balloon can be dilated in graded fashion with progressively increasing pressures (measured in atmospheres) until the lesion finally "cracks" and yields by dilating. The most important first step for balloon dilatation is for the balloon catheter to cross the lesion. Once the balloon crosses the lesion, the balloon diameter will determine the degree of dilatation. More often than not, particularly when the lesion is very severe and/or severely calcified, one has to start with a very small balloon in order to cross the lesion and initiate the dilatation process, followed by a larger balloon to achieve further luminal gain. In general, a lesion must be fully expanded before implanting a stent in order to prevent stent under-expansion. When selecting a balloon, the operator must decide on the diameter, length and compliance of the balloon. Balloons are typically described in terms of diameter and length (for e.g., a 3.0 × 15 mm balloon measures 3.0 mm in diameter and 15 mm in length) as well as either compliant (softer balloons, cross lesions more easily and tend to grow as dilation pressure increases) and non-compliant (stiffer balloons, do not cross lesions as easily, grow very little even at high dilation pressure). In general, compliant balloons are used to pre-dilate a lesion before stent implantation and non-compliant balloons are used for both pre-dilation of a resistant lesion as well as post-dilatation after stenting. An ideal balloon to artery ratio of 0.9–1.1 is needed to minimize the risk of dissection and abrupt closure. Specialty balloons include balloons with blades ("cutting" balloons) or wires around the balloon ("scoring" balloons) that are meant to create "cracks" in hardened and/or calcific plaques and promote the lesion to yield and expand. Structurally, there are two types of commonly-used balloon catheters: over-the-wire and monorail, catheters.

Over-the-wire balloon catheters have a central lumen for the guidewire and another lumen to allow for balloon inflation throughout the catheter. This system has the advantage of maintaining coronary artery access with the guidewire distal to the lesion while exchanging balloon and stent catheters. Guidewires can also be exchanged without losing arterial access by pushing the balloon to the distal portion of the artery. Because of the length of the two balloon lumens, additional personnel are needed to aid in exchange of the catheters and guidewires.

The rapid-exchange or monorail balloon catheters have a short segment that contains two lumens. One lumen, which runs the length of the catheter, is used for balloon inflation, while the second lumen is shorter and contains the guidewire. This creates a lower profile catheter and allows a single operator to exchange catheters while maintaining distal wire

protection. It also allows for the use of a shorter coronary guidewire. These catheters however require more manipulation of the guidewires and balloon catheters by the operator.

Balloon dilatation of a stenosis relieves the obstruction to a varying degree by a combination of vessel stretch as well as plaque compression, fracture and dissection. This "balloon angioplasty" as it is called, was the primary mode of PCI during the early days of the procedure and was limited by a high rate of restenosis (recurrence of the stenosis) via a combined mechanism of vessel recoil as well as negative remodeling. Hence in modern PCI balloon angioplasty alone (often termed "plain old balloon angioplasty or POBA) is almost always followed by implantation of a coronary stent. However, in recent years there has been emerging data to suggest that treating lesions after POBA with drug-coated balloons (coated with antiproliferative agents like paclitaxel and sirolimus) may improve the restenosis rates after POBA. These balloons are currently not approved for coronary use in the United States.

Stents

Stents are balloon-expandable scaffolds made of stainless steel or alloys and are placed within the coronary artery at the site of obstructing lesion following balloon dilatation/plaque modification. The primary role of an intracoronary stent is to mitigate luminal loss following balloon dilatation that presents as either early abrupt closure or late restenosis. As mentioned above, the mechanism of this restenosis is vessel recoil and negative remodeling, which is countered by the scaffolding effect of the metallic implant. However, following stent implantation restenosis may still occur due to a different mechanism—new tissue growth within the stent lumen (neointimal hyperplasia). Clinical predictors of in-stent restenosis (ISR) include diabetes, unstable angina, history of prior restenosis and procedural factors such as long stent length, smaller minimal lumen diameter and smaller acute gain of the target vessel are predictors of restenosis. As with coronary balloons, stents are available in over-the-wire or monorail designs. Stents are also selected based on their diameter and length. Earlier stents were 'bare-metal' devices with relatively high rates of ISR and it was common to deploy relatively larger diameter ($\geq$3.0 mm) and shorter length ($\leq$18 mm) stents to avoid high rates of ISR. Of course, this meant that long lesions in smaller diameter vessels were not suitable for PCI owing to unacceptably high rates of ISR. This paradigm somewhat changed with the next iteration of stents, the "drug-eluting" stent (DES) in which the stent has some sort of coating with an anti-proliferative drug (e.g., sirolimus, biolimus, everolimus, zotarolimus) that is slowly released ('eluted') and prevents neointimal hyperplasia with consequent marked reduction in restenosis. The first drug eluting stent (DES) was approved by the FDA in 2003 and subsequent iterations of various DES platforms has resulted in the current fourth generation of stents with significant improvements in stent thickness (better, thinner stents), flexibility and deliverability, as well as biocompatibility.

Antiplatelet Therapy

Antiplatelet therapy is indicated after all PCI procedures. In the case of an acute coronary syndrome presentation, dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 inhibitor like clopidogrel, ticagrelor or prasugrel is recommended for one-year if the patient is not at high risk for bleeding. This recommendation applies whether just balloon angioplasty is performed or a stent is implanted. For non-ACS situations, aspirin monotherapy is recommended for the uncommon cases treated with balloon angioplasty alone. Owing to the advantages of stenting as described above, the vast majority of PCI involves implanting a stent. The trade-off associated with a metallic implant in the coronary circulation is the risk of stent thrombosis. Randomized trials have shown that treatment with DAPT reduces that risk to an acceptable <1%. Following a bare metal stent, the recommended duration of DAPT is 1 month. For drug-eluting stents, due to delayed healing and endothelialization of the stent (as a consequence of the antiproliferative drug), an increased risk of late (>30 days) and very late (>1 year) stent thrombosis was observed prompting the need of a longer duration

of DAPT after DES implantation. This increase in late stent thrombosis has been markedly mitigated with design changes in later generation DES. The current recommendations are to treat with DAPT for 6–12 months following implantation of a drug-eluting stent after which monotherapy with one agent is appropriate. However, recent trials have suggested that with the current generation of stents, DAPT can be safely truncated at 1 month in high bleeding risk individuals [4, 5].

Technique

Once a stenosis is identified, careful analysis of the clinical characteristics and coronary anatomy is necessary to determine whether or not the patient would be best served by percutaneous revascularization, CABG or medical therapy. A lesion classification system has been developed to categorize the anatomic risk of the lesion undergoing intervention and is related to the likelihood of a successful procedure (Table 33.1). A relatively newer scoring system called the Syntax score is used specifically to compare outcomes of PCI versus CABG surgery in multivessel disease. Patients with a low Syntax score <22 do equally well with PCI whereas those with a high Syntax score >34 tend to perform better with CABG surgery [1, 3]

Table 33.1 Classification system describing lesion characteristics related to the likelihood of a successful PCI

Low risk	Moderate risk	High risk
Discrete (length <10 mm)	Tubular (length 10–20 mm)	Diffuse (length >20 mm)
Concentric	Eccentric	Total occlusions >3 months old and/or bridging collaterals
Non-angulated segment (<45°)	Moderately angulated segment (45–90°)	Extremely angulated segments (>90°)
Non-tortuous	Moderate tortuosity	Excessive tortuosity
Little or no calcification	Moderate calcification	Heavy calcification
No major side branch involvement	Bifurcation lesions requiring double guidewires	Inability to protect major side branches
Little or no calcification	Moderate calcification	Heavy calcification
Absence of thrombus	Some thrombus is present	Degenerated vein grafts with friable lesions
Not ostial in location	Ostial in location	

After the decision to proceed with an intervention is made, a guiding catheter is introduced through an arterial sheath, typically placed in the femoral, radial, or brachial artery. The guiding catheter is then advanced into the aorta and the coronary artery is cannulated so that the catheter is coaxial to the ostium of the coronary artery. Guiding catheters have distinct shapes and are selected based on their ability to provide adequate backup support for advancing equipment into the coronary artery relative to its take-off from the aorta.

Before advancing guidewires into the coronary arteries, the patient should be started on an intravenous anticoagulation regimen. In general, the adequacy of procedural anticoagulation is guided by the activated clotting time (ACT) which should be usually be >300 s with the use of IV heparin. The ACT has limited utility in guiding PCIs in which the direct thrombin inhibitor bivalirudin is utilized. All PCIs require the administration of antiplatelet therapy as described above. A 0.014 in. guidewire is placed in the catheter via a Y-connector (Tuohy-Borst or Copilot) and is maneuvered past the stenosis under fluoroscopic guidance. The guidewire is advanced as far distally into the vessel as needed to support balloon advancement.

Once the lesion is crossed with the guidewire, the balloon catheter is advanced, using the guidewire, as a rail to the target lesion. The balloon is then inflated at the stenosis thereby dilating the lesion. Contrast is then injected through the guide catheter to assess the result of predilation and coronary blood flow. The balloon can be used at this time to help assess, the length of stent required.

A stent is then advanced through the guiding catheter to the target lesion. The stent is deployed at a pressure that will maximize stent expansion within the lesion without causing vascular dissection at the margins of the stent or the much less common complication of perforation. The stent catheter is then removed following stent implantation in the artery. The stent is visualized through a contrast injection to determine if it is

properly deployed. Although direct stenting without balloon predilation can be performed, not all lesions are amenable to this technique. Lesions which are calcified and tortuous may prevent optimal stent implantation and should be predilated with a balloon catheter. Intravascular ultrasound can also be used to verify adequate deployment of the stent by visualizing the relationship of the stent struts to the vessel wall. If the stent does not appear to be fully expanded, a non-compliant balloon may then be advanced into the stent and inflated to fully expand it and better appose the stent against the arterial wall.

Once a satisfactory revascularization result is achieved, the artery is imaged in several views demonstrating the result. The guidewire is then removed. A coronary angiogram after wire removal should be performed to ensure there is no distal perforation and to assess vascular anatomy without wire-induced straightening artifacts. The guide catheter is then removed and the arterial sheath should then be removed and hemostasis achieved either via manual compression or with the aid of a vascular closure device.

Post PCI, the patient should be monitored for recurrent myocardial ischemia until discharge. All patients should be made to understand the importance of adhering to recommended medical therapies, including anti-platelet therapies and risk factor modification proven to reduce morbidity and mortality form coronary artery disease.

Several lesion types represent higher-risk anatomic subsets for intervention and require specific techniques to help ensure optimal procedural and clinical results.

Bifurcation Lesions

Bifurcation lesions usually refer to a diseased arterial segment which involves a parent and sidebranch vessel. PCI in these cases should be approached prudently in order to preserve the parent vessel and side branch. If the side branch is a large diameter vessel and there is critical disease within the proximal vessel, then bifurcation stenting should be strongly considered. When the side branch is free of or minimally diseased, provisional stenting is preferable. This refers to the situation when the parent vessel is stented across the origin of the side branch. The side branch is only rewired for ballooning or stenting if there is reduced flow or if the patient has ischemic symptoms referable to flow obstruction in the side branch. If bifurcation stenting is going to be performed, several approaches have been described and the choice of which approach is employed is based on the angle between the side branch and parent vessel as well as other factors.

Saphenous Vein Graft Intervention

Another challenging lesion subset for PCI are those in degenerated saphenous vein bypass grafts. These lesions are at elevated risk of distal embolization into the native coronary vasculature during balloon and stent inflation and can cause no reflow phenomenon—the occurrence of impedance to blood flow to ischemic tissue following the relief of coronary occlusion, presumably due to microvascular obstruction. Due to the high thrombotic burden present in the diseased graft, a distal protection device (Guardwire, Filterwire, etc) should be used, when feasible, to prevent or decrease any downstream debris embolization. The distal protection device is then retrieved and can be assessed for the presence of debris. Intracoronary medications such as nitroprusside and verapamil can also be delivered prophylactically in an effort to prevent no reflow and potentially as a treatment should it occur.

Calcified Lesions

Severe calcified stenoses are associated with suboptimal stent expansion and increased risk of complications such as dissection and perforation. Risk factors associated with calcific disease include advanced age, prior bypass surgery and end stage renal disease. Calcific disease is an increasingly-common problem in modern interventional cardiology practice. A key step in treating calcified lesions is adequately modifying the calcific plaque such that the lesion compliance is

increased and the vessel expands with balloon dilatation. This ensures that the subsequently implanted stent is able to achieve adequate expansion—the most important determinant of clinical events post PCI. Techniques such as rotational atherectomy can debulk the calcified lesion through the use of a high speed (≈150,000 rpm) diamond tip burr. Orbital atherectomy is a newer technology which ablates calcific plaque via a "sanding" effect and is effective in pretreating calcified lesions to allow for easier delivery of balloons and stents. Orbital atherectomy is contraindicated however for aorto-ostial lesions. Both technologies ablate calcium that leads to (1) modification of the calcific plaque making it more amenable to dilatation and (2) distal embolization of ablated material that can sometimes lead to hemodyanamic instability. The latter can be of particular importance for patients undergoing high risk PCI with compromised left ventricular function, ongoing ischemia, or in cardiogenic shock, where the operator should consider the implantation of a mechanical support device such as an intra-aortic balloon pump or an Impella prior to atherectomy. Limitations of atherectomy include the issue of hemodynamic tolerance, risk of perforation (particularly in tortuous vessels) and need for experienced and skilled operators.

Very recently, a new device to treat intracoronary calcification gained FDA approval—intravascular lithotripsy (IVL). Leveraging on the concept of shockwave lithotripsy for renal stones, IVL delivers acoustic shock waves to the vessel wall via emitters integrated into a balloon [6]. The balloon itself is very compliant and is dilated to a low pressure of 4 atm, enough to ensure that an appropriately sized balloon is in contact with the vessel wall. The emitters are then triggered, delivering a compression-decompression shockwave to the plaque, peaking at approximately 50–60 atm of pressure for a total of ~ 5 μsecs. In contrast, the typical "high-pressure" non-compliant balloon inflation is at much lower pressure (20–30 atm) for significantly more sustained periods of time (15–30 s). The extremely short duration of this very high pressure is a key factor that makes IVL safe, yet effective. Intracoronary imaging suggests that IVL targets both superficial and deep calcium (unlike atherectomy which addresses only superficial calcium) and induces both visible as well as micro-fractures in the calcium that favorably changes vessel compliance. Of note, in a large body of experience, perforation and distal embolization is exceedingly rare. The learning curve for IVL is essentially that of handling a regular balloon. Although IVL is likely to significantly change the landscape of calcium modification in PCI, some important limitations need to be kept in mind. First, the balloon is less trackable and in order to bring the balloon to the lesion several techniques may need to be used including but not limited to the use of more supportive guidewires, use of a GCE and sometimes rotational atherectomy to create the path that allows delivery of the IVL balloon (so-called "rotatripsy"). Second, the coronary IVL balloon comes in only one 12 mm length and is able to deliver only 80 pulses before replacement is necessary. This can be challenging if a long area of calcific plaque requires IVL. Third, IVL works best for concentric calcium (270–360°) and is less effective for nodular and/or eccentric calcium. Concentric calcium allows the acoustic waves to reflect back and forth against the calcific interface and the energy of the wave gets harnessed to "crack" the calcium. With eccentric lesions, acoustic energy of the waves directed towards the non-calcific side is, essentially, lost. It has been suggested that eccentric calcium may respond if a larger number of pulses are delivered to that location. Fourth, IVL is expensive (currently, almost 3X the cost of rotational atherectomy). Overall, IVL is unlikely to replace atherectomy; more likely, they will be complimentary therapies. But it is extremely useful and effective in situations where atherectomy is not feasible (Case 3). At the present time IVL is only indicated for treating de-novo calcific lesions [7]. However, an attractive albeit off-label use of IVL is to treat an under-expanded stent.

Data Interpretation

Angiographic success after percutaneous coronary intervention is defined as decreasing the stenosis diameter reduction to <20% with TIMI-3 flow. Additionally there should be clinical signs of success with relief of signs and symptoms of myocardial ischemia post procedure.

Complications

Acute vessel closure is an important complication of percutaneous coronary intervention and can be caused by dissection, thrombus formation, and spasm. If the target vessel remains closed, then the impaired blood flow can result in hypotension, myocardial infarction, arrhythmia and death. With the advent of coronary stenting and adjunctive pharmacologic therapy, the incidence of acute closure has markedly decreased.

Increased mortality following percutaneous coronary interventions has been associated with advanced age, female gender, diabetes, prior myocardial infarction, multivessel disease and a large area of myocardium at risk. The combined risk of death, nonfatal myocardial infarction, stroke, and emergent bypass surgery as a consequence of PCI is approximately 1%.

The most common complication for patients undergoing PCI, however, is bleeding at the arterial puncture site. This may occur in 1–3% of all cases. Radial access for PCI has been associated with a lower incidence of vascular complications and there are some reports of decreased mortality when radial approach is used for STEMI patients. Moreover, patients with renal insufficiency may develop worsening renal function secondary to the use of iodinated contrast.

Restenosis has been a major determinant of event free survival following coronary intervention and results from elastic recoil and neointimal hyperplasia of the artery. Clinical factors such as diabetes, unstable angina, history of prior restenosis and procedural factors such as smaller minimal lumen diameter and smaller acute gain of the target vessel are predictors of restenosis. With the advent of the antiproliferative drug eluting stents, the incidence of in-stent restenosis has substantially decreased.

Clinical Vignettes

Case 1

A 60 year old female with Type II diabetes presented to the emergency room with 1 hour of chest pain radiating to the jaw and left arm. ECG demonstrated ST elevation in leads II, III, and avF. The patient was given aspirin, lopressor, IV Heparin.

The patient was taken emergently to the cardiac catheterization lab and was found to have a 100% occlusion in the right coronary artery (Fig. 33.4). A JR 4 guiding catheter was placed in the ostium of the right coronary artery and a guidewire was advanced through the target lesion. The lesion was dilated with a balloon (2.0 × 12 mm). A drug eluting stent (3.25 × 20 mm) was then deployed. Angiography demonstrated 0% residual stenosis (Fig. 33.5).

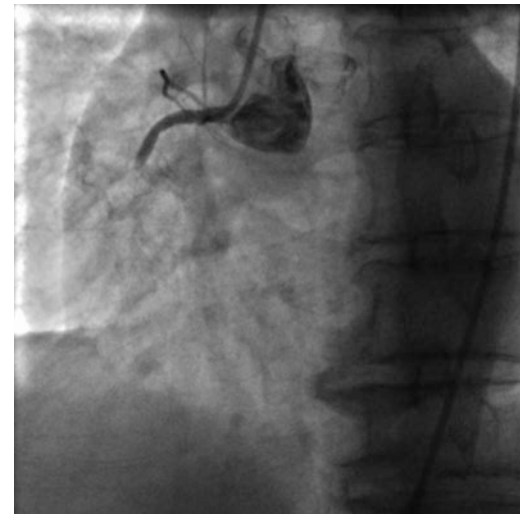

Fig. 33.4 This is a view of the right coronary artery in a left anterior oblique projection which shows a completely occluded mid RCA

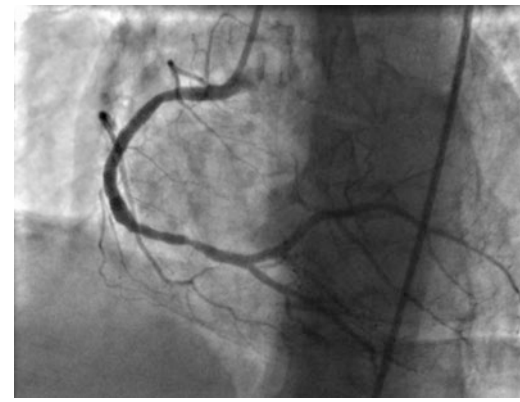

Fig. 33.5 This is an LAO projection of the revascularized RCA

Case 2

A 55 year old male smoker with dyslipidemia presents for an outpatient cardiac catheterization for worsening chest pain with exertion. The patient exercised for 7 min on the Bruce protocol, developed angina with 2 mm ST depression in the precordial ECG leads with a large moderately reversible anterior defect with nuclear imaging.

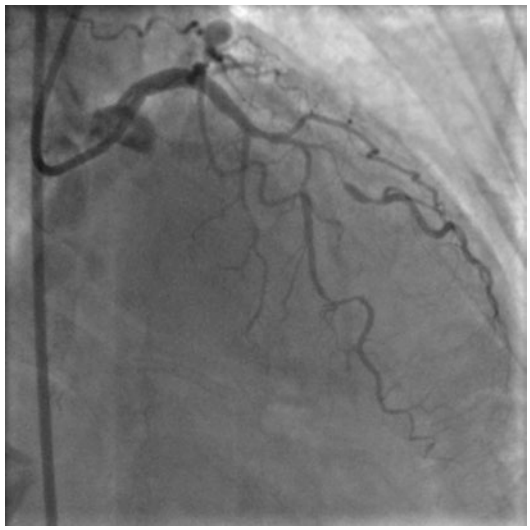

Fig. 33.6 This is an RAO cranial projection of the left coronary system. Once can see that there is a lesion involving the LAD and Diagonal coronary arteries with a 90% stenosis in the LAD and 95% stenosis in the diagonal branch

Angiography revealed a significant stenosis at the LAD/Diagonal bifurcation with a 90% mid left anterior descending coronary artery lesion and a 95% Diagonal coronary artery lesion (Fig. 33.6). A balloon catheter (2.0 × 12 mm) was advanced over a guidewire and was inflated at both lesions. A crush technique was used to treat the lesions with a 2.5 × 20 DES to the Diagonal branch and 3.0 × 24 DES to the LAD (Fig. 33.7).

Case 3

This 66 year-old woman with end-stage renal disease on dialysis presented with a non ST segment elevation myocardial infarction. She underwent rotational atherectomy and stenting of the LAD (not shown) a few days prior with a good result. She now presented for staged PCI of the RCA (Fig. 33.8).

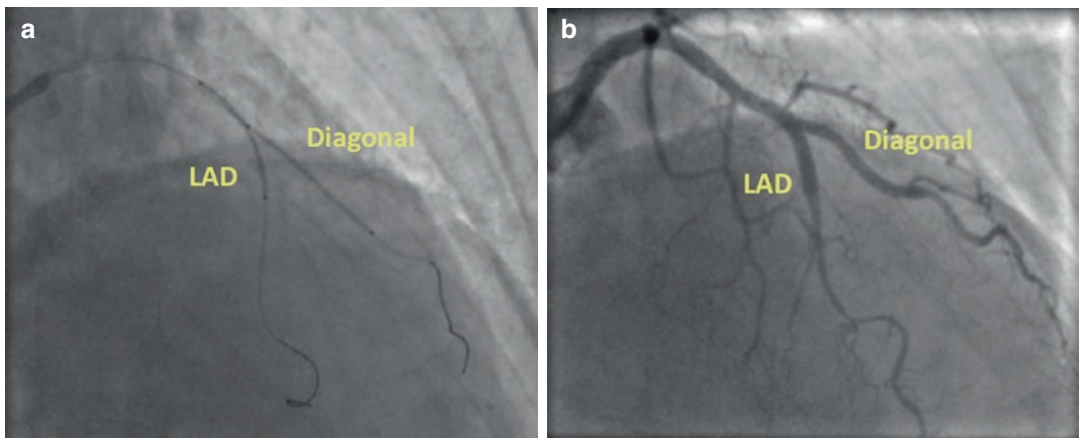

Fig. 33.7 This demonstrates the bifurcation stenting during and after revascularization. A minicrash technique was used. (**a**) A stent is positioned in the diagonal and a second stent placed in the LAD. The diagonal stent is deployed and the balloon and wire are withdrawn. Next the LAD stent is fully deployed. After that the diagonal branch is rewired and kissing balloon inflation is performed. (**b**) The final result after post dilation

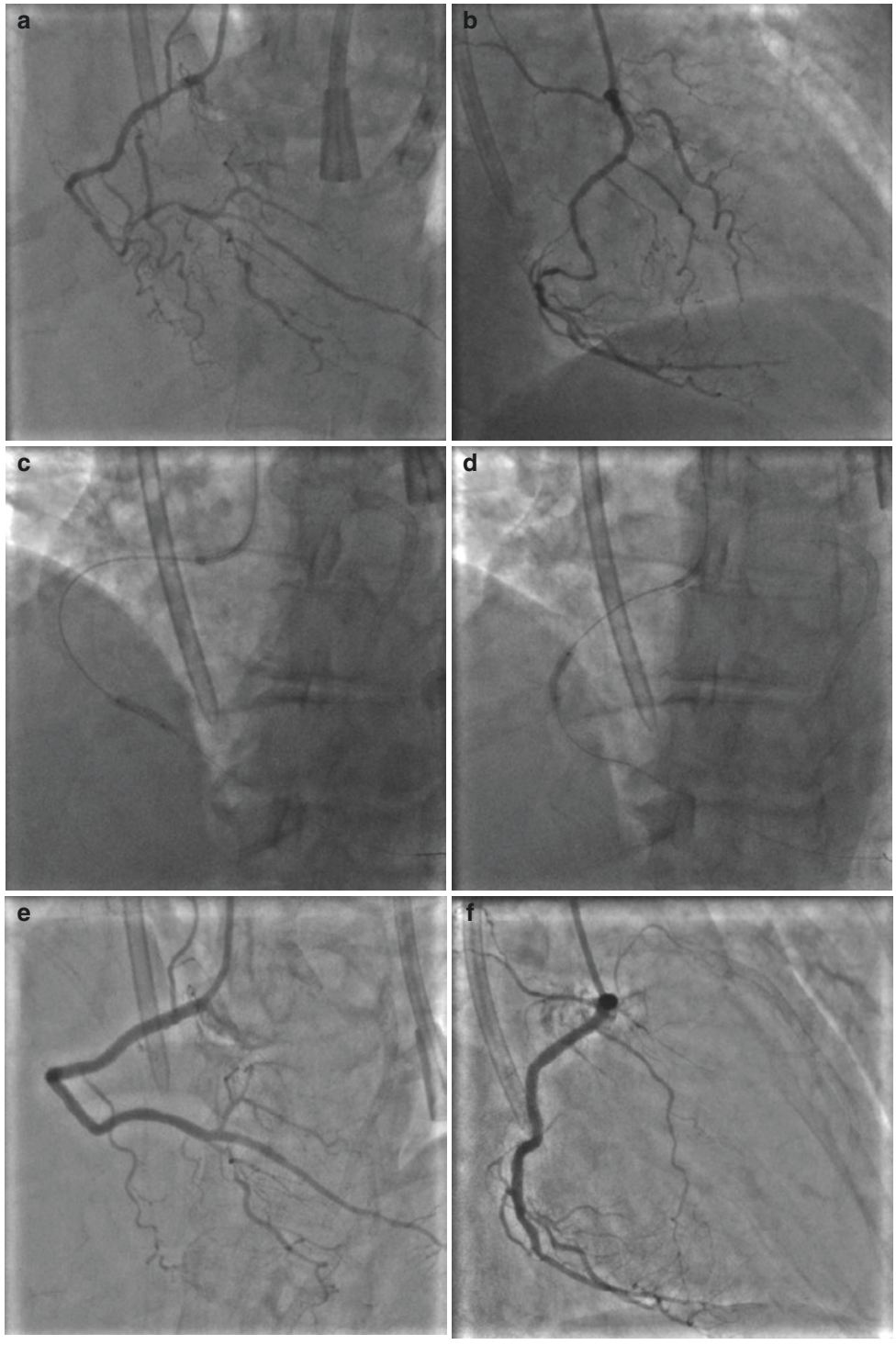

Fig. 33.8 The RCA is heavily calcific and extremely tortuous and was judged not safe for rotational atherectomy (panels A, B). IVUS showed multiple areas of concentric calcium (distal and mid) as well as nodular calcium. After failing to expand the distal RCA lesion with a non-compliant balloon at high pressure, the distal RCA was successfully dilated with a 3.0 × 12 mm IVL balloon (panel C). The mid RCA also failed to dilate with a 3.0 mm non-compliant balloon and was expanded almost completely with a 4.0 × 12 mm IVL balloon albeit with a little 'waist' (D). The mid RCA was then treated with a 3.5 × 15 mm cutting balloon at high pressure (not shown) then successfully stented (panels E, F)

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Alcohol Septal Ablation

34

Carey Kimmelstiel

Indications

Hypertrophic obstructive cardiomyopathy (HOCM) is a relatively common genetic disorder that exhibits wide variability in its clinical expression. Symptomatic patients most frequently experience exertional dyspnea, chest pain, fatigue and, occasionally, orthopnea or nocturnal dyspnea. Five to 10% of symptomatic patients with HOCM are refractory to medical therapy (typically beta blockers and heart rate lowering calcium antagonists) and may require mechanical approaches targeting relief of obstruction and mitral regurgitation. Previously, mechanical approaches were limited to surgical myectomy, however, since the late 1990s increasing experience with a percutaneous technique, alcohol septal ablation, has become a widely-used alternative to surgical myectomy.

General indications for alcohol septal ablation include patients with severe symptoms—New York Heart Association class III or IV, refractory to maximal drug therapy with a left ventricular outflow gradient ≥ approximately 50 mmHg at rest or after provocation, with a basal septal thickness ≥17 mm as measured with echocardiography or MRI [1]. The most current guidelines recommend alcohol septal ablation to be performed in adult patients with obstructive HOCM who remain severely symptomatic, despite guideline-directed medical therapy and in whom surgery is contraindicated or the risk is considered unacceptable because of serious comorbidities or advanced age [2]

Contraindications

Relative contraindications to performing alcohol septal ablation include coexistent abnormalities that are best treated surgically—eg. multivessel coronary artery disease and especially mitral valve or papillary muscle/mitral apparatus abnormalities that contribute to mitral regurgitation and/or left ventricular outflow tract obstruction. These patients, who comprise approximately one-third of the HOCM medication-refractory population, should be referred for surgical myectomy, at which time, coexisting abnormalities can be addressed.

Equipment

Alcohol septal ablation uses standard coronary intervention equipment (Fig. 34.1): a coronary guide catheter, guide wire and angioplasty balloon along with a pulmonary artery catheter to

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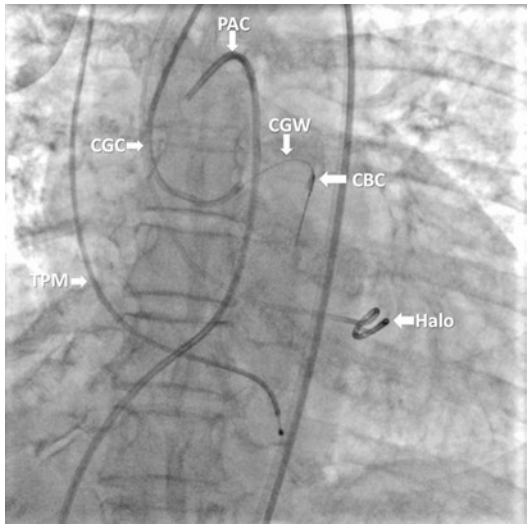

Fig. 34.1 Equipment/catheters used in alcohol septal ablation. *TPM* temporary pacemaker, *CGC* coronary guide catheter, *PAC* pulmonary artery catheter, *CGW* coronary guide wire, *CBC* coronary balloon catheter, *Halo* Halo left ventricular catheter

measure pulmonary pressures and an end-hole pigtail or halo catheter to measure the left ventricular pressure. Comparison of the left ventricular pressure to the central aortic pressure determines the left ventricular outflow gradient. All patients have a temporary pacemaker placed at the right ventricular apex. Transthoracic echocardiography is used in all cases to guide ablation.

Technique

Alcohol septal ablation is performed in the cardiac catheterization laboratory. A right and left heart catheterization are performed at which time pulmonary capillary wedge and pulmonary arterial pressures are measured. Left ventricular outflow gradients are measured, usually with an endhole pigtail or halo catheter so as to be able to record pressure at a precise location within the left ventricle with a catheter whose shape makes entrapment unlikely. Determination of the left ventricular outflow gradient is accomplished by comparing the left ventricular pressure to the central aortic pressure as recorded usually from the coronary guide catheter (Fig. 34.2). It is important to establish the gradient that will be followed to judge procedural efficacy and to establish, with the aid of echocardiography, that the location of obstruction to left ventricular outflow is subaortic. For those patients in whom the outflow gradient is either absent or small at rest, the magnitude of provocable obstruction is most appropriately determined with exercise. If exercise is not feasible, Valsalva maneuver or post-PVC beats are employed.

Prior to proceeding with alcohol infusion, all patients have a temporary pacemaker placed in the apex of the right ventricle as a precaution against the occurrence of complete heart block following alcohol injection. This is usually placed from the right internal jugular vein, as this is a stable route allowing for maintenance of proper positioning following the procedure.

Coronary angiography is performed to assess for the presence or absence of atherosclerotic epicardial coronary artery disease and to identify potential target septal perforator branches, which most often originate from the left anterior descending (LAD) coronary artery. Most practitioners employ myocardial contrast echocardiography, which involves two dimensional echocardiographic imaging during the infusion of 1–2 mL of echo or angiographic contrast through the lumen of an inflated balloon dilatation catheter. This technique enhances the efficacy and safety of the procedure by avoiding septal branches that supply areas of myocardium distant to the targeted region, limiting the number of vessels intervened on, thereby reducing the amount of alcohol used which aids in preventing the complication of complete atrioventricular block. The targeted myocardial region for ablation is that area of the basal septum where contact is made with the anterior leaflet of the mitral valve (Fig. 34.3) [3].

Once the target vessel or branch has been identified, angiographic contrast is injected through the coronary guide catheter and through the distal port of the inflated balloon catheter in the septal vessel. This is done to ensure that the inflated balloon completely occludes the septal vessel, so that upon injection, alcohol cannot leak

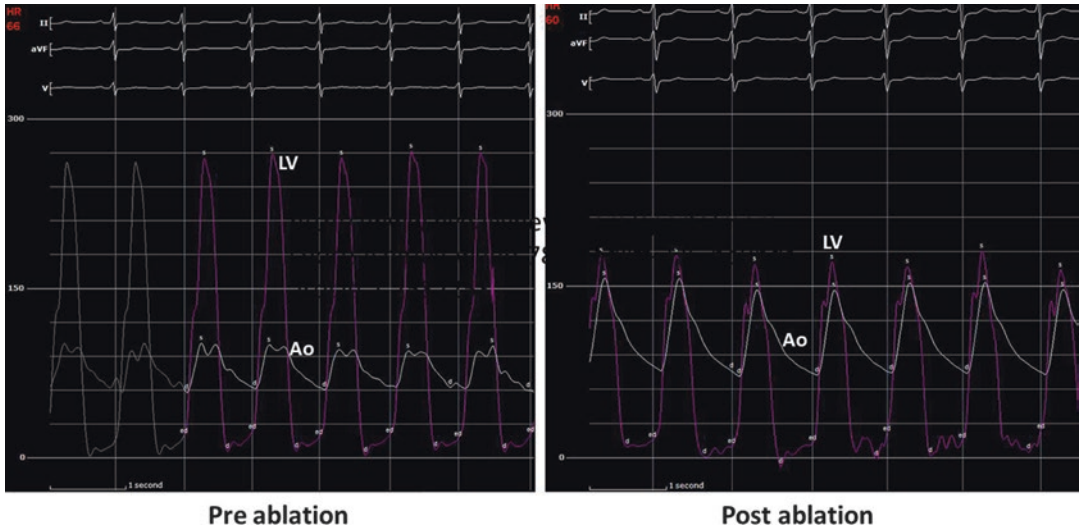

Fig. 34.2 Left ventricular outflow gradients before and following alcohol septal ablation. Before ablation, the gradient is 170 mmHg. Note the bifid aortic waveform, highly suggestive of dynamic outflow obstruction with a narrow pulse pressure. Following ablation, the gradient has been reduced to 20 mmHg. The aortic waveform no longer exhibits a bifid contour and the pulse pressure has increased

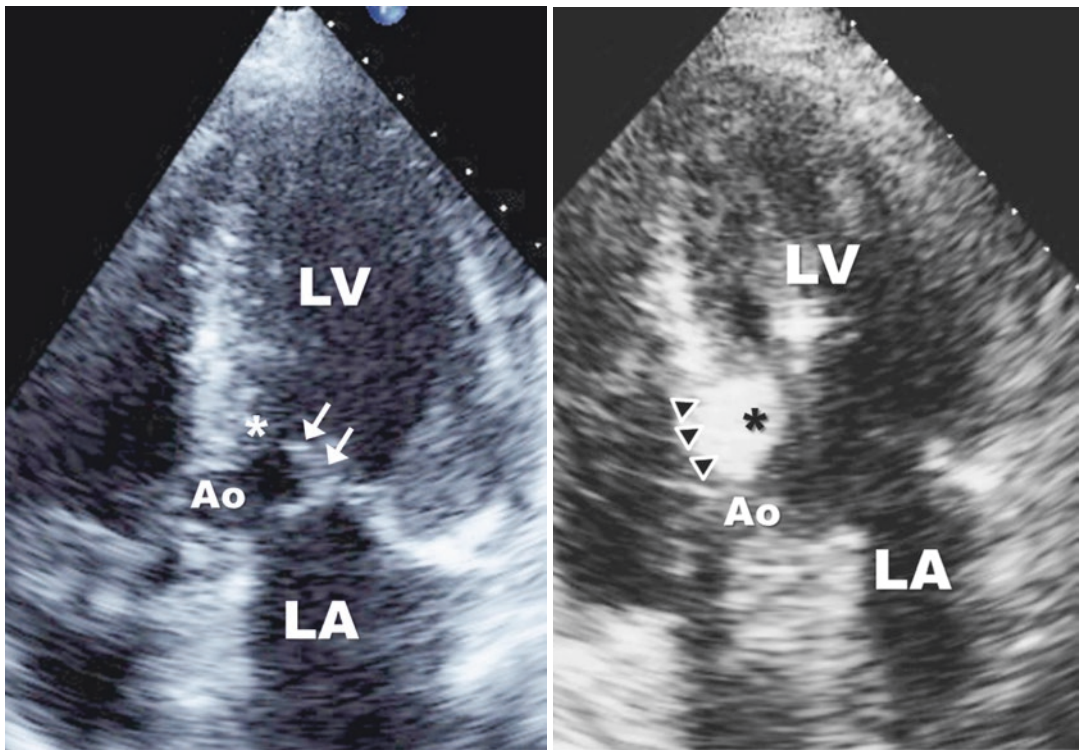

Fig. 34.3 Echocardiographic view during alcohol septal ablation. Panel A demonstrates the anterior leaflet of the mitral valve (*arrows*) making contact with the basal portion of the anterior interventricular septum (*) during systole. *Ao* aortic valve, *LV* left ventricle, *LA* left atrium. Panel B is alcohol (*arrowheads*) in basal anterior septum including the area where the anterior mitral leaflet makes contact (*)

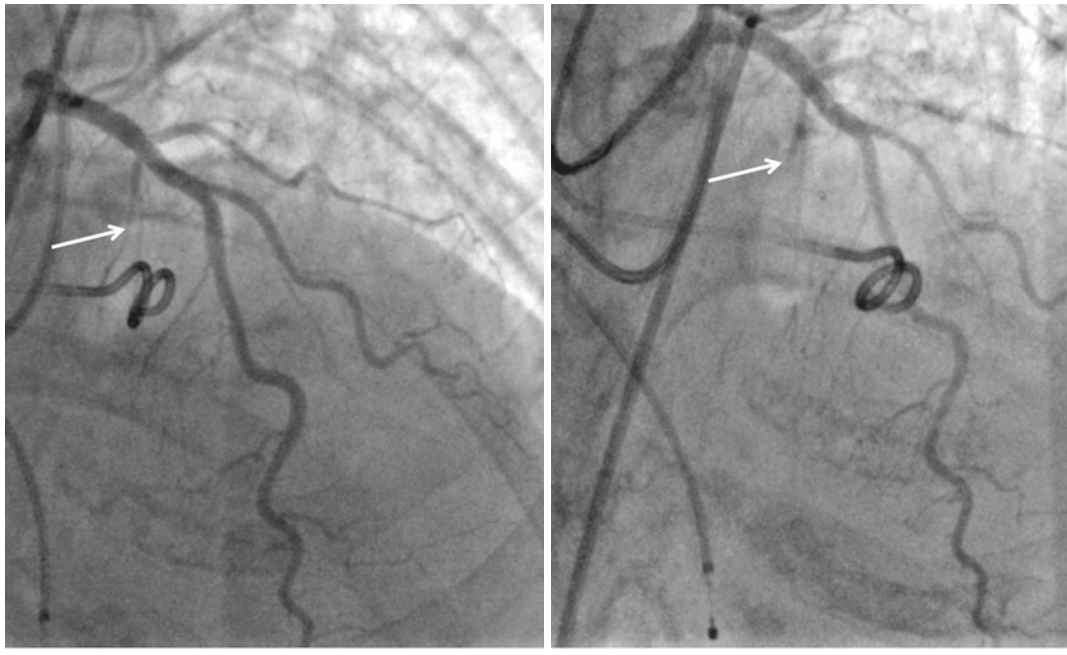

Fig. 34.4 Pre-ablation panel: Coronary angiogram showing the basal septal branch of the first septal perforator (*arrow*) which was documented by myocardial contrast echocardiography to be the target for alcohol ablation. Post-ablation panel: Ablated basal septal branch (*arrow*) following the slow injection of 1.25 cc of alcohol

back into the LAD, which is a potentially disastrous complication. Myocardial contrast echocardiography has taught us that contrary to what was originally thought, the entire septal branch need not be ablated in order to obtain a satisfactory hemodynamic result (Fig. 34.4).

Alcohol septal ablation is accomplished by injection of usually 1–2 mL of 96–98% ethanol into the target septal branch. The alcohol is injected slowly, at a rate of approximately 1 mL/min. This is done to minimize complications, especially high-degree atrioventricular block. Immediately prior to alcohol injection, intravenous analgesia is administered in an effort to mitigate the pain associated with alcohol-mediated myocardial necrosis. During and immediately following alcohol infusion, the patient is scrupulously monitored looking for QRS widening, ST segment changes, the occurrence of complete heart block and for signs of hemodynamic deterioration.

Following alcohol septal ablation, patents remain in the coronary care unit for approximately 24 h, predominantly for monitoring, especially as relates to detecting ventricular arrhythmias and complete heart block. In general, if the patient has not required pacing, the temporary pacemaker is removed.

Data Interpretation

As a general rule, alcohol septal ablation is considered successful when an acute reduction in the resting or provoked left ventricular outflow gradient of greater than 50% or to less than 20 mmHg has been achieved (Fig. 34.2). Comprehensive pressure sampling is usually performed given the dynamic nature of the left ventricular outflow gradient in HOCM. Frequently, the initial improvement in the outflow gradient appears to be lost on follow-up Doppler study the day following the procedure. The immediate gradient reduction is likely secondary to alcohol-induced septal necrosis and stunning, an effect which can be evanescent and is distinct from the permanent

septal thinning and remodeling which is associated with progressive and long-lived gradient reduction seen on long-term follow-up.

To date, there have been no randomized studies comparing alcohol septal ablation to surgical myectomy in patients with medication-refractory HOCM. Meta-analyses of large observational series have suggested that septal ablation and myectomy are comparable in terms of long-term survival and symptomatic relief with septal ablation leading to a higher rate of permanent pacemaker implantation [4–7]. There are suggestions that patients undergoing septal ablation have higher residual gradients as compared to patients treated surgically, however, the clinical significance of this finding is not clear.

Complications

The risk of procedural mortality following alcohol septal ablation is low. Recent series have reported in-hospital mortality of less than 1% [4–7]. The reduction in procedural mortality over the years has paralleled the decline in the volume of alcohol used to accomplish gradient reduction. Approximately 75% of the patients undergoing alcohol septal ablation will develop a right bundle branch block following the procedure which is in contrast to patients undergoing surgical myectomy who almost universally develop a left bundle branch block.

The most frequent complication of alcohol septal ablation is complete heart block. The decision to implant a permanent pacemaker in patients with heart block involves a clinical assessment of risk of recurrence and/or permanence of the heart block involving clinicians caring for the patient which usually involves electrophysiologic consultation. There is some variability in the threshold for pacemaker implantation, with a current frequency in the United States of approximately 10–15% of ablation patients. There is a higher frequency of heart block and pacemaker implantation in the elderly given their higher frequency of intrinsic conduction system disease.

The most feared complication of septal ablation is the application of alcohol outside of the myocardial region targeted by myocardial contrast echocardiography. This can occur when alcohol leaks down the LAD through a nonocclusive balloon or when alcohol enters collateral channels (which may be below fluoroscopic imaging resolution) leading away from the targeted septal branch. The obvious result is infarction in an unintended myocardial region. The consequences depend on the involved area of myocardium and the volume of alcohol entering this region. Patients experiencing this complication may exhibit rapid clinical deterioration due to widespread acute myocardial infarction often with consequent pulmonary congestion. Mitral and tricuspid regurgitation as well as ventricular tachyarrhythmias are also possible in this subset of patients. Echocardiography, which is readily available during this procedure, is a key aid in confirming this diagnosis. Other rare coronary complications include coronary dissection, perforation, and thrombosis.

A potential longer-term complication of alcohol septal ablation is the facilitation of ventricular arrhythmias. Alcohol septal ablation does induce intramyocardial scar formation in a population of patients already prone to reentrant ventricular arrhythmias raising the possibility that the induced septal infarct could enhance the likelihood of sudden death in some patients. This concern has not, to date been realized as interrogation of defibrillators, implanted for primary prevention in HOCM patients undergoing septal ablation has not documented any signal for an increased incidence of ventricular arrhythmias. Comparative analyses have similarly shown no increase in the incidence of sudden cardiac death in ablation patients when compared with similar populations undergoing surgical myectomy.The fear of late ventricular arrhythmias following ablation have not been substantiated, indeed, the survival of patients undergoing either surgical myectomy or alcohol ablation is generally regarded as being similar [2].

Clinical Vignette

A 67 year old, morbidly obese man with a history of prior coronary bypass surgery, COPD and obstructive sleep apnea presented with an 8 month history of progressive dyspnea on exertion, NYHA Class III in severity which severely limited his normal daily activities. Physical exam documented a bifid carotid pulse and a loud apical systolic murmur which increased by 1 grade following a Valsalva maneuver. Echocardiography revealed hyperdynamic left ventricular systolic function, basal septal hypertrophy with a thickness of 21 mm consistent with a diagnosis of hypertrophic cardiomyopathy. There were no noted abnormalities of the mitral valve or the subvalvular apparatus. Continuous wave Doppler study estimated an 80 mmHg subaortic gradient due to dynamic systolic anterior motion of the mitral valve with basal septal contact. Coronary artery angiography documented patent grafts to the distal LAD, right and left circumflex arteries. The LAD was occluded in its mid segment after the second diagonal branch.

Medical management with escalating doses of β-blocking agents and verapamil were ineffective in relieving the patient's symptoms. Due to prior coronary bypass surgery, medical comorbidities and patient preference ASA was recommended. The patient was referred to the cardiac catheterization laboratory where a 100 mmHg resting left ventricular outflow gradient was documented. Myocardial contrast echocardiography identified a basal branch of the first large septal perforating branch of the LAD as supplying the basal septum at the site of contact with the anterior leaflet of the mitral valve. Following the slow infusion of 1.25 mL of alcohol, the resting gradient was reduced to 20 mmHg. The patient required temporary pacing for 10 min following the injection of alcohol, but sinus rhythm returned shortly thereafter, albeit with the emergence of a right bundle branch block. Permanent pacemaker implantation was not required. On follow-up 3 months later, the patient reported marked clinical improvement with NYHA Class I symptoms. Echocardiography with Doppler study documented that the basal septum had remodeled to a maximal thickness of 17 mm with a resting outflow gradient of 20 mmHg.

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35 Transcatheter Closure of Atrial Septal Defects and Patent Foramen Ovale

Francisco Garay and Ziyad M. Hijazi

Atrial Septal Defect

Secundum atrial septal defects (ASD) represent 6–10% of all congenital cardiac anomalies and are twice as frequent in females than males. ASD leads to a left to right shunt which in turn produces right sided cardiac volume overload, increased pulmonary blood flow and eventually pulmonary vascular disease and pulmonary arterial hypertension. The closure of these defects can be achieved safely and efficiently by transcatheter methods [1–3].

Indications

Closure of this defect is indicated in patients with evidence of a significant hemodynamic left to right shunt which is usually documented on echocardiography as evidenced by right ventricular and atrial enlargement. Clinically, this is evident by the presence of a systolic ejection heart murmur with fixed splitting of S2. Patients may or may not have overt symptoms, including shortness of breath, fatigue and palpitations.

Contraindications

- The development of non-reactive pulmonary vascular disease. This is rare (about 5% of patients) and usually occurs in adults older than 40 years of age. A pulmonary vascular resistance indexed higher than 7 Wood units after a trial of vasodilators, such as inhaled nitric oxide is a contraindication for closure.
- Systemic or local infection within 1 month of the procedure.
- Bleeding disorders or other contraindications to aspirin therapy, unless other antiplatelet agents such as clopidogrel can be used for 6 months.
- Presence of intracardiac thrombus.
- Nickel allergy is a relative contraindication. This issue has not been a clinically important one even in patients with documented nickel allergy.
- Patients with primum or sinus venosus types of atrial defects are in general, not candidates for device closure. Patients with sinus venosus/SVC defect could be analyzed individually for the possibility of closure using new techniques with covered stents.

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Equipment

Several devices are available to perform percutaneous ASD closure. The most common occluder device used for ASD closure is the *Amplatzer® Septal Occluder* (ASO). It consists of 2 nitinol wire mesh discs connected by a 3–4 mm waist (Fig. 35.1). The device size is determined by the diameter of its connecting waist with available sizes ranging from 4 to 40 mm. The two flat discs extend radially beyond the connecting waist to secure anchorage. The left atrial disc is larger than the right atrial disc. Dacron polyester patches are sewn into each disc and the connecting waist to increase thrombogenicity of the device. The ASO is delivered through a 6–12Fr sheath based on device size and the delivery sheath is 60–80 cm long which is usually advanced from the right femoral vein, through the right atrium across the interatrial septum into the left upper pulmonary vein. The ASO is pushed through the sheath by a delivery cable, which is unscrewed when proper location and deployment are documented. The use of sizing balloon is optional but recommended to facilitate correct device sizing. Other nitinol mesh occluder devices are available (Occlutech®, Lifetech®, pfm®) with differences on its delivery mechanism but all of them maintain the concept of a double disc nitinol device and share the same implanting routine. The *Gore Cardioform ASD Occluder®* is a different low-profile device constructed on a frame made up of independent nitinol wires and covered by expanded polytetrafluoroethylene (ePTFE). The device is available in 5 sizes, ranging in diameters from 15–35 mm in 5 mm increments.

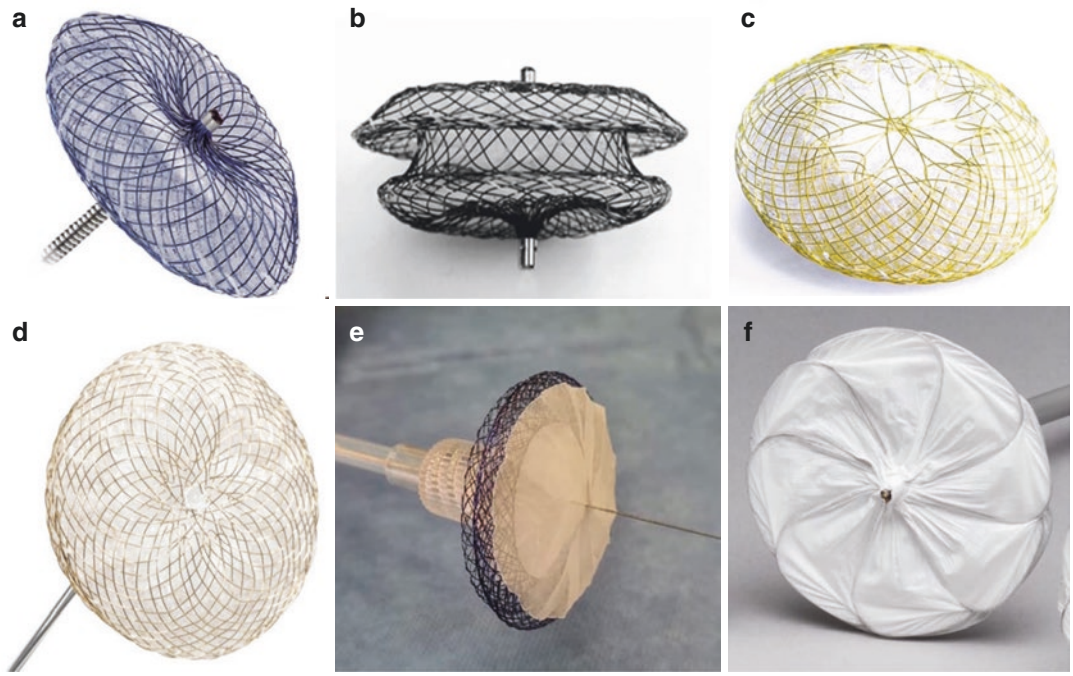

Fig. 35.1 Currently available devices for atrial septal defect closure. Amplatzer Septal Occluder en face (**a**) and lateral view (**b**), Occlutech Figulla Flex II (**c**), Lifetech CeraFlex ASD Occluder (**d**), pfm Nit-Occlud ASD-R (**e**) are made of Nitinol wire mesh and Gore Cardioform ASD Occluder (**f**) has a frame made of independent nitinol wires, covered by expanded polytetrafluoroethylene (ePTFE)

Technique

One should review all previous data related to the patient and the defect to be closed and ensure that appropriate devices and delivery systems are available. Aspirin 81–325 mg should be started 48 h prior or immediately after the procedure. Alternatively, Clopidogrel 75 mg could be used.

The procedure is performed under either transesophageal echocardiography (TEE) or intracardiac echocardiography (ICE) guidance. If TEE is used, due to the length of the procedure and for patient's comfort, the procedure should be done under general endotracheal anesthesia. If the procedure is performed under ICE guidance, mild sedation is given. The procedure is most often performed via femoral venous access. Heparin is administered to maintain an activated clotting time (ACT) above 200 s at the time of device deployment. Broad spectrum antibiotic administration is recommended for the procedure (eg. cefazolin 1 g iv), the first dose at the time of the procedure and two additional doses 6–8 h apart. Right heart catheterization is performed to measure pulmonary artery pressure, calculate pulmonary vascular resistance and shunt (Qp:Qs) ratio. The pulmonary vascular reactivity can be evaluated if necessary. TEE or ICE (Figs. 35.2 and 35.3) images are obtained to assess the ASD anatomy (location, size, additional defects and rims) [4]. It is important to fully evaluate the atrial septal anatomy as well as that of adjacent structures to ensure that the device will be properly seated following deployment.

Angiography in the right upper pulmonary vein can be performed (Fig. 35.4a) to evaluate

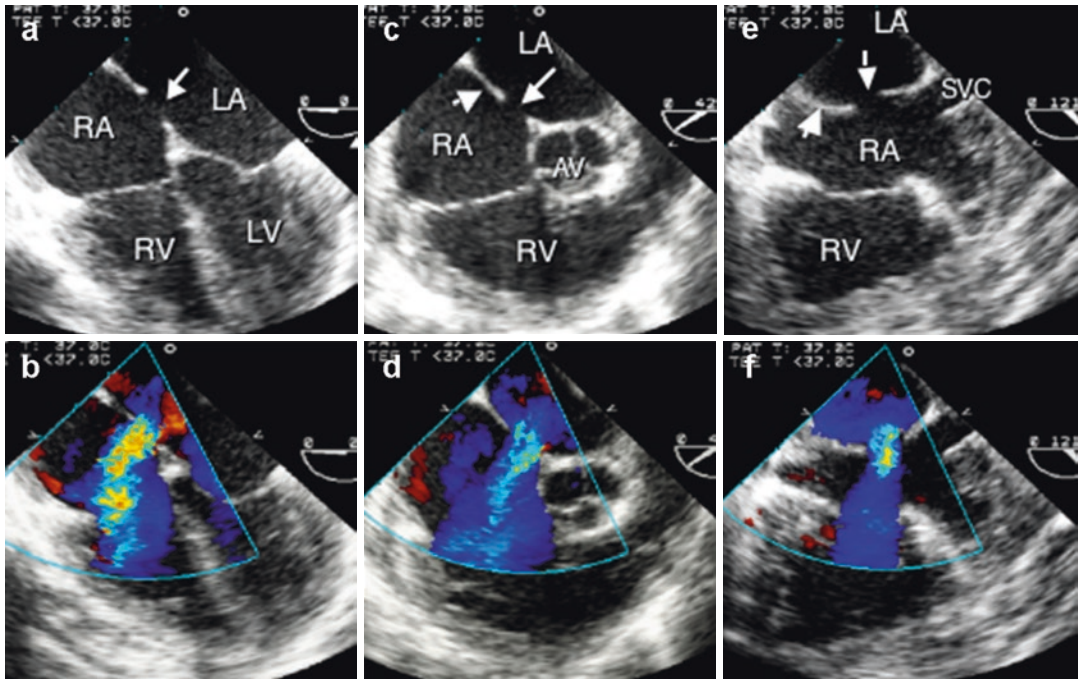

Fig. 35.2 Transesophageal echocardiographic images obtained to assess the ASD anatomy. (**a**, **b**) four chamber view without and with color Doppler demonstrating the ASD (*arrow*) and left-to-right shunt. (**c**, **d**) short axis view without and with color Doppler demonstrating the ASD (*arrow*), the anterior rim near the aortic valve and posterior rim (*arrowhead*). (**e**, **f**) bi-caval long axis view without and with color Doppler demonstrating the ASD (*arrow*), the superior rim near the superior vena cava and inferior rim near the inferior vena cava (*arrowhead*). *RA* right atrium; *LA* left atrium; *RV* right ventricle; *LV* left ventricle; *SVC* superior vena cava

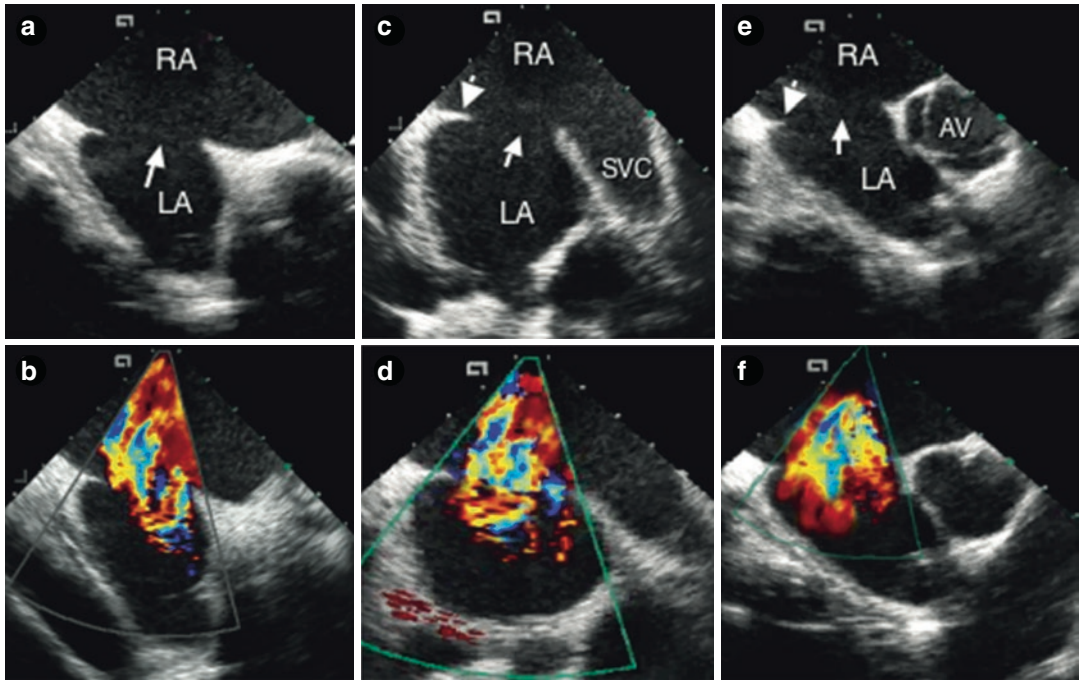

Fig. 35.3 Intracardiac echocardiographic images obtained to assess the ASD anatomy. (**a**, **b**) Septal view without and with color Doppler demonstrating the ASD (*arrow*) and left-to-right shunt. (**c**, **d**) bi-caval long axis view without and with color Doppler demonstrating the ASD (*arrow*), the superior rim near the superior vena cava and inferior rim near the inferior vena cava (*arrow head*). (**e**, **f**) short axis view without and with color Doppler demonstrating the ASD (*arrow*), the anterior rim near the aortic valve and posterior rim (*arrowhead*). Note, with ICE, the left atrium is in the bottom of image and right atrium in top, which is in contrast with TEE images. *RA* right atrium; *LA* left atrium; *SVC* superior vena cava

the atrial septal length and shape or rely on echocardiographic imaging according to the operator's preferences. A stiff guide wire is advanced just distal to the catheter tip into the left upper pulmonary vein (Fig. 35.4b). The angiographic catheter is exchanged for a sizing balloon (Fig. 35.4c). The balloon is placed across the defect under fluoroscopic and echocardiographic guidance and then inflated with diluted contrast until the left-to-right shunt ceases (stop-flow diameter) as observed by color flow Doppler on TEE or ICE. The indentations in the balloon made by the margins of the ASD are measured on echocardiographic or fluoroscopic images (Fig. 35.4c). Usually the echo measurements are more reliable than the fluoroscopic measurements. A device approximately 1–2 mm larger than the measured sizing balloon diameter is selected. The sizing balloon is removed and a delivery sheath is advanced over the super stiff guide wire to the left upper pulmonary vein (Figs. 35.4d and 35.5b). Extreme care must be exercised to not allow passage of air inside the delivery sheath.

The device, attached to the delivery cable is advanced to the tip of the sheath. Then the cable and delivery sheath are pulled back as one unit to the middle of the left atrium. This position and the next steps are verified under fluoroscopy or TEE/ICE (Figs. 35.4, 35.5 and 35.6). The left

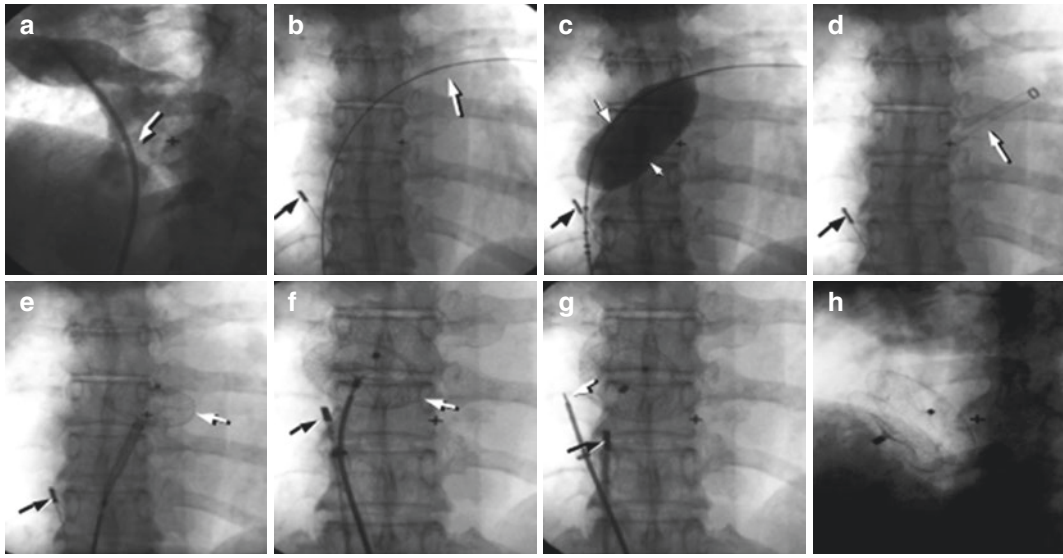

Fig. 35.4 Cine fluoroscopic images in a patient with a large secundum ASD during closure with the Amplatzer device under intracardiac echocardiographic guidance. Black arrow is the AcuNav catheter for intracardiac echocardiographic images. (**a**–**h**) were obtained in the hepatoclavicular projection and the remaining images in straight frontal projection. (**a**) angiogram in the right upper pulmonary vein demonstrating the left-to-right shunt through the ASD (*arrow*). (**b**) cine image during passage of the guide wire (*white arrow*) through the ASD to the left upper pulmonary vein. (**c**) cine image during balloon sizing demonstrating the "stop-flow" diameter of the defect (*white arrows*). (**d**) cine image during passage of the delivery sheath (*white arrow*) to the left upper pulmonary vein. (**e**) cine image during deployment of the left atrial disk (*white arrow*) in the left atrium. (**f**) cine image during deployment of the right atrial disk (*white arrow*) in the right atrium. (**g**) cine image immediately after the cable (*white arrow*) was released from the device. (**h**) final angiogram in the right atrium in the showing good device position

atrial disc is deployed by retracting back the sheath maintaining the cable position and taking care of not to interfere with the atrial appendage. Finally withdrawing the delivery sheath over the cable, the connecting waist and the right atrial disc are deployed in the ASD itself and in the right atrium respectively.

Proper device position can be assessed by fluoroscopy where both discs are seen parallel to each other and separated from each other by the atrial septum (Fig. 35.4h). The echocardiogram (TEE/ICE) must demonstrate the presence of one disc in each atrial chamber. If the position is uncertain or questionable, after all these maneuvers, the device can be recaptured and repositioned. After the position of the device has been verified, the device is released from its delivery cable. Assessment of the final result of the closure procedure is performed immediately with TEE or ICE, and 24 h later with transthoracic echocardiography.

Patients are treated with daily aspirin for 6 months and endocarditis prophylaxis when necessary for 6 months after the procedure. Full activity including competitive and contact sports are allowed after 4 weeks of implantation.

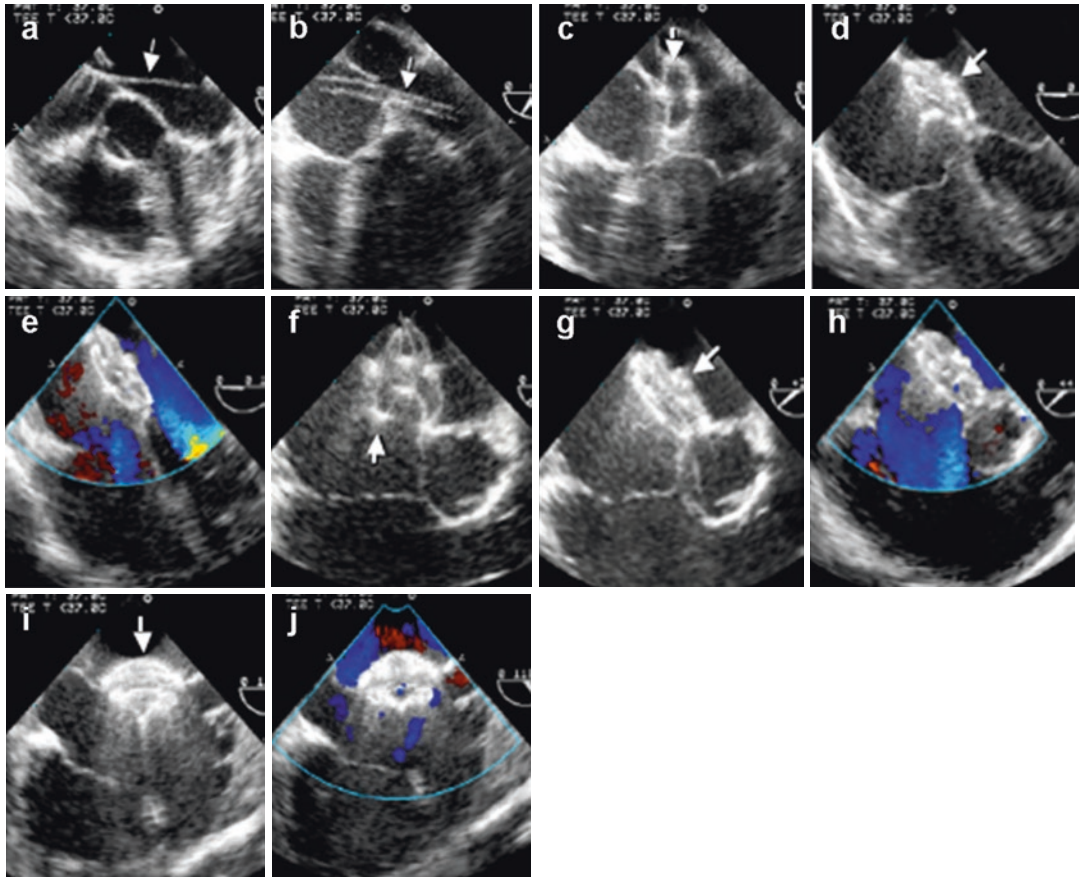

Fig. 35.5 Transesophageal echocardiographic images in the same patient as Fig. 35.2 demonstrating the steps of closure. (**a**) passage of guide wire (*arrow*) in 4-chamber view to the left atrium. (**b**) passage of the delivery sheath (*arrow*) in 4-chamber view to the left atrium. (**c**) deployment of the left atrial disk (*arrow*) in 4-chamber view in the left atrium. (**d**, **e**) device release (*arrow*) in 4-chamber view without and with color Doppler demonstrating good device position. (**f**–**h**) deployment of the right disk (*arrow*), device and assessment of position in short axis view without and with color Doppler. Device looks good and no residual shunt. (**i**, **j**) bi-caval view without and with color Doppler demonstrating good device position

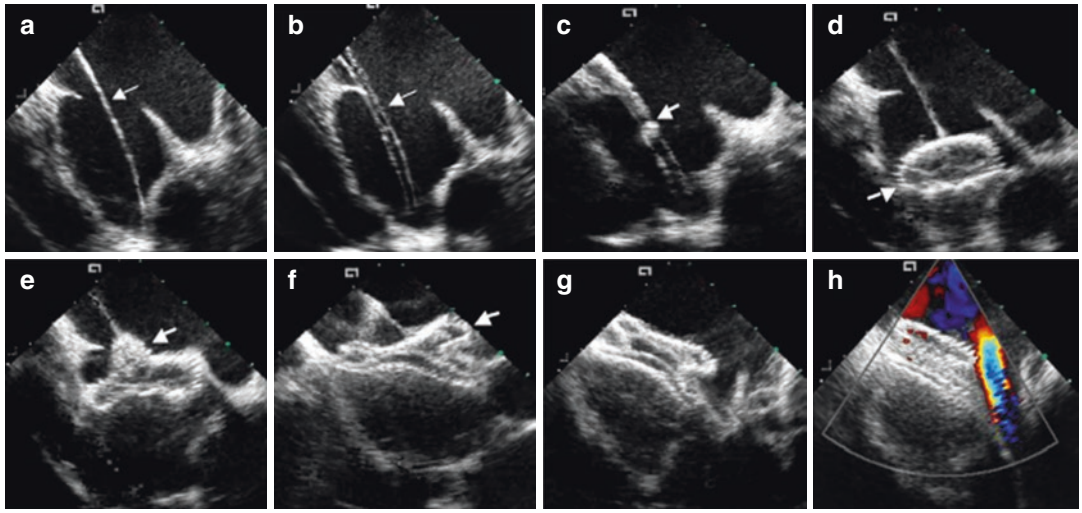

Fig. 35.6 Intracardiac echocardiographic images (ICE) during various stages of device deployment in the same patient as Fig. 35.3 (**a**–**c**) views between septal and bi-caval views demonstrating passage of guide wire (*arrow*) (**a**) delivery sheath (*arrow*) (**b**) and the 32 mm device inside the sheath (*arrow*) (**c**). (**d**) deployment of the left disk (*arrow*) in the left atrium. (**e**) deployment of the connecting waist (*arrow*) in the defect itself. (**f**) deployment of the right disk (*arrow*) in the right atrium. (**g**) device release demonstrating good device position. (**h**) bi-caval view showing good flow in the superior vena cava and good device position

Data Interpretation

Measurement of Qp:Qs ratio in the catheter laboratory is prone to errors, therefore, evidence of the right-sided volume overload is verified mainly by echocardiography. In adults older than 65 years and with large defects or patients with a stiff left ventricle (elevated end-diastolic pressure above 15 mmHg), it is prudent to measure the LA pressure during balloon occlusion of the defect to evaluate the LV compliance. If an increase to > 18 mm of Hg in the LA pressure is observed, then a LV conditioning treatment is started with anti-congestive and afterload therapy for 48–72 h prior to attempting the closure procedure [5]. The use of a fenestrated device could also be considered in these patients [6].

Complications

Air embolism

Meticulous technique should be used to prevent air entry into the left sided cardiac chambers which may result in coronary ischemia and stroke. Free flow of blood from the sheath must be allowed, avoiding forceful negative pressure aspiration.

Device embolization

If this occurs the device has to be removed either surgically or by transcatheter snare techniques. One should avoid pulling the device across valves.

Prolapse of the left disc across the defect during deployment

Especially in patients with large defects and deficient antero/superior rims, resulting in left atrial disc prolapse through the anterior/superior part of the ASD. Several technical maneuvers can correct such malpositioning [7, 8]

Arrhythmias

An increase in atrial arrhythmias occurs following the procedure, but this is a transient phenomenon that usually resolves within 6 months. Heart block has been rarely reported [9].

Right atrial and aortic root perforation (Erosions)

Extremely infrequent (0.1%). To minimize this risk, device oversizing should be avoided [10].

Patent Foramen Ovale (PFO)

The foramen ovale is created by the overlap of septum primum and septum secundum. Anatomic variants exist (flap type, tunnel type and PFO with aneurysmal septum primum). It has been described to remain probe-patent in 25% of the population, being a potential source of paradoxical emboli when a right-to-left shunting is present. PFO has been demonstrated with a higher than normal prevalence in cryptogenic stroke patients less than 55 years old and an association has been suggested with an aneurysmal septum primum increasing this risk. Additionally, conditions associated with elevated RA pressure (chronic pulmonary disease, recurrent pulmonary embolus) and hypercoagulable states increase the potential for right-to-left shunt and paradoxical emboli. In spite of medical management the risk of stroke recurrence remains significant.

Several devices have been designed to specifically close PFO's, even ASD closure devices have also been used for PFO closure (Fig. 35.7). The Amplatzer® PFO Occluder is a self-expandable, double-disc device made from a Nitinol wire mesh 0.005–0.006 in. in diameter (Fig. 35.7a). The two discs are linked together by a connecting waist 2 mm in diameter and 4 m in length (Fig. 35.7b). The discs are filled with polyester fabric sewn securely to each disc by a polyester thread that increases the device closing ability. The device is similar in design to the ASD occluder, differing in that the right atrial disc is larger than the left one. Similar devices from Occlutech®, Lifetech®, pfm® and GORE® are available for PFO closure as well (Fig. 35.7c–f).

Indications

Patients with recurrent cryptogenic stroke due to presumed paradoxical embolus through a PFO and who have failed conventional medical therapy [11]. Numerous randomized trials have documented a reduction in recurrent cryptogenic stroke in patients randomized to device closure compared to those medically treated [12–14].

Contraindications

The same as for secundum ASD closure.

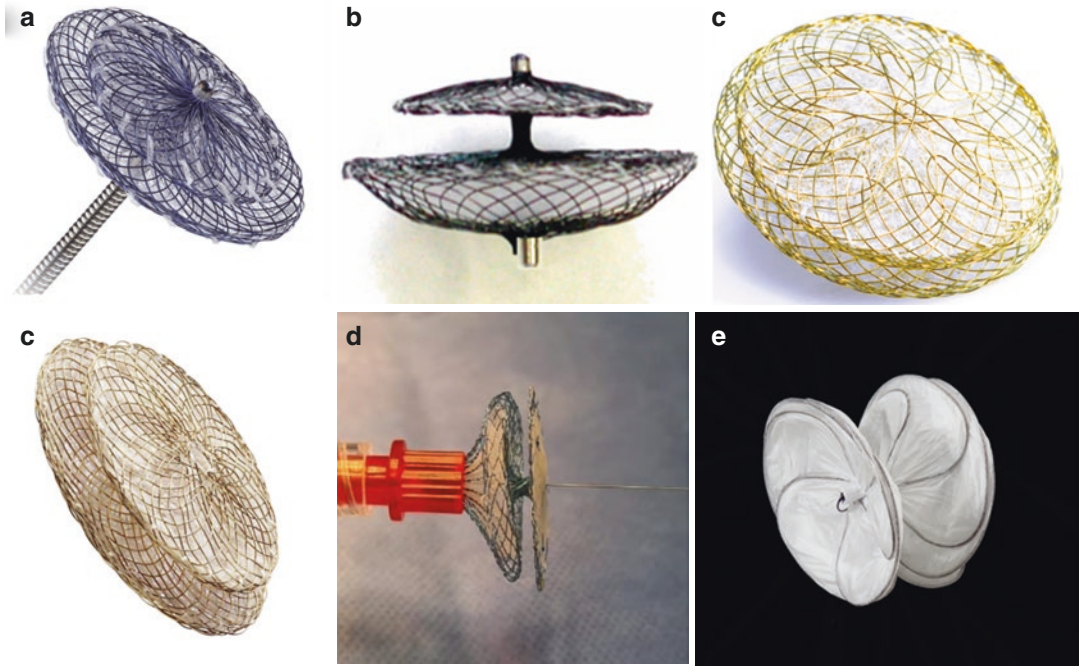

Fig. 35.7 Currently available devices for PFO closure. Amplatzer ® PFO Occluder en face (A) and lateral view (B), Occlutech ® PFO Occluder (C), Lifetech CeraFlex PFO Occluder (D), pfm® Nit-Occlud PFO (E) are made of Nitinol wire mesh and Gore® Cardioform Septal Occluder (F) has a frame made of independent nitinol wires, covered by expanded polytetrafluoroethylene (ePTFE)

Equipment

The delivery system is similar to the ASD delivery system.

Technique

Similar to the ASD procedure. A sheath is inserted into the femoral vein. Heparin and antibiotics are administered. The procedure is performed under general anesthesia or conscious sedation depending on the imaging modality used to guide deployment (TEE or ICE). Assessment of PFO anatomy and rims (Fig. 35.8) should be performed (a minimal distance of 9 mm to the SVC and to the aortic root is required to implant the device). In cases with an aneurysmal septum a larger device is preferred. Unlike the ASD closure procedure, balloon sizing is not usually performed. The device deployment is identical to ASD closure (Fig. 35.9).

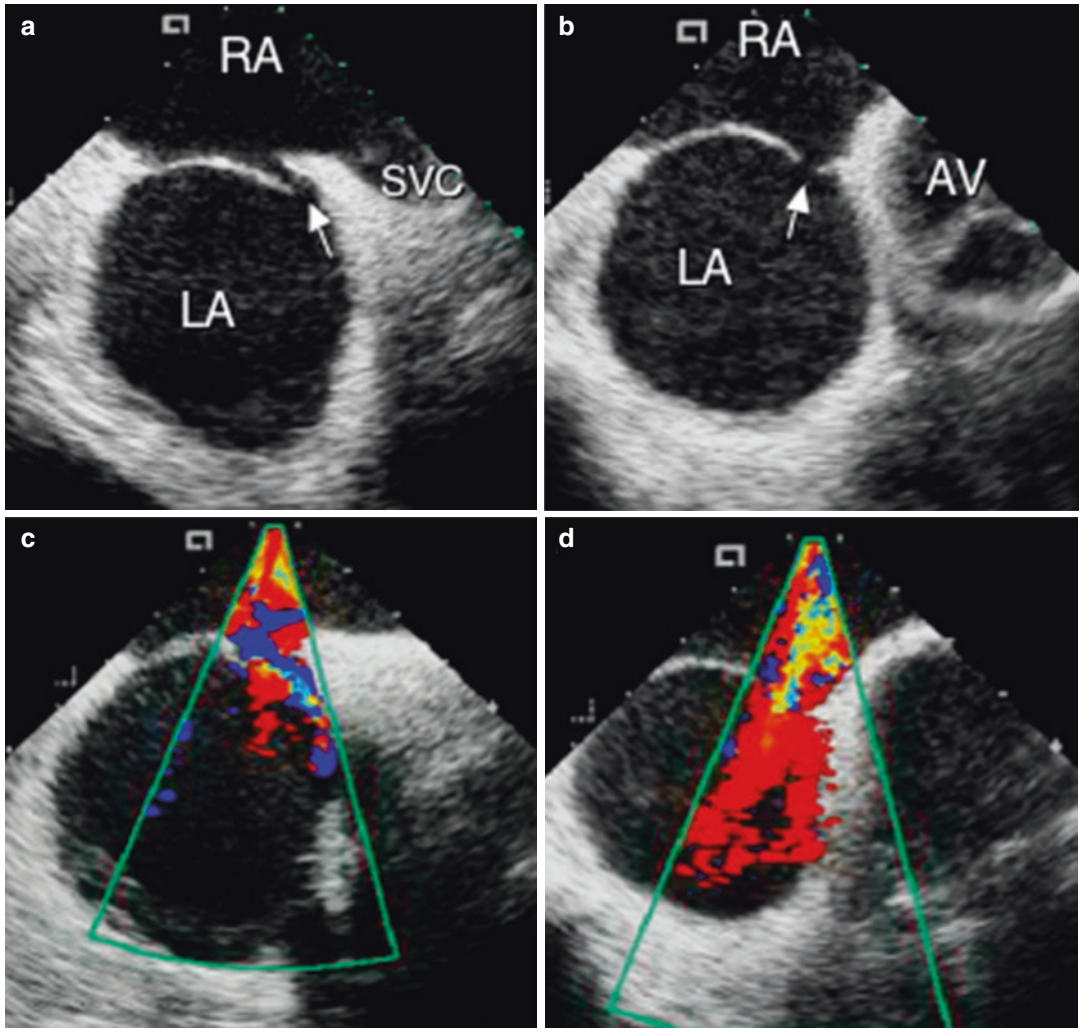

Fig. 35.8 Intracardiac echocardiographic images to assess anatomy of the PFO in a patient who sustained a stroke. (**a**, **b**) septal view without and with color Doppler demonstrating presence of a PFO (*arrow*) with left-to-right shunt. (**c**, **d**) short axis view demonstrating the PFO (*arrow*) and left-to-right shunt

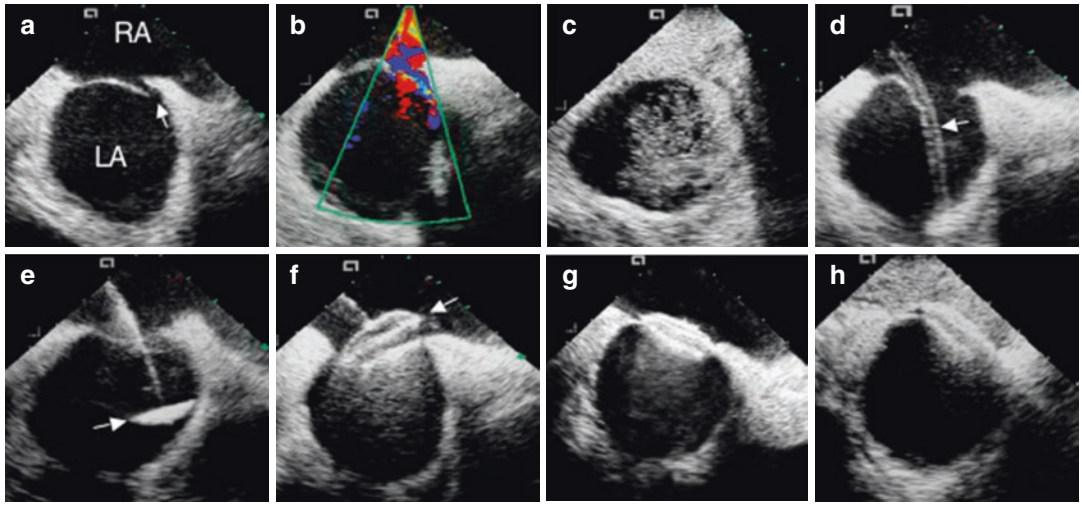

Fig. 35.9 Intracardiac echocardiographic images in same patient as Fig. 35.8 during various stages of device closure. (**a**, **b**) septal view without and with color Doppler demonstrating the PFO (*arrow*). (**c**) contrast bubble study at rest showing passages of bubbles from right atrium to left atrium. (**d**) passage of the delivery sheath (*arrow*) to the left atrium. (**e**) deployment of the left disk of a 25 mm Amplatzer PFO device into the left atrium. (**f**) deployment of the right disk (*arrow*) in the right atrium. (**g**) device has been released showing good position. (**h**) repeated contrast bubble study showing negative result at end of Valsalva maneuver

Data Interpretation

A contrast bubble study with and without Valsalva maneuver under echocardiography or transcranial Doppler (TCD) is necessary to demonstrate right-to-left interatrial shunting and is repeated at the end of the procedure to document successful closure. Closure rates using the Amplatzer PFO device have been over 95% [15].

Complications

Right atrial and aortic root perforation

Extremely infrequent. It has motivated the company to introduce the septal measurements, emphasizing the distance of the free right atrial wall from the defect and device.

Entrapment of prominent Eustachian Valve on the delivery cable

It causes no problem with the deployment, however to avoid the avulsion of the Eustachian Valve, it is suggested to advance the delivery sheath to the hub of the right disc prior to releasing the cable from the device.

Clinical Vignettes

Case 1

ASD Closure

An asymptomatic 28 year young female patient was diagnosed to have a secundum type ASD. On a routine scheduled physical examination she was noted to have a widely split S2 and a grade 2 systolic ejection murmur heard best at the left upper sternal border. The lungs were clear to auscultation. TEE revealed a large secundum ASD measuring 26 mm with left-to-right shunting and evidence of right ventricle volume overload. Cardiac catheterization performed under conscious sedation and ICE guidance showed a significant left-to-right shunt with calculated Qp:Qs ratio of 4.1:1, the mean pulmonary artery pressure was 18 mmHg and PVR was 1.3 Wood units. ICE revealed a large ASD measuring 26 mm in diameter with left-to-right shunt and a deficient anterior rim (Figs. 35.3 and 35.6).

A 32 mm Amplatzer septal occluder device was chosen and a 11 Fr Hausdorf sheath was used to deliver the device. ICE revealed complete closure. The patient was discharged 24 h later with

TTE showing proper device position and no residual shunt.

Case 2

PFO Closure

A 42-year old female patient chronically treated with aspirin, presented reporting the sudden onset of right-sided weakness and dysarthria while driving her car. On examination, she was noted to be aphasic with a facial droop and right upper and lower extremity hemiplegia. She was treated with heparin and aspirin with clinical resolution of most symptoms overnight. One day later, an MRI of the brain revealed an infarct in the distribution of the left middle cerebral artery with evidence for a prior, clinically unrecognized event in the right parietal cortex. Work-up was remarkable solely for a PFO with right-to-left shunting and an atrial septal aneurysm.

She was referred for device closure for recurrent stroke in the setting of anti-platelet therapy. The procedure was done under ICE guidance (Fig. 35.8) and a 25 mm Amplatzer PFO device was successfully implanted (Fig. 35.9). Her ICE and TCD were negative for residual shunt after the closure.

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Balloon Valvuloplasty

36

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Aortic Valvuloplasty

Indications

Balloon aortic valvuloplasty (BAV) is first choice therapy for aortic stenosis in children and young adults, age 21 years or less. In older adult patients, it is infrequently a first choice therapy because restenosis occurs in most patients between 6 months and 2 years after the therapy is initially applied and is considered contraindicated as a stand-alone alternative to definitive valve intervention for aortic stenosis. It is indicated as a bridge to surgery in hemodynamically unstable high-risk patients prior to aortic valve replacement, for palliation in patients with serious comorbid conditions, and prior to noncardiac surgery in some patients. The most common use of BAV in current practice is as a bridge to TAVR for patients with debilitating symptoms or refractory heart failure. Indeed, BAV utilization increased fivefold between 2004 and 2013, mirroring the increasing use of TAVR across this period [1]. Of note, however, as TAVR has become an easier and shorter procedure, the fraction of patients who require BAV in a separate setting as a bridge to TAVR has decreased as the difference in risk between with the two procedures has diminished. Patients are selected on the basis of symptoms of angina, dyspnea or syncope in association with echocardiographic evidence for severe aortic stenosis. Finally, while BAV was once considered mandatory for preparation of the aortic valve prior to delivery of TAVR devices, recent evidence of high procedural success rates for 'direct' TAVR using newer generation devices suggests that the decision to perform balloon predilation should be determined by individual anatomic factors [2].

Contraindications

The major contraindications to BAV are the patient who is a candidate for aortic valve replacement, and then among patients in whom BAV is desired, severe aortic insufficiency or an inability to accomplish retrograde catheterization.

Equipment

- 10–14F sheaths
- 0.032″& 0.035″ extra-stiff 260–300 cm length guidewires
- Temporary pacemaker
- PA catheter (Swan-Ganz)

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- percutaneous suture closure devices
- 18–24 mm balloon catheters with 120 cm shaft

Techniques

The techniques for performing aortic valvuloplasty include the conventional retrograde approach (Fig. 36.1) and the less frequently utilized antegrade transseptal approach [3]. Retrograde valvuloplasty requires a 10–12 French arterial sheath. After placement of a large sheath, the valve is crossed retrograde, and a balloon catheter ranging from 18 up to 24 mm diameter is passed retrograde across the valve and inflated to relieve the stenosis. The balloon size is usually estimated from the annulus diameter on transthoracic echo, from the short axis of the annulus diameter on TEE, or from CT-derived measurement. Rapid right ventricular pacing is used as a method to diminish balloon "watermelon seeding" during balloon inflations. Without this adjunct, ventricular systole, especially in patients with preserved left ventricular systolic function, ejects the balloon during attempts to inflate it in the stenotic aortic valve. Burst pacing at between 160 and 200 beats per minute effectively reduces cardiac output sufficiently to allow the balloon to be positioned stably for inflations. Shorter balloons can thus be used, which diminishes the time of the inflation-deflation cycle. Temporary pacing is also needed if there is underlying bundle branch block.

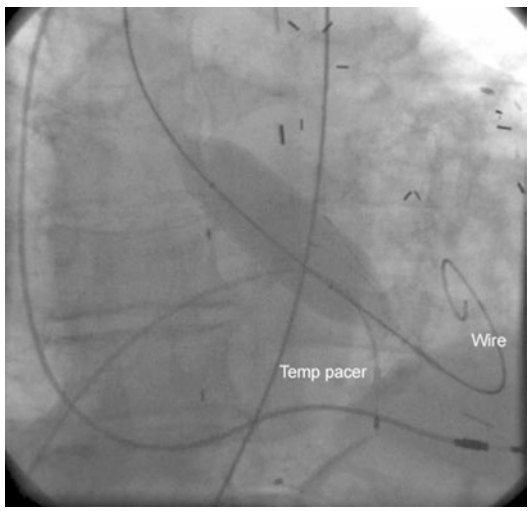

Fig. 36.1 Retrograde BAV. A curved guidewire is placed across the aortic valve into the left ventricular (LV) apex from the retrograde femoral arterial approach. A temporary pacemaker is used to pace the LV at 160–200 bpm while the balloon is inflated

The use of suture preclosure has diminished the challenges in managing the large arterial puncture [4]. Using one or two 6 French Proglide devices, immediate hemostasis can be obtained in the vast majority of patients, without any need to reverse the heparin anticoagulation. Alternatively, post-closure may be achieved with a collagen plug specifically designed for large bore access. Recently, a transradial approach has also been described using 9Fr radial access, and has demonstrated feasibility in the vast majority of patients along with low risk of bleeding complications [5].

Antegrade BAV has been described but is rarely used. A 14 French sheath can be placed in the right femoral vein to allow transseptal access and antegrade passage of a wire loop through the circulation, followed by balloon placement. Venous preclosure may be used as well, which similarly simplifies the management of the large venous puncture. Antegrade valvuloplasty may be performed with a conventional balloon or with an Inoue balloon. The valve areas achieved with the Inoue device are significantly greater than with a conventional balloon. The antegrade approach is more complex technically, but has the advantages of eliminating the need for a large arterial puncture, allowing more stable positioning of the balloon in the valve, and facilitating the delivery of larger balloon into the valve orifice.

Data Interpretation

Interpretation of hemodynamic data during the procedure is based on measurement of transvalvular pressure gradient and cardiac output with calculation of valve areas (Fig. 36.2) [6]. Most patients have an initial aortic valve area between

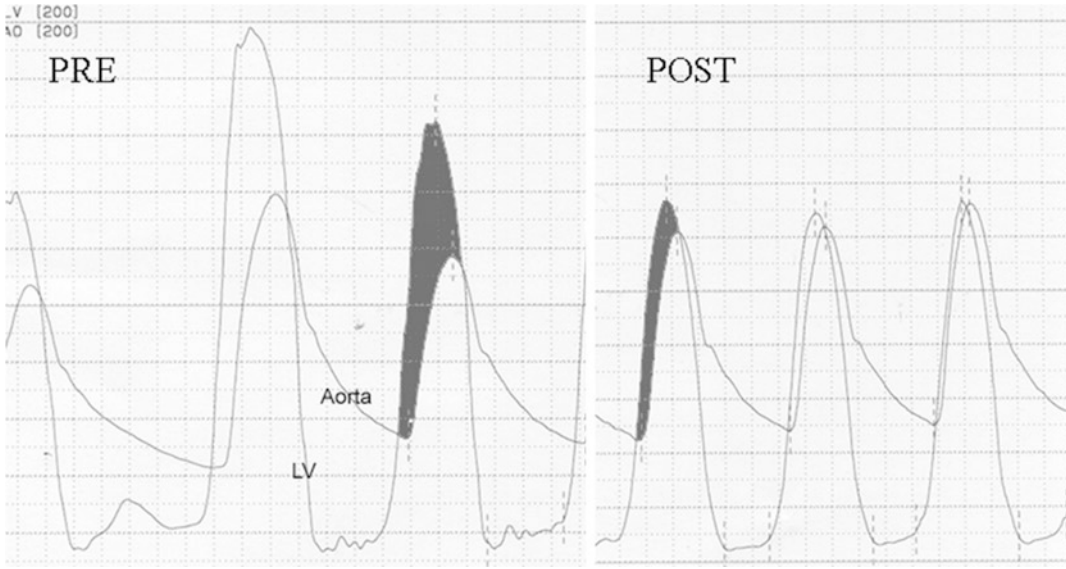

Fig. 36.2 Transaortic valve pressure gradient before and after BAV. The left panel shows a mean gradient of 45 mmHg (*shaded area*), representing the difference between the left ventricular and aortic pressures. The valve area was 0.6 cm^2. After BAV the mean gradient has decreased to 12 mmHg, and the valve area has increased to 1.3 cm^2. *Aorta* aortic pressure, *LV* left ventricular pressure

0.4 and 0.8 cm^2. Typical post-procedure results involve increases in valve area up to 0.9–1.2 cm^2. One standard definition of procedure success is a 50% increase in valve area or a 50% decrease in mean transvalvular pressure gradient.

Complications

Major complications of the procedure are vascular access complications, damage to the aortic valve, or cardiac perforation. Large vascular sheaths are used for either venous or arterial access. Bleeding complications are minimized by the use of suture closure techniques following the procedure. Acute aortic regurgitation causing hemodynamic compromise – although a feared complication – is rare, occurring in less than 2% of cases [7]. Nevertheless, some patients have dramatic hypotension and left ventricular failure immediately following balloon inflations, which in some cases leads to fatality on the catheterization laboratory table. Permanent pacemakers for heart block are required in 1 or 2% of patients, especially if underlying bundle-branch block is present to begin with. Hospital mortality is 5–8% in this elderly, highly sick patient population when BAV is done as primary therapy, and probably less when BAV is done as a bridge to TAVR [8].

Clinical Vignette

An 84 year old man presents with CHF and is found to have aortic stenosis with a Doppler estimated aortic valve area of 0.6 cm^2. The transvalve mean and peak gradients are 54 and 76 mmHg, and left ventricular function is moderately depressed with ejection fraction 40%. He has a history of CABG at age 70 and then again at age 78 years. The ECG shows atrial fibrillation with a rate of 85 bpm. Angiography shows a patent LIMA to LAD, patent native RCA, and occluded native and graft circumflex supply. In addition he has chronic kidney disease and recently diagnosed lung cancer.

His STS risk score is 16% and due his untreated cancer and frailty he is felt not to be a candidate for TAVR. Thus, balloon valvuloplasty is an attractive palliative therapy. BAV was performed using the antegrade approach. Right

femoral venous 6F access was obtained, and a 6F Closer S device was used to place a suture. Baseline right heart pressures were measured. A 14F sheath was placed. After transseptal puncture, baseline transaortic gradient was assessed & valve area calculated. A balloon flotation was passed from LA to LV, and then antegrade across the aortic valve into the descending aorta. A guidewire was passed through the balloon catheter and snared in the descending aorta. The transseptal catheter was exchanged for a Inoue 26 mm balloon. This was passed over the wire to the aortic valve and inflated once to accomplish valve dilatation. Final transaortic valve pressure gradients were measured and valve area calculated. The 14F venous sheath was removed with preplaced suture closure. He was discharged from the hospital the next morning.

Pulmonic Valvuloplasty

Indications

Balloon valvuloplasty (PBV) is the treatment of choice for patients with pulmonic stenosis. It is indicated for patients with pulmonic stenosis and symptoms of exertional dyspnea, angina, syncope, or presyncope. Asymptomatic patients with normal cardiac output and peak gradient greater than 50 mm should be treated as well. Treatment is controversial in patients who are asymptomatic with normal cardiac output and peak gradient between 30 and 50 mmHg. Asymptomatic patients with gradients less than 30 mmHg should not be treated with balloon valvuloplasty. The treatment is highly durable with symptomatic relief in the vast majority of patients lasting for decades [9, 10].

Contraindications

The major contraindication is more than moderate pulmonic insufficiency.

Equipment

- 12–14 F sheaths for femoral venous access
- Dual lumen catheter
- 0.035″& 0.038″ extrastiff 260–300 cm length guidewires
- percutaneous suture closure devices
- 22 & 24 mm balloon catheters with 120 cm shaft
- 26–30 mm Inoue balloon catheters

Technique

The procedure is performed via femoral venous access [11]. A guidewire is passed across the stenotic pulmonic valve, and transvalve pressure gradient measured with a dual lumen catheter. A balloon catheter is passed across the valve. It is important to measure the valve annulus diameter using echocardiography prior to the procedure so balloon sizing can be appropriate. A single large balloon is adequate in the majority of patients. A balloon to annular diameter ratio of 1.2 is ideal. Occasional patients require double balloon technique to achieve an adequate result. The Inoue balloon may be used and is available in diameters up to 30 mm, which will be suitable for the majority of patients.

Data Interpretation

Transvalvular pressure measurement is used before and during the pressure to assess the degree of stenosis. Gradient >50 mmHg at rest is typical. Valve areas are not routinely reported for this procedure, but are useful to follow and should be measured in adult patients. After valvuloplasty the PA pressure changes little. Diminished RV pressure is mostly responsible for the decreases in gradient.

Complications

The major complications include vascular access bleeding, which is not ordinarily

problematic because the access is venous. Pulmonic insufficiency may result and is usually tolerated acutely [8].

Clinical Vignette

A 43 year old man presents with fatigue. After a heart mumur is noted he is found to have congenital pulmonic stenosis on echo. The mean gradient is estimated to be 80 mmHg and there is no pulmonic regurgitation. There is RV hypertrophy without chamber enlargement. The pulmonic annulus diameter measured 23 mm.

Right femoral 14fr access was obtained. Arterial pressure was monitored by cuff. Pressures were measured, and after the transpulmonic gradient was confirmed, a 28 mm Inoue balloon was passed into the valve and inflated twice. The balloon was removed and a double lumen catheter passed back across the valve. Repeat pressure measurement showed a decrease in transpulmonic gradient to 35 mmHg. The single right femoral venous sheath was removed with manual compression. After 6 h of bed rest the patient was ambulated and then discharged.

Mitral Valvuloplasty

Indications

Balloon mitral valvuloplasty is also referred to as balloon mitral valvotomy (BMV), or percutaneous transvenous mitral commissurotomy (PTMC). BMV is indicated for symptomatic patients with mitral valve area 1.5 cm^2 or less and favorable valve morphology [12]. The most important contraindication is left atrial thrombus seen on transesophageal echo, which is necessary for screening all patients, in the absence of moderate to severe mitral regurgitation. Favorable leaflet morphology is related to the pliability of the leaflets, symmetry of commissural fusion, and the degree of leaflet calcification and subvalvular deformity. Asymptomatic patients with valve area less then 1.5 cm^2 and pulmonary artery systolic pressure greater than 50 mm at rest or 60 mm with exercise, may be treated as well. Severely symptomatic patients with highly calcified valves who are high risk for mitral valve replacement can be treated as well. Treatment for asymptomatic patients with new atrial fibrillation is controversial. Patients with mild mitral stenosis should not be treated with balloon valvotomy.

Contraindications

The most important contraindication for BMV is left atrial thrombus, which may be seen in as many as 20% of patients screened for the procedure, even among those taking coumadin anticoagulation therapy. The addition of more intense anticoagulant therapy will result in resolution of the thrombus in most patients within 6–12 weeks, allowing performance of the procedure at a later time.

Equipment

- 14F sheath for R femoral venous access
- Transseptal sheath & needle
- PA catheter (Swan-Ganz)
- percutaneous suture closure devices
- 26, 28, and 30 mm Inoue balloon catheters

Technique

Numerous techniques exist, among them the double balloon technique, Inoue balloon technique, metal commissurotome, and retrograde transarterial technique [13]. Dilatation is usually performed via an antegrade approach using transseptal puncture. The most commonly used device for catheter mitral valvotomy worldwide is the Inoue balloon catheter. This is a novel single balloon that inflates in three stages (Fig. 36.3). After the balloon is passed into the left atrium, the front portion is inflated in the manner a pulmonary artery catheter is inflated, and then the balloon is maneuvered across the mitral valve. This is accomplished with the aid of a steering stylette with a preformed anterior curve. The

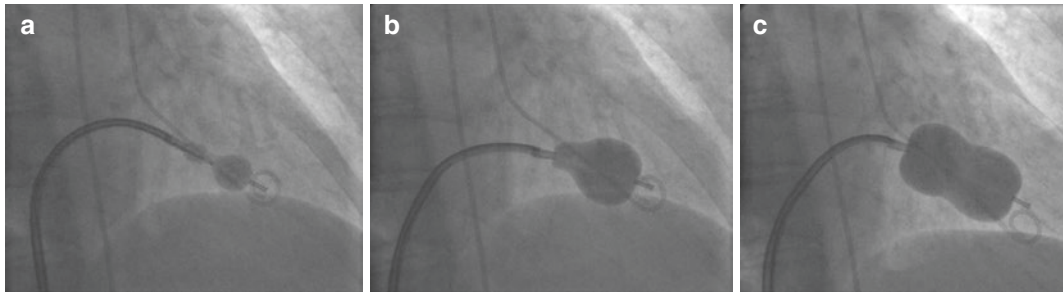

Fig. 36.3 Sequence of balloon inflation for Inoue technique BMV. (**a**) Partially inflated Inoue balloon, across the mitral valve, in the left ventricle. (**b**) the balloon is pulled back to engage the mitral leaflets and (**c**) fully inflated to split the valve commissures

balloon is pulled back until it engages the stenotic mitral orifice. As the balloon is inflated, the middle section opens, applying pressure to the commissures. The balloon may be inflated with increasing volumes of contrast with resultant increases in diameter. After each balloon inflation the pressure gradient can be measured and mitral regurgitation assessed either by echocardiographic visualization or by repeat ventriculography. Successive inflations at larger balloon diameters is then performed until either a minimum gradient is achieved or mitral regurgitation begins to increase. This is called the step-wise method for commissurotomy.

The procedure may also be accomplished using conventional balloons. Typically two balloons of 15–20 mm diameter are used together. Two wires must be passed through the transseptal puncture to accomplish this. The wires are looped in the ventricular apex and sometimes passed into the aorta to provide stability for advancing the balloons into the mitral orifice. The balloon catheters for this approach are longer than the Inoue balloon and either the balloon catheter tips or the guide wire may cause ventricular apical perforation. It is also possible to pass balloons retrograde from the aorta through the left ventricle and across the initial valve. This approach avoids transseptal puncture, but requires large bilateral femoral sheaths.

The metal commissurotome is a mechanical metal dilator placed on a catheter shaft. This can be passed into the mitral valve and opened to split the commissures. The major advantage of this device is that it is a reusable instrument and is especially attractive in parts of the world where catheter reuse is the rule rather than the exception. A disadvantage is the large French size and rigidity of the metal working end of this device. It can be difficult to position in the mitral valve, and cardiac perforation is a risk. This device is not available in the United States.

Data Interpretation

Screening transthoracic echo is the first critical step in patient evaluation. The valve leaflets and subvalvular apparatus must be examined for patient selection for the procedure. An echocardiographic scoring system assigning 4 points to each of these categories (maximum score 16) has been devised as a rough guide to patient selection. Patients with low score (6–9) have the best long-term results. Patients with higher scores may be treated, recognizing that results will be less durable. Poor candidates for surgery may be treated even with severe valve deformity (echo score 10–16) as a palliative procedure. During the procedure results are assessed by hemodynamic measurement of the transvalvular pressure gradient (Fig. 36.4). The mean gradient typically decreases from 12–14 to 4–6 mmHg. Results are also assessed by echo measurement of the mitral valve area. Both left ventriculography in the cath lab and Doppler echo are used to assess mitral regurgitation before and after BMV.

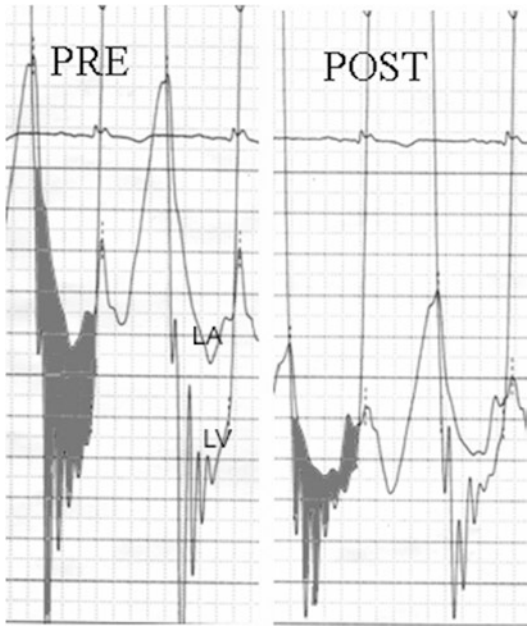

Fig. 36.4 Transmitral pressure gradient before and after BMV. The left panel shows a mean gradient of 16 mmHg (shaded area), representing the difference between the left atrial and left ventricular pressures. The valve area was 1 cm^2. After BMV the mean gradient has decreased to 6 mmHg, and the valve area has increased to 2.0 cm^2. *LA* left atrial pressure, *LV* left ventricular pressure

Complications

Major complications of BMV include worsening mitral regurgitation, which is seen in at least a minor degree in at least 15% of patients [14]. Severe mitral regurgitation necessitating mitral valve replacement during the same hospitalization occurs in 2–4% of patients. Hospital mortality is typically less then 1%. TIA or stroke also occurs in less than 1% of patients. Transseptal puncture is necessary to accomplish the procedure using antegrade approaches, and cardiac perforation occurs in 0.5–1.5% of patients. Atrial septal defect complicating the transseptal puncture with a significant clinical shunt occurs in less than 2% of patients.

Clinical Vignettes

Case 1

A 33 year old Asian woman presents in the fifth month of pregnancy with dyspnea at rest. A murmur is noted, and echo shows mitral stenosis with a transmitral gradient of 20 mmHg, pliable noncalcified leaflets, and no regurgitation. The valve area is 0.6 cm^2. TEE shows no left atrial appendage thrombus.

Once on the catheterization table, right femoral 14 F venous access is obtained. To minimize x-ray exposure, transthoracic echo is used during the procedure to monitor the valve gradient and regurgitation, rather than using hemodynamic measurements. Transseptal puncture is performed. The atrial septum is dilated and the Inoue balloon placed in the left atrium, then maneuvered into the left ventricle. The balloon is inflated partially, pulled back against the stenotic valve, and fully inflated. Echo shows no mitral regurgitation, but the gradient has only decreased to 12 mmHg and the valve area is 0.8 cm^2. A second inflation using a larger inflation volume (and therefore a larger inflated diameter) is performed, with resultant mild mitral regurgitation and a valve area of 1.9 cm^2. The sheaths are removed and after 6 h bedrest the patient is ambulated, She is discharged the next morning.

Case 2

A 157 cm tall, 54 year old woman presents with a history of slowly increasing dyspnea on exertion. She has a history of rheumatic mitral stenosis, and the valve area has decreased from 1.6 cm^2 2 years ago to 1.2 cm^2 on a recent echo exam. The is mild mitral regurgitation. TEE shows no left atrial thrombus, and coronary angiography shows no disease.

Bilateral femoral access is obtained, with left arterial 6 F access for pressure monitoring and ventriculography, left 8 F venous access for right heart catheterization and cardiac output measurement, and 14 F right venous for transseptal puncture and passage of the BMV balloon. After transseptal access, atrial septal dilatation, and passage of the balloon into the left atrium and then left ventricle a first inflation is performed. Initial balloon inflation diameter is estimated from patient height using the empiric formula (height in cm/10) + 10 = expected inflation diameter in mm. In this case the expected inflation diameter is 26 mm, so a first inflation of 24 mm is used. This results in no change in the

LA pressure or mitral gradient. A second balloon inflation to 25 mm has similar results, but after the third inflation to 26 mm balloon diameter the mean gradient decreases to 7 mmHg and the valve area increase to 2.1 cm^2. Repeat left ventriculography shows no change in the mild mitral regurgitation. The sheaths are removed and the patient ambulated after 6 h. She is discharged the next morning.

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37 Transcatheter Aortic Valve Replacement

Samuel P. Powell, Nicholas S. Amoroso, and Daniel H. Steinberg

Indications

Appropriate patient evaluation is of paramount importance. The American College of Cardiology/American Heart Association guidelines recommend the use of a heart valve team in patients for whom transcatheter aortic valve replacement (TAVR) or high-risk surgical valve replacement is being considered [1]. A heart valve team typically consists of an integrated, multidisciplinary group of healthcare professionals with expertise in valvular heart disease, cardiac imaging, interventional cardiology, cardiac anesthesia, and cardiac surgery [2]. Along with the heart valve team, there are several objective risk stratification tools currently available to quantify risk and assist in patient selection for TAVR. The determination of clinical risk typically involves calculation of the Society of Thoracic Surgery (STS) risk score along with assessments of frailty, multisystem disease and procedure specific impediments.

On the basis of pivotal trials in elevated and extreme risk patients, TAVR was initially approved for patients deemed to have an elevated surgical risk as determined by a heart valve team [2–4]. Subsequently, studies in patients with an intermediate surgical risk and low surgical risk have shown similar outcomes in surgical valve replacement compared to TAVR, especially for patients with suitable iliofemoral anatomy for transfemoral access [5–8].

Contraindications

Absolute contraindications for TAVR implantation are limited to patients who have less than 1 year life expectancy for reasons other than aortic stenosis. Relative contraindications for TAVR implantation are largely anatomic in nature. Inadequate coronary heights or a narrow sinus of Valsalva may be considered relative contraindications as the implantation of the TAVR can push that native valve leaflets backwards and potentially obstruct coronary arteries with a low takeoff. This can be overcome by protecting coronary arteries with techniques such as electrocautery of the native leaflets or use of wires and undeployed coronary stents that can then be deployed if there is evidence of coronary obstruction.

Equipment

In the United States, two transcatheter technologies are currently available for commercial use, the balloon expandable Sapien S3 Valve (Edwards Life Sciences, Irvine CA) (Fig. 37.1) and the self-expanding CoreValve Evolut PRO+

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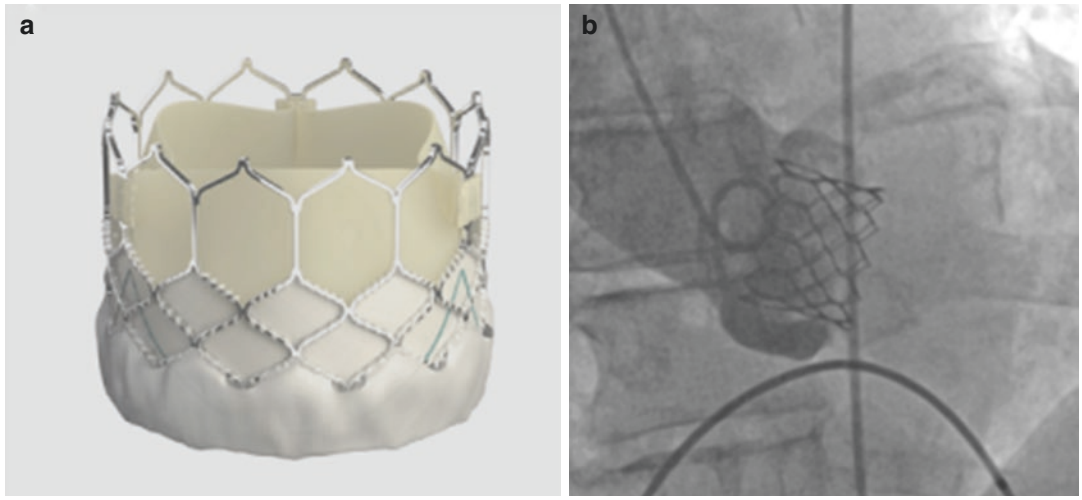

Fig. 37.1 (**a**) Balloon Expandable Edwards Sapien 3 Valve. (**b**) Fluoroscopic Image of deployed Edwards Sapien 3 Valve

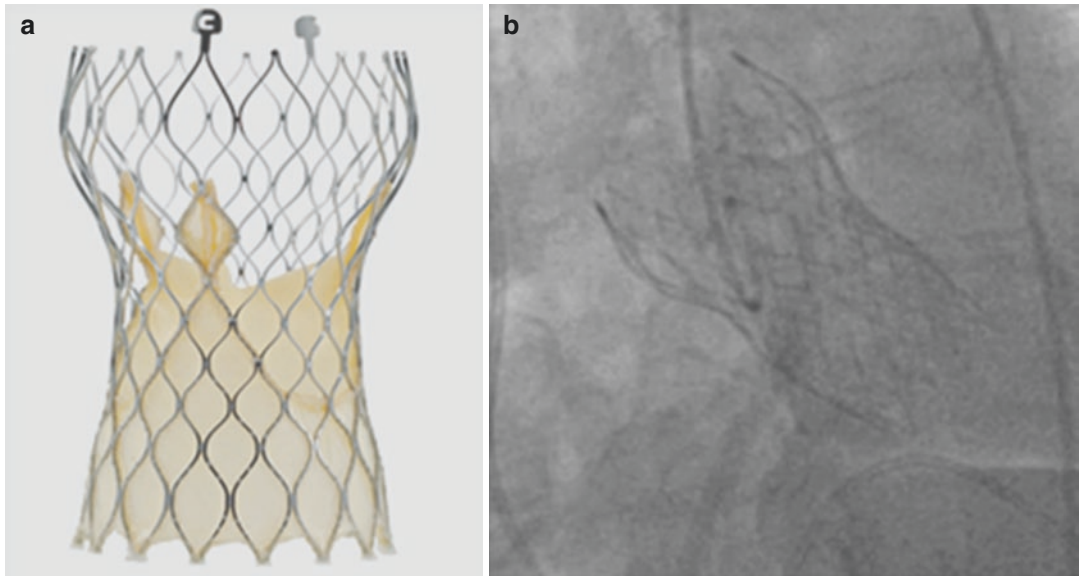

Fig. 37.2 (**a**) Medtronic Evolut PRO+. (**b**) Fluoroscopic Image of deployed Medtronic Evolut PRO+

(Medtronic, Minneapolis, MD) (Fig. 37.2). The S3 platform is available in 20, 23, 26 and 29 mm sizes delivered through a specially- designed expandable 14 French sheath (the 29 mm device requires a 16 French sheath). The Evolut PRO+ platform is available in 23, 26, 29 and 34 mm sizes typically delivered via an in-line 14 French sheath for 23, 26 and 29 mm valves (the 34 mm Evolut R requires 16 French while the 34 mm PRO+ requires 18 French). Equipment used in our current practice is summarized in Table 37.1.

Techniques

Current ACC/AHA guidelines recommend the use of a hybrid operating theatre for implantation of the transcatheter aortic valve, although at some

Table 37.1 Procedural equipment

	Equipment	Comments
Basic Essentials		
	Hybrid Suite	Capable of full catheterization and surgical needs
	Anesthesia Setup	General or conscious sedation
	Surgical Setup	
	Perfusion Pump	Not necessarily primed, but available
	Transvenous pacemaker	
	Transesophageal Echocardiography	As appropriate, not necessary for all cases
	PCI Equipment	Standard guides, wires, stents available
	Covered stents	Available for vascular complication
Sheaths	Standard access equipment	May require longer sheaths
	Specialty sheath	Multiple types available—based on specific procedure and access site
Catheters		
	JR4, AL1	For crossing valve (others as appropriate)
	2 Pigtail catheters	For exchange, aortography and hemodynamic evaluation
Wires	0.035″ angiographic	Both 150″ and 260″
	0.035″ straight tip	For crossing—we prefer hydrophilic wire
	0.035″ extra/super stiff	Depends on valve type, dedicated pre-curved wires available
Specialty		
	Valvuloplasty balloon	Size chosen by purpose (i.e. priming, sizing,)
	Transcatheter Valve	As appropriate

centers, there has been a transition to procedural performance in appropriately outfitted catheterization laboratories. Current guidelines also mandate that both an interventional cardiologist and cardiothoracic surgeon be present for the procedure [1].

The preoperative evaluation is summarized in Fig. 37.3, and it is essentially congruent with a surgical evaluation with the addition of Multidetector Computed Tomography (MDCT). This modality is of particular importance for TAVR as it enables one to choose the appropriate device size based on aortic annular area/perimeter, evaluate left ventricular outflow tract and valvular calcification, assess coronary heights, sinus width, sinotubular junction diameters/calcification, angiographic views and potential access routes (Fig. 37.4). While many of these variables can be assessed through alternative modalities, MDCT is a singular, detailed and 3-dimensional modality with dedicated software systems allowing for reliable and reproducible analyses and pre-TAVR planning.

Regarding access, the transfemoral route is generally favored for patients with suitable iliofemoral anatomy to accommodate currently available devices, and approximately 97% of procedures are now performed via transfemoral access [9]. For patients with iliofemoral disease precluding delivery of the 14–16 French devices, alternative access routes are possible. These alternative sites include: open iliac (via conduit), subclavian, direct aortic or transapical. Additionally, direct carotid or transcaval access (with crossover from the inferior vena cava to the aorta) may be of utility in appropriately selected patients.

Typical procedural steps for each device are outlined here and described in the clinical vignettes below. Regardless of the planned primary access site, additional arterial access is obtained for annular assessment and venous access is obtained for delivery of a transvenous temporary pacemaker. Placement of an embolic protection device may be accomplished through transradial access. A pigtail catheter is advanced

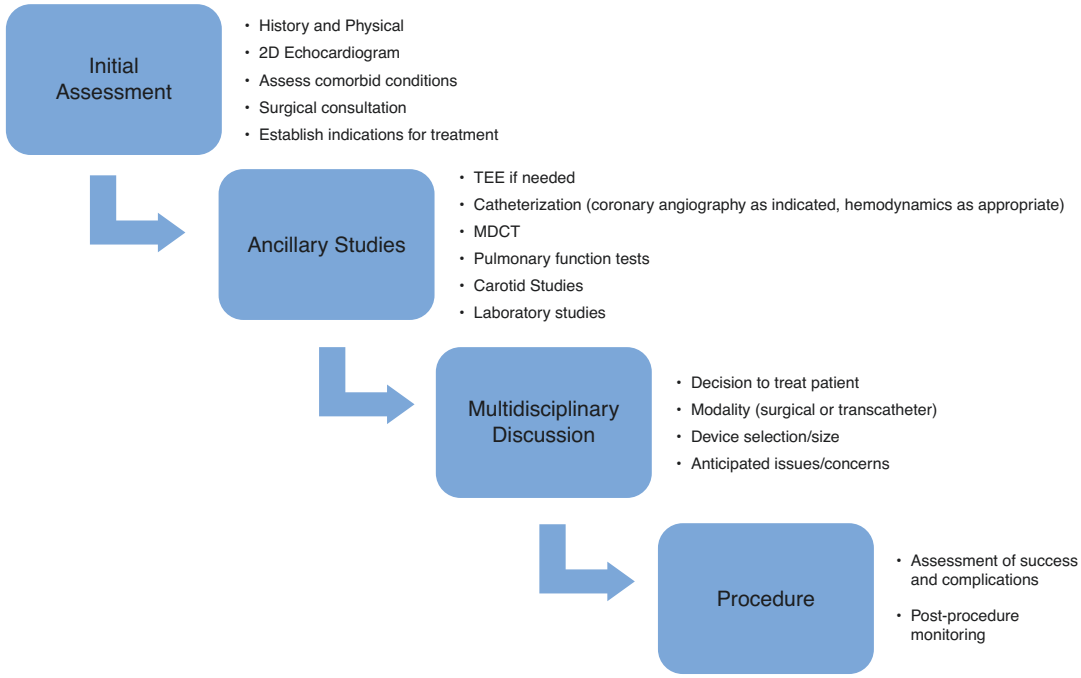

Fig. 37.3 MDCT Preprocedural evaluation

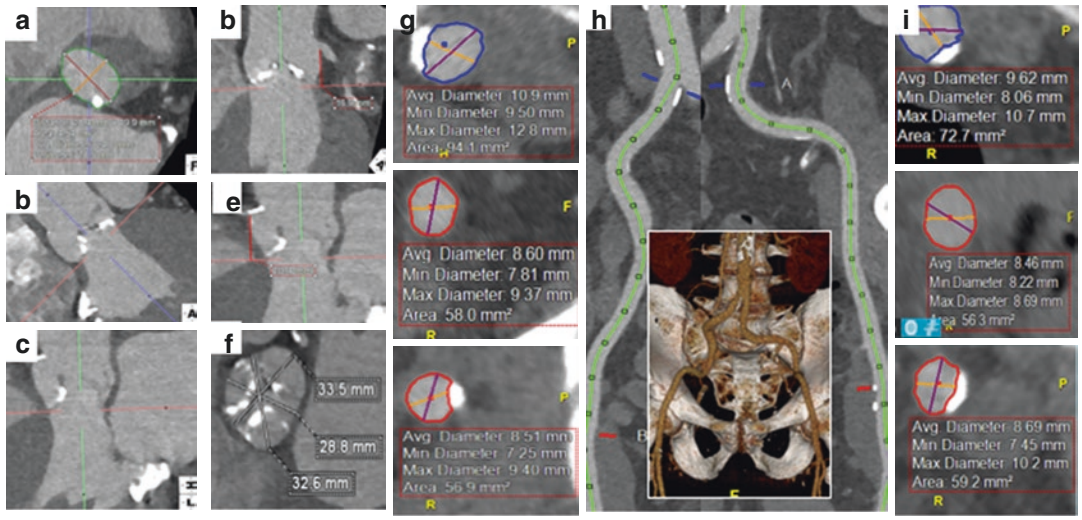

Fig. 37.4 MDCT evaluation. (**a**) Annulus measurement. (**b**) Coronal angle at level of annulus. (**c**) Sagittal angle at level of annulus. (**d**) Left coronary height. (**e**) Right coronary height. (**f**) Sinus of Valsava measurements. (**g**) Right iliofemoral minimums. (**h**) Iliofemoral scout. (**i**) Left iliofemoral minimums

to the aortic root and aortography is then performed to identify the annular plane. The aortic valve is crossed with a straight wire using a FR4 or AL1 coronary catheter, and a second pigtail is exchanged for measurement of simultaneous left ventricle-aortic pressure gradient. A stiff 0.035″ wire is then advanced into the left ventricle. Priming valvuloplasty is typically performed under conditions of rapid pacing. Following priming valvuloplasty, the valve is

placed across the aortic valve with appropriate position confirmed by aortography prior to valve deployment.

The valves are deployed via respective techniques (described in the vignettes below). Hemodynamic assessment is performed with simultaneous left ventricle-aortic pressure measurements to assess post implantation gradient and aortic insufficiency. Positioning and aortic insufficiency is also assessed through aortography and echocardiography as indicated. Post dilation is performed as needed, usually to address perivalvular regurgitation. Access site management/closure is performed based on the chosen access site. In patients undergoing balloon expandable valve implantation, the pacing wire can be removed if there is no evidence of conduction disturbance, while for those receiving a self-expanding valve, the temporary pacing wire may remain in place up to 48 hours prior to removal for those with evidence of conduction system disturbance.

Data Interpretation

After valve implantation the operator must assess multiple factors before the procedure is considered successful. Immediate attention is given to the acute hemodynamics and recovery of systemic pressures. The ECG is examined for conduction disturbances and/or ST changes suggestive of coronary occlusion. Once stable, the post implantation pressure gradient is directly measured via catheters in the left ventricle and aortic root followed by an assessment of aortic insufficiency and coronary patency by aortic root angiography. A transvalvular gradient of <10 mmHg is expected in the majority of cases, and an increased gradient should lead to re-evaluation of the valve for complete expansion.

While trace to mild residual aortic insufficiency is generally acceptable, greater than moderate aortic regurgitation after implantation has been shown to predict long term mortality throughout TAVR trials. Aortic insufficiency is visually assessed by aortography and clinically assessed via assessment of diastolic pressure separation. More than mild-moderate AI should lead to re-evaluation of valve expansion and deployment location for potential remedies such as post dilation or implantation of a second valve.

Complications

For purposes of data collection and consistency, complications have been precisely defined by the Academic Research Consortium and are reported in the Transcatheter Valve Technologies registry (a requirement for reimbursement in the United States) [10]. Procedural success is defined as successful vascular access, appropriate placement of a single valve with less than moderate aortic insufficiency. With increased global experience and device iteration, procedural success approaches 95–100%, and overall complication rates continue to improve with intraprocedural mortality generally less than 1% and in-hospital mortality less than 2% [9]. Major acute complications include annular rupture, ventricular perforation, acute aortic insufficiency, coronary obstruction, complete heart block and vascular compromise. These complications often manifest with acute hemodynamic, electrocardiographic or echocardiographic changes. Identification and treatment depend on the cause and commonly temporizing resuscitative measures are employed while the underlying issue is addressed.

In the post-operative period, the more important complications following TAVR include clinically evident stroke in about 2–3% of cases and conduction disturbances requiring permanent pacemaker implantation in approximately 10% of cases depending on the particular valve used [9]. Conduction abnormalities following TAVR are related to the close proximity of the aortic annulus and specialized conduction tissue, and these are more common with self-expanding valves compared to balloon expandable devices. Rates of complete heart block also appear dependent on the depth of implantation relative to the annulus, and various implantation techniques are proposed to ensure shallower implant depth and ideally lower rates of pacemaker implantation [7].

Clinical Vignettes

Case 1

A 79-year-old male with hypertension, hyperlipidemia, diabetes on oral medications, moderate lung disease, chronic renal insufficiency, coronary artery disease with prior CABG, chronic diastolic heart failure and severe aortic stenosis presented for evaluation. Symptoms were consistent with New York Heart Association Class 3, and after multidisciplinary evaluation, he was considered at elevated risk for surgical AVR with an STS predicted risk of mortality of 8.4%. Physical exam was consistent with severe aortic stenosis. Echocardiogram demonstrated an ejection fraction of 60%, annular diameter 21 mm, aortic valve area of 0.8 cm^2, peak velocity 4.2 m/s and mean gradient 43 mmHg with trace aortic insufficiency. Coronary artery angiography demonstrated multivessel coronary disease with patent grafts. CTA of the chest, abdomen and pelvis revealed a trileaflet aortic valve, a calcium score 6348, annular area 470 mm^2, annular-coronary heights greater than 10 mm bilaterally, and iliofemoral minimal diameters of 6.6 mm at the left common femoral artery, and 6.2 mm at the right common femoral artery.

Percutaneous access was obtained on the right common femoral artery. Contralateral arterial and venous access was obtained percutaneously. The right common femoral artery was preclosed with 2 suture devices, and using standard techniques, a 14 French hemostatic sheath was secured in place. The aortic valve was crossed with a 0.035″ straight-tipped Glidewire and a FR4 catheter. A soft 0.035″ exchange length wire was advanced into the ventricle via the catheter, and a pigtail was then advanced into the ventricle over this wire. Simultaneous pressures were recorded. A 0.035″ extra stiff wire was advanced into the ventricle.

6 French right radial access was obtained. Aortography was performed via a 5 French pigtail placed through the sheath in the right femoral artery. The cerebral embolic protection device was advanced over a 0.014″ wire into the ascending aorta. The proximal basket was deployed in the innominate artery, and the device was then articulated into the left common carotid. Once this was achieved, the distal filter was deployed.

After confirmation of correct orientation of the 26 mm S3 balloon expandable valve on the delivery catheter, the valve was crimped and loaded onto the delivery catheter which was then advanced over the exchange wire into the descending aorta. Proper alignment with the valve and balloon on the delivery catheter was achieved. The valve was advanced across the native aortic valve. With rapid pacing and under both fluoroscopic and aortographic guidance, the valve was positioned precisely across the aortic valve, and the valve was deployed. After full deployment, rapid pacing was ceased. Valve positioning and aortic insufficiency was assessed by aortography and hemodynamics. Post dilation was not performed. The deployment system was removed.

The pigtail catheter was placed into the descending aorta, and the pacemaker wire was removed. The delivery sheath was retracted, and percutaneous closure commenced. A completion angiogram was performed. No complications were noted.

The patient improved post procedure and was discharged the following day. Predischarge echocardiography demonstrated normal LV systolic function with a mean gradient across the aortic prosthetic valve of 16 mmHg with trace paravalvular regurgitation.

Case 2

A 72 year-old female with hypertension, hyperlipidemia, diabetes on oral medications, mild lung disease, chronic renal insufficiency, chronic diastolic heart failure and severe aortic stenosis presented for evaluation. Symptoms were consistent with New York Heart Association Class 3 congestive heart failure, and after multidisciplinary evaluation, she was considered at elevated risk for surgical AVR with an STS predicted risk of mortality of 3.3%. Physical exam was consistent with severe aortic stenosis. Echocardiogram demonstrated an ejection fraction of 50%, annular diameter 20 mm, aortic valve area of 0.7 cm^2, peak velocity 4.0 m/s and mean gradient 40 mmHg with mild aortic insuf-

ficiency. Coronary artery angiography demonstrated insignificant coronary disease. CTA of the chest, abdomen and pelvis revealed a trileaflet aortic valve, a calcium score 1555, aortic annular area 380 mm^2 and perimeter 68.7 mm, annular-coronary heights greater than 10 mm bilaterally, and iliofemoral minimums of 6.4 mm at the left common femoral artery, and 6.2 mm at the right common femoral artery.

Percutaneous access was obtained on the right common femoral artery. Contralateral arterial and venous access was obtained percutaneously. A 6F sheath was inserted in the contralateral femoral artery, and a 5 French pigtail catheter was placed via through the sheath in the ascending aorta. A transvenous pacemaker wire was placed via the right internal jugular vein. Pacing thresholds were optimized, and proper alignment of the aortic cusps was determined via aortography. The right common femoral artery was preclosed with 2 suture devices, and a 14 F hemostatic sheath was secured in place via standard techniques. Anticoagulation was initiated with unfractionated heparin.

6 French right radial access was obtained. Aortography was performed via a 5 French pigtail placed through the sheath in the right femoral artery. The cerebral embolic protection device was advanced over a 0.014″ wire into the ascending aorta. The proximal basket was deployed in the innominate artery, and the device was then articulated into the left common carotid. Once this was achieved, the distal filter was deployed.

The aortic valve was crossed with a 0.035″ straight-tipped Glidewire and a FR4 catheter. A soft 0.035″ exchange length wire was advanced into the ventricle via the FR4, and a 6 F pigtail catheter was exchanged over the wire. Simultaneous pressures were recorded. A 0.035″ Lunderquist exchange length wire was advanced into the ventricle.

The sheath was exchanged over the Lunderquist wire for the in-line 14 F system. A 26 mm self-expanding CoreValve Evolut PRO+ was loaded onto the delivery catheter and advanced over the exchange wire into position across the aortic valve. Under fluoroscopic, aortographic and echocardiographic guidance, the valve was positioned precisely across the aortic valve, and deployment commenced. Once annular contact was achieved, accelerated pacing was started, and the valve was unsheathed further. After 2/3 deployment, pacing was ceased. Valve positioning and aortic insufficiency was assessed by echocardiography and aortography. The valve was fully deployed and detached, the delivery catheter was removed, and the pigtail catheter was advanced over the exchange wire for hemodynamic, echocardiographic and aortographic assessment. The pigtail was then removed.

The second pigtail catheter was placed into the descending aorta, and pacemaker wire was kept in place. The delivery sheath was retracted, and percutaneous closure commenced. A completion angiogram was performed. No complications were noted, and all other equipment was removed.

The patient improved post procedure and was discharged 24 hours post TAVR implant. Predischarge echocardiogram demonstrated normal LV systolic function with a mean gradient across the aortic prosthetic valve of 10 mmHg with trace paravalvular regurgitation.

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Transcatheter Mitral Valve Repair

38

Charles Resor

Indications

The prevalence of significant mitral regurgitation (MR) approaches 10% in patients over 75 years of age [1], with functional MR accounting for > 50% of cases [2]. The COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) Trial [3] has now established transcatheter edge to edge repair (TEER) with MitraClip(Abbott Structural, Santa Clara, California) as first line therapy for patients with heart failure and functional MR with demonstrated improvement in mortality, heart failure hospitalization (HFH) and quality of life measures(QoL) compared to medical therapy. While surgery remains the preferred intervention for patients with primary MR, transcatheter edge to edge repair is an appropriate alternative in patients at high or prohibitive surgical risk. While other mitral repair and replacement devices are in various stages of trials, MitraClip is the only FDA approved such device at this time and will be the only device discussed herein.

Contraindications

Patients with small mitral valve areas (<3.5 cm^2) or severely calcified or fibrotic leaflets which predispose to post-procedure mitral stenosis are poor candidates. Insufficient posterior leaflet length (<5 mm), leaflet perforation and active endocarditis preclude MitraClip placement. Any anatomic or comorbid factors that preclude transseptal puncture or TEE render the procedure largely impossible.

Equipment

TEER with MitraClip requires the MitraClip Steerable Guide Catheter and Clip Delivery System with XTW, XT, NTW and NT clips. Transseptal puncture can be performed with standard equipment such as a Brockenbrough needle and Mullins style sheath. Our preference is to use the Bayliss Versacross ® radiofrequency (Baylis Medical Company, ON, Canada) system, which, at added expense, saves time, equipment and wire exchanges. The 24 French venotomy can be managed with a "preclosed" Perclose device (Abbott Vascular, Santa Clara, Ca) or figure of eight suture.

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Technique

TEER should be performed in a catheterization lab which facilitates transesophageal echocardiographic imaging and contains a monitor which allows side by side fluoroscopic and echocardiographic images to be displayed next to hemodynamic tracings. We obtain radial access for arterial monitoring and, in select patients, perform right heart catheterization from the left common femoral vein. We utilize the right common femoral vein(RCFV) for access for the transseptal puncture/TEER. We start by "preclosing" the RCFV. After the vein is preclosed, we give therapeutic heparin (though this can also be done after the transseptal puncture is safely completed) and insert a 14Fr sheath. Through the 14Fr sheath, we insert the transseptal sheath/needle/wire and perform transseptal puncture under TEE guidance (the 14 Fr sheath is not essential but does facilitate easier catheter manipulation). Care and time should be taken to achieve the optimal transseptal puncture location as this will ultimately facilitate easier leaflet grasping. We utilize x-plane imaging with side by side bicaval and short axis views and aim for a mid (in the inferior-superior plane) and posterior (in the anterior-posterior plane) site. With the transseptal sheath tenting the septum in that location, this site should be confirmed with TEE to be 4–4.5 cm above the mitral annulus to ensure sufficient "height" for the procedure prior to puncture. Once across the septum, left atrial access can be confirmed with fluoroscopy, TEE and/or saturation and pressure tracing. For those operators who choose to give heparin after the transseptal puncture, a therapeutic ACT should then be achieved.

The steerable guide catheter can then be advanced into the left atrium over a stiff wire. Once the wire and dilator are removed the clip delivery system can be advanced through the guide into the left atrium. The clip is then steered down towards the mitral valve using the "M" knob, intermittently retracting the clip handle taking care to avoid the back wall of the atrium and the "Coumadin ridge". Using the intercommissural or 3D *en face* view the clip can be positioned, typically over the largest jet or flail segment. Clip trajectory can then be tested by advancing the clip handle and observing the movement of the clip in the AP and medial-lateral planes. Once the clip arms are opened, clip arm orientation can be assessed in the 3D *en face* view and adjusted by torquing the clip handle in the desired direction until the clip arms are perpendicular to the line of coaptation at the desired grasping site. With the G4 system, the anterior and posterior grippers should be identified by echo prior to crossing the valve. If the C arm is then rotated until the clip arms are parallel to the imaging plane (typically an RAO Cranial projection), the clip can be advanced under the valve with fluoroscopic and echocardiographic guidance and any rotation of the clip can easily be detected fluoroscopically. The clip arms are then opened under the valve and the clip handle is then retracted until the anterior and posterior leaflets of the valve land on their respective clip arms (typically in an LVOT view). The grippers are then dropped and appropriate leaflet insertion should be confirmed by TEE. Visualization of the grippers "bouncing" in concert with the leaflets in an indication that the leaflets were grasped but full leaflet insertion should be confirmed by reviewing the grasping images as well as residual leaflet mobility and length. A "tissue bridge" should be confirmed in the 3D *en face view*. With the independent grasping elements of the G4 system, leaflet grasps can then be optimized individually as needed. Once sufficient insertion is confirmed. The clip arms are then closed, slowly, and tension is "given back" by gently and minimally advancing the clip handle, particularly with the XT clips. Clip arm closure can be performed with color echo imaging to assess the MR change in real time. Multiple measures should then be used to assess residual MR severity and the mitral inflow gradient and area should be measured to rule out significant mitral stenosis. If sufficient tissue insertion is achieved, MR reduction is optimal and no mitral stenosis is present, the clip can be deployed. A subsequent assessment of the valve can then be performed. Additional clips can be placed as

needed and care should be taken to ensure the steerable guide is still across the septum prior to withdrawal of the initial clip delivery system.

Technical Considerations

With the G4 device, there are 4 clip types: NT/NTW and XT/XTW (Fig. 38.1). The W (wide) clip arms are 6 mm in diameter as opposed to 4 mm for the standard clips. The XT clip arms are 12 mm long, while the NT clip arms are 9 mm long. We favor the XTW clip for degenerative MR cases with long leaflets and NTW cases for secondary MR cases with significant tethering. We typically use the wide clips in most cases and the narrow clips when there is a concern for mitral stenosis. We favor the NT/NTW clips for commissural lesions. There are some data to suggest an increased risk of perforation or single leaflet detachment with the longer clip arms [4] so care should be taken to ensure the quality of leaflet tissue and avoid excessive tension on the leaflets. The G4 device allows better left atrial pressure monitoring than the prior device but once multiple catheter manipulations are made, there is often significant pressure dampening. Thus one should pay close attention to the left atrial pressure and arterial pressure immediately prior to and after grasping/closing to accurately assess the hemodynamic change with each clip. For challenging leaflets to grasp, adenosine or rapid pacing can be utilized.

Data Interpretation

Functional MR: On the strength of the COAPT Trial, the 2020 ACC/AHA Clinical Practice Guidelines for Patients with Valvular Heart Disease [5], gave a Class IIA recommendation to TEER for patients with chronic severe functional mitral regurgitation in the setting of a reduced ejection fraction and persistent NYHA Class II-IV symptoms despite guideline directed medical therapy(GDMT). TEER in the COAPT Trial resulted in a nearly 50% reduction in heart failure hospitalizations and nearly 40% reduction in mortality at 2 year follow up when compared to medical therapy alone. While the MITRA-FR [6] (Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regugitation) Trial in a similar patient population was neutral with respect to hospitalization and mortality, it had several major limitations. In contrast to the COAPT Trial, it lacked rigorous GMDT optimization prior to enrollment, it enrolled patients with less severe MR than in

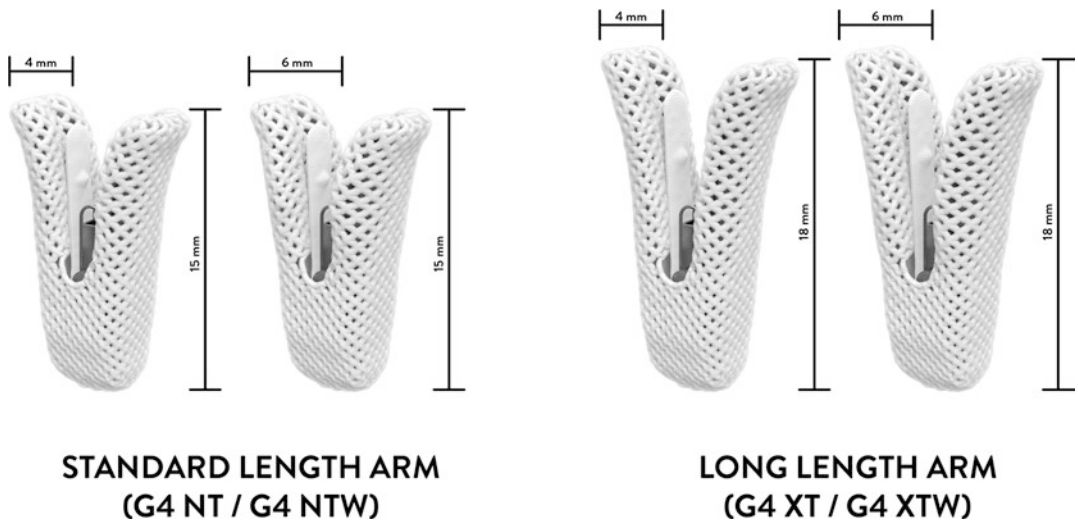

Fig. 38.1 Fourth generation MitraClip

COAPT and in it, procedural outcomes (MR reduction and complications) were worse than in COAPT. Interestingly, while surgical mitral intervention has never been shown in a randomized trial to improve hard outcomes in functional MR, the 2020 practice guidelines still give it a class IIb recommendation in this patient population.

Primary MR: In contrast to the functional MR recommendations, for primary MR, surgical valve intervention remains the gold standard. In the Everest II Trial [7], a randomized trial of mitral valve surgery vs TEER with MitraClip in what was largely a primary MR population, patients randomized to TEER experienced a higher rate of the primary endpoint (a composite of severe MR, mitral valve surgery or mortality). The primary endpoint difference was driven by a 20% increase in the need for mitral valve surgery in patients randomized to TEER with no difference in mortality. As such, per the 2020 ACC/AHA practice guidelines MitraClip received a Class IIa recommendation only in patients at high or prohibitive risk for surgery.

Complications

In the COAPT Trial, the rate of death, stroke, myocardial infarction or emergent surgery within 30 days was less than 4% for patients in the MitraClip arm. While device embolization, single leaflet detachment, cardiac tamponade and vascular complications (related to access and transseptal puncture) occur, they are fortunately rare. Induction of mitral stenosis can occur but if the transmitral gradient is <5 mmHg with the final clip in place, it is unlikely to occur (barring major changes in hemodynamic parameters).

Clinical Vignette

Our patient is an 81 year old woman with a history of CAD status post LAD PCI, CKD, COPD and mitral valve prolapse who was transferred from an outside hospital after presenting with acute decompensated heart failure, acute renal failure and respiratory failure requiring mechanical ventilation. Workup revealed severe mitral regurgitation (Fig. 38.2a) with prolapse of the P2 component of the mitral leaflet with an EROA of 1.1 cm^2 and flow reversal in the pulmonary veins with an ejection fraction of 45%. Coronary angiography revealed a *de novo* 80% mid LAD lesion and right heart catheterization demonstrated a PCWP of 28 mmHg with V waves of 40 mmHg and cardiac index of 1.4 L/min×m^2. After multidisciplinary discussion, she was turned down for CABG and MV repair given an STSPROM of 20% for mitral repair/CABG. Given a GFR of 10, we elected to perform the MitraClip procedure

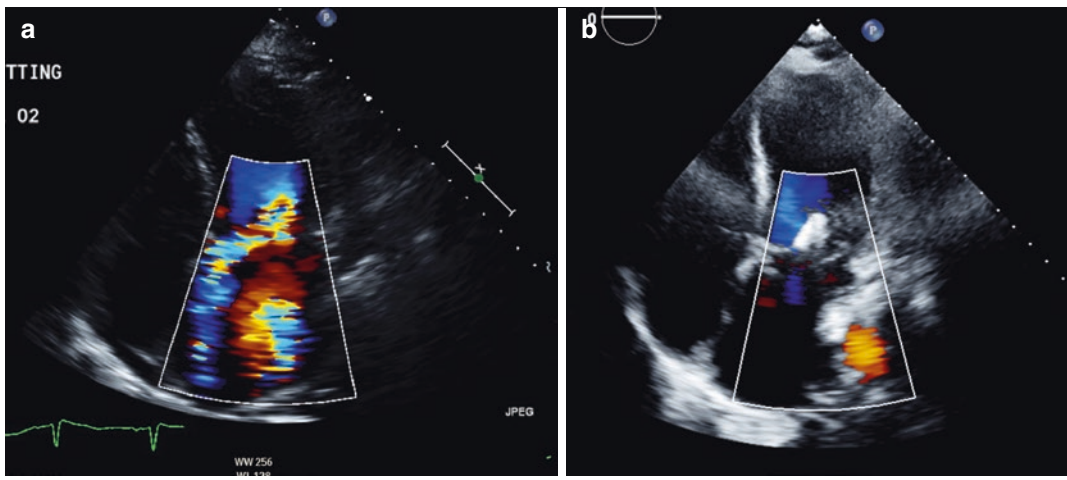

Fig. 38.2 (**a**) Color Doppler of MR pre-procedure; (**b**) Color Doppler of MR post-procedure

first. 1 XTW and 1XT clip were deployed to A2-P2 with improvement in MR from severe to mild (Fig. 38.2b). Left atrial V waves decreased from 40 mmHg to 17 mmHg and mean LA pressure decreased from 22 mmHg to 13 mmHg. She was discharged 3 days post procedure and seen at 30 day follow up with NYHA class 1 symptoms and mild MR on TTE.

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Endomyocardial Biopsy

39

Johny Kuttab and Carey Kimmelstiel

Introduction

Endomyocardial biopsy is an invasive procedure performed by interventional cardiologists. The procedure is widely used to screen and survey transplanted hearts for signs of cellular or humoral rejection allowing for titration of immunosuppressive therapy. Although this remains the strongest indication for the procedure [1–3], its clinical utility could be expanded to the diagnosis of other myocardial processes.

Indications

In general, the use of EMB is recommended in clinical scenarios in which the diagnostic yield of the procedure outweighs the procedural risk.

The following are indications for EMB [3]:

1. Surveillance for cardiac allograft rejection remains the most important indication for EMB.
2. Fulminant heart failure with hemodynamic compromise. The prototype for this group of patients is lymphocytic myocardidites, eosinophilic myocarditis or giant cell myocarditis.
3. New-onset heart failure associated with high degree atrioventricular (AV) block or ventricular arrhythmias. These clinical manifestations could be suggestive of giant cell myocarditis in which case tissue diagnosis is important for treatment and prognosis.
4. Chronic heart failure with high degree AV block or ventricular arrhythmias which could be suggestive of cardiac sarcoidosis.
5. Unexplained restrictive cardiomyopathy. Cardiac amyloidosis and hemochromatosis are diagnoses that fall within this group of infiltrative cardiomyopathies.
6. Hypereosinophilic syndrome and endomyocardial firboelastosis.
7. The workup of cardiac tumors.
8. The monitoring of anthracycline cardiotoxicity.
9. Unexplained cardiomyopathy in children.
10. The diagnosis of arrhythmogenic right ventricular cardiomyopathy when other noninvasive or invasive modalities are inconclusive.

Contraindications

There are no absolute contraindications for EBM. Relative contraindications include [3]:

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1. Coagulopathy.
2. Hemodynamic compromise or active heart failure precluding patient positioning and sedation.
3. Pericardial effusion or tamponade.

Equipment

1. Central venous access kit and sheath: Sheath size depends on the type of bioptome used.
2. Bioptome: There are various types of bioptomes. In general, two types of bioptomes—those with a floppy shaft which requires the use of a long sheath for delivery and the more commonly used stiff shaft which is manipulated into the region being biopsied (usually the right ventricle) after being introduced, via a short sheath, located within a central vein.
3. Ultrasound (echocardiography) machine: Most EMBs are performed using fluoroscopic imaging for bioptome positioning. Occasionally, when a specific region of the heart requires biopsy, echocardiography may be necessary to guide the bioptome to that area of the heart. In addition, echocardiography is frequently used to guide EMB in those instances where the risk of right ventricular perforation is elevated. Examples of this clinical scenario include patients with fulminant myocarditis eg. giant cell myocarditis where the combination of the thin-walled right ventricle and a closed pericardium lead to a heightened risk of myocardial perforation and subsequent cardiac tamponade. In such cases, echocardiography is frequently used to ensure that the bioptome is pointed toward the interventricular septum as opposed to the right ventricular free wall (Fig. 39.1).

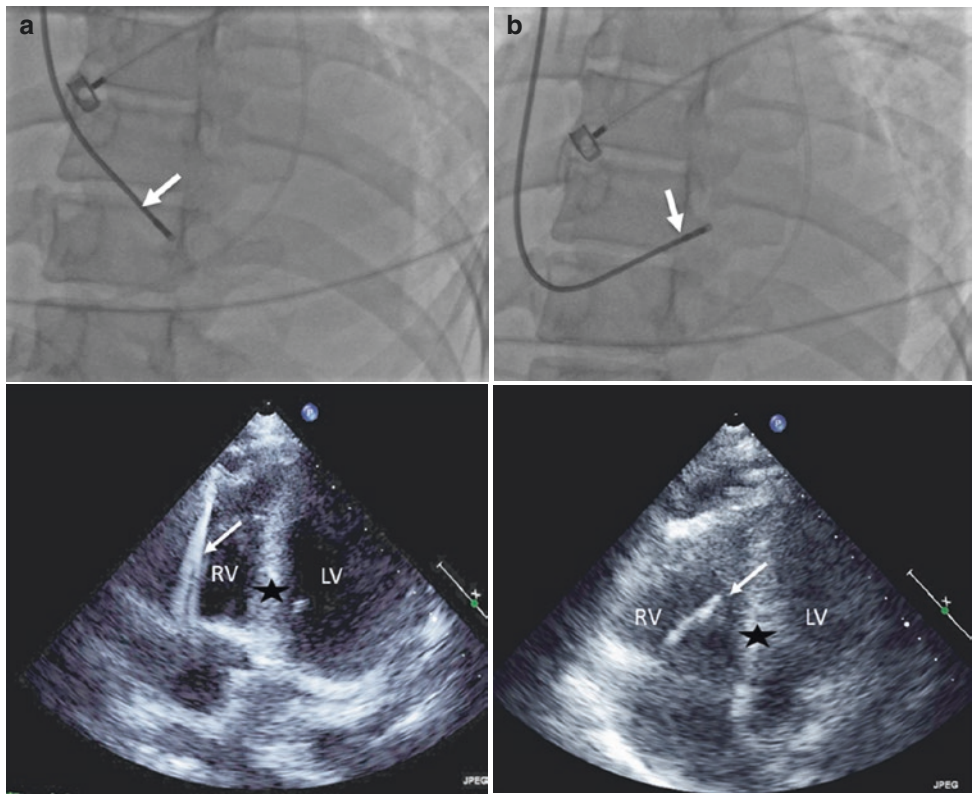


Fig. 39.1 Panel (**a**) Fluoroscopic view (*top*) of bioptome (*arrow*) in an incorrect position. Echocardiography (*bottom*) documents that the tip of the bioptome (*arrow*) is positioned against the right ventricular free wall, near the apex—a position putting the patient at risk for perforation if biopsied there. Panel (**b**) Fluoroscopy shows that the bioptome (*arrow*) has been repositioned to a more appropriate location, pointing superior and posterior (*top*). Echocardiography (*bottom*) documents that the bioptome (*arrow*) is pointing towards the interventricular septum (*star*)

Technique

There are three commonly utilized access sites for EMB. The most commonly used route is the right internal jugular vein. In this technique, the patient is prepped and draped in a sterile fashion. Ultrasonography, although not absolutely necessary, is commonly utilized for obtaining access to the vein. The venous sheath is then inserted over a wire. Once the sheath is flushed, the bioptome is inserted through the venous sheath under fluoroscopic guidance and advanced superiorly and posteriorly towards the interventricular septum. Once positioning is verified, the bioptome jaws are opened (Fig. 39.2), advanced towards the septum, and closed. The bioptome is pulled back gently at this time. Once the bioptome is free, it is pulled out of the venous sheath and the biopsied tissue is removed from the forceps and the procedure is repeated over again. Occasionally, echocardiographic guidance may be utilized to assist in bioptome positioning while performing EMB.

Other commonly used access sites include the subclavian/axillary vein and the femoral venous approach. When the femoral vein is used, a longer bioptome is used (105 cm) which is introduced through a long 7F venous sheath. Internal jugular and subclavian approaches utilize the standard 50 cm bioptome introduced through a standard 7F 11 cm long venous sheath.

In rare instances, the femoral arteries could be utilized for EMB of the left ventricle.

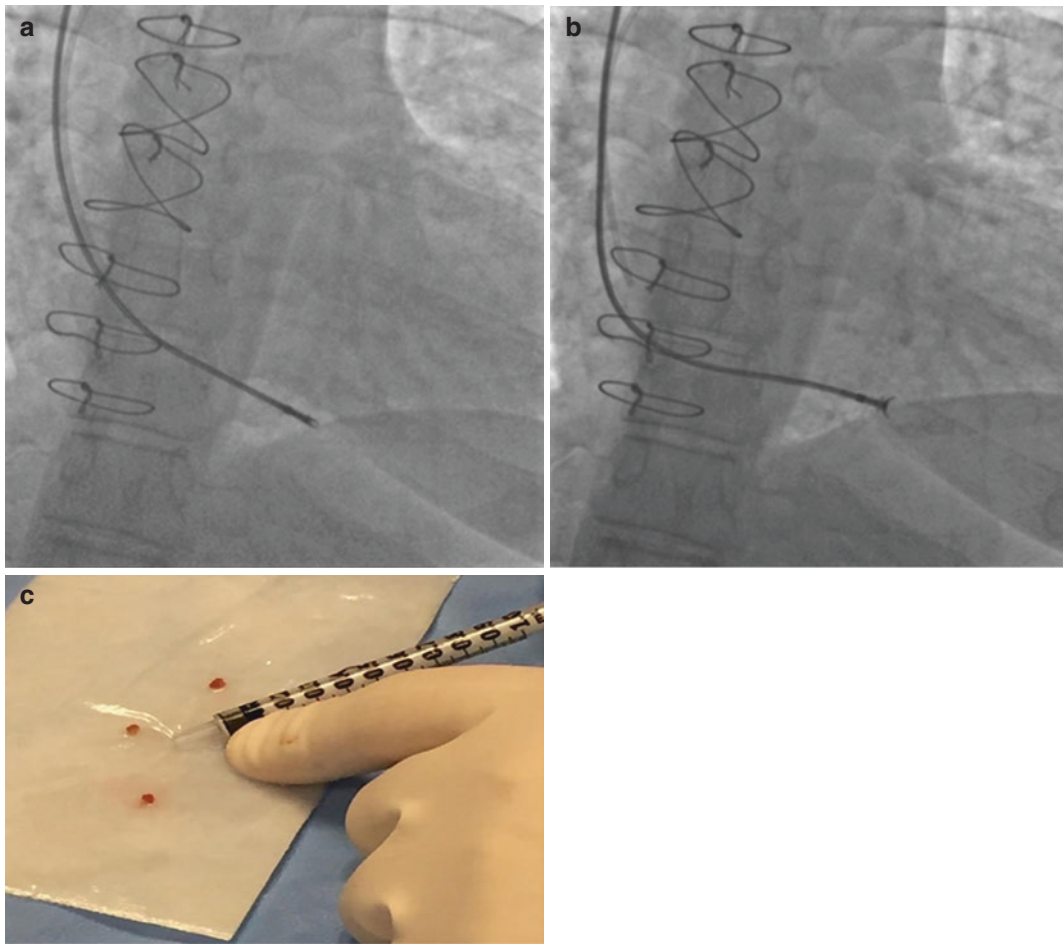


Fig. 39.2 (**a**) A bioptome, in the closed position, which has coursed from the right internal jugular vein through the right atrium, into the right ventricle. (**b**) The bioptome is in the open position as the interventricular septum is biopsied. (**c**) Three biopsies of myocardial tissue obtained during the procedure

Data Interpretation

Storage of the sample is dictated by the clinical question to be answered. A minimum of 5 right ventricular samples should be obtained if possible. Standard histological preparation using paraffin embedding, sectioning and staining can be used in the diagnosis of allograft rejection, myocarditis or amyloidosis. Polymerase chain reaction for the detection of viruses can be performed on paraffin-embedded tissue although the sensitivity is higher when performed on liquid nitrogen frozen tissue.

Complications

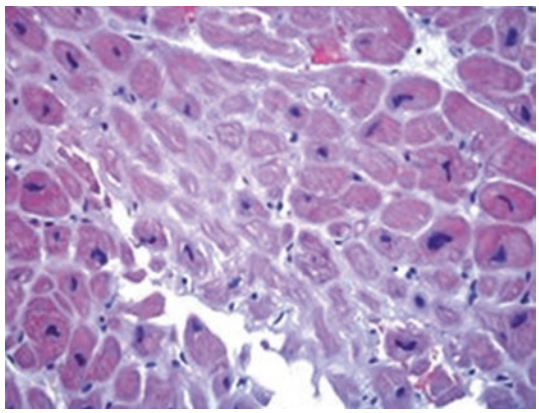
The rate of complications during an EMB depends on multiple factors. It is reported to be <6% in most case series. The following are possible complications [1–3]:

1. Access site hematoma.
2. Supraventricular and ventricular arrhythmias
3. Transient right bundle branch block.
4. Tricuspid regurgitation.
5. Air embolism
6. Occult pulmonary embolism
7. Vein thrombosis.
8. Pneumothorax.
9. Bleeding.
10. Right ventricular perforation.
11. Pericardial effusion with tamponade physiology.
12. Death.

Clinical Vignettes

Case 1

A 58 year old female patient, presented to the Advanced Heart Failure and Transplant clinic with progressively worsening dyspnea on exertion, lower extremity edema, orthopnea, paroxysmal nocturnal dyspnea and cough. She was initially treated at a community hospital for possible flu, however she experienced a progressive clinical decline. Her initial echocardiographic assessment revealed an ejection fraction of 30%, with left ventricular hypertrophy, bi-atrial enlargement, and Doppler parameters consistent with stage III diastolic dysfunction. On initial assessment, she was found to have elevated levels of serum free light chains. A cardiac MRI was pursued at that time and was significant for multifocal thickening of the myocardium with sparing of the anterior wall, multifocal delayed transmural hyperenhancement with relative sparing of the anterior wall, and diffusely decreased T1 signal, findings consistent with amyloidosis. Shortly after, she underwent a fat pad biopsy to look for evidence of systemic amyloid. Unfortunately this was non-diagnostic. An endomyocardial biopsy was ultimately done. Histological findings (Fig. 39.3) were diagnostic for cardiac amyloidosis.



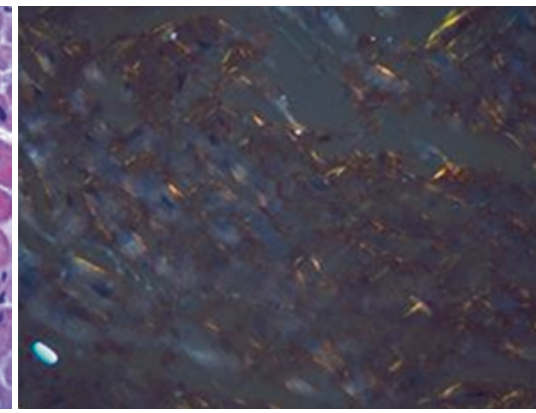


Fig. 39.3 *Left*—Endomyocardial biopsy from the patient in Case 1. Amyloid deposits appear as light-pink hyaline extracellular deposits displacing cardiac myocytes. *Right*—Congo red staining of the biopsy sample shows apple-green birefringence of the amyloid deposits

Case 2

A 57 year old man with a history of familial hypercholesterolemia, complicated by coronary artery disease requiring multiple coronary artery bypass surgery developed worsening heart failure secondary to ischemic cardiomyopathy despite optimal heart failure medications, necessitating an orthotopic heart transplantation. His immediate post-transplant course was uneventful. Six months following transplant, he presented with new onset cardiogenic shock, a newly depressed ejection fraction and refractory ventricular tachycardia. He underwent a right heart catheterization with an endomyocardial biopsy which was significant for high grade cellular rejection. Based on the biopsy results, he underwent treatment with thymoglobulin and high dose intravenous steroids with stabilization of his clinical status.

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Circulatory Support Devices

40

Navin K. Kapur and Michele Esposito

Introduction

The role of percutaneously-delivered mechanical circulatory support (pMCS) devices in the cardiac catheterization lab has grown exponentially over the past two decades. Current pMCS options include the intra-aortic balloon pump (IABP), Impella axial flow catheters, TandemHeart centrifugal pump, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO). The overall goals of pMCS systems are to: (1) increase vital organ perfusion, (2) augment coronary blood flow, or (3) reduce ventricular volume and filling pressures. Clinical scenarios where these devices are commonly used include: advanced heart failure, cardiogenic shock, mechanical complications after AMI, high risk coronary and non-coronary intervention, and high-risk electrophysiologic ablations. This chapter will outline various aspects of IABP and continuous flow support devices.

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Intra-aortic Balloon Counterpulsation

Optimal performance of IABP counterpulsation should improve myocardial oxygen supply and demand balance. By rapidly expanding a balloon positioned in the descending aorta in early diastole, an IABP can augment diastolic pressure and increase coronary perfusion pressure. Rapid deflation of the IABP at end-diastole can decrease left ventricular (LV) afterload by driving aortic volume forward and reducing aortic pressure during systole (Fig. 40.1). Expected effects on the hemodynamic profile of patients with cardiogenic shock include an increase in the diastolic pressure; a decrease in the systolic pressure; an overall maintenance or slight improvement in the mean arterial pressure; a reduction in the heart rate; an elevation in the cardiac output; and a decrease in the pulmonary capillary wedge pressure (Table 40.1) [1].

Indications

Hemodynamic Compromise

Indications for IABP placement include patients with acute myocardial infarction (MI) and cardiogenic shock secondary to continued ischemia or myocardial stunning. The IABP-Shock II randomized controlled trial showed no benefit with rou-

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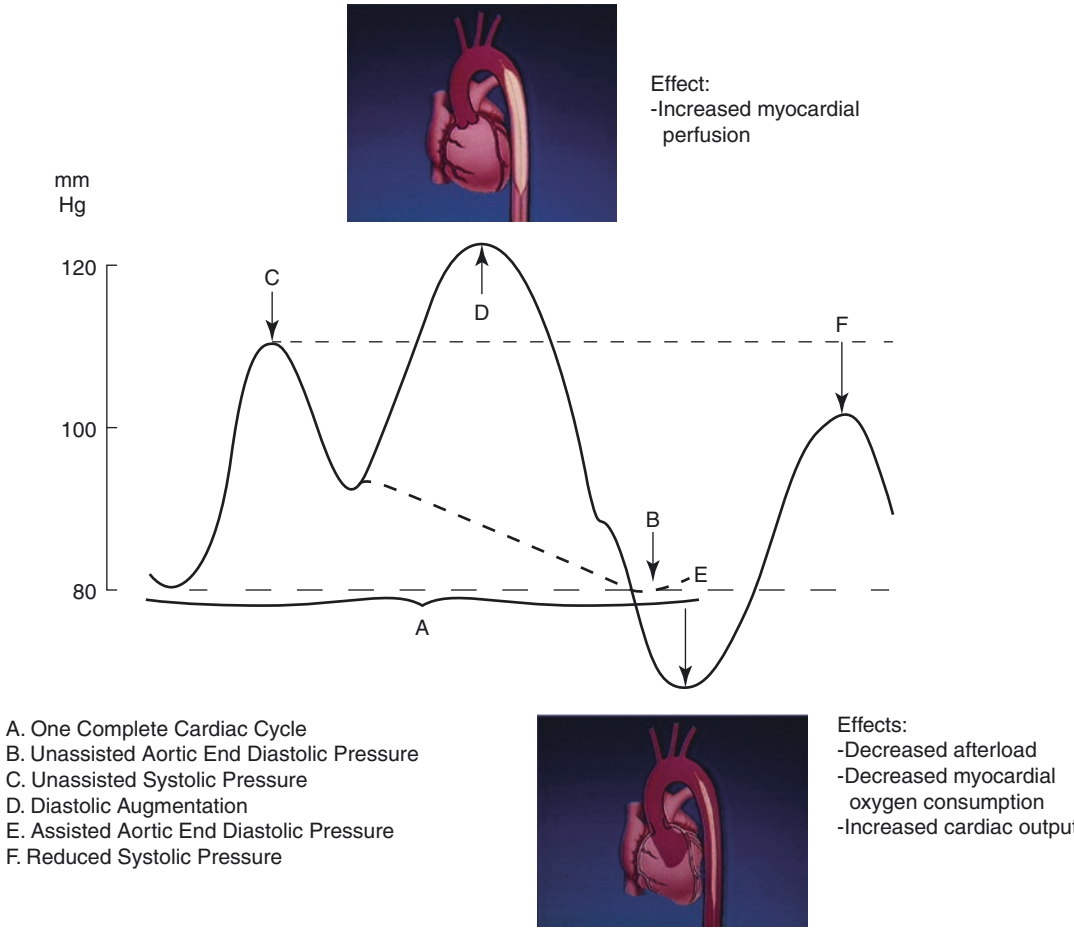

Fig. 40.1 The IABP may improve myocardial oxygen supply and demand balance by increasing myocardial perfusion during diastole and decreasing resistance to left ventricular ejection during systole, while increasing systemic mean arterial pressure. (with permission from Datascope)

Table 40.1 Hemodynamic effects of the IABP

Systolic BP	Diastolic BP	MAP	HR	CO	PCWP
↓	↑	No change or ↑	↓	↑	↓

tine IABP support during cardiogenic shock for acute myocardial infarction (REF). Without revascularization, survival rates in patients with cardiogenic shock supported with IABP and medical therapy are quite poor. The IABP provides temporary hemodynamic stabilization until definitive revascularization can be performed. The IABP might also be used to support patients with cardiogenic shock due to mechanical complications of MI—e.g. ventricular septal rupture—until corrective surgery can be performed. Additionally, it has been shown to be an effective temporary therapeutic option in patients with non-ischemic reversible causes of shock, such as myocarditis or drug toxicity. IABP support is often used in patients who are difficult to wean off bypass after cardiac surgery due to severe LV dysfunction or secondary to myocardial stunning from prolonged cardioplegia. Patients with refractory heart failure and those with end-stage cardiomyopathy awaiting advanced therapies—i.e., "bridge to transplantation" "or "bridge to decision"—might also benefit from IABP support. No randomized controlled studies have tested the efficacy of IABPs in heart failure [1, 2].

Absence of Hemodynamic Compromise

IABPs can be used to alleviate medically refractory unstable angina in patients awaiting definitive revascularization—e.g., a patient with severe triple vessel coronary artery disease awaiting bypass surgery. Prophylactic IABP placement is commonly employed in patients with severe left main coronary obstruction or severe aortic stenosis to avoid clinical deterioration while awaiting surgery. IABPs are also commonly placed to mitigate continued ischemia during complex/complicated percutaneous coronary intervention (PCI) or to support patients after failed PCI. The Intra-aortic Balloon-pump Coronary Interventional Study (BCIS-1) failed to show any reduce in major adverse cardiovascular or cerebral events with prophylactic IABP use in complex PCI (REF) [1].

Contraindications

Major contraindications to IABP placement include significant aortic regurgitation, abdominal or thoracic aortic aneurysm, aortic dissection, severe peripheral vascular disease (aorto-iliac or femoral artery disease), severe bleeding diathesis, and uncontrolled septicemia.

Equipment

The intra-aortic balloon pump consists of a polyurethane balloon, which surrounds a double lumen catheter that is mounted onto a flexible shaft and connected to a console. It is inflated by a helium gas control system, which is housed within the console.

Technique

Insertion

After the leg is shaved and prepped with antiseptic solution, the femoral artery is accessed and J-tipped guide wire is passed through a needle to the aortic arch. After an introducer sheath is inserted, the balloon is advanced over the guide wire with the radiopaque tip positioned in the descending aorta just distal to the origin of the left subclavian artery (generally at the level of the carina). When available, fluoroscopic guidance should always be employed for IABP placement. If fluoroscopic guidance is not available, the distance from the angle of Louis (or between the second and third intercostal spaces) to the umbilicus and then obliquely over to the femoral insertion site can be measured to determine the approximate distance the balloon should be advanced. After positioning of the IABP is confirmed, the helium gas line extending from the console is connected. Balloon counterpulsation is then initiated at 1:2 setting (balloon inflation with every other beat) and fluoroscopy again is used to confirm uniform expansion. Sheathless insertion is sometimes performed in patients with peripheral vascular disease in an attempt to reduce the incidence of lower limb ischemia. However, sheathless insertion does not allow for repositioning once the balloon is placed, and is associated with higher rates of infection [1].

Inflation and deflation of the balloon are usually timed and triggered by the surface electrocardiogram. Triggering can also be initiated by the arterial pressure waveform or set to a fixed asynchronous cycle for patients with significant arrhythmias—e.g., ventricular fibrillation—or patients on bypass. Pacing spikes should be used to trigger the balloon in patients with 100% paced rhythms. Adjustments to timing are performed with initial pump triggering set at 1:2, thereby allowing comparison of the arterial tracing with and without counterpulsation (Fig. 40.2). Timing of inflation is delayed after the R wave on the surface ECG such as to begin on the downslope of the systolic pressure waveform, just before the dicrotic notch (when the aortic valve closes). Deflation should be timed just before the opening of the aortic valve to allow for the maximum reduction in aortic systolic pressure compared with an unassisted beat. After timing of inflation and deflation is adjusted, the balloon counterpulsation is then set at 1:1 (Fig. 40.3) [1].

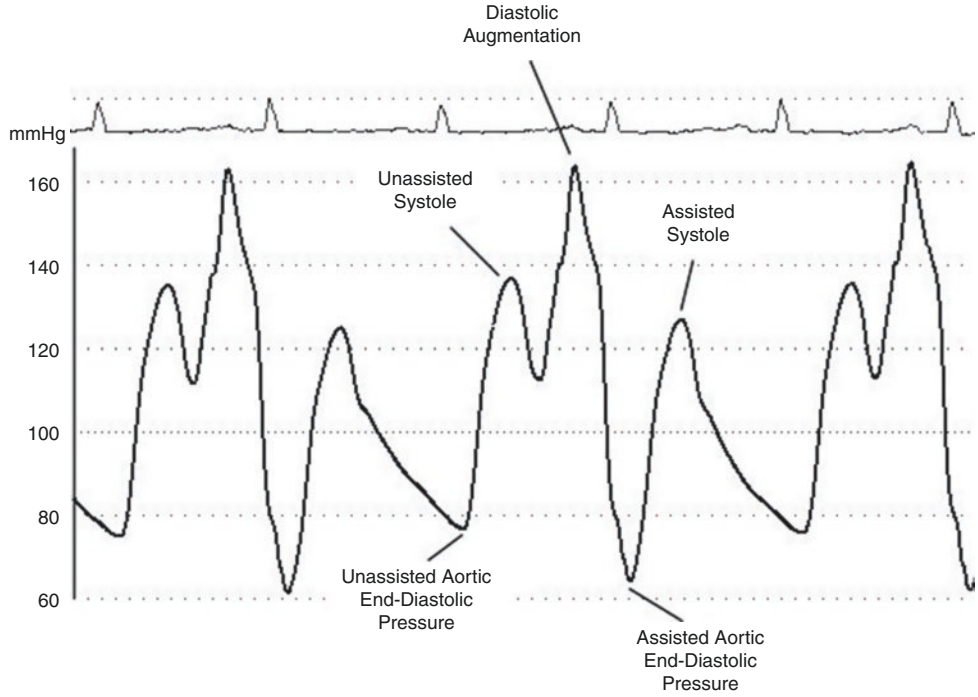

Fig. 40.2 Adjustment to timing is performed with the IABP set at 1:2 to allow comparison of the arterial tracing with and without counterpulsion. Timing of inflation is delayed after the R wave on the surface ECG such as to begin, just before the dicrotic notch on the aortic pressure waveform. Deflation is timed to allow for the maximum reduction in aortic systolic pressure compared with an unassisted beat

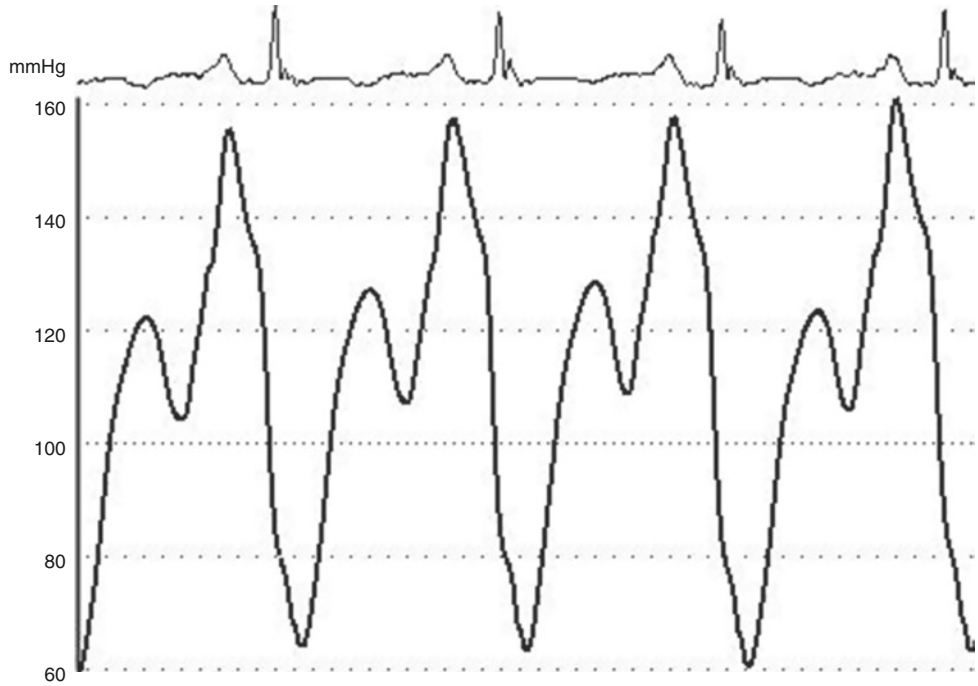

Fig. 40.3 IABP set at 1:1

More recently, several reports have described IABP deployment via the axillary artery using percutaneous or via a surgically grafted conduit (REF). No studies have compared outcomes between femoral versus axillary IABP deployment.

Management of the Patient During Counterpulsation

When the patient is returned to the appropriate unit, a chest x-ray should be immediately obtained to again verify balloon position and check for any possible migration during transfer. To prevent thrombus formation, the patient is heparinized, the activated partial thromboplastin time being carefully maintained at 50–70 s. The patient must be kept at bedrest and the head of the bed should not be elevated more than 30°. Daily chest x-ray should be obtained to evaluate balloon position and migration. During counterpulsation, evaluation of circulation should take place on every nursing shift (or at least Q8h). Daily monitoring for evidence of sepsis, bleeding, hemolysis, and embolus should also be performed [1].

Weaning from Counterpulsation

Before an IABP is removed, a patient is progressively weaned from its support. Under close hemodynamic supervision the counterpulsation mode is decreased step-wise from 1:1 to 1:2, and then to 1:3. The patient should be monitored for 2–3 h at each downgraded level to ensure tolerance to reduced support. When safety of withdrawal is established, the balloon is set back to 1:1 and the heparin drip is discontinued for at least 4 h. The activated clotting time is checked until it falls below 160 s. The balloon and sheath are then removed as a single unit to prevent any tearing of the balloon membrane. Manual pressure is then applied proximal to the insertion site for 30–60 min until hemostasis is achieved. After removal the patient is kept at strict bed rest avoiding hip flexion on the affected side for the next 6–12 h [1].

Complications

Vascular complications remain the major risk associated with IABP placement. Among the significant vascular complications, the most common are limb ischemia, vascular laceration, and major hemorrhage. Other vascular complications include arterial dissection, pseudo-aneurysm formation, cholesterol embolization, and cerebrovascular accident (CVA). Risk of CVA increases if the IABP has been placed too high or has migrated proximally. Vigorous flushing of the central lumen should also be avoided, as it can result in dislodgement of thrombus. Overall, major complications (severe bleeding, major limb ischemia, balloon leak, or in-hospital mortality related to IABP) associated with IABP placement are relatively rare with an incidence of 2.6% in the Benchmark Counterpulsation Outcomes Registry [1, 3].

Non-vascular complications include groin infection, sepsis (especially when counterpulsation is carried out for longer than a week), hemolysis, thrombocytopenia, and balloon rupture. Although rare, balloon rupture should be considered when blood is detected in the gas drive-line or if augmentation failure develops.

Continuous Flow Support Devices

The pMCS) systems have grown from counterpulsation balloon systems to rotary flow pump systems that include extracorporeal centrifugal pumps or intracorporeal catheter-mounted axial-flow pumps. Both surgical LVADs and pMCS rotary flow systems are subject to changes in preload and afterload. Inadequate LV preload due to volume depletion, poor right ventricular function, hypotension, pulmonary obstruction, or valvular disease will reduce flow generation. Similarly, increased afterload due to hypertension, elevated systemic vascular resistance or valvular disease will reduce device flow. For these reasons, careful hemodynamic interrogation before, during, and after initiation of pMCS is essential for optimal device function. Percutaneous circulatory support devices can be

categorized by the type of pump used as either pulsatile or continuous blood flow devices. Each device impacts native ventricular function in a unique way and requires adequate preload for optimal use.

Both the Impella (Abiomed Inc) and TandemHeart (CardiacAssist Inc) devices are rotodynamic pumps that generate continuous, minimally pulsatile blood flow (Fig. 40.4) [4, 5]. The Impella devices are catheter-mounted axial-flow pumps that are placed into the left ventricle in retrograde fashion across the aortic valve. The pump transfers kinetic energy from a circulating impeller to the blood stream, which results in continuous blood flow from the left ventricle to ascending aorta. The Impella 2.5 LP and CP devices can be deployed without the need for surgery, while the Impella 5.0 and 5.5 devices require surgical vascular access [4–6]. At present, there is growing use of the Impella CP device in the United States. In contrast, the TandemHeart device is an extra-corporeal centrifugal flow pump that reduces left ventricular *preload* by transferring oxygenated blood from the left atrium to the descending aorta via two cannulas: a trans-septal inflow cannula in the left atrium and an arterial outflow cannula in the femoral artery. The net effect of these devices is to reduce native left ventricular volume and pressure, while increasing mean arterial pressure without greatly influencing ventricular afterload [7]. An advantage of the Impella 2.5 and CP devices is ease of insertion via a single arterial access, while advantages of the TandemHeart device are the magnitude of support provided without the need for surgical vascular access and the ability to splice an oxygenator into the circuit. Several studies have evaluated the clinical utility of these devices, but large randomized controlled trials are lacking [8]

Other centrifugal pumps include the Centrimag, Rotaflow, and Biomedicus pumps are used to provide flow for veno-arterial extra-corporeal membrane oxygenation (VA-ECMO). VA-ECMO is more commonly used to enhance systemic oxygenation during

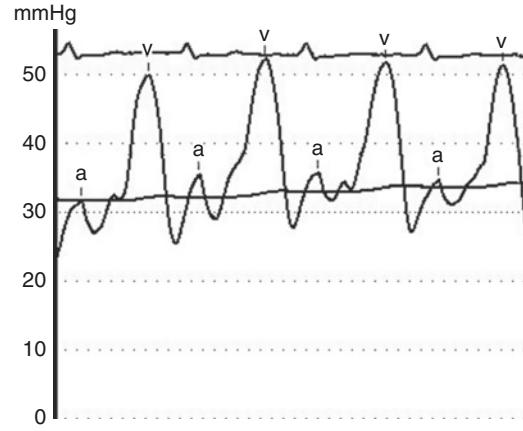

Fig. 40.4 Percutaneous non-durable mechanical circulatory support systems. (**a**) The Impella axial flow catheters are deployed in retrograde fashion across the aortic valve and directly displace blood from the LV into the proximal aorta. Immediate effects of the Impella activation include reduced left ventricular pressures and volume as shown by pressure-volume (PV) loops. (**b**) The TandemHeart centrifugal flow pump displaces oxygenated blood from the left atrium (*LA*) to a femoral artery, thereby reducing left ventricular preload. The net effect of immediate TandemHeart activation is a reduction in total LV volume and native left ventricular stroke volume (width of the PV loop). (**c**) Venoarterial extracorporeal membrane oxygenation (VA-ECMO) displaces venous blood from the right atrium (*RA*) through an extracorporeal centrifugal pump and oxygenator, then returns oxygenated blood into the femora artery. The immediate effect of VA-ECMO without a left ventricular decompression mechanism is an increase in left ventricular pressure and a reduction in left ventricular stroke volume

cardio-respiratory collapse or biventricular failure. Over the past decade, VA-ECMO use has grown by over 11-fold in the United States and Europe [9, 10] The major effect of VA-ECMO is to displace blood volume from the venous to the arterial circulation (Fig. 40.4) [7, 11]. As a result, a reduction in both right and left ventricular volumes can be observed with a concomitant increase in mean arterial pressure and both LV systolic and diastolic pressures. This increase in LV afterload or wall stress occurs in contrast to the Impella or TandemHeart devices since there is no direct venting of the left ventricle with VA-ECMO (Fig. 40.5). For this reason, operators have

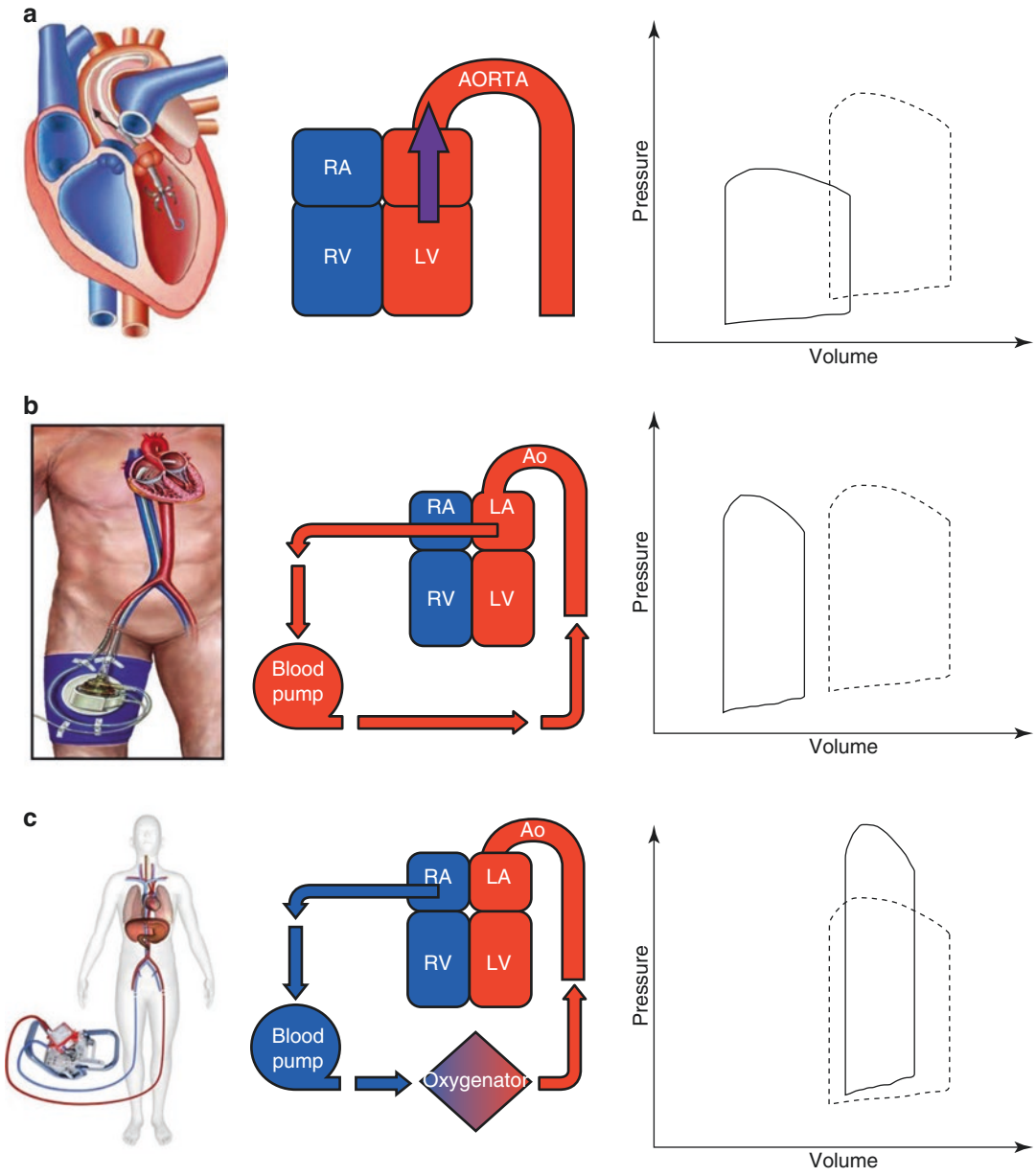

Fig. 40.5 Hemodynamic profile of veno-arterial extracorporeal membrane oxygenation (*VA-ECMO*) with and without left ventricular venting. (**a**) A double-lumen pigtail catheter during activation of VA-ECMO shows increased LV systolic pressure and reduced aortic pulse pressure. (**b**) Initiation of an IABP with VA-ECMO shows reduced LV systolic pressure (venting) and elevated aortic diastolic pressure. (**c**) Venting of the LV with either an IABP, Impella device or trans-septal left atrial cannula during VA-ECMO support, reduces LV end-systolic pressure and end-diastolic volume

combined VA-ECMO with either an IABP, Impella device, or a trans-septal left atrial cannula to negate the effect of increased left ventricular afterload during VA-ECMO support [11, 12]. Advantages of VA-ECMO include the relative ease of insertion, the ability to support systemic oxygenation or biventricular failure, and the ability to provide cardiopulmonary support during ventricular tachycardia or fibrillation.

Indications

Clinical scenarios where these devices are commonly used include: cardiogenic shock, mechanical complications after AMI, high-risk coronary and non-coronary intervention, and for high-risk electrophysiologic ablations.

Contraindications

Major contraindications to Impella placement include the presence of a left ventricular thrombus, severe aortic valve insufficiency, and severe peripheral vascular disease. Major contraindications to TandemHeart placement include bleeding diathesis, severe peripheral vascular disease. Major contraindications for VA-ECMO include severe peripheral vascular disease, coagulopathy, and severe aortic valve insufficiency.

Equipment

The TandemHeart consists of a 21-Fr inlet cannula placed into the femoral vein and through the right atrium into the left atrium through a trans-septal puncture, an external impeller, and a 15-Fr outflow cannula placed into the femoral artery. The Impella consists of a catheter-mounted microaxial flow pump and a pigtail catheter that is inserted into the left ventricle, with the inlet and outlet areas on either side of the aortic valve. VA-ECMO employs a venous inflow cannula and an arterial outflow cannula. Both are attached to an extracorporeal centrifugal pump and oxygenator.

Technique

To deploy the Impella device, femoral artery access is first obtained and a guidewire is advanced into the apex of the left ventricle. The placement guidewire is then inserted into the lumen at the tip of the pigtail, until the catheter is successfully backloaded onto the guidewire. The catheter is then advanced under fluoroscopic guidance over the guidewire across the aortic valve using a fixed wire technique. The inlet area of the catheter should sit 3.5 cm below the level of the aortic valve. The guide is then removed, and proper placement is confirmed with fluoroscopy as well as using pressure waveforms from the Impella console. The TandemHeart requires a trans-septal puncture to deliver a left atrial inflow cannula and a separate arterial puncture for an outflow cannula. In contrast, percutaneous VA-ECMO requires a single venous puncture for delivery of a venous inflow cannula into the superior vena cava and an arterial puncture for an outflow cannula.

Complications

Potential complications of all pMCS) devices include clinically significant hemolysis, device malfunction, major bleeding, aortic insufficiency, perforation, hematoma, arrhythmias, cerebrovascular accidents, cardiac tamponade, renal failure, or vascular injury. Appropriate placement of the Impella device is crucial for proper functioning and to avoid the risk of device outflow obstruction. Echocardiography as well as the utilization of aortic and ventricular pressure waveforms from the device console should be used to guide placement. Similarly, the TandemHeart left atrial inflow cannula can dis-

place into the right atrium and requires close monitoring with echocardiography. The major complication associated with VA-ECMO is left ventricular pressure overload, which requires close monitoring with a pulmonary artery catheter.

Clinical Vignettes

Case 1

A 65 year old woman with history of heavy tobacco use, HTN, and hypercholesterolemia presents to a community hospital emergency department (ED) with history of 3 days of intermittent chest pain and worsening shortness of breath. On arrival to the ED she is noted to be in respiratory distress secondary to pulmonary edema and is urgently intubated. ECG is consistent with inferior ST elevation myocardial infarction). Due to hypotension dopamine is initiated and she is taken emergently to the catheterization laboratory (cath lab). Coronary angiography reveals three-vessel coronary artery disease with acute right coronary artery occlusion. Right heart catheterization is performed and reveals right atrial (RA) pressure 12 mmHg, pulmonary artery (PA) pressure 64/29 (43) mmHg, and pulmonary capillary wedge pressure (PCWP) 33 mmHg with large V waves noted on the PCWP tracing consistent with heart failure and severe mitral regurgitation. Transesophageal echocardiogram performed in the catheterization lab reveals papillary muscle rupture with severe, new onset, mitral regurgitation—a mechanical complication of acute myocardial infarction that can result in heart failure and cardiogenic shock. An intraaortic balloon pump is placed to stabilize the patient for transfer to a tertiary care center for coronary bypass surgery and mitral valve replacement.

Case 2

A 77 year old male with history of diabetes and hypertension) is admitted with unstable angina. Cardiac catheterization reveals triple vessel coronary artery disease with 80% left main coronary artery stenosis, 90% mid left anterior descending stenosis, 85% proximal left circumflex stenosis, and 70% mid right coronary stenosis. The patient is evaluated by cardiothoracic surgery and planned for CABG surgery in the morning. Chest pain free and hemodynamically stable, he is transferred to the coronary care unit for monitoring until surgery. Despite medical therapy with beta blockers, nitrates, and heparin the patient develops recurrent chest pain with ischemic ECG changes. He is returned to the cath lab for IABP placement.

Case 3

A 44 year old man with a history of hypercholesterolemia presents after a witnessed cardiac arrest in the field, where an EKG on site showed an anterior ST elevation myocardial infarction. He was resuscitated, and then taken to a local hospital where he underwent coronary angiography, which showed severe triple vessel disease. He underwent PCI to the left anterior descending and left circumflex arteries. His LV end-diastolic pressure was measured at 40 mmHg. An IABP was implanted, and he was transferred to our institution for further management of cardiogenic shock. Upon arrival, he became hypotensive and was taken back to the cardiac cath lab. There, stenting of his right coronary artery was performed, followed by implantation of an Impella CP device. His LV ejection fraction was measured) at 15%. Later that night, he sustained another cardiac arrest and was upgraded to VA-ECMO support, while using the previously implanted Impella device as an LV vent (Fig. 40.6). Over the course of the next two weeks, his hemodynamics gradually improved. His LV ejection fraction recovered to 65%, and he was weaned from all mechanical support. He was discharged home in stable condition.

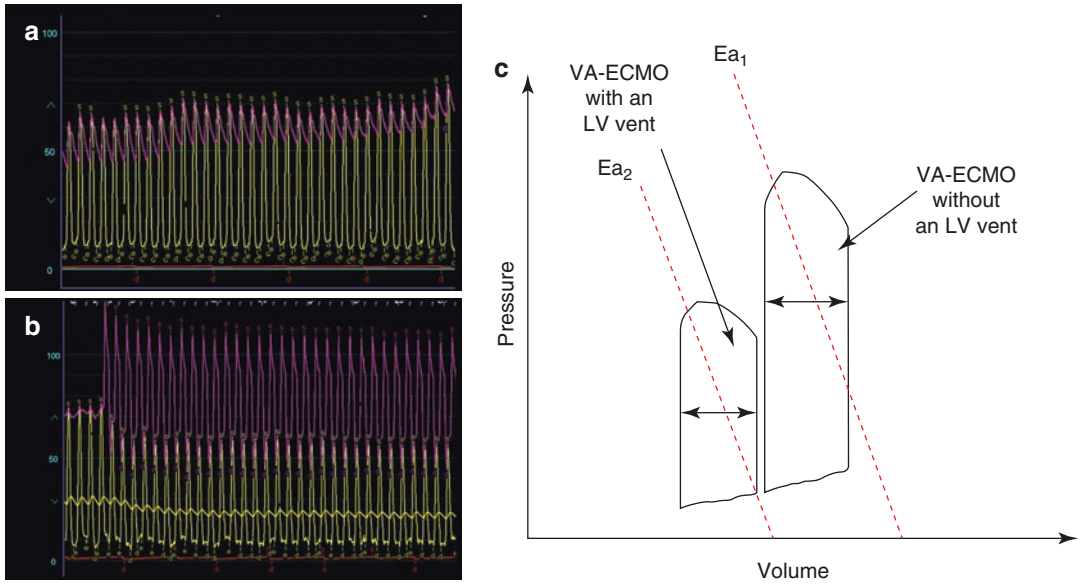

Fig. 40.6 (**a**) Pressure tracing of both LV (yellow) and Ao (pink) waveforms in a patient supported on VA-ECMO. (**b**) The pressure tracing demonstrates LV and Ao uncoupling after the activation of the Impella CP device while on VA-ECMO. (**c**) Pressure-volume loops demonstrate both reduced pressure and volume in the setting of VA-ECMO in the presence of the Impella CP which acts as an LV vent

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