Case-Based Device Therapy for Heart Failure

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Eric Adler
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Editors
Ulrika Birgersdotter-Green
Division of Cardiovascular Medicine
University of California, San Diego
La Jolla, CA, USA

Eric Adler
Division of Cardiovascular Medicine
University of California, San Diego
La Jolla, CA, USA

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Case Vignette

A 50 year-old female with past medical history of breast cancer and chemotherapy, paroxysmal atrial fibrillation and diabetes mellitus, presents with dyspnea on exertion, orthopnea and paroxysmal nocturnal dyspnea. On exam, she is hypotensive (83/61 mmHg), tachycardic (100 beats per min), and tachypneic (20 breaths per min). She has a regular rhythm, systolic ejection murmur at the left apex 3/6, jugular venous distention up to the mandible, sign of hepatojugular reflex, leg edema 2+, and cool distal peripheries. Her blood work is significant for a BUN 33 mmol/dL, creatinine 1.64 mg/dL, total bilirubin 2.42 mg/dL, lactate 2.4 mmol/L. Her NT pro-BNP is 6310 pg/mL, HS-troponin 18 ng/L. Her echocardiogram shows an LV ejection fraction of 12%, end diastolic dimension 6.7 cm, reduced RV function, pulmonary artery systolic pressure of 47 mmHg, moderate-severe mitral regurgitation and severe tricuspid regurgitation. A pulmonary artery catheter was placed showing the following hemodynamics:

Variable	Value	Variable	Value
RA, mmHg	11	SVR, dyn/cm/sec^5	1600
PA, mmHg	55/33/39	PVR, woods units	237
PCWP, mmHg	21	RA:PCWP ratio	0.52
PA Saturation, %	47	PAPi ratio	2.0

J. Silva Enciso (✉)
Cardiology Division, Sulpizio Cardiovascular Center, University of California, San Diego, USA
e-mail: jsilvaenciso@health.ucsd.edu

Division of Cardiovascular Medicine, Advanced Heart Failure, Mechanical Circulatory Support and Heart Transplant Program, UC San Diego Health, 9300 Campus Point Drive, MC 7411, La Jolla, CA 92037, USA

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Variable	Value	Variable	Value
AO Saturation, %	99	CPO, watts	0.41
Cardiac Output, L/min	2.3	BP, mmHg	106/67/80
Cardiac Index, L/min/m^2	1.8	HR, bpm	132

The patient is started on Norepinephrine that is promptly escalated to 11 μg/kg/min, Vasopressin 0.04 UI/hr, Dobutamine 3 μg/kg/min and Milrinone 0.25 μg/kg/min.

Definition

Cardiogenic Shock (CS) complicates 5–10% of acute myocardial infarction (AMI) cases with an in-hospital mortality of 41–50% which has been unchanged over 2 decades. Among survivors of AMI, up to 19% of patients will experience a readmission after discharge, with 30% of them developing recurrent heart failure symptoms. Furthermore, 30% of all CS cases present as acute decompensation of chronic systolic heart failure [1]. A higher incidence of CS is seen in elder patients, female gender, patients with diabetes or a prior history of LV dysfunction. Classically, cardiogenic shock has been defined as tissue hypoperfusion and hypoxia due to impaired cardiac function and low cardiac output. It is manifested by abnormal clinical and biomarkers of end organ dysfunction that require either pharmacological or mechanical circulatory support interventions [1]. However, the parameters that define CS differ due to the complexity of its presentation.

Clinical trials defining CS have resolved to count on 3 indicators of cardiac performance: (1) a systolic blood pressure <90 mmHg and use of drugs or devices to maintain BP above 90 mmHg; (2) Cardiac Index of ≤2.2 ml/min/m^2 and a capillary wedge pressure ≥15 mmHg; (3) altered mental status, decreased urine output ≤30 ml/h and lactate ≥2 mmol/L. Clinical features of CS have varied across clinical trials leading to lack of uniformity in defining CS patients which has impact clinical trial outcomes. Recently, The Society of Cardiovascular Angiography and Interventions (SCAI) has developed a classification system as a referendum to differentiate patient subsets and risk stratify their morbidity and mortality risk. This schema allows rapid interpretation and categorization of patients to strategize which therapeutics will benefit each individual (Table 1) [2].

Causes

1. **Acute myocardial infarction (AMI)**. Accounts for 30–80% of the causes of CS, with ST-segment elevation MI being the most common presentation compared to Non-ST elevation MI. ST-segment elevation MI is the leading cause

Table 1 SCAI Cardiogenic shock classification

SCAI shock stage	Physical exam	Biomarkers	Hemodynamics
A	• Normal JVP, clear lung sounds, • Strong distal pulses • Normal mentation	• Normal renal function and lactate	• SBP > 100 mmHg • CI > 2.5 • CVP < 10 • PASAT ≥ 65%
B	• Elevated JVP, rales • Strong distal pulses • Normal mentation	• Minimal renal function impairment • Elevated BNP • Normal Lactate	• SBP < 100 OR MAP < 60 OR > 30 mmHg drop • Pulse ≥ 100 • CI ≥ 2.2 • PASAT ≥ 65%
C	• Ashen, mottled, dusky skin • Volume overload, extensive rales, Killip 3–4, Bipap or mechanical ventilation • Acute AMS	• Lactate > 2 • Creatnine doubling or > 50% drop in GFR, UO < 30 mL/hr • Increased BNP • Increased LFT	• Drugs/Device to maintain BP above Stage B • CI ≤ 2.2, PCWP ≥ 15, RA/WP ≥ 0.8, PAPi < 1.85, CPO ≤ 0.6
D	• Any stage C	• Stage C + Deteriorating	• Any stage C AND requiring multiple pressors, OR addition of MCS to maintain perfusion
E	• Near Pulselessness, cardiac collapse, defibrillator use • Mechanical Ventilation	• Lactate > 5 • pH < 7.2	• No SBP w/o resuscitation • PEA or refractory VT/VF • Hypotension despite maximal support

of death in patients with AMI with an in-hospital mortality close to 36–50% [3]. The clinical presentation of patients with CS are predominantly left ventricular failure (78.5%), severe mitral regurgitation (6.9%), ventricular septal rupture (3.9%), right ventricular failure (2.8%) and cardiac tamponade (1.4%) [4]. Among those who survive to discharge 18.6% have a 30-day risk of readmission (median time of 10 days) with the most common cause being heart failure (39%) followed by new myocardial infarction (15%) and arrhythmias (11%) [5]. Compared to other causes of CS, patients with CS-AMI present with a higher number of cardiovascular co-morbidities including hypertension, diabetes mellitus and smoking. Similarly, compared to other causes of CS, a significant number of CS-AMI patients require mechanical circulatory support, mechanical ventilation and renal replacement therapy at the time of their presentation due to the clinical severity of CS with substantial metabolic disturbances (i.e. higher lactate acidemia, elevated liver function test and renal dysfunction) [6].

2. **Acute Heart Failure (AHF)**. Accounts for 46% of causes of CS based on contemporary data from critical care registries. It is associated with a 31% in-hospital mortality. Patients within this group present with high filling pressures,

low oxygen delivery, higher burden of atrial arrhythmias or ventricular arrhythmias, pulmonary hypertension, chronic kidney disease and severe valvular disease requiring often invasive hemodynamic monitoring, higher use of vasoactive medications and mechanical circulatory support for stabilization (26% of Non-Ischemic Cardiomyopathy compared to 61% of AMI patients) [6]. MAY NEED TO EXPAND THE AHF CAUSES SECTION TO TYPES OF AHF ICM VERSUS NICM

3. **Non-AMI causes**. Other causes of CS are less common and can occur concomitant to the most common causes of CS including valvular heart disease (valvular stenosis or acute insufficiency,) (11%), myocarditis (2%), stress induced cardiomyopathy (2%), post-partum cardiomyopathy, hypertrophic cardiomyopathy and aortic dissection, all which can rapidly deteriorate through direct or indirect impact on the myocardial function (Table 2).

Pathophysiology

Cardiogenic shock precipitates when there is profound depression of the myocardial function resulting in deleterious consequences to end organ perfusion triggering a downward spiral of low cardiac output, reduced blood pressure, ischemia

Table 2 Causes of cardiogenic shock

Acute Myocardial infarction	Heart failure	Valvular-native or prosthetic	Electrical
Mechanical complication • Ventricular septal rupture • Papillary Muscle Rupture • Free Wall Rupture • Cardiac tamponade	• Ischemic Cardiomypathy • Dilated Cardiomyopathy	Stenosis	Atrial arrhythmias
Mitral regurgitation	Myocarditis	Acute regurgitation	Ventricular Tachycardia
Right Ventricular Infarction	Stress induced cardiomyopathy	Valvular Obstruction	Bradycardia
Left Ventricular Dysfunction	Pregnancy associated • Peripartum cardiomyopathy • Coronary Artery Dissection	Leaflet failure	
	Post-Cardiotomy shock	Valve dehiscence	
	Outflow obstruction • Hypertrophic cardiomyopathy		

with the latter enhancing the vicious cycle of perpetual shock. Mechanisms to counterbalance this negative cycle include vasoconstriction and fluid retention with the goal to maintain tissue perfusion and cardiac output. However, in the presence of cardiogenic shock, a cascade of inflammatory markers is released due to poor perfusion. Reactive oxygen species, nitric oxide synthase, peroxy-nitrite and interleukins among other markers will promote vasodilation, reduce catecholamine sensitivity and reduce contractility ultimately affecting myocardial performance [7]. With persistence of inadequate forward flow, the remaining viable myocardium starts to increase its oxygen demand and consumption, compromising further global ventricular function due to ischemia. When left ventricular dysfunction progresses over the course of the shock stage, pulmonary artery pressures and left sided pressures commence to increase leading to interventricular septum displacement to the right ventricular cavity reducing preload to the right ventricle (RV). The acute changes in pressure load deteriorate RV function triggering a rise in venous pressures. This leads to alterations in right ventricular structure causing cavity dilation and displacing the interventricular septum to the left ventricular space, compromising left ventricular diastolic filling and reducing coronary and systemic perfusion causing end organ damage [8].

Similar to CS from left ventricular dysfunction, the pathogenesis of cardiogenic shock due to right ventricular dysfunction (RVD) is associated with poor prognosis. In the presence of acute myocardial infarction, acute RVD presents with ischemia, arrhythmias, cytokine releases (i.e. tumor necrosis factor-α, interleukins) inducing further impact on systolic and diastolic function, poor tolerance to changes in afterload, pulmonary vasoconstriction due to hypoxia and increase risk of microthrombi and emboli. Furthermore, in those patients that require mechanical ventilation, RV function is negatively affected by acute changes in preload an afterload from elevated intra pulmonary pressures, especially when high positive end expiratory pressure ventilation is required [9]. With the abrupt changes in load, RV stroke volume is decreased, RV systolic pressure is reduced prompting reduction in LV end diastolic filling which in turn will contribute to coronary and systemic hypoperfusion. Overtime reduction in RV contractility results in annular and cavity dilation leading to tricuspid regurgitation. The increased regurgitant volume will further exacerbate RV dilation and drive ventricular inter-dependence to affect LV filling begetting a vicious cycle of hypoperfusion. As 20–40% of the RV systolic function is derived from interventricular and LV contraction, once ventricular interdependence develops, it is paramount to maintain and enhance ventricular performance to halt the shock sequence.

Early Recognition of Shock

Clinical features present during the Initial evaluation of the individual with CS include hypotension (systolic blood pressure less than 90 mmHg), diminished pulses, elevated jugular venous pressure, dyspnea, cool peripheries, delated

Table 3 Clinical distinct features of ventricular dysfunction

Features of LV dysfunction	Features of RV dysfunction
Pulmonary rales and/or wheeze	Increase jugular venous pressure
Displaced point of maximal impulse	Tricuspid regurgitation
Mitral or aortic regurgitation	Hepatomegaly
	Hepato-jugular reflex
	Lower extremity edema

capillary refill and altered mental status. However distinct characteristics upon presentation can guide the clinician to elucidate between which ventricle is compromised (see Table 3).

It is important to recognize however that presence of elevated JVP can be seen in both right and left ventricular dysfunction as recent studies show that more than 70 percent of individuals with acute heart failure present with left and right sided concordant hemodynamics (right atrial pressure $\geq$ 12 mmHg equates to a pulmonary capillary wedge pressure $\geq$ 30 mmHg) supporting the notion of JVP as an estimator of pulmonary capillary wedge pressure [10].

- **Electrocardiogram Interpretation**

  In patients with initial presentation of CS-AMI, ECG is essential in the decision process for management of patients suspected of ACS. The ECG should be ordered within 10 min of arrival to the emergency room and If the initial ECG is non-diagnostic, serial ECG should be obtained every 15–30 min. Any ST segment deviation should promptly be determined for acute coronary intervention. Presence of ST segment elevation in 2 or more contiguous leads indicates urgent reperfusion, ST segment depressions, transient ST-elevation ($\geq$0.5 mm [0.05 mV]), or new T wave inversion symmetrical in the precordial leads ($\geq$2 mm [0.2 mV]) are strongly suspicious for acute coronary syndrome (ACS) [11]. Presence of Q waves reflect size and extension of the MI and predicts lower ejection fraction [12]. Ventricular or atrial arrhythmias can also be suggestive for ACS as up to 6% of patients can develop ventricular tachycardia or ventricular fibrillation within an hour of symptom presentation. Most commonly however patients with ACS can present with non-sustained monomorphic in the first 24–48 h after an AMI and usually associated with regional ischemia. Sustained VT is less common but can be seen in ST-elevation AMI associated with larger infarction areas [13].

Risk Assessment

Once clinical identification of CS is established, phenotyping the hemodynamic presentation is essential to guide therapy. The common presenting theme is a low cardiac index with a variable preload, volume and systemic vascular resistance.

A framework has been defined to characterize the hemodynamic status of patients presenting with CS. The classic cold and wet profile is seen in more than 60% of patients with CS-AMI while those with cold and dry profile (isolated hypoperfusion) are seen in close to 30% of patients with CS-MI (Table 4). Moreover, the mortality associated with each profile relies vastly on the presence of hypoperfusion independent on the presence or absence of pulmonary congestion. In the SHOCK trial, hypoperfusion was defined by oliguria <30 ml/hr or cold peripheries which identifies individuals with evidence of end organ dysfunction. The study showed an in-hospital mortality of 70% for those with hypoperfusion without pulmonary congestion compared to 60% with presence of both hypoperfusion and congestion. Those with no hypoperfusion with or without congestion had a 20% mortality [14]. Similarly those patients presenting with the wet and warm profile have a commensurate mortality risk to those in other profiles. This group is characterized by low cardiac index, low-normal systemic vascular resistance and elevated wedge pressure. In those presenting with ST segment elevation AMI, 25% met systemic inflammatory response syndrome (SIRS) criteria defined as presence of two or more of the following: 1. heart rate >90 beats/min; 2. respiratory rate >20 breaths/min; 3. body temperature >38 or <36 °C; 4. leukocyte count >12 or $<4 \times 10^9$/L. For those with SIRS at the time of AMI presentation prognosis is poor with a mortality risk of 31% and a 2–threefold risk for death, shock, heart failure and stroke at 90 days [15].

The basis of profiling patients with CS remotes to the early era of AMI managed by thrombolytic therapy. Originally developed in 1967, the Killip-Kimball classification is based on the bedside clinical assessment of patients presenting with left ventricular dysfunction due to AMI. The classification is divided in 4 categories: class (I) no clinical signs of heart failure; class (II) HF with jugular venous distention, rales and S3 on heart auscultation; class (III) overt pulmonary edema and class (IV) cardiogenic shock and hypoperfusion. The significance of this classification remains relevant today as many studies continue to validate its association with mortality. A recent study examining the temporal trend in outcomes of AMI patients stratified by Killip class showed that this classification remains an independent predictor of mortality with a 3 to fourfold risk of death post-MI specifically in those with Killip class greater than or equal to 2. Patients

Table 4 Hemodynamic profiles in cardiogenic shock

	Volume		
Perfusion		Dry	Wet
	Warm	Increased CI Low SVRi Low-Normal PCWP	Low CI Low-Normal SVRi High PCWP
	Cold	Low CI High SVRi Low-Normal PCPW	Low CI High SVRi High PCWP

CI: Cardiac Index; PCWP: Pulmonary Capillary Wedge Pressure; SVRi: Systemic vascular resistance index

with higher Killip class exhibited more complications including acute kidney injury, new onset atrial fibrillation and ventricular arrhythmias [16].

Risk Scores

Risk prediction in CS is limited due to the heterogeneity of its presentation and causes leading to CS. About one fifth of the causes are not related to AMI however all CS cases share similar variables that can forecast patient outcomes. However, their use in predicting short-term mortality and survival after MCS is helpful. The advantage of risk classifying CS patients is to rapidly determine severity of presentation and facilitate clinical decision making utilizing readily available data obtained with in 24 hr of CS presentation (Table 5).

Biomarkers

Evaluation of myocardial injury severity through biomarker data is paramount as they serve to support the diagnosis of CS, distinguish the hemodynamic profile, determine prognosis. The continuous assessment of the biomarker profile can portend the temporal status of a patient in shock and define treatment effects that may identify responders and non-responders to therapy. The changes in biomarkers overtime can also help predict myocardial recovery.

Table 5 Risk scores utilized in cardiogenic shock

This table 5 Risk ScoreRisk score/trial	Components
Shock trial	Clinical Score: Age, shock on admission, end-organ hypoperfusion, anoxic brain injury, systolic blood pressure, prior CABG, noninferior MI, and creatinine ≥ 1.9 mg/dL. Hemodynamic Score: LV stroke work, LVEF < 28%. The limitations of this score is based on the treatments offered at the time period (1993–1999), and not with contemporary therapeutic resources existent to treat shock [38]
CardShock trial	ACS etiology, age, previous MI, prior CABG, confusion at presentation, low LVEF, lactate levels, eGFR. The risk tool was validated in 384 patients from the IABP-SHOCK II trial and showed an AUC 0.85 for mortality prediction [39]
IABP-SHOCK II score	Age > 73 years (1 point); 2) history of stroke (2 points); Glucose > 191 mg/dL (1 point); Creatinine > 1.5 mg /dL (1 point); lactate > 5 mmol/L (2 points); TIMI flow < 3 after PCI (2 points). Risk categories based on the points where low 0–2 points, intermediate 3–4 points and high 5–9 points with mortality rates of 23.8%, 49.2% and 76.6% respectively. The AUC for short-term mortality in AMI-CS was 0.73. When validated with patients included in CardShock, IABP-SHOCK II score showed a similar AUC 0.73 [40]

Within 12 h of Ý metabolic panel, blood count, arterial blood gas and lactate should be obtained. Electrolyte evaluation, liver and renal function parameters are important elements of end organ perfusion Cardiac enzymes should be obtained serially and trend every 6 h. Frequent monitoring of cardiac markers can reveal the degree of injury the myocardium has sustained since the initial event. The following are some biomarkers that have demonstrated prognostic value in patients with cardiogenic shock:

- **N-terminal pro-B-type natriuretic peptide (NT-proBNP)**. NT-proBNP should be obtained as it can help prognosticate outcomes in cardiogenic shock patients. In a sub study from the IABP shock trial, NT-proBNP values were higher among non survivors compared to survivors specially in those with impaired renal function, signaling a degree of advanced shock stage and end organ dysfunction [17]. It is important to note that high natriuretic peptide levels do not necessarily correlate with elevated filling pressures however in those admitted to ICU with shock, NT-proBNP remain an independent predictor of ICU mortality with a 15-fold risk of death compared to those with levels <1200 pg/mL [18].
- **Lactate**. As a marker of tissue hypoperfusion, it has been associated with a high 30-day mortality. In patients presenting with ACS, admission lactate is predictor of in-hospital mortality when added to other indicators of shock including, systolic blood pressure, LV ejection fraction and peripheral hypoperfusion [19]. Similar to patients presenting with ACS, those with admitted to the ICU with acute decompensated heart failure (ADHF) can be risk stratified by determining the lactate on admission. In a study of 754 consecutive patients with CS-ADHF, the admission lactate had a greater power to predict in-hospital mortality with a twofold risk, especially in those with levels greater than 3.2 mmol/L [20]. Others have also shown that even in the absence of shock, patients with heart failure related to AMI, there is a 28% thirty day mortality when lactate is greater than 2.5 mmol/L [21]. It is recommended that lactate measurements should be obtain every 1–4 h and that repeated assessments can inform about persistence of shock. Absence of lactate clearance from blood is associated with a poor prognosis, as studies have shown that a clearance of less than 10% in 12 h from admission identifies a high-risk subset of patients for death [22]. Additionally, determining the level of bicarbonate at admission has been associated with a high mortality risk at short and long term follow up. In a study of 165 ischemic patients admitted with cardiogenic shock, those with in the lowest tertile of bicarbonate levels had a 15.5 (IQR 12.8–16.6) were associated with a twofold risk for 1 year mortality [23].
- **Troponin**. Cardiac troponin beyond its diagnostic power for detecting AMI, has been determined to be a successful tool in predicting mortality. The degree of troponin elevation can determine outcomes in patients presenting with CS-AMI. In the Global Registry of Acute Coronary Events, the maximum 24-h troponin (either I or T) presenting with non-ST segment elevation MI (NSTEMI) was analyzed in 16,318 patients. For each ten-fold increase in the baseline value, there was a significant linear trend for worse outcomes including ventricular arrhythmias, cardiogenic shock, new onset heart failure and death. The degree of troponin elevation was found to be a strong predictor for early and late mortality [24]. Furthermore, in patients that continue to have elevated circulating

troponin levels over the first 30 days following a hospitalization, it suggests ongoing myocardial injury associated with chronic remodeling and risk for all-cause mortality [25].

Echocardiography

Echocardiography in the acute setting can be beneficial in differentiating the causes of cardiogenic shock. A focused echocardiogram should be done in the initial evaluation of CS patients as it provides vital information about LV and RV contraction, intravascular fluid status, presence of pericardial effusion and tamponade. In those presenting with AMI, detecting mechanical complications is of sum importance to dictate the opportune therapies for stabilization. In other cases of CS, it help assess left ventricular function, right ventricular function and acute valvular heart disease. In the SHOCK trial, mechanical complications accounted for 12% of the causes of CS with severe valvular heart disease being the most common one (predominantly moderate mitral regurgitation), followed by ventricular septal rupture and tamponade. Moreover, in CS patients presenting with moderate MR, there is a 6 to sevenfold risk of 30-day mortality [4, 26]. However, in recent years the mortality related to mechanical complications in ST segment elevation MI (STEMI) patients have decreased to almost 25%, with free wall rupture representing now the most common complication, requiring pericardiocentesis due to cardiac tamponade with hemodynamic compromise [27].

In cases of cardiogenic shock secondary to acute heart failure (CS-AHF), distinct echocardiographic markers have been found to provide additional information to stratify patients at risk of worsening shock and poor prognosis. Studies have shown that a reduced ejection fraction, high wall motion score index, elevated E/e' ratio>13 m/s, moderate to severe mitral regurgitation, presence of LV outflow obstruction, elevated pulmonary systolic pressure and right ventricular involvement are associated with increase in hospital mortality [28]. Early recognition of these high-risk individuals can rapidly triage which patients need to escalate their hemodynamic support with either intravenous inotropic drugs and/or mechanical circulatory support (MCS). Furthermore, once hemodynamic stabilization occurs, daily echocardiograms at the bedside can determine myocardial recovery or persistent systolic dysfunction, myocardial complications post-AMI and short term MCS device adjustment.

Hemodynamic Monitoring

Urgent assessment of signs of hypoperfusion in all patients with CS is recommended by obtaining continuous blood pressure monitoring through an arterial line, telemetry for heart rate and arrhythmia evaluation, continuous pulse

oximetry for oxygen saturation, temperature and urine output. Additionally, pulse pressure should be closely monitored with a goal SBP ≥ 90 mmHg and MAP 60–65 mmHg. Central venous catheter insertion should also be obtained to administer vasopressors or inotropes, monitor CVP and mixed central venous oxygen saturation.

The use of invasive hemodynamic through a pulmonary artery catheter (PAC) is critical for establishing the diagnosis of cardiogenic shock. Determining the cardiac index and filling pressures ascertains the category and severity of shock and risks stratify patients. It can also provide information about the fluid status, adequate oxygen delivery as determined by the mixed venous oxygen saturation (SVO2) and pulmonary vascular resistance. The PAC can also distinguish cardiogenic vs. mixed shock as the latter can be seen in 20% of CS cases.

Although PAC utilization in CS has decreased over the past decade, studies have shown that its use is associated with corrections in reclassification of CS, improved outcomes and increased survival. The goal of hemodynamic monitoring is directed towards improving tissue perfusion through stabilization or enhancing parameters that will make a significant impact on outcomes. It should not only focus on improving cardiac function but also reducing filling pressures. A sub-analysis from the CardSHock study investigating the use of PAC in a real-world setting showed that those managed by PAC received more often inotropes, vasopressors, mechanical ventilation, renal replacement therapy and mechanical assist devices. The cardiac index, cardiac power output index and stroke volume index where the highest predictors for 30-day mortality allowing for reclassification of CS patients [29]. This is partly due to better decision strategies to guide therapy based on the hemodynamic data obtained [30].

The PAC can assist in choosing which vasopressor or inotropic drug to initiate and titrate, select which patient will benefit from acute MCS insertion for isolated LV, isolated RV or biventricular support and guide weaning of pharmacological or mechanical support. This is of importance as response to any intervention is dependent on volume status, intrinsic RV function, systemic and vascular resistances, and presence of valvulopathy.

A multitude of hemodynamic parameters can be obtained by PAC measurement which the clinician can integrate into their decision making:

	Mean	Range
Right Atrium, mmHg	4	−1 to 8
Right Ventricle Systolic, mmHg	24	15 to 28
Right Ventricle End Diastolic, mmHg	4	0 to 8
Pulmonary Artery Systolic, mmHg	24	15 to 28
Pulmonary Artery Diastolic, mmHg	10	5 to 16
Pulmonary Artery Mean, mmHg	16	10–22
Pulmonary Capillary Wedge, mmHg	9	6 to 15

	Mean	Range
Cardiac Output, mL/min	6	4 to 8
Cardiac Index, mL/min/m^2	3.4	2.8 to 4.2
Systemic Vascular Resistance	14.4 (1150)	11.3 to 17.5 (900 to 1400)
Pulmonary Vascular Resistance	2.5 (200)	1.9 to 3.1 (150 to 250)
Transpulmonary Gradient	<12 mmHg	PAP mean—PCWP mean
Diastolic Pulmonary Gradient	<7 mmHg	PAP diastolic—PCPWP mean

The PAC can also assess if there is RV involvement in CS. Right ventricular dysfunction (RVD) can be defined by readily available hemodynamic parameters obtained by PAC which include:

1. Right atrial pressure (RAP) >10 mmHg
2. Right atrial to pulmonary capillary wedge ratio >0.63
3. Pulmonary artery pulsatility index (PAPi) <2. This parameter represents the ratio of PA pulse pressure to RAP calculated as: pulmonary artery systolic pressure—pulmonary artery diastolic pressure/right atrial pressure
4. Right ventricular stroke work index <450 g-m/m^2, determined by mean PA pressure—mean RAP x stroke volume index

Recognizing markers of RVD is important as 23–24% of CS-AMI present with RVD (CVP > 10 mmHg), while 15% present with severe RVD (CVP > 15 mmHg). Even more, biventricular failure (represented by elevated CVP > 15 mmHg and PCWP > 15 mmHg) is the most common hemodynamic profile occurring in 38% of patients which is associated with poor prognosis and not uncommonly requiring biventricular mechanical support [31].

Other important hemodynamic parameters that have proven to be significant prognosticators in CS are the cardiac power output (CPO) and cardiac power index (CPI) is derived from obtaining the cardiac output and mean arterial pressure. The CPO is calculated as CO x MAP/451. A CPO <0.6 W/m^2 which been associated with increased 30 day in-hospital mortality in patients with CS at 24 h after CS diagnosis and implementing supportive therapies [32, 33].

Since PAC is an invasive procedure, its insertion should be guided with caution as complications can occur in 5% of the cases including: insertion site hematoma, arterial puncture, pulmonary artery hemorrhage, pulmonary artery puncture, arrhythmias catheter related blood stream infections and endocarditis.

Hemodynamic Risk Profiling

The SCAI stages serves as a robust indicator for profiling CS patients based on their initial presentation (Table 1). With each incremental stage there is a 1.53 to 6.8-fold increase in-hospital mortality risk [34]. Among those with ongoing hypoperfusion and deterioration based on presence of hemodynamic indicators of

biventricular failure (high RAP:PCPW ratio, low CPO, low PAPi), requiring multiple vasopressors for ongoing support, are at highest risk for becoming refractory to therapy and at greatest need for MCS. The in-hospital mortality for those in refractory shock can range from 40 to 67% [35]. Thus, early recognition and rapid progression of the severity of CS is critical for survival and improved outcomes.

Hemodynamic Goal Directed Therapy

Initial evaluation of invasive hemodynamics during the acute phase of shock can serve to identify and institute adequate support measures for stabilization. The initial measurements of cardiac index, pulmonary capillary wedge pressure, pulmonary artery oxygen saturation, pulmonary artery pulsatility index can assist clinicians in determining which therapies provide the maximum benefit. Studies have shown that when interventions are started on early hours of CS, survival outcomes improve. In patients with CS-AMI requiring MCS in the first 12–24 h of presentation, a CPO >0.6 W and lactate <4 mg/dL show a 95% in-hospital survival to discharge compared to those with a CPO < 0.6 W and lactate >4 mg/dL who have a predicted 30% survival. Additionally, once MCS is initiated more than 50% of patients reduce the number of inotropes, improve cardiac performance measures, oxygenation, lactate and achieve a lower heart rate. Establishing shock protocols emphasizes standard practices that can promptly identify patients in need of early MCS.

Even though macro-circulatory changes can be seen with prompt fluid resuscitation, micro-circulatory dysfunction can persist signaling poor perfusion pressure. Correction of flow alterations occurring at tissue level is critical as impaired endothelial vasoreactivity, reduced blood cell rheology, platelet aggregation and micro-thrombosis can accelerate organ failure and make all efforts of MCS futile. Optimization of oxygen transport based $ScvO_2$, lactate, veno-arterial difference in CO_2 and sublingual microcirculatory flow by administration of fluids, red blood cell transfusions, and inotropes is in parallel important to MCS initiation [36].

Establishing Weaning Versus Dependence

One of the overarching goals of every shock patient should be to achieve myocardial recovery and survival to discharge. Daily assessments are required to evaluate underlying cardiac function, hemodynamic changes, biomarker trend and vasopressor requirements. The later has been proven to be a marker of poor prognosis when the number of vasopressors or inotropes escalates rapidly. Indeed, patients who required more than 2 inotropes have a 65% 30-day mortality risk compared to those with one or none vasopressors. By assessing hemodynamic trends, the clinician can rapidly identify if escalation or de-escalation of support is warranted. Several observational studies and inherent institutional protocols have been established to dictate when a patient can be weaned off support. These include:

1. Cardiac index ≥ 2.2 L/min/m^2
2. Cardiac power output > 0.6 W
3. PCWP ≤ 18 mmHg
4. PAPi ≥ 1.5
5. MAP ≥ 65 mmHg
6. CVP ≤ 15 mmHg
7. Heart Rate < 120 bpm
8. LVEF $\geq 25\%$
9. TAPSE > 14 mm

If such recovery parameters are not met then consideration for increasing hemodynamic support should be considered with either a short-term MCS (impella, intra-aortic balloon pump, VA-ECMO). If such weaning trials are occurring while on MCS then evaluation for advanced therapies are to be sought including durable left ventricular assist device or heart transplantation.

Timing of Percutaneous Mechanical Circulatory Support

The initial management strategies to stabilize CS includes IV fluids, inotropes and vasopressors, however about 8% of patients evolve into progressive or refractory shock with an expected mortality of ~70%. Moreover, mortality increases rapidly with the number of vasoactive drugs use with only 35% survival when 2 or more inotropes are used and are associated with increase myocardial oxygen consumption, increase afterload and vasoconstriction that may impair microcirculation [37]. In these stages aggressive interventions are needed to stop the accelerated pace of shock. Short-term MCS inserted either percutaneously or surgically can be used as a bridge to myocardial recovery, bridge to decision when neurological function is unclear or multi-organ failure may preclude a decision for advanced heart failure therapies including LVAD or heart transplant; or as bridge to another durable device. The advantage of short-term MCS is to allow hemodynamic optimization and potential reversal of end-organ dysfunction before moving forward with other therapies or palliative care.

It is important then to recognize the initial insult leading to CS and understand the underlying myocardial reserve to withstand circulatory collapse. The primary objective of managing CS patients is to achieve coronary perfusion via revascularization when needed, achieve circulatory support to preserve a viable mean blood pressure and unload the left and/or right ventricle to reduce the deleterious effects of increase afterload and oxygen demand.

The 2015 SCAI statement on the use of percutaneous MCS recommends implementing early placement of approved MCS devices in those who failed to stabilize with initial support. Prompt ventricular unloading enhances myocardial performance and reduces mechanical power expenditure by: (1) lowering PCWC; (2) minimizing myocardial wall stress and ventricular work; (3) reducing myocardial oxygen demand; (4) augmenting coronary perfusion. Studies have shown that early MCS implementation with the impella device is associated with better

survival specially in those when MCS is implemented less than 75 min from shock onset. In a study of 287 patients presenting with CS-AMI who underwent percutaneous coronary intervention with a mean LVEF of 25%, only 44 survive to discharge. Time to MCS was associated with improved survival before PCI or requiring inotropes and vasopressors [37].

Although observational and registry data suggest that early initiation of MCS favors good outcomes, appropriate patient selection including patient age, comorbidities, hemodynamic and laboratory values institutional experience and device related complications are key elements that have to be taken into account when consider MCS.

Shock Team Approach

Our current understanding of CS has evolved over the past decade with attention being focused towards preservation of end organ perfusion while minimizing adverse events when patients are supported on conventional therapy. The key to improve outcomes in CS is to stablish a pattern of early recognition markers of CS to allocate appropriate therapies. The success of door-to balloon time in STEMI has been in large part due to training of emergency personnel to detect clinical, ECG, and laboratory criteria of acute ischemia due to coronary occlusion. A similar approach should be boarded for early triage of patients and avoid delaying evaluation and management of CS patients. Cardiac shock centers have demonstrated improved outcomes when care pathways are established and followed based on current best practices standards. When a standardized approach is use survival from CS can improve dramatically. In a study of 204 patients, from the INOVA group from a task force to develop a management protocol for CS patients. The algorithm approach focused on 5 objectives:

1. Rapid identification of the CS state
2. Early invasive hemodynamic implementation
3. Minimize use of vasopressors and inotropes
4. Early MCS implant for the left and/or right ventricle
5. Assess and achieve myocardial recovery

The authors noted that after implementing the shock team approach the survival increased from 47% for CS-AMI and CS_ADHF to 58 and 77%. The most common cause of death was multiorgan failure in 80% of the patients. Those who required MCS for every 1-h delay in escalation to MCS was associated with a 10% increase risk of death. Overall, the complexity of CS etiologies requires a multi-disciplinary team approach with the clinical skills, hemodynamic expertise and technical skills for percutaneous MCS insertion and management. In tertiary shock care centers, the team is mostly conformed of interventional cardiologist, advanced heart failure specialist, nephrologist, critical care specialist, cardiac surgeon, palliative care, neurologist, pharmacist. A proposed algorithm based on current scientific statement for CS management (Fig. 1).

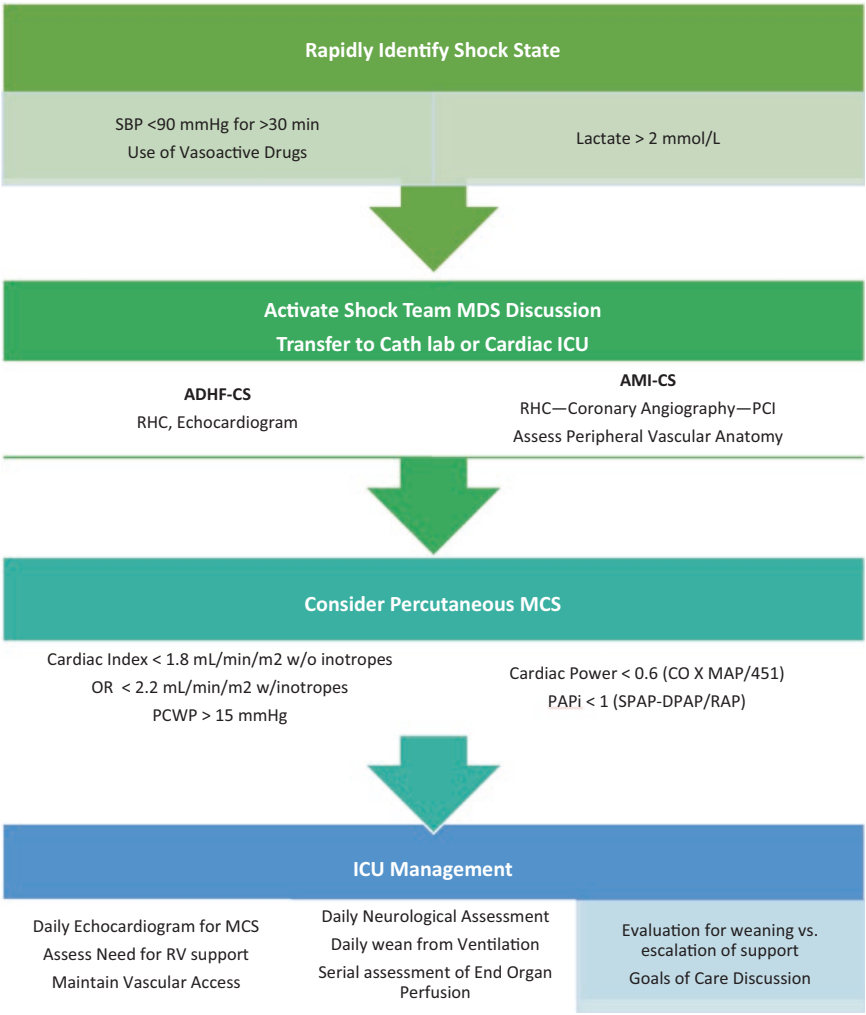

Fig. 1 Cardiogenic shock management algorithm

Key Points

1. Identify Type and severity of Cardiogenic Shock: ACS vs non-ACS
2. Use hemodynamic data to guide clinical decision making
3. Use Vasoactive Drugs to maintain MAP > 65 mmHg
4. Trend hemodynamic and biomarker data (CPO, PAPi, lactate, CO2, creatinine)
5. Expedite Early Ventricular Unloading with MCS and Select type
6. Enhance Coronary perfusion

7. Preserve Renal and Hepatic Function
8. Maintain Vascular access
9. Achieve recovery and survival
10. Refractory Shock = Escalation to MCS

Case Conclusion

After unsuccessful improvement in the patient's hemodynamic, clinical and perfusion status, a decision is made to start mechanical circulatory support with notable improvement in atrial and ventricular filling pressures, cardiac index and lactate. Weeks after maintaining stabilization with MCS the patient underwent successful heart transplantation without complications:

	Inotrope	24 hours post-MCS
RA, mmHg	11	8
PA, mmHg	55/33/39	44/20/29
PCWP, mmHg	21	17
PA Saturation, %	47	58
AO Saturation, %	99	100
Cardiac Output, L/min	2.3/1.8	2.9/2.2
Cardiac Index, L/min/m^2	1.8	2.2
SVR, dyn/cm/sec^5	1600	2041
PVR, Woods unit	237	248
RA:PCWP ratio	0.52	0.47
PAPi ratio	2	3
CPO, watts	0.41	0.51
BP, mmHg	106/67/80	96/44/79
HR, bpm	132	88
Lactate mmol/L	2.4	1.6

Conclusion

Cardiogenic shock is complex syndrome that requires a multidisciplinary approach to improve outcomes. The current SCAI classification can allow for proper differentiation of CS subsets and determine the hemodynamic profile. The advantage of utilizing PAC hemodynamic guided therapy can confirm eh presence and severity of CS where the cold and wet is the most frequent CS phenotype.

The use of vasopressors and inotrope for initial stabilization of CS patients is beneficial, however the longer duration on these vasoactive drugs is counterbalanced by their negative side effects. Trending arterial lactate is helpful in prognosticating and identifying refractory CS. The early recognition of high-risk CS patients will allow for prompt implementation of MCS to improve cardiac while avoiding the cardiotoxic effect of vasopressors. Similarly, those patients that fail to achieve myocardial recovery should be considered for long term durable MCS.

Future Direction

The Shock team approach has been popularized in tertiary centers and has quickly been adopted by many hospital systems. The early mobilization of a multidisciplinary team to address medical and surgical needs of the patient may prove to be cost-effective and timely. Early recognition of cardiogenic shock as well has been the center of discussion with artificial intelligence embedded in electronic medical record systems. These ubiquitous systems actively collect continuous variables to alert practitioners by the use of best practice advisories.

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Temporary Mechanical Circulatory Support

Daniel Walters and Ryan Reeves

Clinical Vignette 1

A 55 year-old man with a past medical history notable for HIV infection and AIDS, tobacco abuse, coronary artery disease, and a prior percutaneous coronary intervention (PCI) to an unknown vessel presented with acute chest pain and anterior ST-segment elevations. He was hypotensive with a blood pressure of 85/52, tachycardic with a heart rate of 112 in sinus rhythm, and demonstrated crackles on pulmonary auscultation. Emergent angiography demonstrated left anterior descending artery stent thrombosis. Successful angioplasty and stenting were performed, however he remained persistently hypotensive and required norepinephrine for blood pressure support. Subsequently, a 50 mL IABP was placed from the right femoral artery. He was brought to the cardiac care unit, where over the next 48 h his condition improved. The IABP was weaned and removed on hospital day three with manual pressure for hemostasis, and discharged to home on hospital day five (Tables 1, 2, 3).

Introduction: IABP

The IABP was the first widely available non-pharmacologic modality that could alter cardiovascular hemodynamics and for decades was the standard therapeutic device for percutaneous MCS [1]. It continues to be the most widely used system

D. Walters · R. Reeves (✉)
Division of Cardiology, Department of Internal Medicine, University of California, San Diego, USA
e-mail: rreeves@health.ucsd.edu

R. Reeves
9452 Medical Center Dr #7411, La Jolla, CA 92037, USA

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Table 1 SCAI/ACC/HFSA/STS consensus statement summary

Suggested indications for percutaneous mechanical circulatory support
• Complications of acute myocardial infarction
• Severe heart failure in the setting of non-ischemic cardiomyopathy
• Acute cardiac allograft failure
• Post-transplant right ventricular failure
• Patients slow to wean from cardiopulmonary bypass following heart surgery
• Refractory arrhythmias
• Prophylactic use for high risk percutaneous coronary intervention*
• High-risk or complex ablation of ventricular tachycardia
• High-risk percutaneous valve interventions

*HR-PCI encompass those age 70, ongoing ischemic and LV systolic dysfunction EF < 40%, previous CABG, acute coronary syndromes complicated by unstable hemodynamics (wedge pressure ≥ 15 mmHg, mean pulmonary arterial pressure ≥ 50 mmHg), post-AMI angina, Killip class III-IV and CS

with approximately 50,000 per year being implanted for cardiogenic shock alone [2]. Indications for use include the following: acute or chronic cardiogenic shock, decompensated congestive heart failure refractory to medical therapy, acute myocardial infarction (AMI), critical left main or three vessel coronary artery disease, adjunctive support for high risk/complex PCI, and refractory arrhythmia [3, 4]. Introduced through the peripheral vasculature, the IABP is advanced over a guidewire to the proximal descending thoracic aorta, just distal to the great vessels. The hemodynamic effects of counterpulsation include: increased diastolic pressure and coronary perfusion, decreased afterload, increased stroke volume, and decreased stroke work and myocardial consumption, which lead to an improvement in cardiac output (0.5–1.5 L/min) and metabolic clearance of lactate [3, 5–7]. The hemodynamic benefits are dependent on balloon position, presence of cardiac arrhythmias and tachycardia, timing of balloon inflation, and systemic vascular resistance. Systemic anticoagulation may reduce device-associated thrombosis, and is recommended. If ongoing bleeding precludes anticoagulation, a systole to balloon inflation ratio of 1:1 is recommended to reduce stasis and the potential for thrombosis.

IABP and Acute Myocardial Infarction

Initial reports demonstrated the benefits of the IABP in AMI complicated by cardiogenic shock, with a significant reduction of in-hospital mortality, however, patients receiving IABP were younger, more often received inotropic support, and were more aggressively treated with coronary angioplasty and bypass surgery [8–10]. This early experience, although derived from a sub-analysis of

Table 2 Societal recommendations regarding the use of percutaneous mechanical circulatory support

Societies	Publication	Year	Recommendation(s)	Strength	LOE
ACC/AHA/SCAI	Guidelines for Percutaneous Coronary Intervention	2011	• A hemodynamic support device is recommended for patients with CS after STEMI who do not quickly stabilize with pharmacologic therapy	I	B
			• Elective insertion of an appropriate hemodynamic support device as an adjunct to PCI may be reasonable in carefully selected high-risk patients	IIb	C
AHA	Scientific Statement on Recommendations for the use of Mechanical Circulatory Support: Device Strategies and Patient Selection	2012	• Urgent nondurable MCS is reasonable in hemodynamically compromised HF patients with end-organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile	IIa	C
ISHLT	Guidelines for Mechanical Circulatory Support	2013	• The use of temporary mechanical support should be strongly considered in patients with multiorgan failure, sepsis, or on mechanical ventilation to allow successful optimization of clinical status and neurologic assessment prior to placement of a long-term MCSD	I	C
ACCF/AHA	Guidelines for the Management of Heart Failure	2013	• Nondurable MCS, including the use of percutaneous and extracorporeal ventricular assist devices (VADs), is reasonable as a "bridge to recovery" or "bridge to decision" for carefully selected patients with HFrEF with acute, profound hemodynamic compromise	IIa	B
ACCF/AHA	Guidelines for the Management of ST-Elevation Myocardial Infarction	2013	• The use of mechanical circulatory support is reasonable in patients with STEMI who are hemodynamically unstable and require urgent CABG	IIa	C
			• The use of IABP counterpulsation can be useful for patients with cardiogenic with CS after STEMI who do not quickly stabilize with pharmacological therapy	IIa	B
			• Alternative LV assist devices for circulatory support may be considered in patients with refractory CS	IIb	C

Table 3 Percutaneous mechanical support device characteristics

Device	Augmentation	Access	Flow (L/min)	Contraindications
IABP	Pneumatic counterpulsation	Femoral artery	Approx. 0.5	Severe AI, aortic dissection, AAA, anticoagulation intolerance, severe PAD
Impella 2.5	Continuous axial flow	Femoral artery	Up to 2.5	Severe AI/AS, mechanical AV, significant VSD/ASD, LV thrombus, severe PAD, anticoagulation intolerance
Impella CP	Continuous axial flow	Femoral artery	Up to 3.8	As above
Impella 5.0	Continuous axial flow	Femoral artery	Up to 5.0	As above
TandemHeart	Continuous centrifugal flow	Femoral artery, central vein	Up to 5.0	Atrial thrombus, severe PAD, VSD, anticoagulation intolerance
ECMO	Continuous centrifugal flow	Femoral artery, central vein	Up to 7.0	Severe PAD, right atrial thrombus, anticoagulation intolerance

non-randomized data, was convincing enough that the IABP soon became a pivotal component of post infarction cardiogenic shock care.

The first randomized controlled trial investigating the use of counterpulsation in post infarction cardiogenic shock was the IABP-SHOCK II trial [11]. Six-hundred patients with post infarction cardiogenic shock were randomized to IABP or standard care. At 30 days there was no difference in the primary outcome of all-cause mortality, approximately 40% in each arm. There was also no difference in major secondary endpoints including ICU length of stay, lactate levels, renal function, major bleeding, peripheral ischemic events, stroke, and sepsis. Twelve month follow-up confirmed no difference in mortality, repeat revascularization, reinfarction, and stroke between the two groups [12]. Limitations of the trial included a high cross-over rate of 10% to IABP in the standard care arm. Furthermore, IABP placement occurred after coronary intervention in over 85% of patients, making it unclear if earlier insertion might show greater benefit. Given that these findings lacked clear evidence of the use of IABP in post-infarction cardiogenic shock, the 2013 ACC/AHA reduced the recommendation for the use of IABP in cardiogenic shock after ST-elevation myocardial infarction not rapidly reversed by pharmacologic therapy from a Class I indication to a IIa indication (LOE B) [13].

Clinical Vignette 2

After two weeks of intermittent chest pain, a 53 year-old male presented to the emergency room with severe chest pain and shortness of breath. He rapidly developed hypotension requiring dopamine and hypoxic respiratory failure for which he was intubated. During intubation the patient became progressively more hypotensive and electrocardiography demonstrated diffuse ST-segment depression in the precordial and limb leads. He was emergently brought to the catheterization laboratory and was found to have complete thrombotic occlusion of the left main coronary artery. Femoral access was rapidly obtained and an Impella CP was placed followed by successful revascularization of the left main coronary artery with a drug-eluting. The patient ultimately stabilized with three days of hemodynamic support. After successful weaning of the Impella CP, device removal was planned in the catheterization laboratory. Radial artery access was obtained, and a long sheath advanced along with a 7.0 mm peripheral balloon over a long wire to the level of the arteriotomy within the femoral artery. The device was removed, and the balloon inflated at four atmospheres of pressure for a duration of five minutes. During this time period, light manual pressure was applied. Subsequently five minutes of manual pressure was applied, after which visual inspection demonstrated no external extravasation and angiography demonstrated no internal extravasation nor dissection, thrombus formation, or other concern. All equipment was thus removed, and a compression band placed at the radial arteriotomy.

Introduction: Impella

The Impella (Abiomed Inc., Danvers, MA) is an axial flow pump that is seated in the left ventricle (LV) across the aortic valve. The device first received CE Mark approval in 2005 and FDA approval in 2008. The pump is placed via femoral, subclavian, or axillary arterial access and provides continuous flow from the LV directly into the ascending aorta. The left ventricular Impella family consists of three devices with different maximum flow capabilities that increase as device caliber increases. The Impella 2.5 and Impella CP are able to provide up to 2.5 L/min and 3.5 L/min of flow, respectively, and can be placed percutaneously, while the larger Impella 5.0 provides up to 5.0 L/min of flow and is placed with a surgical cutdown. The motor housing is at the distal end of the catheter and is significantly larger than the catheter shaft, which determines the size of the respective access sheaths. After achieving an activated clotting time greater than 250 s, the device is placed over a guidewire in the left ventricle. Heparinized saline is continually infused through the pump catheter while the device is in place. After placement, the access sheath may be removed and a maintenance sheath that tapers to a smaller caliber within the vessel is secured in place. This allows for

increased distal perfusion relative to the access sheath and decreases the risk of limb ischemia. In order to prevent endovascular trauma and limb ischemia, a surgical cutdown and synthetic graft anastomosis are typically required for placement of the larger Impella 5.0 access and maintenance sheaths.

The device was first used as an alternative to the IABP in the early 2000s for post-cardiotomy patients, as adjunctive hemodynamic support during high risk PCI, and in patients with AMI associated cardiogenic shock [14–18]. Investigations for other indications have been limited by clinical trial enrollment issues [19]. The Impella 2.5 and CP are FDA approved for elective and urgent high-risk PCI, as well as cardiogenic shock within 48 h of acute myocardial infarction for a duration of up to four days. The Impella 5.0 is approved for up to fourteen days of shock-related circulatory support. In clinical practice these devices are used for extended periods as dictated by a patient's response to therapy and the occurrence of complications.

The Impella RP uses a similar principle to unload the right ventricle and improve pulmonary arterial flow. After obtaining femoral venous access, the device is placed antegrade through the right-sided cardiac chambers to deliver blood through the proximal inflow port in the right ventricle to the more distal pulmonary artery. The device is approved for up to fourteen days of support for right ventricular failure after left ventricular assist device (LVAD) placement, transplant, infarction, or open-heart surgery [20].

Impella and Cardiogenic Shock

There have been two major trials assessing the use of Impella in cardiogenic shock. The first was the ISAR-SHOCK trial in 2008, where the Impella 2.5 was compared to IABP in post infarction cardiogenic shock in a randomized, non-blinded fashion [17]. There was a statistically significant improvement in cardiac index in the Impella group, with an increase of 0.49 L/min/m^2 versus 0.11 L/min/m^2. Secondary endpoints of mortality, hemolysis, and serum lactate were not statistically different. Mortality in each arm was 46% and highlights the elevated baseline risk of the trial subjects. The second trial, RECOVER I, was a prospective, single-arm trial to assess post-cardiotomy use of the Impella 5.0 [21]. Sixteen patients underwent implantation immediately after CABG and/or valvular surgery or heart transplantation. The device was implanted upon identification of cardiogenic shock after weaning from cardiopulmonary bypass. The primary safety endpoint was the frequency of death and stroke at 30 days or discharge. The primary efficacy endpoint was survival of the patient to implementation of the next therapy, including recovery. After insertion, cardiac index and mean arterial pressure (MAP) increased from 1.65 to 2.7 L/min/m^2 and 71.4 to 83.1 mmHg, respectively, and pulmonary artery diastolic pressure decreased from 28.0 to 19.8 mmHg. There was one death and one stroke; native heart recovery occurred in 15 of 16 patients. Survival at 30 days was 93%, and 75% at one year [22]. The current ACC/AHA

guidelines for the use of Impella indicate that the device may be considered as an alternative to IABP for circulatory support in patients with refractory cardiogenic shock (Class IIB, LOE C) [20].

Clinical Vignette 3

A 74 year old male with coronary artery disease and remote CABG surgery presented with acute decompensated heart failure. His ejection fraction was moderately depressed and there was a torn chordae resulting in severe eccentric mitral regurgitation on echocardiography. After initial medical interventions, he remained in cardiogenic shock and was transferred to a tertiary center. He underwent emergent veno-arterial ECMO and Impella CP placement on arrival and patent bypass grafts were confirmed. Multi-organ dysfunction persisted and twenty-four hours later, he returned to the catheterization laboratory for placement of a Tandem Heart (LivaNova PLC, London, UK), cannula in the left atrium. The cannula was inserted in a Y-configuration into the ECMO circuit so as to further unload the left ventricle and decrease the impact of the severe mitral regurgitation (Fig. 3). His clinical status markedly improved as the degree of mitral regurgitation was significantly less. His urinary output increased, liver function returned, and the vasoactive agents were successfully titrated down. After review by the heart team, he was felt to be at prohibitive risk for surgical repair of the mitral valve, therefore the left atrial cannula was removed and percutaneous mitral valve repair was performed with the MitraClip (Abbott Vascular, Santa Clara, CA) system through the trans-septal puncture. His hemodynamics improved and within three days he underwent ECMO decannulation and removal of the Impella catheter (Figs. 1, 2, 4).

Introduction: TandemHeart

The TandemHeart is a centrifugal flow pump that entirely bypasses the left ventricle. Introduced via the femoral vein, the catheter is placed across the interatrial septum into the left atrium; blood is displaced through the pump, circulating back to the body via a femoral arterial catheter. The TandemHeart cannulae does not enter the left ventricle, reducing structural concerns associated with Impella use, however it does require a septal puncture for placement. The system provides up to 5.0 L/min of output and anticoagulation is achieved within the circuit. Research into device use began in the early 2000′s in patients with shock, direct comparison with the IABP, indirect comparisons to Impella, and high risk coronary intervention [23–26]. Currently, the device is FDA approved for support for up to 6 h, although as with the Impella device, in clinical practice use can extend well beyond this time period.

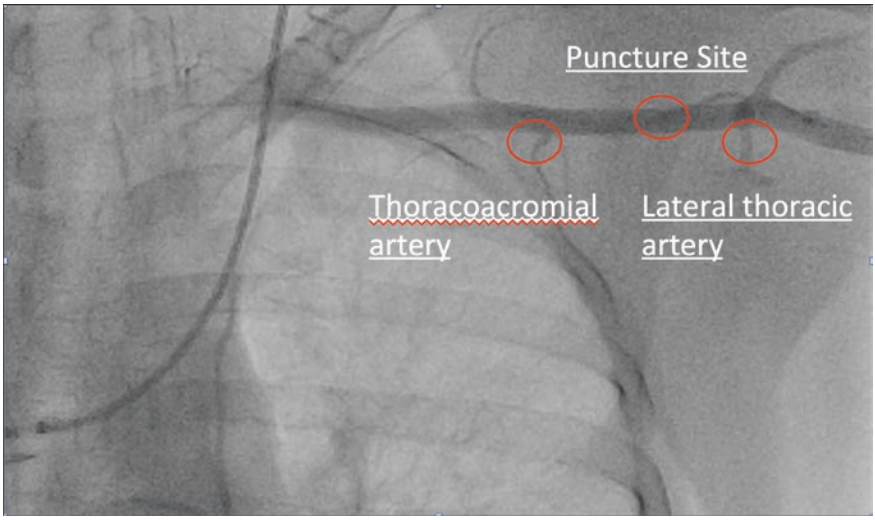

Fig. 1 Axillary access: The ideal location is between the thoracoacromial and lateral thoracic arteries. The axillary segment between these two branches is extra-thoracic and proximal to the crossing of the branches of the brachial plexus

TandemHeart and Cardiogenic Shock

A case series of TandemHeart demonstrated safety and efficacy of use for acute myocardial infarction complicated by cardiogenic shock, with a 30-day mortality rate of 44%. This led to a randomized, prospective, non-blinded trial comparing TandemHeart to IABP [24]. While TandemHeart was found to reduce lactate and intracardiac pressures along with a higher cardiac power index, mortality was no different between the groups, and those randomized to TandemHeart had a higher risk of limb ischemia and severe bleeding. A subsequent case series found similar hemodynamic and complication rates, and importantly, a comparable mortality rate at 30 days and 6 months (40.2% and 45.3%, respectively) [27]. A meta-analysis comparing percutaneous LVAD including TandemHeart and Impella to the IABP found that percutaneous LVAD had significantly higher cardiac index and mean arterial pressure, and significantly lower PCWP [28]. A 30-day mortality difference did not exist between the groups. Percutaneous LVAD support had a higher, albeit not significant, incidence of leg ischemia (RR 2.59, $p = 0.31$) while significant bleeding was more frequently observed with TandemHeart (RR 2.35).

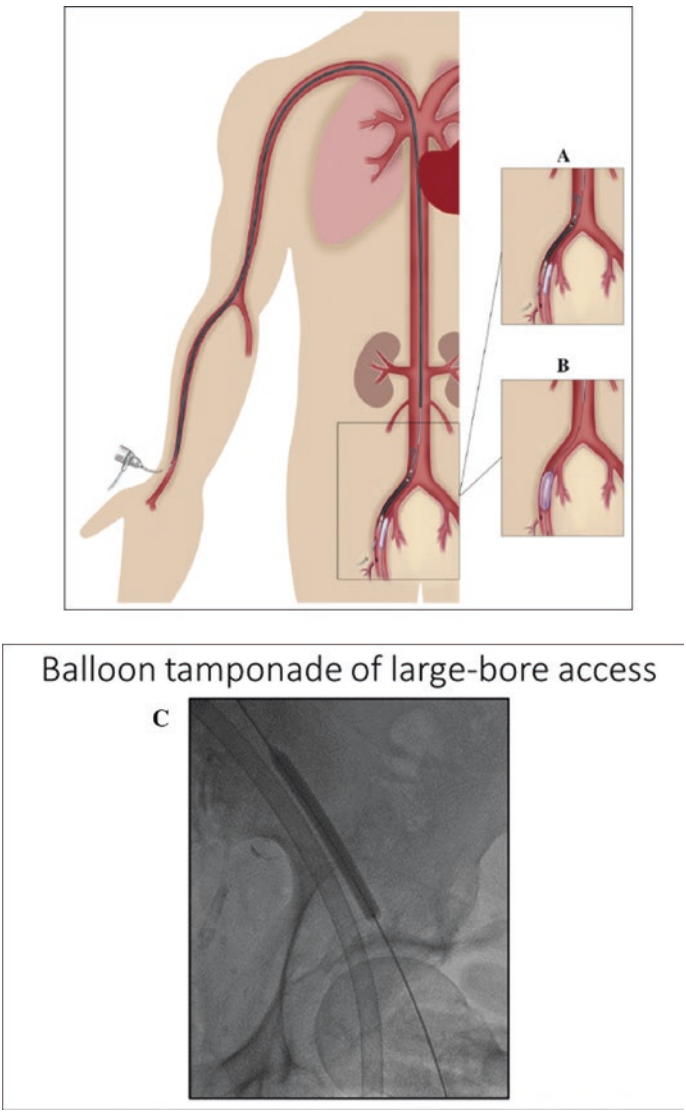

Fig. 2 Balloon assisted closure to remove a femoral sheath from a secondary access site. Panels A and B detail the approach and major steps when the radial artery is used as the secondary access site (Reprinted with permission from Pourdjabbar et al, Cardiovascular Revascularization Medicine April-May 2017 (pp. 215–220); copyright 2017 Elsevier). In panel C, the fluoroscopic image depicts an inflated balloon providing hemostasis after removal of an Impella catheter in an anticoagulated patient with an ECMO venous cannula in place

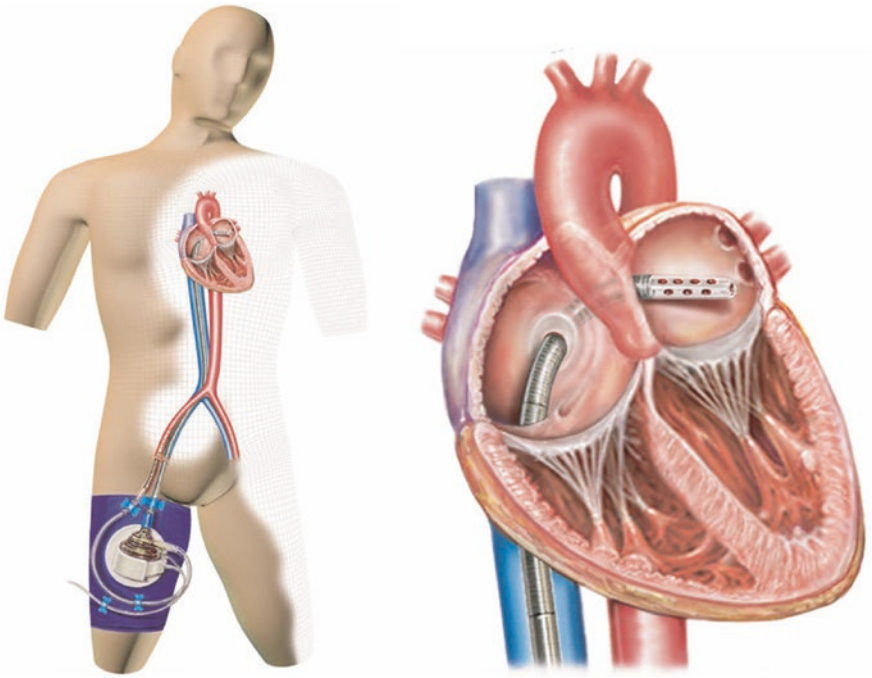

Fig. 3 TandemHeart device

Impella and TandemHeart have not been evaluated against one another in the context of cardiogenic shock. The TandemHeart has been employed for allograft rejection, postcardiotomy cardiogenic shock, and in right heart failure after durable left ventricular assist device implantation [29, 30]. When used for right heart support dual venous access is used for removal of blood from the right atrium and return into the pulmonary arteries. Complications associated with device use include limb ischemia and significant bleeding.

Special Considerations

Percutaneous MCS as a Bridge to Placement of a Durable LVAD or Heart Transplantation: IABP has been utilized as an effective bridge to transplant (BTT) or durable VAD in patients with acute decompensated HF [31, 32]. In a retrospective study of 32 patients treated with IABP due to severe hypo-perfusion, counterpulsation support allowed for improvement in clinical condition, serum creatinine, total bilirubin, and aminotransferases [33]. It may also allow for optimization of HF patients prior to durable VAD or transplantation to improve the postoperative course [34]. Overall patients on long-term IABP support have a low rate of complications and no increases in hemorrhagic episodes after VAD surgery [35]. Similarly, successes have been noted with the Impella family of devices as a bridge to definitive therapy [36, 37] as well as the TandemHeart device [29].

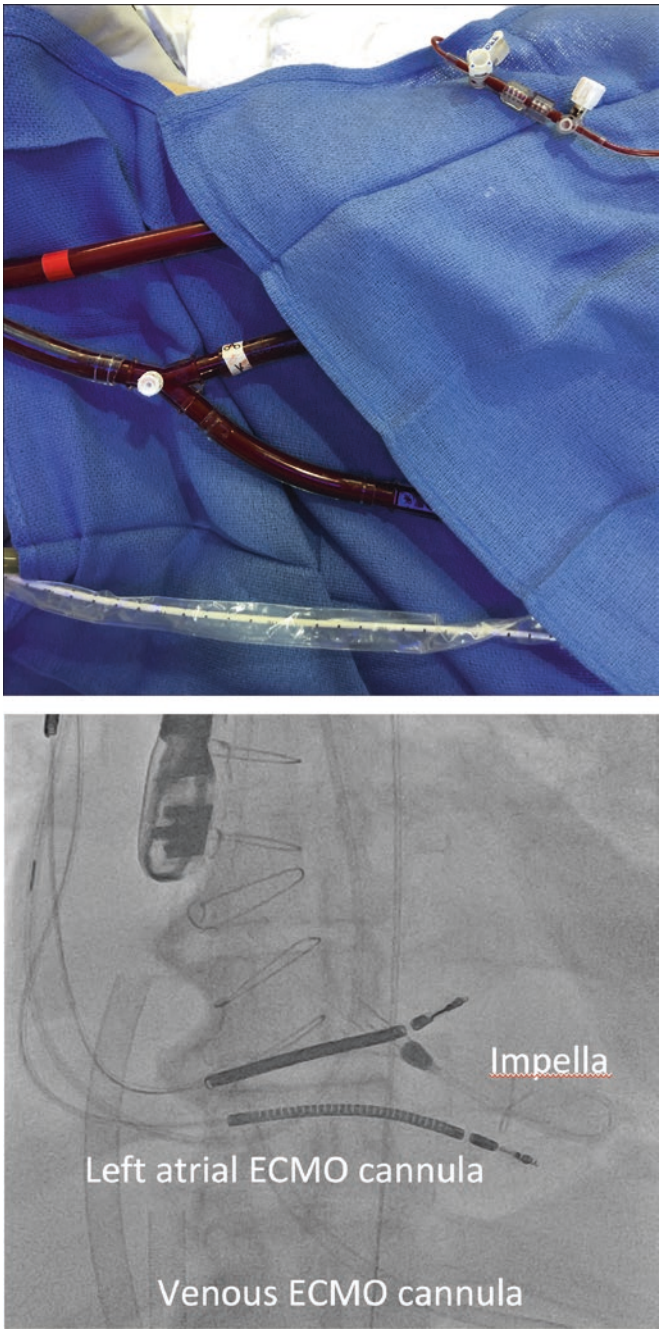

Fig. 4 Optimal stabilization may require multiple support devices for the severe cardiogenic shock. Here, VA ECMO was initiated after the patient presented with cardiogenic shock due to acute mitral regurgitation. An Impella CP catheter was then placed to unload the left ventricle, however hemodynamic improvement was suboptimal. A left atrial cannula was then added to the ECMO circuit via trans-septal puncture in order to adequately unload the left ventricle and reduce the impact of the mitral regurgitation. An antegrade catheter was placed to allow perfusion distal to the ECMO arterial cannula

Adjunctive Percutaneous MCS during PCI: High-risk PCI is a rapidly evolving field with a fluid definition. Generally speaking, it is accepted that PCI may be deemed high-risk when meeting any of the following broad criteria: ejection fraction <35%, unprotected left main disease or last remaining vessel, active/ongoing ischemia or shock, or multivessel disease with factors increasing the complexity of the revascularization procedure, such as calcification or large at-risk side branches. Hemodynamic support should be considered and often utilized for these interventions. Data is limited, however a randomized trial, PROTECT II, randomized over 450 patients undergoing high risk, non-emergent PCI to either IABP or Impella 2.5 [31]. High-risk was defined as unprotected left main coronary artery or last patent coronary vessel with an ejection fraction <35%, or three-vessel coronary artery disease and an ejection fraction <30%. At 30 days, no difference in the primary outcome of major adverse cardiovascular events was seen between the groups, however at 90 days a trend toward an absolute reduction was seen with an 8.7% absolute reduction in major adverse cardiovascular events (40.6% Impella versus 49.3% IABP). A per protocol analysis of the 90-day data met statistical significance favoring Impella 2.5, largely driven by a reduction in repeat revascularization. Subanalysis also demonstrated that in the subset of patients from PROTECT II who underwent rotational atherectomy, more aggressive atherectomy was performed in the patients randomized to Impella versus IABP [38]. This was associated with an overall reduction in the need for repeat revascularization but a higher incidence of peri-procedural myocardial infarction. TandemHeart for high risk PCI has not been studied in a randomized trial, however a case series found that in patients deemed high-risk for surgical revascularization (STS scores predicting 13% mortality), TandemHeart support allowed for successful intervention in 97% of cases, with 10% mortality at 30-days, 13% mortality at 90-day, and a 13% rate of significant vascular complications [26].

Non-Femoral Access for Percutaneous MCS: Alternative access for device placement is a consideration in patients for a multitude of reasons including peripheral vascular disease, body habitus/obesity, vascular calcification and tortuosity, aortic pathology, ambulatory status, and when prolonged MCS will likely be required. The IABP and Impella devices can be safely introduced via access sites other than the femoral artery, most commonly the axillary artery; the TandemHeart device is not routinely placed percutaneously at an alternate access site.

IABP placement via the axillary artery was first described in 1989 [39]. Published case series have noted an overall low rate of acute vascular complications, 0 out of 50 in the largest published series, and few late complications, 2 out of 50 in that same series [40, 41]. A noted advantage of the axillary approach is the potential for increased mobility with simultaneous hemodynamic support. The use of physical therapy after placement, in particular with patients awaiting cardiac transplantation, has been shown to increase overall daily ambulatory distance five-fold [35]. Arm movement and increased mobility, however, may lead to device malposition and technical complications, such as kinking, and may require pump exchange in nearly one quarter of patients [40, 41]. Device migration into the abdominal vessels may occur spontaneously or with device manipulation,

therefore if the device retracts into the subclavian artery, advancement over a guidewire that has been placed into the distal aorta is recommended. However, bedside, image-guided device manipulation often solves malposition issues, while device exchange is most safely performed in the catheterization laboratory.

Impella placement through the axillary artery is more complex than IABP placement due to device caliber, however data is similar regarding the safety and efficacy. The initial percutaneous experience was first published in 2016, and demonstrated the technique for both Impella placement and removal [42]. The total vascular complication rate from device placement to removal was 12% in a multicenter registry, occurring in 6 of 51 patients with an axillary device with over 80% of the devices being an Impella CP [43]. Two-thirds of patients with a device survived to hospital discharge after a median implant time of 2.5 days; three quarters of these patients experienced myocardial recovery, while the other third underwent durable LVAD placement or heart transplantation. Bedside device manipulation, as with a femoral Impella device, can be performed under echocardiographic guidance for minor manipulation, however given critical requirement of cannula placement across the aortic valve, significant manipulation or complete maneuvering across the valve should be performed in the catheterization laboratory.

Axillary percutaneous support placement has increased with the continued growth of LVAD and transplant programs. In our practice it is common to use the femoral artery for access if there are no issues with vessel caliber or anatomical contraindications and the device is likely to be in place for less than 72 h or it is being placed for an emergent indication. There may be significant anatomical variability of the aortic arch and great vessels which may affect access and device placement in the left ventricle, while the less variable iliofemoral arterial system is less likely to affect device delivery once traversed successfully with a guidewire. Furthermore, to prevent trauma to the brachial plexus, axillary access should be performed proximal to where the nerve bundles commonly course over the axillary artery. The ideal location is between the thoracoacromial and lateral thoracic arteries (Fig. 1). The axillary segment between these two branches is extra-thoracic and proximal to the crossing of the branches of the brachial plexus. The steps for placement of axillary MCS devices are summarized in Table 4. Once placed and secured, frequent radiographic and echocardiographic monitoring for placement is essential to optimize device performance and outcomes.

Device Removal: Multiple arterial closure devices are available for MCS access site closure immediately after supported PCI, however the optimal method of device removal for prolonged MCS support has yet to be defined. Depending on body habitus and vascular characteristics, an IABP access sheath may safely be removed with the application of manual pressure for hemostasis. No randomized data is available regarding the time to hemostasis, however, the minimum time of manual pressure should be three minutes per access sheath French size, with longer times for larger sheaths and consideration given to anticoagulation status. In larger patients or patients with calcified vessels or suboptimal arteriotomy locations (above or below the level of the femoral head or in one of the distal branches

of the common femoral artery), maintaining vascular control and appropriate pressure for safe, successful hemostasis may be difficult. In these scenarios, removal of a sheath in the catheterization laboratory may be performed with balloon-assisted closure through a secondary arterial access site. Impella access sheaths are significantly larger and while a device may be removed and manual hemostasis attempted at the bedside, the potential for bleeding complications is higher. While both devices may be removed while maintaining wire access followed by immediate sheath replacement, the potential complications of prolonged large bore access remain as does the need for eventual removal and hemostasis. Furthermore, details regarding the access procedure, including the site and iliofemoral vascular anatomy, are often unknown after inter-hospital transfer. Therefore, removal in the catheterization laboratory allows for immediate balloon-assisted hemostasis and angiographic assessment. Removal of an axillary access sheath poses greater risk due to anatomical considerations and unfamiliarity in obtaining manual hemostasis over the pectoralis muscles and against the humeral head. Therefore, sheath removal should routinely be performed in the catheterization laboratory with secondary access and balloon assisted tamponade. The standard steps of MCS device removal in the catheterization laboratory are summarized in Tables 5 and 6.

If the preclose method with the Perclose Proglide system (Abbott Vascular; Lake Park, Illinois) is performed and the MCS device is not removed after supported PCI or the preclose method is used routinely with MCS device implantation, the sutures may be used to obtain hemostasis at a later date. However, the externalized suture ends must be secured and covered in a sterile fashion. The post-close technique, in which the Impella access sheath is closed using the Perclose system, allows for safe and successful closure after device removal without requiring preclosure at the time of placement. First described in 2019, the technique involves access site preservation followed by the sequential deployment of two Perclose devices [44] and summarized in Table 7. When performing vascular closure in a scenario remote from device placement, there is a theoretical increased risk of infection. Therefore, meticulous preparation of the patient, access sheath, and MCS device is warranted to mitigate this risk and all options of device removal and arteriotomy closure should be considered. The TandemHeart device is explanted by removal of the cannulae followed by primary vascular repair.

Choosing a Percutaneous Support Device: Clinical Decision-Making

In determining the level of support to provide a patient with acute myocardial infarction complicated by cardiogenic shock, first consider potential contraindications, including peripheral vascular disease, intra-cardiac or intra-vascular thrombus, valvulopathies, infectious status, and coagulopathy. If the patient is in refractory shock on presentation the preferred method of support is placement of an Impella CP device due to the level of support that may be provided.

Table 4 Axillary access for percutaneous mechanical circulatory support

Percutaneous Access of the Axillary Artery for MCS	
1. Mark the delto-pectoral groove and, using fluoroscopy, evaluate the location of the humeral head and mark its location	
2. If the anatomy permits, obtain femoral or ipsilateral radial access. Place a small radio-opaque marker on the skin at the proposed puncture site and perform angiography to define the arterial anatomy relative to the skin marks. Place an 0.035 inch wire in the axillary artery across the proposed arteriotomy site (this may be used to assist in access and for bailout in the case of immediate bleeding complications)	
3. Plan for access between the thoracoacromial and lateral thoracic arterial branches (Fig. 1). Using ultrasound, identify the axillary artery (the 0,035 inch wire should be identifiable). Using a micropuncture system, obtain axillary artery access in the standard ultrasound-guided fashion. Perform angiography to identify the arteriotomy; if distal to the lateral thoracic artery, consider manual pressure and repeating the attempt at access in order to decrease the risk of damage to the brachial plexus	
4. Advance a standard J-wire along with a 5F JR4 catheter into the descending aorta; exchange the J-wire for a stiff wire such as an Amplatz wire	
5. Remove the micro-puncture sheath, dilate the tract, and advance the MCS access sheath over the stiff wire. Remove the wire from the non-axillary access site placed in step 2	
IABP	Impella
6. Exchange the stiff wire for the standard balloon pump guidewire and insert the IABP such that the proximal marker is at the level of the carina	6. Advance a standard J-wire along with a 5F JR4 catheter through the Impella sheath into the ascending aorta; exchange the JR4 catheter for a pigtai catheter, and cross into the left ventricle using this catheter and the J-wire,
7. Ensure normal function of the IABP and secure the catheter along the arm or the thorax to minimize kinking of the system at the level of the sheath	7. Continue Impella placement and advancement of the re-positioning cheath in the standard fashion. Subclavian tortuosity and a distal take-off of the left subclavian artery may complicate placement of the Impella catheter, Care must be taken to maintain guidewire access to the left ventricle

If angiography is performed first and the territory at risk is large, including a large anterior myocardial infarction or in the presence of severe multivessel disease, Impella placement is likely to be the optimal MCS device. Pilot data from the ongoing UNLOAD trial has shown that delaying revascularization while unloading the left ventricle with the Impella CP device did not impact MACE at 30 days [45]; the completion of the trial and long-term data is forthcoming. In patients with persistent shock despite primary PCI, who are responding to vasoactive agents and not exhibiting signs of vasoplegia, placement of an IABP will often provide adequate support and allow for de-escalation of pharmacologic support. Measurement of left ventricular end diastolic pressure and placement of a pulmonary artery catheter in the catheterization laboratory is almost universally performed and will be helpful in guiding subsequent therapy after MCS placement.

As the field of interventional cardiology continues to accept higher risk patients for PCI, the use of MCS is becoming increasingly performed. When choosing a device, a number of key factors play a role. Potential device-specific

Table 5 Balloon assisted femoral arteriotomy closure

Balloon assisted closure during femoral MCS device removal	
1. Obtain secondary femoral or radial arterial access in a vessel appropriately sized to accommodate a balloon that may occlude flow across the MCS arteriotomy site. Systemic anticoagulation should be discontinued	
Femoral secondary access site	Radial Secondary access site
2. Access the proximal iliac system above the MCS access with an appropriate sheath and perform angiography. Ideally, place a stiff guidewire distal to the closure site	2. Access the proximal iliac system above the MCS access with a Terumo R2P sheath (available lengths 119150 cm; Terumo Medical, Tokyo, Japan) and perform angiography. Ideally, place a stiff guidewire distal to the closure site
3. In the external iliac artery, place a balloon > 40 mm in length, sized just under 1:1 to the vessel caliber	3. In the external iliac artery, place a balloon > 40 mm in length on a long shaft, sized just under 1:1 to the vessel caliber
4. Remove the device and the sheath allowing for a 1–2 s of bleed back. Apply manual pressure at the site while slowly inflating the balloon to the minimum atmospheres necessary for complete inflation	
5. Release manual pressure and assess for bleeding, which should be minimal. Gentle manual pressure may then be reapplied as necessary	
G, After five minutes, deflate the balloon and apply five minutes of occlusive manual pressure. Alternating inflations and pressure may then be performed as necessary until hemostasis has been achieved. Drain and flush the delivery sheath/catheter regularly	
7. Drain and flush the delivery sheath/catheter. Perform angiography to assess for hemostasis and possible complication. If a peripheral complication has occurred treat accordingly (thrombus aspiration, angioplasty for flow-limiting dissection, etc.). Standard closure or manual pressure of the secondary access site may be performed immediately or once MCS access site hemostasis is confirmed	
Note: If a diagnostic catheter with an 0.035 inch lumen is being used, an 0.018 inch guidewire will need to be used if angiography is performed after wire placement. If a sheath or coronary guide catheter is being used, angiography may be performed with an 0.035 inch guidewire in place. Ensure the delivery sheaths and catheters will accommodate the balloon size that will be required for hemostasis	

contraindications and bleeding risk must be considered. In the presence of severe left ventricular systolic dysfunction when PCI is to be performed on the last remaining vessel, when multivessel PCI is to be performed, or significant atherectomy is required in the setting of multivessel disease, support with an Impella device is normally preferred. Anatomical features, the severity of the left ventricular dysfunction, the amount of revascularization required, and the presence of pulmonary hypertension are often used to determine whether an Impella 2.5 or CP will be used. In patients deemed to be at the highest risk, such as those with multivessel disease and very poor systolic function, TandemHeart provides the highest level of support, although it is the most complex to place and often requires surgical removal. In lower risk settings, such as left main or multivessel PCI with severe aortic stenosis and normal systolic function, or in single vessel

Table 6 Balloon assisted axillary arteriotomy closure

Balloon assisted closure during axillary MCS device removal	
1. Obtain secondary femoral or radial arterial access in a vessel appropriately sized to accommodate a balloon that may occlude flow across the MCS arteriotomy site	
Femoral secondary access site	Radial secondary access site
2. Access the proximal subclavian artery with with an appropriate catheter or sheath and perform angiography. Ideally place a stiff guidewire distal to the closure site	2. Navigate a guidewire into the descending aorta and place an appropriate catheter just before the access site. Perform angiography. In most cases, the radial artery will not accommodate a catheter large enough to deliver an appropriately sized balloon and will need to be removed. The current Terumo Destination sheaths do not have a hydrophilic coating along the entire sheath and are not recommended
3. In the subclavian artery, just distal to the vertebral artery, place a balloon >40 mm in length, sized just under 1:1 to the vessel caliber. If a long sheath or large caliber guide catheter is not placed in the subclavian artery, it will have to be removed before balloon advancement	3. In the subclavian artery, just before the vertebral artery, place a balloon >40 mm in length, sized just under 1:1 to the vessel caliber. If the balloon will not cross the MCS access site it will have to be advanced over the wire immediately after device removal
4. Remove the device and the sheath allowing for a 1–2 s of bleed back. Apply manual pressure at the site while slowly inflating the balloon to the minimum atmospheres necessary for complete inflation	
5. Release manual pressure and assess for bleeding, which should be minimal. Gentle manual pressure may then be reapplied as necessary. When the delivery sheath/catheter position may be maintained from the femoral approach, angiography will allow for confirmation of vertebral artery flow	
6. After five minutes, deflate the balloon and apply five minutes of occlusive manual pressure. Alternating inflations and pressure may then be performed as necessary until hemostasis has been achieved. Drain and flush the delivery sheath/catheter regularly	
7. Replace the delivery sheath/catheter if necessary. Perform angiography to assess for hemostasis and possible complication. If a peripheral complication has occurred treat accordingly (thrombus aspiration, angioplasty for flow-limiting dissection, etc.). Standard closure or manual pressure of the secondary access site may be performed immediately or once MCS access site hemostasis is confirmed	
Note: If a diagnostic catheter with an 0.035 inch lumen is being used, an 0.018 inch guidewire will need to be used if angiography is performed after wire placement. If a sheath or coronary guide catheter is being used, angiography may be performed with an 0.035 inch guidewire in place. Ensure the delivery sheaths and catheters will accommodate the balloon size that will be required for hemostasis	

disease requiring atherectomy in the setting of moderately reduced systolic function, support with an IABP will likely be adequate. Regardless of the chosen level of support, proper pre-procedure evaluation and planning will minimize the risk of complications and increase the chances of optimal outcomes.

Table 7 Arteriotomy post closure technique

Post closure technique for Impella device removal
1. Insert a stiff 0.035 inch guidewire through the Impella repositioning sheath side-port. A > 145 cm wire is recommended to prevent inadvertent wire removal
2. With no or minimal device flow, retract the Impella catheter so the outflow port remains at least 5 cm above the distal end of the repositioning sheath without retracting the guidewire
3. After ensuring that there is no device flow and that the distal end of the wire is well above the distal end of the Impella catheter, retract the catheter and sheath together while maintaining wire access. If there is a sufficient length of wire distal to the Impella catheter, the wire may be retracted simultaneously with the catheter and sheath; otherwise removal may be performed in a standard 'walking-out' fashion
4. Once the catheter and sheath exit the skin puncture site, the wire is secured, and a 14F sheath is placed
5. After removing the sheath dilator, a second 0.035 inch guidewire may be placed, the 14F sheath removed, and two 8F sheaths placed, one over each wire. If this is not hemostatic, mild pressure may be placed
6. One sheath is then removed and one Perclose may be placed over the bare guidewire and deployed
7. The remaining sheath is then removed and a second Perclose placed and deployed
8. If significant extravasation persists, a third Perclose may be placed or a sheath may be re-advanced over the wire for balloon-assisted closure

Conclusion

The third vignette highlights the creativity that may be required for the most complex cases. The simultaneous use of multiple support devices may be performed safely in select scenarios as a bridge to recovery, durable VAD placement, heart transplantation, or other therapies. With the evolution of contemporary percutaneous and surgical procedures, early hemodynamic improvement is critical in stabilizing the severely decompensated patient to create an optimal scenario for future therapeutic interventions.

Percutaneous hemodynamic support may be considered in any case of cardiogenic shock when inotropic agents are required. The level and duration of support is dependent upon the clinical picture and often cannot be predicted based on the initial presentation. Larger devices that provide a higher level of support carry an increased risk profile, and prolonged use increases the amount of time that a complication may occur. On the contrary, inadequate left ventricular unloading and organ perfusion will not allow for reversal of the shock state and the delay in stabilization may not allow for a meaningful recovery. Future iterations of support devices will likely include smaller caliber catheters with functional designs that decrease the risk of red blood cell injury and thrombus formation. It is essential that medical centers develop either local or referral pathways for advanced care, and the impetus is on the heart failure and interventional cardiology communities to continue to expand the options for all patients, especially the sickest of the sick.

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Extra Corporeal Membrane Oxygenation

Kimberly Hong, Scott Chicotka, and Travis Pollema

Case

A 32-year-old female with World Health Organization (WHO) group 1 pulmonary arterial hypertension (PAH), presented to the hospital with right lower lobe pneumonia. Her echocardiogram demonstrated severe PAH with a pulmonary artery (PA) systolic pressure of 110 mmHg, an enlarged right ventricle with reduced function, a patent foramen ovale (PFO) with left to right shunt, and mild mitral regurgitation. She was initially trialed on high flow oxygen with a non-rebreather, however, she remained persistently hypoxic with a SaO_2 of 80%. The decision was made to cannulate for veno-venous (VV) ECMO as a bridge to recovery and possible bridge to transplant. Over the next 5 days her SaO_2 was maintained above 90% on VV ECMO and high flow oxygen, however she experienced multiple anxiety attacks with significant desaturation. Additionally, there was not enough of a right-to-left shunt to provide oxygenated left ventricular preload nor offload the right ventricle and augment forward flow through the pulmonary circulation. ECMO flow was increased to 5 L/min but this did not address her right ventricular failure. She began to demonstrate evidence of worsening end organ function, rising NTpro BNP and creatinine levels, consistent with worsening RV failure. Her right ventricular function continued to deteriorate despite an increase in epoprostanil. It was evident that she would require RV support, and the decision was made to convert to veno-arterial (VA) ECMO. Femoral-femoral VA ECMO was

K. Hong · T. Pollema
Division of Cardiovascular Medicine, University of California, San Diego, USA

S. Chicotka
Division of Cardiovascular and Thoracic Surgery, University of California, San Diego, USA

T. Pollema (✉)
University of California San Diego Health System, 9300 Campus Point Drive #7892, La Jolla, CA 92037, USA
e-mail: tpollema@health.ucsd.edu

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established with adequate flow approximately 3.5 L/min, and she demonstrated a marked improvement in hemodynamic status with near immediate improvement in urine output and decrease in creatinine. The following day, however, she began to experience persistent desaturation to around SaO_2 80%.

Introduction

Depending on cannulation strategy, extra corporeal membrane oxygenation (ECMO), is instituted for life threatening respiratory and/or cardiac failure, and has progressed remarkably over recent years [1]. As a temporary support device, ECMO is often used while awaiting recovery of end organ function, as support for intrathoracic surgeries in unstable patients, or as a bridge to transplantation [2]. In recent years, ECMO utilization has increased, with annual ECMO deployment exceeding 12,000 units since 2017 [3]. This is due in part to ECMO being the only temporary mechanical support device that can offer full cardiopulmonary support, as well as technological improvements in the device that have simplified its implementation. Even though ECMO use has become increasingly widespread, the morbidity and mortality associated with it remains high. This is driven largely by the acuity of patients who need full cardiopulmonary support, as well as the vascular, thrombotic and infection risks associated with the institution and maintenance of ECMO Itself. The purpose of this chapter is to describe patient selection criteria, specifically indications and contraindications, as well as, anticipated complications and management strategies.

Mechanism of ECMO Support

As a form of cardio-pulmonary life support, blood is drained from the venous system, circulated extracorporeally using a mechanical pump into an oxygenator and returned to the body either via the venous (VV ECMO) or arterial system (VA ECMO). The former provides support for pulmonary failure, while the latter provides cardiopulmonary support by bypassing the heart and lungs entirely. An oxygenator placed in series to the mechanical pump saturates hemoglobin with oxygen while carbon dioxide is removed. Both oxygenation and CO_2 removal can be controlled by the adjustment of the flow rate and countercurrent gas flow, respectively [4].

Modes of Vascular Access [5]

Indication, degree of intrinsic cardiac function and vascular access will determine the cannulation strategy utilized. An understanding of cannulation options and access is important for troubleshooting complications as well as for

confirming optimal cannula placement via x-ray, fluoroscopy and echocardiogram. An important distinction between VA-ECMO compared to VV-ECMO is that while VA-ECMO provides a parallel circuit that bypasses the heart and lungs, VV-ECMO provides a circuit that lies in series with the heart and lungs. Thus, while differential hypoxemia can occur with VA-ECMO, VV-ECMO will provide the same oxygenation to all organs.

In VV-ECMO, the most common cannulation strategy is with two cannulas. The venous return cannula is placed via the right internal jugular to the SVC-RA junction or RA directly and the venous drainage cannula is placed via the femoral vein to the IVC-RA junction. Alternatively, there is also a single cannula strategy which utilizes a dual lumen cannula placed via the right internal jugular. This dual lumen cannula drains blood from the IVC and SVC through distal and proximal ports respectively and returns oxygenated blood via a second lumen towards the tricuspid valve. Unlike, VA-ECMO which involves cannulation of both the venous and arterial systems, the VV-ECMO circuit is contained in the venous system alone. Because of this, there is a risk that blood will recirculate if the cannulas in the dual cannula strategy are in close proximity to one another.

In VA-ECMO, cannulation can be obtained centrally (blood drained directly from the right atrium and returned to the proximal ascending aorta) or peripherally (blood drained from the proximal femoral or jugular vein and returned to the carotid, axillary, or femoral artery) [6]. With central cannulation, because the blood is returned to the ascending aorta, intrinsic cardiac and lung function will not impact oxygenation or result in differential hypoxemia. Furthermore, because central cannulation requires an open approach, a direct apical or left atrial vent can be placed at the same time. Limitations with central cannulation are that an open approach is required, and patients' mobility is impacted due to aortic cannulation.

Patient Selection

The primary goals for both VV and VA-ECMO is restoration of tissue perfusion and avoidance of permanent end organ dysfunction. Indications for support can be divided into three broad categories: pulmonary, cardiac, or cardiopulmonary support [7] (see Tables 1 and 2).

As mentioned previously, mortality rates are high in patients requiring ECMO support, with just 60% of patients requiring VV-ECMO and 42% of patients requiring VA-ECMO surviving to discharge in the ELSO registry [8]. This is driven by the acuity of the patients requiring ECMO, as well as the risks for complications associated with device support which accrue with time on support. Appropriate patient selection, including exclusion of patients who have sustained irreversible end-organ damage and are unlikely to recover even with prolonged circulatory support, is very important to mitigating some of the complication risks. Table 3 lists both absolute and relative contraindications to ECMO.

Table 1 Indications for VA ECMO

Cardiogenic shock	Other causes
Acute coronary syndrome	Post-cardiotomy: inability to wean from cardiopulmonary bypass after cardiac surgery
Cardiac arrhythmic storm (refractory to other measures)	Post-heart transplant: primary graft failure after heart or heart–lung transplantation
Sepsis with profound cardiac depression	Chronic cardiomyopathy: as a bridge to longer term VAD support, or as a bridge to decision
Drug overdose/toxicity with profound cardiac depression	Periprocedural support for high-risk percutaneous cardiac interventions
Myocarditis	Bridge to transplant
Pulmonary embolism	
Isolated cardiac trauma	
Acute anaphylaxis	

Table 2 Indications for VV ECMO

Acute respiratory distress syndrome	Extracorporeal assistance to provide lung rest
Severe bacterial or viral pneumonia	Airway obstruction
Aspiration syndromes	Pulmonary contusion
Alveolar proteinosis	Smoke inhalation
Lung transplant	**Lung hyperinflation**
Primary graft failure after transplant	Status asthmaticus
Bridge to lung transplant	**Others**
Intraoperative circulatory support	Pulmonary hemorrhage or massive hemoptysis, congenital diaphragmatic hernia, meconium aspiration, smoke inhalation

Table 3 Contraindications to ECMO

Absolute: largely futile treatment without exit strategy	
Unrecoverable heart and not a candidate for transplant or destination therapy LVAD support	Disseminated malignancy
Known severe brain injury	Unwitnessed cardiac arrest
Prolonged CPR without adequate tissue perfusion	Unrepaired aortic dissection
Severe chronic organ dysfunction (emphysema, cirrhosis, renal failure)	Severe aortic regurgitation
Compliance (financial, cognitive, psychiatric, or social limitations in patient without social support	Peripheral vascular disease in peripheral VA ECMO
Relative: anticoagulation issues, advanced age, obesity	

Management Strategies and Troubleshooting

Although VA-ECMO offers near full cardiopulmonary support, the aforementioned complications with prolonged use limit its application long term. Patient survival after VA-ECMO is contingent on appropriate management while on support, to allow for end organ recovery and successful weaning or bridge to definitive therapies such as durable mechanical support or transplant. Below are common issues that are encountered by individuals on ECMO.

Hypotension

A common issue in individuals on ECMO is hypotension. This will manifest in both low mean arterial pressures readings, as well as "chatter" in the circuit, which occurs because the negative pressure from the rotational pump causes intermittent suction at the inflow cannula. Absent flows will not only cause blood pressure to fall, but also tissue trauma and turbulence which can worsen lysis of blood components and further exacerbate the body's inflammatory response to the circuit. Understanding that pump flow rate is dependent on the inflow cannula size as well as preload, i.e., the blood pool at the inflow cannula site (the right atrium or the inferior vena cava) is critical to troubleshooting hypotension. Intravascular volume depletion from blood or fluid loss, both sensible and insensible, as well as vasodilatory shock from either infection or an inflammatory response are common causes. In addition to volume resuscitating, management also includes reducing the pump flow rate or RPMs. Considerations of mechanical reasons for circulatory arrest need to be considered as well. Specifically, cardiac tamponade or arterial dissection, should also be ruled out. Because of this, imaging with either a surface or transesophageal echocardiogram are important diagnostics for ruling out cardiac tamponade and for confirming inflow and outflow cannula placements.

Differential Hypoxia—VA ECMO

In VA ECMO with peripheral cannulation, fully oxygenated blood from the femoral artery travels retrograde to the ascending aorta and mixes with deoxygenated blood coming from the left ventricle. It is thus important to understand that in peripheral cannulation, VA ECMO sends pressurized oxygenated blood retrograde and works against native cardiac output. The point within the aorta where native cardiac output mixes with ECMO blood flow is called the mixing point. In individuals with poor intrinsic cardiac function, there is minimal resistance to ECMO

flow, and oxygenated blood from the ECMO outflow cannula can travel over the aortic arch and supply oxygen to head vessels and coronaries. In this situation, the mixing point is proximal to brachiocepalic and carotid arteries.

In individuals with recovered cardiac function, but persistently poor lung function due to pulmonary edema, from elevated left sided filling pressures, pulmonary embolus, pneumonia or ARDS, deoxygenated blood will be ejected from the heart and result in a mixing point that is more distal. This is of concern because if deoxygenated blood resists ECMO flows, and the mixing point is distal to the brachiocephalic and carotids arteries, the brain will be perfused with deoxygenated blood. Specifically, the deoxygenated blood will perfuse the upper limbs, heart and brain, while oxygenated blood will perfuse the lower thoracic organs, abdominal viscera, and lower limbs. This phenomenon is known as Harlequin syndrome or North South syndrome. Resultantly, monitoring of the SaO_2 on the right hand with an arterial line is mandatory and can help establish the diagnosis, as well as initiate interventions to improve oxygenation and ventilation of the lungs including unloading the LV by concomitant use of Impella, IABP or a surgical left ventricular vent, which will be discussed later. Lastly, with central cannulation where the outflow cannula is placed into the ascending aorta, and Upper body VA ECMO (UBVA ECMO), ECMO support is provided to the head vessels and body with decreased competitive effect from native cardiac output, thereby eliminating the Harlequin effect.

Recirculation—VV ECMO

As mentioned previously, in VV ECMO, because the circuit is contained within the venous system, there is a risk for recirculation. This is where oxygenated blood from the outflow cannula is pulled back into the inflow cannula, resulting in 2 parallel circuits: 1—an oxygenated VV ECMO circuit and 2—the patient's deoxygenated intrinsic circulation. A low peripheral oxygenation saturation, a high SVO_2 on the circuit, or bright blood red blood in both the inflow and outflow circuits are suggestive of this. Determining cannula location via echocardiogram and volume status are important first steps to troubleshooting recirculation. Specifically, if the inflow and outflow cannulas are placed to closely together, or if the outflow cannula is not directed towards the tricuspid valve, there is a risk for higher recirculation fraction. Additionally, because there is always an amount of recirculated blood, increasing the total volume of blood can reduce the recirculation fraction.

LV Venting Strategies

In VA ECMO, particularly in cases where the indication for support is cardiogenic shock, daily evaluation of intrinsic cardiac function is important. Loss of aortic pulsatility implies that the aortic valve is not opening because the intrinsic

cardiac function is not enough to overcome the ECMO outflow pressure head. Increased left ventricular end diastolic pressure, resulting in LV distention, pulmonary edema and poor oxygenation of blood within the patient's intrinsic circulation will result. Additionally, if the left ventricle is not unloaded, stasis of blood occurs and thrombi can form within the left ventricle, placing the patient at risk for central and systemic embolization. Both invasive hemodynamic monitoring by a pulmonary artery catheter, as well as an arterial line are important for monitoring pulmonary capillary wedge pressure and arterial pulsatility, respectively. Echocardiogram can also be used for direct visualization of aortic valve opening and left ventricular function. Management includes balancing ECMO flow rates for adequate tissue perfusion and afterload and considering inotropic support. In cases where the left ventricle is not adequately unloaded even after titration of inotropes, vasodilators and/or ECMO parameters, then mechanical unloading needs to be considered. Specific cannulation strategies including left atrial drainage spliced into the venous return circuit is one strategy, as is direct left ventricular venting via a surgical approach. Other percutanous strategies include intra-aortic balloon pumps and Impella 2.5, CP and 5.0 devices. Of the percutaneous devices, the Impella is more effective at reducing left ventricular end diastolic pressure [9].

Complications

Although ECMO can improve survival to hospital discharge, it is associated with significant morbidity, with complication rates directly related to duration of support. A meta-analysis of 20 studies that included 1866 patients found bleeding to be one of the most common complications (40.8%), followed by requirement for dialysis (46%), significant infection (30.4%), limb ischemia (16.9%), and stroke (5.9%) [10]. In VA-ECMO, there are inherent risks associated with the deployment of this technology. Below we discuss the most common complications which can be stratified into the following categories: hematologic, vascular, neurologic and infectious.

Hematologic

Due to the mandatory contact between blood and non-endothelialized surfaces in the external circuit and oxygenator, anticoagulation is necessary in all individuals. As a result, patients on ECMO are at high risk for both bleeding and thrombotic complications [11].

Bleeding is the most frequent complication observed in critically ill patients supported by ECMO. In a retrospective study analyzing 149 ECMO runs (111 VA ECMO and 38 VV ECMO), 89 episodes (60%) were complicated by at least one bleeding event [12]. The most common bleeding complications include bleeding at ECMO cannulation sites (37%), hemothorax or cardiac tamponade (17%),

and intracranial hemorrhage occurred in 5 (2.2%) patients. As can be expected, patients with bleeding complications experienced worse survival (adjusted HR 2.17, 95% CI, 1.07–4.41, p = 0.03). Several factors may contribute to high risk bleeding including systemic anticoagulation, platelet dysfunction, shear stress causing hemolysis from the filter and centrifugal pump, blood loss in the device circuit, heparin induced thrombocytopenia, systemic inflammation, acquired von Willebrand syndrome, and coagulation and fibrinolysis activation. To avoid hematological complications, activated clotting time (ACT), activated partial thromboplastin time (aPTT), prothrombin time and platelet count should be monitored. In some instances, the use of thromboelastography (TEG) can assist in tailoring anticoagulation to each patient and allow reductions in transfusions of blood products. Target goals for aPTT is 50–75 s, anti-factor xa is 0.3–0.7 IU/ml, ACT is 180–220 s and platelets, which is controversial, 50,000–100,000/mm^3. In patients with heparin induced thrombocytopenia, anticoagulation can be accomplished using bivalirudin and argatroban, with an aPTT target of 50–60 s [13].

Thrombosis, similar to bleeding is a common complication, and can have devastating consequences depending on where it has occurred. The most common location for clots to form is within the oxygenator [11]. Although clot formation on the oxygenator can impact its function, patients are not at risk for embolic events because the oxygenator is a barrier between the clots and the arterial system. Clots that occur distal to the oxygenator within the pump and circuit, or within the heart, in patients with low intrinsic cardiac pulsatility, are at risk for systemic embolization. Daily visualization of the oxygenator and circuit, as well as monitoring of d-dimer levels, with acute rises predicting oxygenator failure, are critical to anticipating circuit exchanges [11].

Vascular

Many of the complications relate to the vascular access site, with femoral cannulation requiring surgical intervention in 20% of the cases [14]. Arterial cannulation during emergent cases can increase the risk of vessel injury. With the large size cannulas inserted and the hemodynamic instability of patients contributing to the already high risk of limb ischemia. A negative downstream effect of cannulation is distal ischemia which can lead to arterial thrombosis and gangrene. The most frequent vascular complications associated with ECMO insertion are lower extremity ischemia (16.9%), compartment syndrome (10.3%) and amputation (4.7%) [10]. Cannula size greater than 20 FR, female gender, lower body surface area, and peripheral arterial disease increase the risk of limb ischemia [15]. This complication can be mitigated by preemptively placing a small antegrade perfusion cannula in the proximal femoral artery to bypass the area of obstruction from the ECMO arterial cannula in those identified to be at high risk for limb ischemia (Fig. 1). In cases where this is not done, frequent monitoring of bilateral distal flow with doppler can identify those who will require subsequent antegrade cannulation.

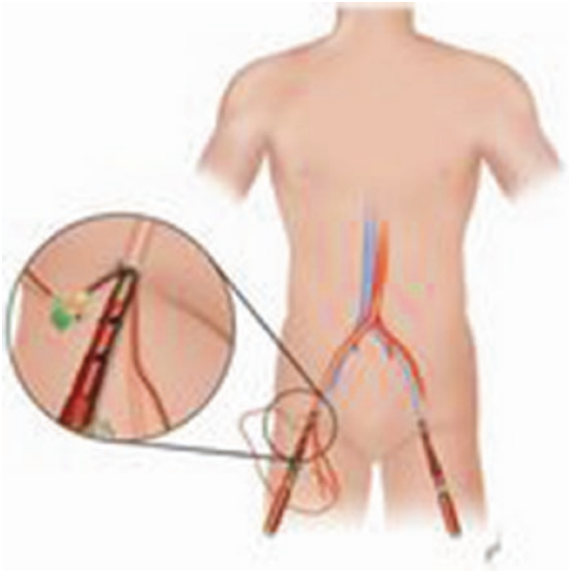

Fig. 1 Right common femoral artery cannulation with right superficial femoral artery antegrade sheath

Neurologic

Neurological complications are a common complication and range from cognitive impairments to peripheral neuropathies to intracranial ischemic and hemorrhagic events and lastly anoxic brain death. Based on data from meta-analyses, the combined rate for both ischemic and hemorrhagic strokes is reported to be 5.9–7.8% [16]. The occurrence of either ischemic or hemorrhagic stroke is a poor prognostic indicator with an almost fivefold increase in in-hospital mortality and remains the leading cause of death in patients supported by ECMO. Intracranial hemorrhage, in particular, is associated with a mortality rate of 89.5% [15]. Factors associated with intracranial hemorrhage include prolonged ECMO duration, antithrombotic therapy, coagulopathy and need for blood transfusions as well as renal failure. Pre-existing patient specific characteristics associated with intracranial hemorrhage include cardiac arrest before ECMO, lower body surface area and female gender [17].

Cerebral hypoxia can result in devastating consequences including cerebral edema, seizures and encephalopathy. While, circuit and intracardiac thrombi are a frequent cause of ischemic stroke, global ischemia can result from hypoperfusion due to vasoconstriction from rapid corrections of severe hypercapnia, systemic hypotension due to vasodilatory shock, or impaired cerebral autoregulation due to sedation. Factors predisposing individuals to intracranial bleeding include the systemic inflammatory response to the interfacing of blood with the ECMO circuit and the cytokines released, in conjunction with the activation of coagulation pathways. These factors result in both prothrombotic and coagulopathic states. Additionally, as blood circulates through the oxygenator, pump and circuit, blood

products including platelets, red blood cells and von Willebrand factor get lysed, predisposing individuals to anemia and bleeding [17].

Clinical diagnosis of neurological events in ECMO patients can be challenging, particularly because patients may require deep sedation and even paralysis. The use of computed tomography, EEG and transcranial doppler can be helpful in estimating extent and severity of brain injury. Lastly are biomarkers for neuronal injury including glial fibrillary acidic protein and neuron-specific enolase. In situations where there is clinical suspicion for neurologic injury, these biomarkers may be helpful in guiding decisions regarding additional imaging diagnostics [16].

Infection

Nosocomial infections pose a high risk for ECMO patients and more than 53% of patients will have some infection within 14 days of ECMO support. This high rate of infection is due to the invasiveness of the cannulas, other vascular catheters placed at the time of resuscitation, as well as the associated comorbidities that are typical of patients requiring ECMO support, including need for mechanical ventilation, continuous renal replacement therapy and high transfusion requirements. Blood stream infections are reported in 3–18% of patients, with lower respiratory tract infections being the most common source. Similar to strokes, infection is associated with an increase in mortality and is cited to be as high as 60% [13]. It is important to keep in mind that monitoring for infection may be confounded by the heat exchanger controlling body temperature and the concomitant presence of systemic inflammatory response syndrome in patients with acute coronary syndrome and cardiogenic shock. Biomarkers such as procalcitonin and trending C-reactive protein to detect the presence of bacterial and fungal infections in critically ill patients may be helpful in detecting infections early [18].

Conclusion

In our patient's case, she was experiencing the Harlequin effect and her hypoxemia was due to significant pulmonary edema and pneumonia with preserved LV function. This was managed by increasing ECMO flow to 3.8 L/min, intubation and mechanical ventilation, thereby increasing her inhaled O_2 content, and also diuresis to decrease pulmonary edema. This strategy worked as her right hand SaO_2 increased to 88–93% with these changes, well within acceptable ranges for patients supported on ECMO.

Her transplant workup continued but this configuration of intubation and femoral cannulation with low normal saturation left her immobile and increasingly deconditioned. Over the next 10 days she was slowly weaned from VA ECMO, and she eventually tolerated decannulation from ECMO support.

The above cases highlight many of the pitfalls and complications that can be encountered during veno-venous and veno-arterial ECMO. There are many ways to configure and re-configure a patient on ECMO in the setting of these problems. They often require a multi-faceted approach and willingness to change strategies based on underlying diagnoses and acute or unexpected changes in the patient's condition.

Key Points

- Underlying diagnoses are very important in successful ECMO configuration
- Complications of ECMO occur and necessitates a thorough troubleshooting process
- Changes in a patient's condition sometimes requires changes in ECMO strategy
- ECMO support can be utilized as a bridge to recovery, decision, transplant, or other procedures
- A multidisciplinary team is essential in the care of the ECMO patient.

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Section II
Chronic Device Therapy in the Advanced Heart Failure Patient

Section Editor: Hao A. Tran

Selection Criteria for Durable Mechanical Circulatory Support

Behram P. Mody and Eric D. Adler

Clinical Case

A 75-year-old male with long standing history of heart failure with a reduced ejection due to ischemic cardiomyopathy dependent on continuous intravenous milrinone presents to your clinic with progressively worsening dyspnea on minimal exertion. He is unable to perform his activities of daily living independently. Currently, he is taking high dose furosemide and only able to tolerate low dose lisinopril and spironolactone. His blood pressure is 95/80 mm Hg. His physical exam is remarkable for jugular venous pressure of 12 cm of water, bibasilar crackles, lukewarm extremities and bilateral 2+ pitting edema. His labs are remarkable for a N-terminal pro-brain natriuretic peptide of 10,000 pg/ml and a serum creatinine of 1.9 mg/dL (previously 1.2 one year ago). His most recent transthoracic echocardiogram reveals a left ventricular (LV) internal dimension in diastole of 7.2 cm, LV ejection fraction of 15%, a normal sized right ventricle with reduced systolic function, moderate mitral regurgitation and trivial aortic regurgitation. Interrogation of his biventricular implantable cardioverter defibrillator reveals 100% bi-ventricular pacing with 5 episodes of non-sustained ventricular tachycardia. He has had 3 hospitalizations for decompensated heart failure over the past year. You perform a right heart catheterization which is remarkable for elevated left and right intracardiac filling pressures, moderate post-capillary pulmonary hypertension and low cardiac output. Concerned for his progressively worsening decline on inotropes, you request an urgent referral for potential durable mechanical circulatory support.

B. P. Mody · E. D. Adler (✉)
University of California San Diego, San Diego, USA
e-mail: eradler@health.ucsd.edu

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Introduction

Mechanical circulatory support (MCS) is a well-established modality of restoring the circulation in a patient with severe heart failure or fatal arrythmias. By ensuring adequate cardiac output, durable MCS or a long-term left ventricular assist device (LVAD) can improve a patient's overall condition. Durable MCS can be utilized as a bridge-to-transplant (BTT), destination therapy (DT) or as bridge-to-decision (BTD). Regardless of the indication, the benefits of utilizing LVADs can be substantial with regards to rehabilitation, quality of life, and reversing cardiac cachexia and multiorgan failure. By optimizing hemodynamics, nutritional status and functional class with LVAD support, select patients may improve their candidacy for becoming recipients of a heart transplant and survival thereafter.

Currently the five general indications for MCS are the following:

1. Cardiogenic shock resulting from acute myocardial infarction
2. Post-cardiotomy myocardial dysfunction
3. Acute cardiac failure from myocarditis
4. Severe chronic heart failure (New York Heart Association Functional Class IIIb-IV), with or without fatal incessant arrhythmias not responding to maximum medical support and at high risk for 1-year mortality
5. Chronic inotrope dependence with evidence of end-organ dysfunction

Patients presenting with one of the above clinical criteria and not responding to maximum medical support, may benefit from short- or long-term MCS. The goal of this chapter is to provide an overview of the selection criteria for durable LVAD support.

Patient Selection

Patient selection for advance therapies is not as simple as checking boxes. It involves meeting stringent criteria and requires a detailed evaluation by a multidisciplinary team including a cardiothoracic surgeon, an advanced heart failure cardiologist, dietician, social worker and palliative care specialist. There are universally accepted criteria with regards to heart transplant listing and endorsed by multiple societies including the International Society for Heart and Lung Transplantation (ISHLT) and the American College of Cardiology, American Heart Association and Heart Failure Society of America (ACC/AHA/HFSA) [1]. Until recently, no validated selection criteria existed for LVAD implantation. In 2013, ISHLT published new guidelines for MCS including a section discussing candidate selection for LVAD support [2]. There are some similarities and clear distinctions between the criteria for cardiac transplantation and LVAD implantation which will be addressed below. In general, candidates for either therapy should have a severely reduced LV ejection fraction, New York Heart Association (NYHA) class III-IV

Table 1 Stages of HF and functional classification

ACC/AHA stages of HF		NYHA functional classification	
A	At high risk for HF but without structural heart disease or symptoms of HF		
B	Structural heart disease but without signs or symptoms of HF	**I**	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
C	Structural heart disease with prior or current symptoms of HF	**I**	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest
D	Refractory HF requiring specialized interventions	**IV**	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

ACC = American College of Cardiology; AHA = American Heart Association; NYHA = New York Heart Association; HF = heart failure [3]

heart failure (HF) symptoms (Table 1), be intolerant of guideline directed medical therapy and with a history of multiple hospitalizations for decompensated HF.

INTERMACS

An important consideration for patient selection is INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) classification. INTERMACS profiling subclassifies the severity of patients with advanced heart failure (NYHA Class III-IV) prior to LVAD implantation (Table 2) [4, 5]. As of the most recent analysis of the INTERMACS database, the largest category of patients receiving LVADs nationwide are patients in INTERMACS Profile 3 (stable but inotrope dependent) followed by Profile 2 (progressive decline on inotropes) and Profile 1 (critical cardiogenic shock) representing 38%, 33.7% and 15.9% of all implants, respectively [6]. LVAD implantation in INTERMACS Patient Profiles 1 and 2 have been associated with increased mortality as early as 3 months (Profile 1: HR 1.98, $p<0.0001$; Profile 2: HR 1.59, $p<0.0001$). Consequently, LVAD implantation is preferred in patients with Profile 3 or greater given better survival outcomes [7, 8].

Table 2 INTERMACS Profiles

Level	Description	Hemodynamic status	Time frame for intervention
1	Critical Cardiogenic Shock (Crashing and burning)	Life threatening hypotension and rapidly escalating inotropic pressor support, with critical organ hypoperfusion often confirmed by worsening acidosis and lactate levels	Within hours
2	Progressive decline (Sliding on inotropes)	Dependent on inotropic support and shows signs of steadily worsening nutrition, renal function, fluid retention, or other major status indicator. Can also be a patient with refractory volume overload, with evidence of impaired perfusion, in whom inotropic infusions cannot be maintained due to tachyarrhythmias, clinical ischemia, or other intolerance	Within days
3	Stable but inotrope dependent (Dependent stability)	Clinically stable on mild-moderate doses of intravenous inotropes (or has a temporary circulatory support device) after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal).	Weeks to months
4	Resting symptoms (Frequent flyer)	Tolerating home oral therapies but has frequent symptoms of congestion at rest or with activities of daily living	Weeks to months
5	Exertion intolerant (Housebound)	Comfortable at rest but unable to engage in any activity, usually housebound with no congestive symptoms	Variable urgency, dependent on organ function and nutritional status
6	Exertion limited (Walking wounded)	Comfortable at rest but able to do some mild activity but fatigue results within a few minutes of meaningful physical exertion	Variable urgency, dependent on organ function and nutritional status
7	Advanced New York Heart Association Functional Class 3	Clinically stable with reasonable level of comfortable activity. Usually can walk more than 1 block	Not indicated

INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support

Indications

As mentioned above, long-term MCS is typically indicated for patients with advanced heart failure who continue to clinically deteriorate despite optimal medical and/or cardiac resynchronization therapy. There are three groups of patients that benefit from long-term MCS (Fig. 1). The first group consists of patients with end-stage heart failure who remain hemodynamically unstable despite maximally tolerated pharmacologic support with or without temporary MCS, and who met criteria for heart transplantation. These patients undergo LVAD implantation as a "bridge to transplant." The second group of patients are similar to the prior but are not transplant candidates. Consequently, these patients receive an LVAD as "destination therapy." Similar to the prior two, the last group of patients present in cardiogenic shock however candidacy for cardiac transplantation is not yet determined. The indication for durable MCS in this group of patients is as a "bridge to decision."

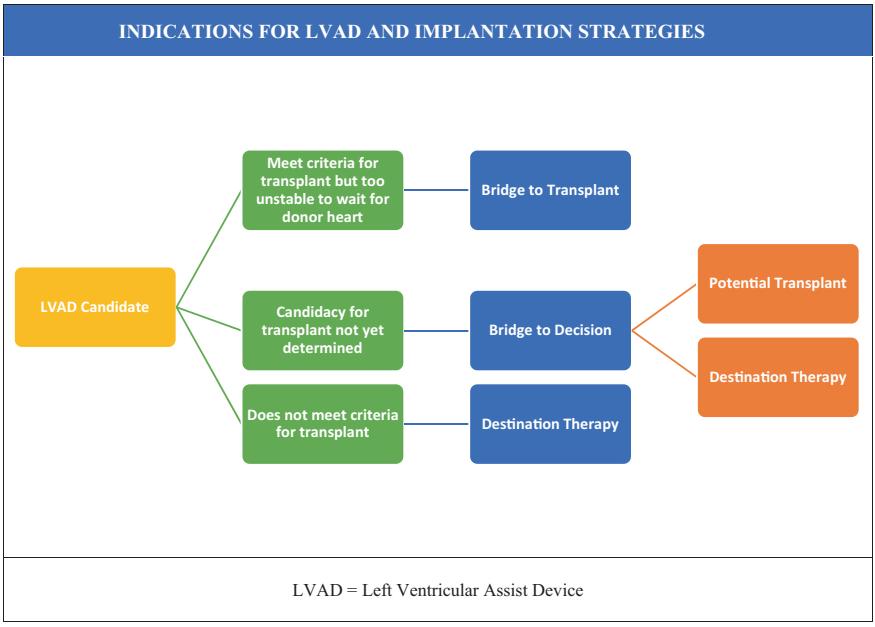

Fig. 1 Indications for LVAD and implantation strategies

Patients who receive an LVAD as BTT should qualify for cardiac transplantation. Our current practice is applying the following criteria for BTT but not limited to those only:

1. Suitable candidate for cardiac transplantation
2. NYHA Functional Class IV heart failure symptoms
3. Imminent risk of death before donor heart availability despite maximal medical support
4. Absence of irreversible liver or renal failure, though exceptions may be made in those being considered for multi-organ transplantation
5. Absence of fixed pulmonary hypertension
6. Adequate psychological criteria and external psychosocial support for transplantation and for possible prolonged LVAD support
7. General hemodynamic data: cardiac index $\leq$2.2 L/min/m^2, pulmonary capillary wedge pressure $\geq$20 mm Hg despite appropriate pharmacologic management (i.e. vasoactive and/or inotropes)
8. Acceptable right heart function assessed by echocardiogram and hemodynamics. If there is an evidence of severe right heart dysfunction, a patient may be evaluated for biventricular assist device support (BiVAD) in bridge to transplant patients
9. Left ventricular systolic function unrecoverable or unlikely to recover without device support
10. Chronic inotrope dependence with 1-year high risk mortality
11. Patient size (body surface area) to accommodate a device:

    a. HeartMate II system $\geq$1.5 m^2
    b. HeartMate 3 system >1.2 m^2
    c. Syncardia TAH: $\geq$1.7 m^2
    d. Heartware HVAD: $\geq$1.0 m^2

Criteria for implantation of a DT device are based on the current requirements from the Center for Medicare Services.

1. Not a candidate for heart transplantation
2. NYHA Functional Class IV symptoms for at least 90 days
3. Life expectancy less than 2 years and meet <u>all</u> the following conditions:

    a. Symptoms have failed to respond to optimal medical management, including beta-blockers, and angiotensin converting enzyme inhibitors (if tolerated) for at least 45 of the last 60 days
    b. Has a LV ejection fraction <25%
    c. Functional limitation with a peak oxygen consumption of $\leq$14 ml/kg/min; or the patient has a continued need for intravenous inotropic therapy owing to symptomatic hypotension, decreasing renal function, or worsening pulmonary congestion
    d. Appropriate body size to support the VAD implantation

Furthermore, clinically perceived frailty, history of non-adherence to medical therapies, and social factors are deemed relative contraindications for LVAD support (Fig. 2).

General Considerations

Age is taken into great consideration when selecting patients for advance therapies especially for cardiac transplantation. Similar to almost any intervention in medicine, age is inversely related to survival post-LVAD implantation [6, 9]. As per the latest annual INTERMACS report, patients greater than 65 years of age are at a high risk with regards to early (less than 3 months) and late mortality (HR 1.41, $p<0.0001$; HR 1.16, $p<0.0001$) [6]. Most programs typically will consider transplantation in patients 70 years or younger; therefore, patients who receiving an LVAD as BTT strategy would typically need to be in this age strata [1]. However, advanced age does not remain an absolute contraindication for LVAD implantation especially those being selected for DT. LVAD implantation in patients 70 years of age or greater have similar outcomes specifically good functional recovery, survival and quality of life at 2 years compared to those less than the age of 70 [10].

Body surface area (BSA) is an important factor to evaluate prior to placing a durable LVAD. Historically, BSA cutoff for LVAD support was $\geq 1.5\ m^2$ putting women and children at a disadvantage. As a consequence of their lower utilization of LVADs, this population had a high waitlist mortality [11, 12]. Our current

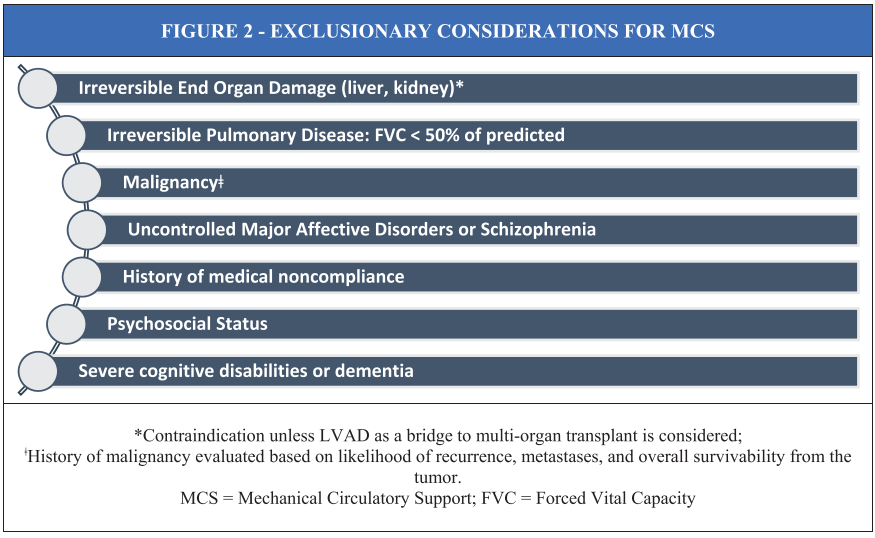

Fig. 2 Exclusionary considerations for MCS

generation of LVADs are small, continuous flow pumps which permit a BSA as low as 1.0 m^2. As per a recent retrospective analysis of the INTERMACS registry, smaller patients (BSA $\leq$ 1.5 m^2) who receive an LVAD tend to be female, of Hispanic origins, and on intravenous inotropes [13]. They have more perioperative bleeding, driveline infections while exhibiting lower rates of right ventricular failure and renal dysfunction compared to larger patients (BSA $\geq$ 1.5 m^2). Most importantly, there are no differences with overall survival.

Cardiovascular Considerations

Most programs nationwide implant durable LVADs in patients with dilated LV with reduced ejection fractions (<35%). Dilated LVs are preferred for LVAD implantation as they can easily facilitate placement of the inflow cannula along the long axis and avoid the LV free wall and interventricular septum. However, having a preserved LV ejection fraction is not an absolute contraindication. LVAD implantation is feasible in patients with end-stage restrictive cardiomyopathies (RCM) such as hypertrophic cardiomyopathy, infiltrative heart disease, or chemotherapy/radiation-induced cardiomyopathy. Patients with RCM typically have impaired hemodynamics secondary to small LV dimensions, low stroke volume and significant diastolic dysfunction. Consequently, medical management can be challenging and thus have an overall poor prognosis [14, 15]. One of the largest studies of patients with end-stage RCM who have received LVAD therapy noted that implantation was associated with an improved survival compared to medical therapy regardless of the etiology of RCM [16]. Furthermore, the study identified that patients with end-stage RCM who have LV end-diastolic diameters of $\leq$46 mm had reduced mean survival times (112 versus 678 days, $p < 0.01$) compared to those >46 mm. Thus, LVAD implantation could be a therapeutic option in patients with end-stage RCM with large LV dimensions.

Valvular heart disease can also be a challenge when implanting an LVAD for various reasons. LV unloading by an LVAD can impair aortic valve (AV) opening and decrease leaflet opening time during systole by increasing the transvalvular pressure (aortic pressure—LV pressure) [17]. As a consequence of disuse, perivalvular thrombus generation can occur as well as deterioration and fusion of the AV leaflets. The result of such pathology either could lead to aortic stenosis (AS) or aortic insufficiency (AI) if there is retraction of the leaflets and a central orifice were to be generated. Thus, pre-implant aortic insufficiency could theoretically worsen and result in worsening heart failure as blood would be travelling in a closed loop without truly unloading the LV. Historically in this scenario, bioprosthetic aortic valves were being co-implanted along with LVADs however this additional procedure typically required increasing the duration of cardioplegic arrest, increased the long term risk of prosthetic valve thrombosis and mortality [18]. In our current era, suture repair of the AV for moderate to severe native AI has been adopted to reduce the potential risk of further

worsening AI [2]. Pre-existing functioning bioprosthetic aortic valves do not require removal or replacement at the time of implant [2]. However, patients with mechanical aortic valves may require replacement with a biologic valve or be surgically closed. Despite patients being on full anticoagulation, mechanical aortic valves pose a thromboembolic risk as blood stasis due to an inactive valve or intermittently opening can lead to thrombus formation followed by potential embolization.

Secondary tricuspid valve regurgitation (TR) can develop as a result of biventricular dilation and failure. Right ventricular (RV) failure, an immediate postoperative complication with LVAD implantation which will be discussed below in further detail, can worsen TR. RV failure is usually multifactorial due to limited flow across the pulmonary vasculature (high RV afterload), aggressive perioperative volume resuscitation (worsening RV dilation and TR), and results in a leftward shift of the interventricular septum (restriction of tricuspid valve leaflets). Currently there is no contraindication for implantation of a durable LVAD in the setting of significant TR but further studies are needed to assess the benefit of concomitant tricuspid valve replacement or intervention. Functional mitral regurgitation typically improves with LV unloading by an LVAD and thus is not of concern prior to implantation.

RV Failure

RV failure is one of the leading causes of morbidity and mortality post-LVAD implantation [19, 20]. Not only can it occur immediately post-operatively but can even occur at a later time (i.e. post-discharge after index hospitalization). In general, RV function is dictated by preload, afterload, contractility, ventricular interdependence and heart rhythm [21]. LV dysfunction can essentially lead to RV dilation and dysfunction over time as a consequence of high RV afterload. Chronically elevated pulmonary capillary wedge (PCW) pressures can result in remodeling of the pulmonary vasculature and eventually post-capillary pulmonary hypertension [22]. This increase in RV afterload leads to RV dilation with potentially worsening TR and hepatic congestion. After LVAD placement, greater unloading of the LV shifts the interventricular septum to the left and provides increased venous return to a dilated and dysfunctional RV. This functionally impaired chamber leads to a decline in RV stroke volume and cardiac output. As a result, LV preload suffers leading to a reduction in LVAD flow and decreased end-organ perfusion.

Assessment of RV function is typically performed by various cardiac imaging modalities (echocardiography, cardiac computed tomography and magnetic resonance imaging) and invasive hemodynamics with a Swan Ganz catheter. Hemodynamic parameters of utmost importance in predicting RV failure include central venous pressure to pulmonary capillary wedge pressure ratio, pulmonary artery pulsatility index, RV stroke work index, and pulmonary vascular resistance

[19, 23]. Abnormal RV hemodynamics should prompt optimization pre-operatively with diuretics, inotropes, pulmonary vasodilators and temporary MCS with the goal to improve end-organ perfusion. It is important to note, RV function can be overestimated in the setting of volume overload or underestimated while on inotropes or temporary MCS. Therefore, it is important to repeat hemodynamic assessment of the RV after a patient has been optimized from a volume standpoint and off RV inotropy.

Echocardiography is great tool to objectively and subjectively characterize RV function. However, there are limitations when assessing RV function with conventional two dimensional (2D) or Doppler echocardiography mainly because of the retrosternal position of the RV and intra-observer variability. In addition, methods evaluating RV dysfunction have been inconsistent, in part due to differing definitions of RV dysfunction and lack of reproducible quantitative measurement analyses. Interestingly, RV function with 2D strain can provide a better assessment of global function of the RV more than tricuspid annular plane systolic excursion (TAPSE) or tricuspid peak systolic annular velocity (S') and can be obtained independently from the load-status or Doppler angle. In addition, strain imaging has been known to detect subclinical deterioration of the myocardium without abnormalities in 2D or Doppler images being noted. Further research with this novel technique is being conducted in the advanced heart failure population. Recently, a few studies have shown that greater (more negative) pre-operative RV longitudinal strain has been associated with RV failure post-LVAD implantation [27, 28].

Risk scores have been developed for predicting RV failure and potentially the need for RV assist device support however have limitations as they are derived from retrospective single center data compiled from a heterogenous LVAD population (pulsatile vs. continuous flow) with different indications (BTT vs DT) [24, 29]. A recent meta-analysis evaluated 36 primarily single center case control studies to identify predictors of RVF (within 2 weeks of implant) after LVAD implantation [28]. The findings of this study revealed multiple variables associated with the occurrence of RVF: use of supportive devices for end-organ dysfunction (mechanical ventilation, intra-aortic balloon pump and continuous renal replacement therapy), various biomarkers (NT-pro brain natriuretic peptide, international normalized ratio, white blood cell count), hemodynamic parameters (central venous pressure, RV stroke work index, mean arterial pressure) and echocardiographic assessment (qualitative RV function, RV/LV diameter ratio, RV free wall longitudinal systolic strain). Despite the inherent limitations of this meta-analysis, it is clear that RV failure is multifactorial and challenging to predict from a sea of parameters.

End-Organ Considerations

Renal Function

Many patients with end-stage HF tend to have renal dysfunction often attributed to cardiorenal syndrome from high central venous pressures or chronic low output state. A thorough assessment of renal function prior to LVAD implantation after patients are hemodynamically optimized includes serum creatinine, blood urea nitrogen and a 24-hour urine collection for creatinine clearance and proteinuria [2]. When selecting a patient with chronic kidney disease for LVAD support, the goal is to hopefully reverse renal impairment and prevent HD after LVAD implantation.

Renal insufficiency typically improves significantly with improvements in GFR usually within the first 30 days of LVAD implantation [30]. On the other hand, acute kidney injury can occur immediately post-operatively due to hemodynamic insults during the index surgery as well as from RV failure; some of these patients may even require temporary hemodialysis. The requirement for continuous venous-venous hemodialysis post-operatively has been shown to be associated with older age (mean 53 years of age), pre-operative intra-aortic balloon pump use, low serum total protein (mean 5.8 g/dL) and albumin (mean 1.2 g/dL) levels [31].

Pre-existing end stage renal failure requiring long term hemodialysis is a general contraindication to LVAD, as studies have shown extremely high mortality in this cohort [2]. In select patients on dialysis LVAD could be considered with the following caveats: volume shifts related to hemodialysis are usually not well tolerated in patients requiring LVAD support with concerns for frequent low flow alarms; the availability of dialysis centers which are trained to manage patients with LVADs are very limited throughout the nation; and, lack of pulsatility can make obtaining frequent blood pressures during hemodialysis sessions troublesome.

Hepatic Function

Patients with end-stage heart failure typically develop congestive hepatopathy, a consequence of increased systemic venous pressure and chronic ischemic injury from systemic hypoperfusion [32]. The syndrome of ischemic hepatitis due to low output results in centrilobular liver necrosis which leads to an elevation in serum aminotransferase levels. Preoperative hepatic dysfunction has been shown to be associated with poor survival and other perioperative complications including right heart failure, renal failure and bleeding events requiring blood transfusions [33, 34]. The Model for End-Stage Liver Disease (MELD) score was initially designed

to predict survival in patients undergoing the trans-jugular intrahepatic portosystemic shunt procedure [35, 36]. The MELD score contains the following parameters: serum creatinine, total bilirubin and international normalized ratio (INR). More recently, this prognostic score has been utilized in predicting mortality in patient undergoing LVAD implantation and heart transplantation [33, 37, 38].

Significant hepatic dysfunction (MELD score $\geq$ 12.6) is associated with poor 90-day and 1-year postoperative survival as well as a higher rates of neurologic events, and need for re-exploration due to early bleeding following LVAD implantation [39]. Generally, markers of liver function improve post-implantation regardless of baseline liver dysfunction suggesting the reversal of congestive hepatopathy. One of the components of the MELD score, the INR, may be inaccurate in the assessment of liver function while on LVAD support as patients are typically on warfarin which increases the INR. Another measure of hepatic dysfunction is the MELD-XI (MELD eXcluding INR) score which has been validated in predicting survival in patients with liver cirrhosis not on oral anticoagulation and correlates with the MELD score (Table 3) [40]. Utilizing the MELD-XI score to assess liver dysfunction is more appropriate in our current era of LVADs as almost all patients are on oral anticoagulation. In fact, both MELD and MELD-XI scores of <17 have been shown to be predictive of on-VAD survival, overall and post-OHT survival [34]. In addition, patients who have an elevated MELD or MELD-XI score ($\geq$17) may benefit from liver imaging and an evaluation by a hepatologist.

Pulmonary Function

In general, patients with severe obstructive or restrictive pulmonary disease are at risk of longer durations on mechanical support and prolonged intensive care unit stays following LVAD implantation. At baseline, patient with end-stage heart failure have poor baseline spirometry measurements. The abnormalities in seen in pre-operative pulmonary function tests (PFT) can be due to pleural effusions,

Table 3 MELD versus MELD-XI

MELD components	MELD-XI components
1. Serum Total Bilirubin (mg/dL) 2. Serum Creatinine (mg/dL) 3. INR	1. Serum Total Bilirubin (mg/dL) 2. Serum Creatinine (mg/dL)
Formula	
3.78 × Ln [bilirubin] + 11.2 × Ln [INR] + 9.57 × Ln[creatinine] +6.43	5.11 × Ln [bilirubin] + 11.76 × Ln [creatinine] +9.44

Model for End-Stage Liver Disease = MELD; MELD-XI = MELD eXcluding INR
INR = International Normalized Ratio; Ln = Logarithm

interstitial edema, reactive fibrosis, prior pulmonary infarctions and decreased lung volumes with compressive atelectasis [41]. If the forced vital capacity, forced expiratory volume at 1 s and carbon monoxide diffusing capacity are all less than 50% predicted, exclusion from LVAD should be considered. Also, if PFTs are abnormal, consider evaluation for obstructive sleep apnea. At present, there is no relationship between baseline PFTs and post-LVAD outcomes [42]. In fact, PFTs typically worsen post-LVAD implantation which is likely multifactorial due to restriction from shared intrathoracic space with an LVAD, respiratory muscle weakness, direct pulmonary injury from cardioplegia, mechanical changes due to sternotomy and manipulation of the lung.

Hematologic Function

Oral anticoagulants and anti-platelet agents are required in patients with LVADs to prevent pump thrombosis. The preferred anticoagulant is a vitamin K antagonist typically with a goal INR 2-3. Baseline thrombocytopenia and anemia are markers of hematologic function which are scrutinized during selection for durable LVAD support. It is important to assess and potentially resolve the reasons for these abnormalities prior to implantation to avoid future adverse events.

Preoperative thrombocytopenia (platelet count $\leq 148 \times 10^3/\mu L$) has been shown to be highly associated with 90-day in-hospital mortality post-implantation [43]. Prolonged anticoagulation with heparin is typically required in the immediate perioperative period. The use of cardiopulmonary bypass and systemic heparinization can make LVAD patients more prone to heparin-induced thrombocytopenia (HIT) [44]. Screening for antibodies to anti-platelet 4 complex, can prevent potential thrombosis and thrombocytopenia in patients with HIT by avoiding future heparin exposure and initiating an alternative anticoagulant in the perioperative period.

Bleeding post-LVAD implantation occurs more commonly as a result of acquired von Willebrand syndrome (aVWF). High shear stress from the LVAD results in proteolysis of large multimers of von Willebrand factor (VWF). The reduction of high-molecular VWF multimers leads to decreased function of VWF hence platelet dysfunction and bleeding. Bleeding typically occurs from mucosal surfaces (oral cavity, gastrointestinal tract) but can even result in menorrhagia, epistaxis, hematuria, and intracranial bleeds. In addition to aVWF, gastrointestinal (GI) bleeding can also be due to arteriovenous malformations. Continuous flow from LVADs create a chronic narrow pulse pressure affecting neurovascular physiology, increasing intraluminal pressure, smooth muscle relaxation, and distension of submucosal venous plexus leading to angiodysplasia [45]. Fortunately, the overall incidence of GI bleeding has reduced significantly with the latest generation of continuous flow LVADs [46]. Regardless, most centers will screen potential LVAD candidates for GI malignancies or arteriovenous malformations with a colonoscopy as their findings increase risk for potential bleeding post-implantation.

Psychosocial Considerations

When considering patients for durable LVAD support it is important to select for those who will be compliant with medical therapy and outpatient follow up. The burden of care for LVADs is high. It requires one to carry a device and batteries which can be up to a weight of 14lbs. Dressing changes at the driveline exit site and adherence to oral anticoagulants are only just a tip of the iceberg. Maintenance of an LVAD requires a basic fundamental of good hygiene and vigilant monitoring of LVAD alarms which may signal device malfunction. Therefore, it is recommended for every multidisciplinary committee to have an advanced licensed clinical social worker who is trained in evaluating potential LVAD candidates [2]. Social workers perform a thorough psychosocial assessment including a patient's social network, potential caregiver plan and history of substance abuse including illicit drugs and alcohol.

The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) score is a popular tool used in the evaluation of potential solid organ transplant candidates (Fig. 3) [47]. The score is calculated based off the answers to 18 questions which envelop 4 psychosocial domains including patient's readiness, social support, psychosocial stability and lifestyle. SIPAT scores are now being utilized in assessing potential LVAD candidates and its questions being modified to be specifically related to knowledge of the device. Evidence supporting the use

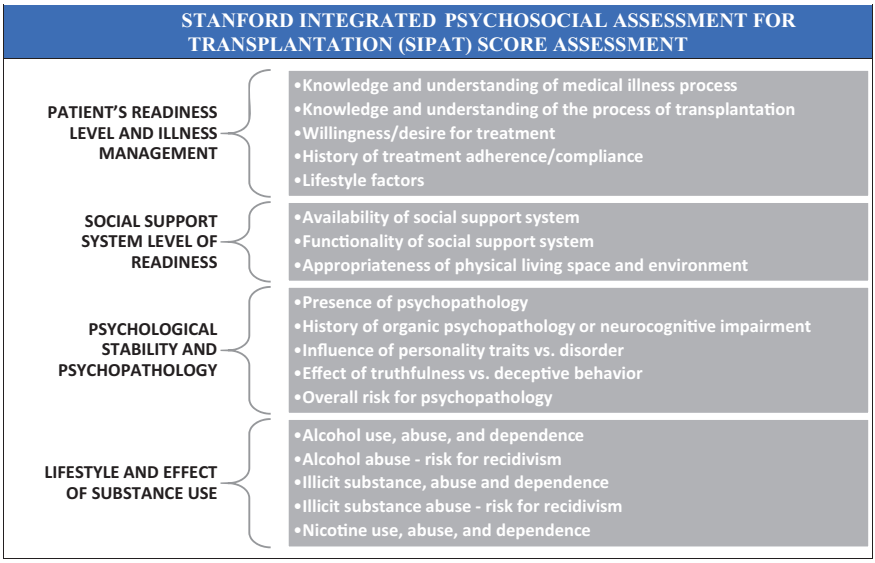

Fig. 3 Stanford Integrated Psychosocial Assessment For Transplantation (SIPAT) score assessment

of SIPAT in this patient population has been controversial. A large single-center retrospective study identified that a high SIPAT score pre-LVAD was associated with a burden of adverse events including readmissions, device exchanges and death post-implantation [48]. However, another single-center retrospective study concluded that a high SIPAT score did not predict cumulative re-admission [49]. Despite its limitations, the SIPAT score is a quick and objective assessment that institutions may consider using as a quality metric to assess the degree of psychosocial risk they are taking programmatically, but not be used to make absolute decisions regarding candidacy [50].

Case Conclusion

After a multidisciplinary committee review, the patient was deemed an appropriate candidate for an LVAD as DT. A continuous flow LVAD was surgically implanted and he required 1 unit of packed red blood cells perioperatively. His post-operative course was complicated by RV failure which resolved after a short course of intravenous diuretics and a slow wean off his milrinone. After a 12-day hospital stay, he was discharged with a serum creatinine of 1.1 mg/dL (pre-LVAD implantation 1.9 mg/dL). Repeat transthoracic echocardiogram was remarkable for a LV internal dimension in diastole of 6.1 cm, trace mitral regurgitation and aortic regurgitation. He has been compliant with medical therapy and outpatient follow up visits. He is now able to perform his activities of daily living without any limitations and enjoys spending time with his grandchildren.

Key Points:

- Durable MCS is a well-established modality of improving cardiac output, functional capacity, quality of life, and reversing cachexia and multi-organ failure.
- Indications for an LVAD include bridge-to-transplant, bridge-to-destination and destination therapy.
- Selection for durable LVAD requires a thorough evaluation by a multidisciplinary team.
- LVAD implantation is preferred in patients who meet INTERMACS Profile 3 or greater given better survival outcomes.
- Cardiac considerations prior to LVAD implantation include assessment of LV cavity size, presence of baseline valvular heart disease and right heart failure.
- Renal and hepatic impairment are typically reversed post-LVAD implantation.
- Psychosocial assessment is important to identify high risk patient features including medical non-compliance, substance abuse and neurocognitive impairment.

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LVAD Inpatient Management

Johannes Steiner and Hao A. Tran

Case Vignette

A 61-year-old woman with a remote history of diffuse large B cell lymphoma received a doxorubicin-based chemotherapy, chest wall radiation and autologous stem cell transplant presented with worsening biventricular systolic dysfunction. She rapidly decompensated necessitating inotropic agents and percutaneous mechanical support (Impella CP, Abiomed Inc, Danvers, MA, USA). Transthoracic echocardiogram revealed a left ventricular ejection fraction 10% with left ventricular end-diastolic diameter 5.5 cm, moderate right ventricular failure (RV), and moderate-to-severe tricuspid regurgitation (TR). Pulmonary artery catheterization revealed mean RA pressure 15 mmHg, PA pressure of 46/24 mmHg and pulmonary artery pulsatility index (PAPI) of 1.5.

The patient was ultimately listed for transplantation and received an urgent HeartWare HVAD (HeartWare, Framingham, MA, USA) and tricuspid ring placement. The pump speed was started at 2500 rpm and immediate post-operative management consisted of epinephrine, milrinone, vasopressin and nitric oxide. After weaning from cardiopulmonary bypass, the device achieved flows only up to 2.5 L/min with pump speed increased to 2600 rpm. Transesophageal echocardiogram (TEE) documented severe RV, systolic dysfunction and residual severe TR with a ventricular septum bulging into the LV causing continued suction events.

Despite an aggressive pharmacological RV support strategy including inotropes and pulmonary vasodilators, the LVAD remained underfilled and was unable to

J. Steiner
Division of Cardiology, Department of Internal Medicine, Oregon Health and Science University, Portland, USA

H. A. Tran (✉)
Division of Cardiology, Department of Internal Medicine, University of California, 9452 Medical Center Drive, La Jolla, San Diego, CA 92037, USA
e-mail: hatran@health.ucsd.edu

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provide adequate systemic flows ultimately necessitating the insertion of temporary RVAD in the form of a RA to PA configured Centrimag RVAD (Abbott, Pleasanton, CA, USA). Postoperative PA chest x-ray suggested an inflow cannula orientation towards the interventricular septum rather than the mitral valve apparatus with the RVAD already in place (Fig. 1).

Pre-Operative Optimization

Inpatient mortality and length of stay after VAD placement in advanced cardiogenic shock states, INTERMACS profiles 1-2 (Interagency Registry for Mechanically Assisted Circulatory Support, more critical patients have lower profiles) are significantly increased compared to VAD placement in stable inotrope dependent or even ambulatory heart failure patients [3]. While the ideal timing for VAD placement is still being debated on the basis of potential risks and benefits of earlier implantation [4], the importance of preoperative optimization and its effects on postoperative outcomes is well recognized.

1. Decompensated RV failure prior to LVAD implantation. Regardless of which definition of RV failure is being used, RV failure after LVAD implant has consistently been associated with worse clinical outcomes, including increased hospital length of stay, worse end-organ function, decreased bridge-to-transplant success, and increased short-term and long-term mortality [5]. This was covered earlier in the previous chapter, but several important points will be discussed here.
    - Pre-operative RV systolic dysfunction is in particular vulnerable to the effects of cardiopulmonary bypass, peri-operative volume shifts and increased RV afterload due to pulmonary edema and/or positive pressure ventilation.

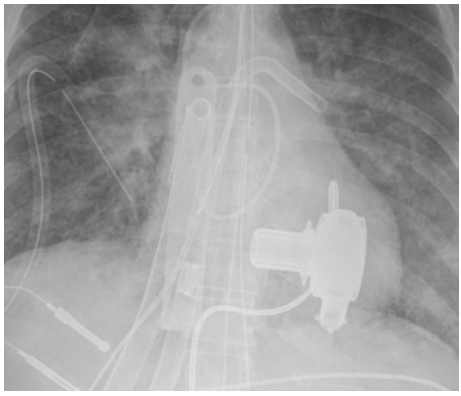

Fig. 1 Chest x-ray indicates an inflow cannula orientation towards the interventricular septum rather than towards the mitral valve apparatus. Centrimag cannulas from the RA to the PA already in place. Moderate pulmonary edema

- While short-term RV assist devices do exist, durable long-term RVAD therapy currently remains off-label
- Several risk scores, echocardiographic or hemodynamic metrics are associated with postoperative RV failure, however, no single metric has been identified to guide patient selection [6].
- Hemodynamic guided heart failure management pre-implant to reduce central venous pressures to below 15 mmHg utilizing aggressive diuresis, inotropic right ventricular support, or even pulmonary vasodilator therapy is strongly advised in at risk patients.
- Minimal invasive approaches via lateral thoracotomy have the potential to maintain an intact pericardium and reduce the incidence of post-operative RV failure [7].

2. Malnutrition is frequently encountered in end-stage cardiomyopathies, impacts postoperative wound healing and the incidence of nosocomial infections.
   - Albumin levels less than 3.5 mg/dL have been associated with increase in postoperative VAD mortality [8].
   - Nevertheless, optimizing pre-implant nutrition potentially requiring weeks needs to be weighed against the potential risk for delaying VAD implant.
3. Active infections need to be excluded prior to implantation. Potential infectious sources including indwelling catheters and dental infections should be removed or treated otherwise. Preoperative antibiotic prophylaxis should be given [9].
4. Renal Failure. Although frequent improvement of the glomerular filtration rate is observed immediately post VAD implant, long-term improvements are less evident and ongoing renal dysfunction is associated with increased morbidity and mortality during the post VAD placement clinical course.
   - Permanent dialysis requirements are still considered a contraindication especially for DT VAD placement and might render BTT VAD patient not being a cardiac transplantation candidate any longer; therefore, efforts should be spent in the pre-operative period to optimize renal function through providing decongestion and adequate renal perfusion [10].

Intra-Operative Management

1. Tricuspid Regurgitation is commonly encountered in end-stage heart failure patients resulting from long-standing pulmonary venous hypertension, right atrial remodeling, and the presence of transvalvular leads. (see Table 1)
   - Despite some early evidence to support a strategy of tricuspid repair at the time of LVAD implant [11] suggesting improved RV reverse remodeling thereafter, these findings did not translate into any clinical benefits in later registry based publications [12] and remain an area of clinical uncertainty.
2. Mitral Regurgitation (severe) is regularly observed prior to LVAD placement, this rarely requires surgical attention at the time of implant and typically

Table 1 Summary of Intraoperative Valvular Interventions

Valvulopathy	Concomitant valvular surgery
Aortic insufficiency or mechanical aortic prothesis	Surgical repair or closure if aortic insufficiency at least moderate
Mitral stenosis	Bioprosthetic mitral valve replacement
Tricuspid regurgitation	No definite recommendations available

improves with LVAD driven ventricular unloading and reverse remodeling. In the rare circumstances of underlying significant mitral valve stenosis, this commonly requires replacement with a bioprosthetic mitral valve to assist with LVAD filling and reduce the risk for intracardiac emboli.

3. Aortic Insufficiency (at least moderate) can create a reentry circuit throughout the cardiac cycle severely jeopardizing systemic perfusion and left ventricular unloading. The progression of aortic insufficiency can be propagated by a reduced systolic excursion of the valve during LVAD support and should be addressed at the time of LVAD implant especially if the patient is expected to remain on LVAD support for a longer duration.
   - Options for surgical management of aortic regurgitation include repair by over-sewing the valve completely (Park stitch) or replacing the valve with a biological prosthesis [13].
   - Options for surgical management of aortic regurgitation include repair by over-sewing the valve completely (Park stitch) or replacing the valve with a biological prosthesis [13].
   - Mechanical prosthesis in the aortic position are typically over-sewn or replaced with a tissue valve due to increased incidence of thrombotic phenomena during a relative low flow state if the patient is expected to remain on LVAD support for a prolonged amount of tie.
4. Right Ventricular Dysfunction. Pulmonary edema, lung injury caused by excessive transfusion requirements, and prolonged cardiopulmonary bypass time all have a direct impact on RV afterload and should be minimized.
   - Most centers utilize aggressive inotropic support and empiric use of pulmonary vasodilators such as inhaled nitric oxide or prostaglandin in case of preexisting pulmonary hypertension and struggling RV function in the immediate perioperative period.
   - To avoid increased pulmonary vasoconstriction and stress on the RV, optimal oxygenation and acid base balance should be achieved prior to separation from bypass.
   - CVP should be closely monitored with attention to avoid over distention of the RV.
   - If right ventricular failure persists, a temporary RVAD should be considered electively before leaving the OR rather than emergently thereafter. This can be achieved either by converting the cardiopulmonary bypass circuit to a right atrial to pulmonary artery configuration or even through

placement of a temporary RVAD (Centrimag RVAD, Abbott Laboratories, formerly Thoratec Corporation, Pleasanton, CA, USA). There may be an emerging role for percutaneously placed right ventricular assist devices (Impella RP, Abiomed, Inc, Danvers, MA, USA or TandemLife Protek Duo, TandemLife, Pittsburgh, PA) in selected cases requiring only short-term support. As may be expected, patient outcomes are improved with planned RV support instead of delayed/emergent upgrade to biventricular support [14].

Post-Operative Management

1. Initial LVAD pump speeds ideally will be adjusted under ongoing TEE and hemodynamic guidance. A strategy of "partial" unloading may be preferable to higher speeds especially in patients at increased risk of post-LVAD RV failure in order to avoid excessive RV preload and leftward septal bowing, which may worsen RV function in the already dysfunctional and perhaps stunned RV following cardiopulmonary bypass. Short and midterm goals include adequate left ventricular unloading as reflected by complete or intermittent aortic valve closure and reduction in left ventricular distention, as well as preventing right ventricular overload or compromise of the septal geometry.
   - Typical pump speeds are 5000–6000 rpm for the HeartMate 3, and 2400–3200 rpm for the HVAD. Optimal speed settings are very dependent on postoperative volume shifts, systemic vascular resistance, and therefore can require ongoing reevaluations.
2. Post-operative hemodynamic scenarios leading to abnormal VAD flows are summarized in Table 2. During this post-operative period, triggers of pulmonary hypertension (acidosis and hypoxia) that may compromise RV function should be remediated. Bleeding should be controlled by correcting any coagulopathies as needed. In patients who have a significantly elevated PVR that does not improve in the early postoperative days, particularly in those with significant, concomitant RV dysfunction, use of an oral phosphodiesterase type 5A inhibitor is a reasonable therapeutic strategy [15].

Anticoagulation Management

Efforts to minimize the risk of bleeding at the time of LVAD implantation typically focus on full reversal of anticoagulation and washout from antiplatelet agents before surgery. The prevention of occlusive or non-occlusive pump thrombosis in the immediate postoperative period needs to be carefully weighed against the risk of postoperative bleeding and its associated morbidity. Valuable lessons were

Table 2 Common postoperative hemodynamic scenarios leading to abnormal VAD flows. Low pump output and significant CVP elevations greater than 20 mm Hg necessitate urgent echocardiographic evaluation to rule out tamponade or other technical complications

Diagnostic Indices	Hypovolemia or bleeding	RV failure	Tamponade	Systemic hypertension	Aortic insufficiency	Ventricular arrhythmias
LVAD flows	Low	Low	Low	Low	High	Low
LVAD pulsatility	Reduced, possible suction events	Reduced, possible suction events	Reduced, possible suction events	Increased	Reduced	Reduced, possible suction events
PAC data	Low CVP	Elevated CVP, reduced PAPi and CI	Elevated CVP		Reduced CI, eventually elevated CVP	Elevated CVP
MAP	Reduced or normal	Reduced or normal	Reduced	Elevated	Normal	Reduced or normal
Echo	Small left ventricular diameter with closed aortic valve, decompressed IVC	Enlarged right ventricle with the septum bowing to the left, dilated IVC	Compressed right ventricle due to circumferential or localized pericardial effusion, increased IVC diameter	Unchanged	Dilated left ventricle and aortic insufficiency throughout systole and diastole	Unchanged
Management strategy	- Volume resuscitation - Monitor for intrathoracic bleeding and increased chest tube output - Adjust hematocrit in LVAD settings	- Evaluate VAD settings to prevent distortion of the septal geometry and RV overload - Inotropic and pulmonary vasodilator support - Aggressive diuresis eventually including u ltrafiltration -Reevaluate vent settings - Low threshold to consider temporary mechanical support for the right side	- Surgical re-exploration	- Optimize pharmacological blood pressure control and eventually reassess pain control	- Echo guided ramp study and potentially speed increase - Consider aortic valve repair or replacement in case of prolonged VAD support anticipated	- Evaluate VAD speed settings, inflow cannula orientation and volume status (suction events) - Eventually antiarrhythmic therapy

leant from the increased incidence of HeartMate 2 pump thrombosis reported on in 2013 [16].

- PREVENTion of HeartMate II Pump Thrombosis trial involved nine strategies believed to influence the risk of thrombosis, including surgical techniques, antithrombotic therapy, pump speed, and blood pressure management strategies.
  - Patients who received heparin bridging, maintained pump speeds of at least 9,000 rpm, and those who had all implant techniques followed experienced significantly fewer pump thrombosis events at six months (1.9% vs. 8.9%; $p<0.01$) [17].
  - Consensus documents from the International Society for Heart and Lung Transplantation (ISHLT) provides guidelines for the utilization of anticoagulation and antiplatelet therapy post LVAD placement [18], however, significant institutional variability still persists in regard to the post-operative management [19].

1. Post-operative heparin:
   - Unfractionated heparin is initiated after the first 24 h with a lower anti-Xa goal range, and then gradually increased for target anti-Xa goal (0.35–0.5). Significant discordances were observed between therapeutic aPTT assays and anti-Xa activities in postoperative LVAD patients especially in the presence of lupus anticoagulants. [20] Heparin administration may be delayed due to ongoing significant bleeding as defined by hemodynamically significant GI bleeding, thoracic cavity bleeding leading to hemodynamic compromise and/or intracerebral bleeding. Heparin bridging is being continued until the first INR reaches a value of 2 or more. For patients with a history of heparin-induced thrombocytopenia (HIT) in whom it is not feasible to wait for disappearance of the heparin-PF4 antibodies, anticoagulation with a direct thrombin inhibitor is the preferred choice.
2. Oral anticoagulation
   - Oral vitamin K antagonists remain the standard of care long-term anticoagulation agent in LVAD patients and are typically initiated once the chest tubes have been removed. A small randomized control trial investigating the utility of novel oral anticoagulants (dabigatran) had to be stopped prematurely due to increased risk of thromboembolic events in the novel oral anticoagulant treatment arm [21].
   - Current guidelines suggest an INR target of 2-3 post VAD placement. Embolic events have been reported to inversely correlate to INR with the highest event rates occurring with an INR lower than 1.5 and significantly increased event rates with INR between 1.5 and 1.9. Significant bleeding events seem to increase significantly for INRs beyond 3 [22]. Long-term warfarin management in LVAD patients can be challenging due to varying levels of hepatic congestion, nutritional status, and polypharmacy.

The time-in-therapeutic range (TTR) for LVAD patients has been reported at between 31 and 51%, which is significantly worse than in other conditions [23]. The anticoagulation approach for each patient is typically individualized. For example, sustained low pump flow states or increasing markers of hemolysis (e.g. lactate dehydrogenase, LDH) would mandate increasing anticoagulation to the upper limits of normal and higher. On the other hand, patients frequently require downward adjustments of INR targets over time in the setting of uncontrollable bleeding complications.

- De novo pump thrombosis remains a rarity in the newest generation HeartMate 3, which was especially designed to reduce hemocompatibility related events and provides the rational for less aggressive anticoagulation strategies. Initial HeartMate 3 pilot data suggest the safety of lower INR targets (1.5–2) in the mid-term for patients at increased risk for bleeding. However, larger and longer-term data are required to apply these findings to the general public [24].

3. Antiplatelet regimen
    - Regarding anti-platelet therapy current guidelines recommend the initiation of aspirin 24–72 h postoperatively. ASA may be stopped or reduced for bleeding. Care should be taken dose reducing ASA in HVAD supported patients due to the evidence that ASA 325 mg is associated with fewer cerebrovascular events and device thrombosis compared with lower doses [25].
    - In the future, platelet activation assays might be able to routinely risk stratify patients at risk for thromboembolic complications and thus might guide patient-tailored pharmacological strategies to balance bleeding and clotting risks [26]. Thromboelastography (TEG) is already used by some centers to manage and adjust anticoagulation. Protocols vary, although many include daily TEG to assess antiplatelet needs until satisfactory.

Infectious Prophylaxis

Next to bleeding driveline associated infections are one of the most common adverse events in LVAD patients. Driveline infection occurs in up to 20% of patients in the first year of LVAD support, and the cumulative risk is continuous during support.

- Algorithms pertaining to infection prevention, antibiotic prophylaxis and driveline site care differ between institutions. However, all patients receive some form of perioperative antibiotic prophylaxis at least including gram positive coverage with many centers also including gram negative coverage and antifungal prophylaxis bases on pivotal trial protocols [9].
- Meticulous driveline exit site care is paramount in the immediate postoperative period and patients require daily driveline dressing changes during the

first postoperative week. Patients are actively educated on daily dressing changes and identifying signs and symptoms of driveline exit site infection. Patients should avoid showering until after adequate tissue-in-growth into the velour has occurred and until there is no drainage at the exit site.

- Most infections are the result of trauma to the driveline exit site such as dropping a controller or pre-existing driveline instability. The use of dedicated percutaneous lead management kits and anchoring devices has been shown to improve driveline stability, thus minimizing trauma and tension at the exit site [27]. Prophylactic use of antibiotics should be considered after documented trauma to the driveline site. However, there is no evidence to support long-term chronic prophylactic use of oral antibiotics [28].

Blood Pressure Management and Hemodynamic Optimization

Based on the continuous flow nature of current era LVADs aortic flow is present throughout the cardiac cycle. With increasing LVAD speeds diastolic pressures rise, systolic pressures remain fairly constant, and the pulse pressure gradually decreases (Fig. 2). Pulse pressure is also affected by several other variables including intravascular volume, remaining cardiac contractility as well as afterload. Therefore, arterial blood pressures and waveforms can provide additional information regarding the interaction between LVAD in the cardiovascular system [29].

- The amount of cardiac output supported by continuous flow devices is inversely proportional to the systemic vascular resistance. Hence, mean arterial blood pressures should remain in the range of 70–80 mmHg to provide adequate ventricular unloading. Optimal blood pressure control is not only affecting the LVAD specific flow features, but also significantly reduces the incidence of hemorrhagic stroke, aortic insufficiency, and thromboembolic

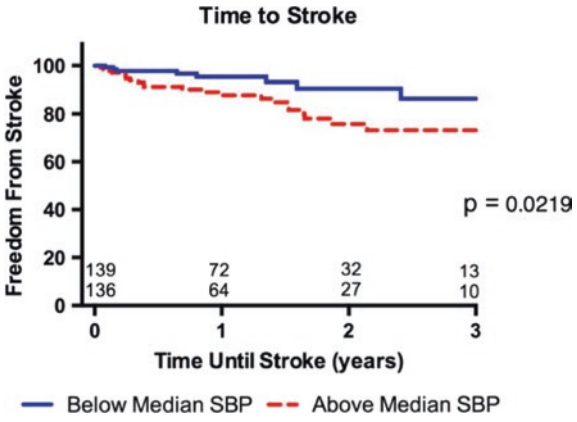

Fig. 2 Association of blood pressure control on discharge with subsequent stroke [30] (permission obtained Nassif et al. J Heart Lung Transplant, 2015. 34(4): 503-8)

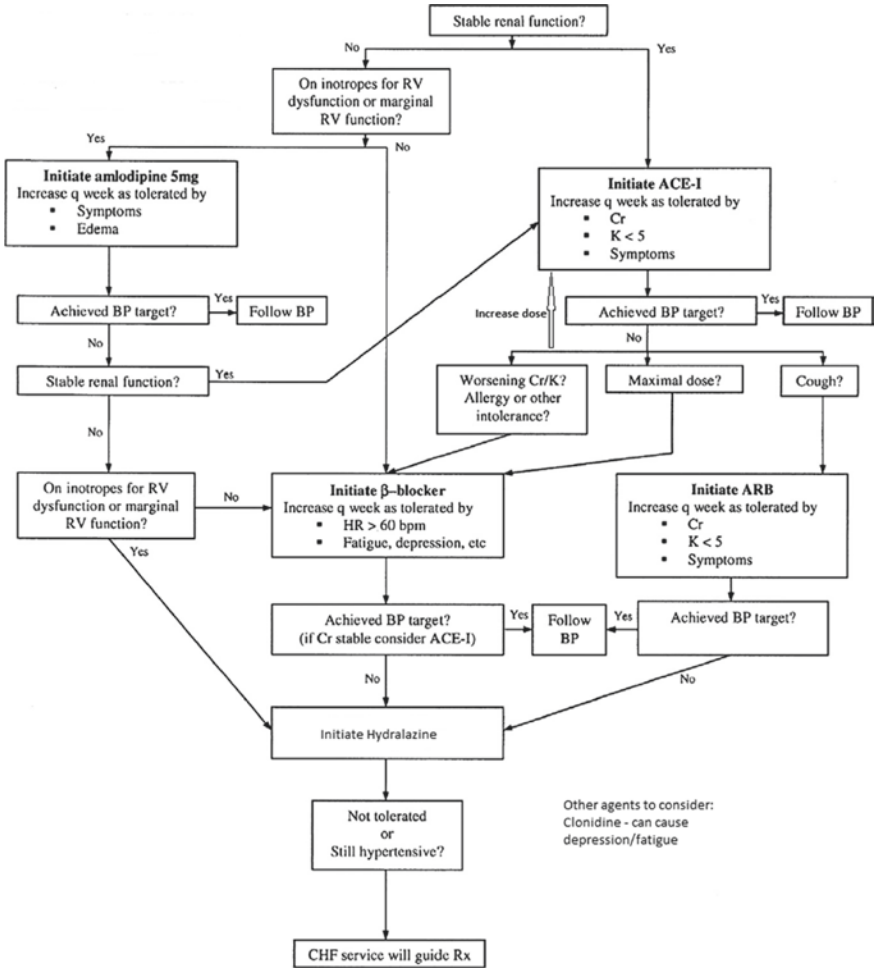

Fig. 3 Blood pressure control algorithm post LVAD placement [33] (permission obtained from Lampert et al. Ann Thor Surg 2014;97:139-46)

events (Fig. 3) [30]. Current generation centrifugal flow pumps have a larger change in flow for given pressure gradient change across the pump compared to the prior generation axial flow device HeartMate 2. Therefore, those new devices are even more sensitive to change in preload and afterload. In the early post-operative period, an arterial catheter is necessary to monitor blood pressure properly. After the arterial catheter is removed, the arterial blood pressure is most reliably assessed using Doppler in the absence of significant pulsatilty.

- A specific blood pressure control algorithm post VAD implant is depicted in the graphic below (Fig. 4). Especially in the destination therapy LVAD cohort

and in patients considered for recovery protocols [31] standard heart failure guidelines regarding the up titration of evidence-based neuro-hormonal blockade agents should be applied.

Reverse remodeling induced by the LVAD is dependent on the operating speed of the LVAD and the flow generated in response to the pressure gradient between the LVAD inflow cannula and the ascending aorta. Short-term changes in LV shape can be demonstrated by changing the LVAD operating speed (ramp study).

- Those findings provide a rationale for pre-discharge optimization studies (ramp) under stable preload and afterload conditions. During these efforts VAD speed would be incremented from the lower speed limit to the upper speed limit under echo and/or pulmonary artery catheter guidance. Device parameters including pulsatility index, power and flow should be recorded simultaneously with hemodynamic data and echo derived LV geometry, mitral valve regurgitation and aortic valve opening frequency.
- Based on these data the device speeds should be set based on optimal hemodynamics including pulmonary wedge pressure of less than 18 mmHg and a central venous pressure of less than 12 mmHg with a secondary goal of minimal mitral regurgitation and intermittent aortic valve opening. Absent pulsatility can suggest that the set pump speed is close to exceed available preload and could provoke ventricular collapse and suction events. Additionally, intermittent aortic valve opening can reduce the incidence of valvular thrombosis and slows down the progression of aortic insufficiency.
- In the Heartmate 3 population recent data suggest that 62.5% of patients displayed favorable hemodynamics at baseline, a number which improved to 81.3% after speed optimization. Most patients had optimal hemodynamics in a narrow speed range of between 5,200 and 5,600 rpm, arguing against routine ramp testing in speed optimization for this device unless there are clinical concerns suggesting inadequate hemodynamics [32].

Key Points

- Two-thirds of all deaths during the first year on LVAD support occur during the implant hospitalization highlighting the importance of careful peri-operative VAD management.
- Surgical implantation techniques focusing on proper pump pocket creation, optimized positioning of inflow cannula and outflow graft, proper pump position in the body, and fixation immediately impact post implantation complications, in particular low VAD flows and pump thrombosis.
- “Optimal” speed settings depend on postoperative volume shifts, systemic vascular resistance, and therefore require ongoing adjustments postoperatively. Midterm goals include adequate left ventricular unloading as reflected by complete or intermittent aortic valve closure and reduction in left ventricular distention, as well as preventing right ventricular overload or compromise of the septal geometry.

- The progression of aortic insufficiency can be propagated by a reduced systolic excursion of the valve during LVAD support and should be addressed at the time of LVAD implant especially if the patient is expected to remain on LVAD support for a longer duration.
- Heparin bridging and antiplatelet therapy should be promptly initiated post-operatively in the absence of clinically significant bleeding events.
- Prophylactic use of antibiotics remains standard of care for peri-operative prophylaxis. However, there is no evidence to support long-term chronic prophylactic use of oral antibiotics.
- Optimal blood pressure control (mean arterial pressure 70–80 mmHg) is not only affecting the LVAD specific flow features, but also significantly reduces the incidence of hemorrhagic stroke, aortic insufficiency, and thromboembolic events.
- Most patients have optimal hemodynamics in a narrow speed range of between 5,200 and 5,600 rpm (HeartMate 3). Ramp testing for speed optimization can provide additional information in case of clinical concerns suggesting inadequate hemodynamics.
- A multidisciplinary teaching approach has been proven to be most effective and directly effects post discharge clinical outcomes.

Case Vignette Conclusion

The patient was unable to be separated from his right ventricular support system and was fortunate to receive an adequate donor heart several days later without any further post-operative complications. This case illustrates the importance of patient selection, optimized surgical LVAD implantation technique, as well as a management approach to perioperative right ventricular failure which has the potential to drastically impact patient post-operative outcomes.

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Outpatient Management of LVAD

Rayan Yousefzai and Marcus Urey

Clinical Vignette

A 39-year-old male with a past medical history of hypertension and 12 pack-year of tobacco use presents to the hospital worsening dyspnea. On presentation, his blood pressure was 124/94, oxygen saturation was 90% on the room air, and his heart rate was 120 beats per minute (sinus tachycardia). He was overloaded on exam with cool periphery. Labs were notable for elevated BNP, mildly elevated troponin, acute renal failure with serum creatinine of 1.9 mg/dl, and normal liver function.

His wife is pregnant with their second child, and he has a 3-year-old son. He is a Veteran, and he is attending a nursing school. Echocardiogram showed severely dilated left ventricle with severely reduced function (ejection fraction of 15%), mildly dilated right ventricle with moderately reduced function and moderate mitral regurgitation. He underwent left, and right heart catheterization, which showed normal coronary arteries elevated filling pressures, and low cardiac output of 3 L/min and cardiac index of 1.5 L/m^2/min. He was started on Milrinone infusion and intervenous diuretics. His cardiac output improved marginally by inotrope support. He underwent Impella placement.

His admission was complicated with significant depression. He underwent therapy and consultation during the hospitalization. HeartMate 3 was implanted as a bridge to transplant, and the patient was discharged home. His daughter was born after the LVAD implantation. He faced significant life changes, suffered from severe depression, and started smoking cigarette again. He was deactivated from the transplant list due to concern for his significant depression and relapse on using tobacco.

R. Yousefzai
Houston Methodist Hospital, Houston, TX, USA

M. Urey (✉)
Cardiovascular Institute, University of California, 9452 Medical Center Drive, La Jolla, San Diego, CA 92037, USA
e-mail: murey@health.ucsd.edu

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Introduction

The incidence and prevalence of patients with heart failure are increasing. Heart failure has become one of the largest cardiovascular epidemics [1, 2]. Despite the significant advancement in heart failure therapy, a subset of the patients with heart failure (0.5–5%) respond poorly to standard guideline-directed medical therapy (GDMT) and progress to stage D heart failure with a very poor prognosis [3, 4]. LVAD offers an alternative for this patient population that can improve survival and quality of life. LVADs have been approved as a bridge to transplant therapy (BTT) and destination therapy (DT). Once outpatient, patients with LVAD face significant lifestyle modification and long-term management challenges. This chapter will review the outpatient management of the LVAD patients.

Preparing for Life Outside Hospital

The success and outcome of LVAD patients depend on adequate preparation of the patients and their caregivers for life outside the hospital. Prior to discharge, LVAD patients and their caregivers must be comfortable with daily monitoring, device maintenance, and performing the daily activities.

Patient and Caregiver Education

Patient and caregiver education are important steps in LVAD care and has a direct association with the outcome. Education should start while the patient is being considered for LVAD and/or heart transplantation and includes (1) understanding the LVAD alarms, (2) daily care of LVAD, (3) managing equipment, (4) nutrition, (5) medication safety, (6) limitations, and (7) the importance of communication with the LVAD team. These guidelines are developed to prepare the patients and their caregivers for out of hospital LVAD management. The following is used in the process of preparing the patients for discharge.

- Completing patients and caregivers training: The patients and the caregivers should read the handbook, attend all training sessions, complete the written knowledge assessment tool and successfully pass the hands-on assessment.
- Reviewing the LVAD equipment and supplies for discharge.
- Reviewing the contact information: patients and their caregivers need to know the contact information for questions and in case of emergency, local resources, designated outpatient labs, designated pharmacy for outpatient medication refills and contact information for emergency medical providers and services.

Home Safety

Home safety should be assessed before discharge. The following are required for a safe home discharge: electricity at home, appropriately grounded outlets, appropriately labeled circuit breakers for power module and AC adaptor, telephone within easy reach at bedroom, a well-lit pathway at bedroom, bathroom safety, good condition and well-lit hallways, and stairs, easy-to-grasp railing, and secure carpets and runners (Fig. 1).

Rehabilitation

Cardiac rehabilitation, including physical therapy, occupational therapy, and nutritional therapy is an essential part of the recovery after LVAD implantation. Even though this effort starts after surgery and during the hospitalization, most of the patients will tremendously benefit from long-term rehabilitation. After discharge, it is highly recommended that LVAD patients continue to improve their physical activity by participating in an outpatient cardiac rehabilitation program. After LVAD implantation by unloading the left ventricle and improving the volume and pressure of the left ventricle [5], patients rest and exercise hemodynamics measured by peak oxygen consumption (VO_2), minute ventilation/carbon dioxide production (VE/VOC_2), cardiac output (CO) and mean pulmonary artery and wedge pressure improves significantly [6, 7]. Assessing the nutritional status of LVAD patients is vital since a significant percentage of patients with advanced heart failure suffer from malnutrition. Patients who have malnutrition are predisposed to immune system dysfunction, impaired healing, and infection [8, 9]. LVAD patients should be referred to the nutritionist for assessment. Changes in inflammation can be used to monitor the metabolic response to nutrition by measuring C-reactive protein and pre-albumin [10].

Optimization Study

It is recommended that the patients with new LVAD implantation undergo optimization study before discharge. An optimization study involves an echocardiogram to evaluate LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), septal position, frequency of aortic valve opening, presence and severity of aortic and mitral valve regurgitation, cannula position and left and right ventricular function. LVAD parameters including flow, pulsatility index, power, and speed are recorded at baseline.

Once baseline values are obtained, the LVAD speed can be changed in either direction by 200 rpm (for the HeartMate II) or 100 rpm (for the HeartWare and HeartMate 3). Echo and LVAD values described above are repeated at every change of speed, after 2 min to allow equilibration. At optimal speed, the aortic valve should open every 3–5 beats with the ventricular septum at midline, and valve regurgitation minimized.

Outpatient Clinic Visits

The frequency of the office visit depends on individual patient requirements. The visits are more frequent initially and decrease subsequently. The frequency of the visits depends on the LVAD programs but generally are weekly initially, followed by bi-weekly visits, and eventually, every four to eight weeks indefinitely. The following will be addressed in each visit: vital signs, LVAD parameters, physical exam, review of medications, functional capacity assessment, laboratory data, LVAD supplies, and follow up appointments and tests. Echocardiograms are performed when it is medically indicated. Right heart catheterization (RHC) is performed to assist in the diagnosis of heart failure symptoms in the setting of right heart failure or suspected LVAD malfunction. RHC is also indicated for the assessment of pulmonary hypertension for BTT patients.

Blood Pressure Management

Blood pressure (BP) management is strongly associated with life-threatening complications, such as pump thrombosis and stroke in LVAD patients [11]. Although the pumps durability and patients' survival have improved significantly by implementing continuous flow (CF) LVADs [12], there are still significant complications associated with CF-LVADs [13–17].

High blood pressure is associated with significant consequences, including stroke and pump thrombosis [18, 19], which is caused by the change in LVAD flow due to changes in afterload with the centrifugal pumps being more susceptible to changes compared to the axial flow pumps [20]. Suggested blood pressure targets are much lower than the general population, related to unique hemodynamic and pathophysiology of CF-LVADs. Current International Society of Heart and Lung Transplantation (ISHLT) guidelines [21] recommends maintaining mean arterial pressure (MAP) of 80 mmHg.

Accurate measurement of BP in patients with CF-LVADs is challenging due to the continuous flow of blood from the left ventricle to the aorta. For a set-speed, flow varies inversely with pressure gradient [22] (Fig. 2) resulting in more flow during systole and less during diastole. In the end-stage heart failure patients due to the reduced contractility systolic blood pressure (SBP) is lower which resulted in lower

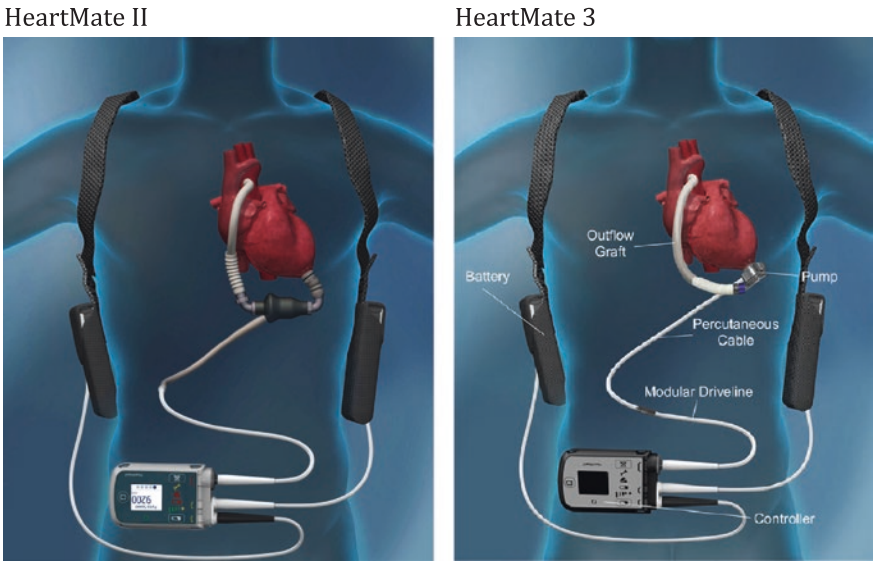

Fig. 1 HeartMate device comparison as seen after implant—HeartMate II and HeartMate 3. HeartMate II and HeartMate 3 are trademarks of Abbott or its related companies. Reproduced with permission of Abbott, © 2020. All rights reserved

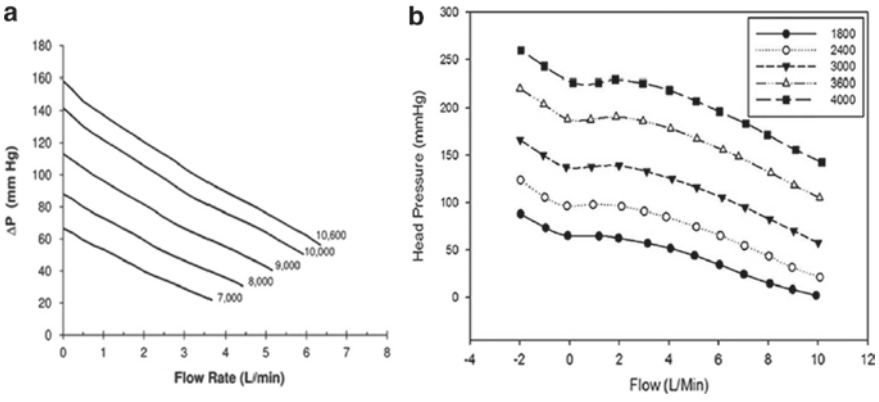

Fig. 2 Flow versus change in afterload for continuous flow-left ventricular devices (CF-LAVD) is shown for (**A**) HeartMate II axial CF-LVAD and (**B**) HeartWare HVAD Centrifugal CF-LVAD. Increasing in afterload is reversely associated with flow. Reprinted from: Frazier OH et al. Optimization of axial-pump pressure sensitivity for continuous flow total artificial heart. J Heart Lung Transplant 2010; 29:687–91, with permission from Elsevier

pulse pressure (PP); furthermore, the continuous flow of blood in LVAD patients at the entire cardiac cycle results in a further reduction in pressure decay during diastole. Therefore PP can be reduced to the extent that may not be measurable by palpitation or routinely used blood pressure monitor systems. A higher speed of LVAD

unloads the left ventricle and reduces the peak systolic pressure as more blood is removed by the device resulted in closing the aortic valve and decreasing pulse pressure while the opposite is correct by reducing the speed of LVAD (Fig. 3) [23].

Measurement of the blood pressure in LVAD patients can be challenging. An indwelling arterial catheter is the most reliable and accurate way to measure blood pressure in CF-LVAD patients however this method is invasive, and it is used in selected patients admitted to the intensive care unit. Commonly used blood pressure monitoring devices are not reliable due to low PP as it has described above. The common BP monitoring devices have a cuff connected to a pressure transducer. Cuff inflates above the SBP and then gradually deflates until the transducer senses increase in oscillation, which registers it as SBP. As cuff continues to deflate the maximum oscillation is registered as mean arterial pressure (MAP), and diastolic BP (DBP) can be estimated. In CF-LVAD patients, the narrow PP significantly decreases the difference between SBP and MAP. Terumo Elemano BP monitor (Terumo Elemano, Hatagaya, Shibuya, Japan) could overcome this issue [24] however the production of this device was discontinued since 2014.

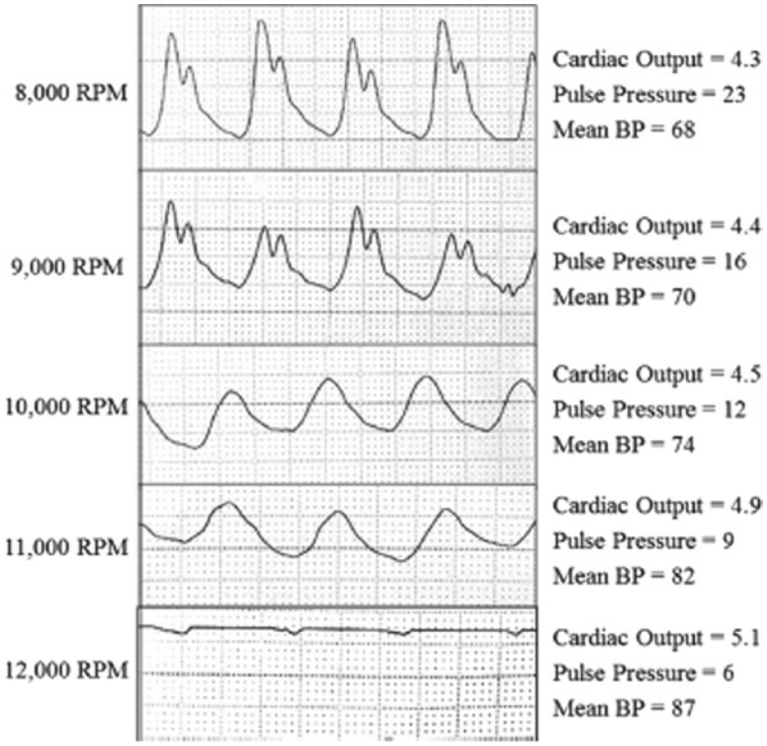

Fig. 3 A display of arterial blood pressure. As LVAD speed increases, the arterial waveform flattens and cardiac output and blood pressure increase. Reprinted from: Nelson JA et al. Left ventricular assist devices and noncardiac surgery. Advances in Anesthesia 2018; 36:99–123, with permission from Elsevier

Doppler ultrasound is the most widely used method for the measurement of BP in CF-LVAD patients [25]. However, depending on the PP, the Doppler measurement can represent SBP or MAP, which creates significant controversial [24]. The validity of Doppler BP as a surrogate for MAP closely depends on PP and markedly worse among patients with high PP [26, 27]. In one study [27] the difference between the mean absolute differences between Doppler and the arterial line was 13.6 mmHg and 3 mmHg among patients with higher PP versus lower PP, respectively. To improve accuracy, another study used a combination of both Doppler and standard automated BP measurement [28]. This study proposed three BP measurements with an automated BP monitor followed by Doppler BP measurements; if automated BP monitor cannot obtain BP, Doppler pressure = SBP = MAP, If BP was obtained successfully one time, Doppler pressure = SBP, if BP was obtained two or more times successfully, then automated BP measurement can be used for SBP, DBP, and MAP measurement.

The new generation of CF-LVAD (HeartMate 3) adds another level of challenge to the measurement of BP, by the creation of an artificial pulse. Every 2 s this pump decreases the speed by 2000 rpm for 0.15 s then increases the speed by 4000 rpm for 0.20 s, before returning to the set speed [29]. These changes are timed independently from the cardiac cycle therefore BP tracings vary based on the relationship between the heart and LVAD cycles. This creates multiple components to the BP tracings thus measurements and interpretation of BP are more complex in HeartMate 3. Non-invasive BP measurement method needs to be validated. One way to overcome this challenge is to measure BP over an extended period.

MAP target is 60–80 mmHg in most of the patients with LVAD. For patients who need hypertensive medications, commonly used heart failure medications are recommended. Some studies [30] have shown mortality benefit by using angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blocker (ARB) in LVAD patients. Mineralocorticoid antagonists such as spironolactone and calcium channel blockers (CCB) such as amlodipine can be utilized as well.

Driveline Exit-Site Management

Driveline infections are most frequent in the early postoperative period but continues throughout support by LVAD due to the presence of percutaneous driveline [31]. The prevalence of LVAD infection has increased since LVADs indication has expanded to longer-term use in destination therapy (DT) [32]. The driveline exit-site is the most susceptible to infection and is most often precipitated by trauma to the tissue surrounding the site. Driveline infections can be divided into deep and superficial infections; both infections involve the soft tissue surrounding the driveline exit-site and are associated with erythema and/or drainage. Deep infections also involve the fascia and muscle layers [33]. The diagnosis and management of the driveline infection are discussed in a separate section, in this section, we will focus on outpatient management and prevention of driveline infection.

There are ongoing efforts to decrease the rate of driveline infection by studying implantation techniques and exit-site management. A study by Dean et al. [34], showed implanting the entire Dacron velour portion of the driveline under the skin decreases the driveline infection significantly compared to partially exposed vel our portion (9% vs. 23%, respectively). Nutrition has shown as an independent predictor of driveline infection. In a study by Imamura et al. [35], serum albumin concentration and low body mass index at hospital discharge after LVAD predicts readmission due to driveline infection. Authors developed a scoring system to risk-stratify the patients as low, intermediate, and high for developing the infection. This study suggests that optimizing nutrition is essential for LVAD patients to decrease the rate of driveline infection.

Driveline stabilizations and exit-site management are essential for the prevention of driveline infections. Trauma at the skin site is associated with increase driveline infection. Avoiding trauma is difficult due to the rigidity of the driveline [36, 37]. One method for driveline stabilization is using the binders, which can be effective however some patients consider it uncomfortable, and they are less likely to be used. The stabilization approach comparing the Sorbaview Ultimate Dressing and the Foley anchor increases the comfort and stabilize the driveline. This method has been used more widely. Different centers have different protocols for a dressing change. RESIST (REduce Driveline Trauma through StabIlization and Exit Site ManagemenT) [38] was a multicenter prospective, self-controlled study was designed to evaluate the use of percutaneous lead management kit (PLMK). PLMK was intended to (1) simplify the dressing change procedure, and (2) reduce the frequency of dressing changes.

PLMK improved comfort and stability in at least 50% of the patients, decreased the required frequency of changing to once weekly and reduced the risk of driveline infection. The content of PLMK include Kendall Webcol swab (70% isopropyl alcohol) for removing adhesive, Chlorascrub Maxi Swabstick and Swab for skin preparation, 3 M Cavilon No Sting Barrier Film to prevent skin irritation, Silverlon Wound Pad Dressing 1.5×1.5 inch to reduce bacterial colonization around exit site, Foley anchor for strain relief, hair cover, face mask, sterile saline and styrofoam tray.

The frequency of the dressing change depends on the time from the implant and the status of the driveline site. In a newly implanted LVAD, and infected would, it is recommended to change the dressing daily and as needed for dressing saturation. In a dry wound or a crusty wound, it is recommended to change the dressing twice weekly.

Responsibilities of Other Providers and Local Teams

Primary care doctors have an essential role in caring for LVAD patients and should be aware of the complications associated with the LVAD. Home visiting nurses are essential in taking care of LVAD patients: they assist in wound care, driveline

exit site management, home blood draws, and routine communication with LVAD team. Local first responders and emergency department should become familiar with the basic of LVAD care and appropriate triage and transfer for designated LVAD centers as needed. Most of the LVAD programs created outreach programs in order to educate the local teams about the issues related to LVAD and basic troubleshooting [39–41]. Electric utility companies are notified to place LVAD patients on the priority list for power restoration as well as to arrange for portable generators. Power companies are asked to avoid planned outage and not to stop the service for a billing issue. The local police and fire department should be aware of the LVAD patients at their districts.

Pharmacological Consideration

LVAD Effect on Coagulation System

Beside the hemolysis, LVAD also alters coagulation proteins, platelets, and von Willebrand protein. Coagulation proteins decrease in the first two weeks after LVAD implantation due to consumption [42]. Elevated levels of prothrombin fragment, D-Dimer, thrombin-antithrombin, and plasmin-antiplasmin suggest thrombus formation and activation of the fibrinolytic system with LVAD. These findings are more pronounced postoperatively and usually normalize within 6–12 months postoperatively however endothelial cell activation persists [42–44]. There is conflicting evidence regarding the platelet activation in the presence of LVAD [45, 46]. Almost all the patients with LVAD developed acquired von Willebrand syndrome due to loss of high molecular weight von Willebrand [47].

Antithrombotic Therapy

LVAD patients are treated with anticoagulation and antiplatelet due to the thromboembolic complications associated with LVAD. The medications used and intensity of the therapy varies depending on patient factor, risk of thrombosis, risk of bleeding, and institution [48]. Before LVAD placement, most of the patients are on anticoagulation for other indications. Heart failure can also cause renal and liver failure, which can compromise the coagulation system. Post LVAD surgery the bleeding is common, and the anticoagulation should be adjusted. Heparin is reversed using protamine after completion of cardiopulmonary bypass. Activated clotting time (ACT) normalization is used to target protamine dose. The ACT is insensitive for residual heparin and thromboelastography (TEG) can be used [49]. Anticoagulation with heparin is recommended to start when hemostasis is achieved on post-op day one.

Long-Term Anticoagulation Management

Vitamin K antagonists (VKA) are commonly used for long-term anticoagulation in LVAD patients. Anticoagulation goals for VKA vary between different studies however the guidelines recommended an international normalized ratio (INR) of 2.0-3.0. Anticoagulation by VKA is challenging due to the frequent need for a dose change. One study [50] found that 54% of the patients on VKA therapy needed dose adjustment without adding any new medications. LVAD patients only spend 31–51% of the time-in-therapeutic INR range [51, 52]. Patient self-testing has improved the time-in-therapeutic range however outcome of LVAD patients is not clear [52].

Antiplatelet Therapy

The choice of antiplatelet and dose vary significantly in different institutions. A majority of institutions use aspirin 81–325 mg daily, and guidelines have recommended aspirin as a drug of choice [53]. In addition to aspirin, some centers use dipyridamole, an antiplatelet medication that inhibits platelet activation through increases in cyclic AMP with unclear clinical benefit [54]. The literature review has shown aspirin dose variation from 81–325 mg once daily and dipyridamole dose of 75 mg once daily to three times daily.

Caregivers' Issues

Most LVAD programs require for patients who will receive LVAD to identify a designated caregiver. Patients and LVAD programs rely on caregivers after hospital discharge. There is significant variability in the requirement for the caregivers among the centers. The caregivers are usually spouses, family members, or close friends. Caregivers help with the daily management of the patients including driveline dressing changes, equipment maintenance, changing the batteries, responding to alarms, managing medications, taking patients vitals, helping with arranging appointments and transportation and helping with recovery [55–57]. Caregivers also support patients psychologically. Generally, caregivers must commit to the daily care of patients for a minimum of 3 months, however for most patients, caregiving extends beyond the first three months period and continues for the life of the patients [58]. The caregiving responsibility can be burdensome [59, 60].

In a study by Bunzel et al. [59], reported 26% of the spouses of the patients with LVAD, met the criteria for post-traumatic stress disorder. The burden on the caregivers depends on the stages of the caregiving course that they were in. The early-stage includes the time before LVAD implantation, decision, and hospital course, the middle-stage covers the time after hospital discharge and after and the late-stage covers the end of the caregiver care for the patient [61–68]. A

meta-analysis by Magid et al. [69] has put together the existing data to evaluate the perceptions of caring for LVAD patients in different stages. The early-stage includes three periods: Pre-LVAD, Decision, and Hospital course. In the Pre-LVAD period, caregivers often feel fear, anxiety, shock, and disbelief, which are described as "emotional rollercoaster." In the decision period, caregivers play a crucial role in decision-making, and sometimes they have to make the decisions for the patient. They have described the feeling as "no option." During the hospital course, caregivers were given relevant information and felt confident in their ability to take care of the patients however they were reluctant to take the patient home and felt they want to "leave it (the LVAD) at the hospital." The middle-stage starts after discharge from the hospital. In the beginning, caregivers felt overwhelmed and found the LVAD patients very fragile but soon was able to develop strategies to adapt to changes. Having support from other family members and friends and receiving a break from caregiving has been identified as crucial in this stage [69]. The late-stage carries different meaning for caregivers who take care of BTT versus DT LVAD patients. For the caregivers who are taking care of BTT LVAD patients, LVAD is not a permanent therapy, and it seems easier to accept the burden, and the late-stage means receiving a heart transplant. They have expressed hope for the future and relief when patients receive a heart transplant. For the caregivers who are taking care of DT LVAD patients, the late-stage means the end of patients' life. Caregiving can be stressful. Caregivers for patients with chronic illnesses are at extremely higher risk for developing anxiety, depression, loneliness, fatigue, and insomnia; they are also in a higher risk for infection, cardiovascular disease, and early mortality, and caregivers for LVAD patients.

There is a significant gap in our knowledge regarding the assessment of caregivers' stability, need, and providing the necessary support for them. Future studies are required for a better understanding of the caregivers' burden and need.

Case Conclusion

He and his wife, as his primary caregiver, were referred to the psychologist and smoking secession program. He quit smoking, and his depression improved significantly. He was activated on the transplant list. He was transplanted seven months later. He is doing well and started taking classes in the nursing school.

Equipment Management

HeartMate II and HeartMate3:

Power Module (PM):
PM is the main source of power, and the patient must always be on PM while sleeping. The PM must be plugged into a designated three-prong outlet all the time.

Symbols on PM:

– Power indicator (upper right):

  - Green: PM is plugged into the outlet.
  - Orange with beeping audio tone: AC failure.

– Internal battery symbol (middle right):

  - Green: the battery is fully charged.
  - Yellow: the battery is being charged.

– Battery advisory symbol (bottom right):

  - Yellow with beeping audio tone: less than 15 min of back-up battery: promptly switch to another power source.
  - Red with continuous audio tone: less than 5 min of back up battery: immediately switch to batteries.

– Alarm silence key (upper left):

  - Silence alarm
  - Perform PM self test

– Yellow wrench symbol (lower left):

  - Yellow wrench with beeping audio tone: advisory fault. Recommend switching to battery power.
  - Yellow wrench with continuous audio tone: critical fault. Recommend switching immediately to battery power.

Pocket Controller (PC):

System controller self-test should be performed daily while on PC. To perform self-test, hold the battery button for five second, all symbols and indicators illuminate at the same time and system controller will make a load audio. Release the battery button, the lights and symbols will stay on for 15 s and when they turn off and screen goes black, the system controller self-test is complete.

– Pocket controller modes:

  - Run mode: running and in use
  - Sleep mode: not in use, but ready to use
  - Charge mode: connected to a power source and charging the system controller's back up battery

– Pocket controller symbols:

  - Pump running circle:

    Full circle: the pump is running
    Half circle: the pump is in backup controller mode

- Battery button:

  Battery fuel gauge: when in battery operation
  Yellow diamond: less than 15 min of battery power is left.
  Red low battery symbol: less than 5 min of power is left.
  System controller test
  Running controller sleep mode

- Silence alarm button:

  Silence active alarms
  Displays last 6 alarms when pressed simultaneously with display button.

- Status symbols:

  Green bars: battery power gauge
  Red heart: low flow hazard alarm
  Yellow wrench: advisory alarm, which can indicate mechanical, electrical, or software issue with the system.
  Cable disconnect symbol: represents cable disconnect — yellow light near cables and the red light near driveline.

Batteries:
Batteries provide 10–12 h of support, depending on the age of the batteries, charge, and pump speed. Batteries are depleted and charged in pairs. There are two ways to check the amount of battery power while in use.

(1) Battery symbol button on the battery and
(2) Battery power gauge on the system controller.

Universal Battery Charger (UBC):

UBC charges and performs diagnostic testing on up to 4 batteries. It takes 4 h or less to charge the batteries.

– Light status:

- Green: ready to use
- Yellow: charging or undergoing calibration
- Flashing yellow: battery requires calibration. Batteries need periodic calibration; this usually occurs after approximately 70 to 75-battery usage. It is best to start battery calibration at night when batteries are not in use. The calibration can take up to 12 h. To start the calibration, press the numbered pocket with flashing yellow light. The light will return to green when calibration is complete.
- Red: defective battery or charging pocket

HeartWare:
Pocket controller:

– Pocket controller symbols:

  - AC/DC indicator: indicates the power source, it will be green if one of the power sources is the AC adaptor or DC adaptor (car adaptor)
  - Alarm indicator: displays active alarm

– Two battery indictors: Battery fuel gauge, which indicates the percentage of battery charge
– Controller display: displays LVAD parameters
– Scroll button: used to see all active alarms and pump information on the controller display.

Batteries and power source:
HeartWare is designed to operate with 2 power sources: external power (AC adaptor or car power adaptor) and 1 battery or 2 batteries. Each battery provides 4–6 h of support, depending on the age of the batteries, charge, and pump speed. Batteries are depleted one battery at a time. Pressing battery test button shows remaining battery power.

Battery charger:
Battery charger charges up to 4 batteries in 4–5 h, performs diagnostic testing.

– Status:

  - Ready status:
    No lights: battery is resting after charge
    Green: ready for use
  - Yellow: charging not ready to use
  - Flashing yellow: battery not charging, check battery connections
  - Red: battery too hot or too cold
  - Flashing red: defective battery

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Evaluation and Management of LVAD Complications

Enrico Perna and Nicholas Wettersten

Clinical Vignette

A 67-years-old man with a long history of ischemic cardiopathy type II diabetes mellitus and carotid artery disease underwent HeartWare HVAD (HeartWare Boston MA) implantation as destination therapy via sternotomy. Surgery and postoperative recovery were uneventful and the patient was discharged home on standard antithrombotic therapy (warfarin with INR range 2–3 and aspirin 325 mg daily). He remained stable until over a year later he presented with hematuria prompting admission to the hospital. There were no signs of pulmonary or abdominal congestion or signs of cardiogenic shock. HVAD parameters showed a progressive increase in power (2.8 Watts → 3.6 Watts) and flow (3.9 L/min → 6 L/min) with an unchanged speed of 2360 rpm. How should this patient be managed?

Introduction

Mechanical circulatory support with ventricular assist devices (VADs) is an important treatment strategy for patients with end-stage heart failure (HF) that is refractory to medical therapy. The use of left ventricular assist devices (LVADs) has increased significantly over the past few years with more than 22,000 devices implanted by 2019 in the United States and more than 2,500 new implants occurring annually [1]. These patients have a 1-year and 2-year survival of 81% and 70%, respectively; however, almost 80% of LVAD patients will be hospitalized

E. Perna
Transplant Center and de Gasperis Cardio Center, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy

N. Wettersten (✉)
Cardiovascular Institute, University of California, La Jolla, San Diego, CA 92093, USA
e-mail: nwettersten@health.ucsd.edu

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within the first year after implantation for some complication. The management of these devices is complex, and these patients still experience high rates of VAD-related adverse events. The most common of these directly related to the LVAD are gastrointestinal bleeding, infection, and neurologic events. However, other LVAD associated complications such as arrhythmias and aortic insufficiency are as important in the care of LVAD patients. Thus, clinicians must be familiar with common and serious complications. This chapter will give an overview of complications to assist clinicians in evaluation and management. This will focus largely on complications in HeartMate II (HMII), HeartMate 3 (HM3) and Heartware (HVAD) devices, which are those most commonly used in the United States.

Basic LVAD Physiology

The LVAD provides an alternate parallel path for blood flow from the left ventricle (LV) to the aorta [2, 3]. Contemporary continuous-flow LVADs consist of a blood pump, percutaneous lead, external power source, and system controller. The blood pump consists of an inflow cannula (inserted into and draining from the apex of the LV), an impeller, and an outflow cannula, which by means of a graft delivers the blood into the aorta. The impeller rotates at a high speed inside its housing, which accelerates the fluid forward along the axis of the impeller in axial-flow pumps (HMII) or outwardly in centrifugal pumps (HVAD and HM 3) (Fig. 1). General characteristics of contemporary devices are shown in Table 1.

Pump Parameters

Contemporary continuous-flow LVADs display the following parameters on the controller or the monitor, and Table 2 gives a brief overview of clinical scenarios causing abnormal pump parameters. (Tables 1 and 2):

Pump Flow is defined as: Flow = Rotor Speed/(P outflow − P inflow)

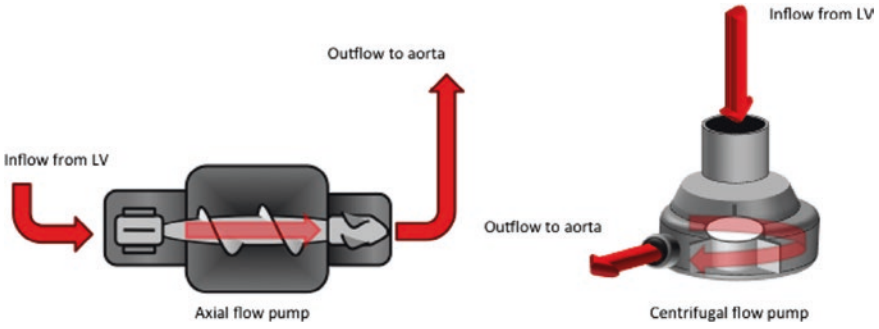

Fig. 1 The two types of impellers most commonly used clinically

Table 1 General characteristics of the three devices

Device	HeartMate II	HeartMate 3	HeartWare
Flow	Axial	Centrifugal	Centrifugal
Placement	Preperitoneal	Intrapericardial	Intrapericardial
Bearing	Ball and cup (blood immersed)	Magnetic levitation	Hydrodynamic
Speed range (rpm)	6000–15000	3000–9000	2400–3200
Maximum flow	10 L/min	10 L/min	10 L/min
Blood flow gaps, mm	0.08	0.12	0.05
Artificial pulsatility	No	Yes	No
FDA approved indications	BTT (2008) DT (2010)	BTT (2017) DT (2017)	BTT (2012) DT (2017)

Table 2 Alterations of pump parameters may suggest different clinical scenarios

Pump parameters	High pulsatility	Low pulsatility
High power/flow	Normal physiology, Improvement in cardiac function, exercise	Hypotension, high pump speed, pump thrombus (affecting rotor/bearings)
Low power/flow	Hypertension, low pump speed, inflow/outflow graft obstruction	Hypovolemia, tamponade, right heart failure, arrhythmias, inflow/outflow graft obstruction

The Flow is derived from pump power consumption and correlates:

- Directly with the speed of the rotor
- Indirectly with the pressure differential between LV and the aorta

Power ("the energy consumed to spin the impeller at the speed we have set"), is a function of:

- Patient status (volume status, degree of afterload, activity)
- Pump status (kinked outflow graft, obstructive inflow cannula, rotor and bearing thrombus)

Pulsatility Index (only reported for HMII and 3 but can be derived from HVAD screen) is defined as: PI = (maximum flow − minimum flow)/average flow × 10. PI has been used as a surrogate for the degree of LVAD support: the lower the PI, the greater the amount of support provided by the pump.

Evaluation of Abnormal LVAD Parameters

Approach

LVAD parameters are an additional vital sign. Like any vital sign, when a parameter is out of the normal range for a patient, assessment for a possible cause should

occur. The prior section provided differentials for some causes of abnormal parameters. Further assessment to narrow this differential is similar to any HF patient with a thorough history, physical exam, and selective laboratory and diagnostic testing (Tables 3, 4, 5 and 6). Early invasive hemodynamic monitoring should be considered for many LVAD complications, but especially in situations of recurrent HF to optimize patient hemodynamics and LVAD function. Clues from these evaluations can direct the clinician to the appropriate issue and management as outlined in following sections.

Table 3 History findings and differential

Symptoms	Clinical condition	Differential
Dyspnea, orthopnea, edema, abdominal bloating	Recurrent HF	Non-compliance, RHF, arrhythmia, pump malfunction
Fatigue, dyspnea, epistaxis, melena, hematochezia	Blood loss	Gastrointestinal bleeding, hemolysis
Fevers, chills, malaise, driveline drainage	Infection	Community acquired infection, driveline infection, pump/pocket infection, endocarditis
Focal weakness, slurred speech, sensation disturbances	Neurologic event	Stroke (ischemic or hemorrhagic)

Table 4 Physical exam findings and differential

Findings	Clinical considerations
Low MAP	Increased LVAD flow, hypovolemia, infection
High MAP	Low LVAD flow, hypertension
Abnormal temperature	Infection
Abnormal heart rate	Arrhythmia
Abnormal LVAD sound	Pump thrombosis, inflow/outflow obstruction
Jugular venous distension	HF, arrhythmia, tamponade
Pallor	Blood loss
Driveline erythema/discharge	Driveline infection
Lung crackles	Heart failure, pneumonia
New weakness, loss of sensation	Stroke

Table 5 Laboratory testing

Test	Clinical considerations
Complete blood count	Leukocytosis—infection Anemia—blood loss
Renal function	Acute kidney injury
Liver function	Abnormalities with congestion, infection, hemolysis
INR	Within therapeutic range?
LDH/plasma free hemoglobin	Markers of hemolysis

Table 6 Diagnostic testing

Test	Clinical considerations
Electrocardiography	Arrhythmia detection
Echocardiography	Assessment of left ventricular size—inadequate unloading? Right ventricular size/function—RHF Valvular heart disease—regurgitant lesions Thrombus
Chest X-ray	Pulmonary edema Infiltrate
Computed tomography	Head—signs of ischemic or hemorrhagic stroke Chest—infection, effusion, fluid collections Abdomen—assessment of driveline, fluid collections

Pump Thrombosis

Background

Pump thrombosis (PT) is defined as an obstruction that limits blood entering or exiting the pump or otherwise impinges the impeller from properly rotating. Recently, the MOMENTUM 3 trial showed 0.12 events per patient-year (EPPY) of PT in the HMII arm with very few events in the HM3 arm [4]. The ADVANCE trial reported an incidence of 0.04 to 0.09 EPPY in the HVAD population [5]. Notably there has been a drastic reduction in the incidence of PT since 2015 with the progressive growth in the number of HM 3 implants. Though an uncommon complication, its clinical implications are substantial as they can lead to catastrophic pump failure or other complications such as stroke.

When clot does form, the location and histology of the clot formation can differ depending on VAD type (Fig. 2). Globular clot formations have been reported on

Fig. 2 Pump Thrombosis

the inflow bearings and in regions of sharp angulation of the HMII inflow/outflow grafts. In contrast laminar fibrin formations may develop on the impeller of HVAD pumps if a thrombus event occurs. The HM 3 was designed to prevent pump thrombosis by employing three innovations:

- Use of wider blood flow passages to reduce shear stress and minimize disruption of red blood cells as they pass through the pump
- Magnetic levitation technology to create a frictionless pump with no mechanical bearings
- Incorporation of an artificial fixed pulse that speeds up and slows every two seconds to minimize blood stasis and facilitate pump surface washing.

Presentation of Pump Thrombosis

Patients experiencing PT may present with four possible scenarios:

(1) Asymptomatic sustained power elevations (defined as power $\geq$ 10 watts or power > 2 watts above baseline for > 24 h)
(2) Isolated elevation of LDH levels (>3 times the upper limit of normal) or plasma free hemoglobin (pfHb) (>40 mg/dL)
(3) Clinical signs of hemolysis (hemoglobinuria)
(4) Symptoms of HF (with or without hemodynamic abnormalities including shock)

Diagnostic Evaluation

In addition to the assessment of abnormal device parameters, the following tests are commonly used for diagnosing PT (Table 7):

Serial recording of LV end-diastolic diameter with increasing VAD speeds (known as a ramp study) may diagnose pump thrombus or other obstructions to blood flow within the rotatory pump and cannula system.

Management

At present, the ideal strategy for treating PT in contemporary devices has yet to be defined. Surgical device exchange or urgent heart transplantation represent the most definitive treatment modalities, in particular for HMII patients because clots are generally detected after they are no longer amenable to medical therapy.

Table 7 Diagnostic testing for pump thrombosis

Laboratory findings	Chest X-ray	Echocardiography	Chest computed tomography
High LDH	Malposition of inflow	Dilated ventricle	Malpositioned inflow cannula
Low hemoglobin/ hematocrit	Misaligned outflow graft protector	Severe mitral regurgitation	Kinked outflow graft
Low haptoglobin	Pulmonary congestion	Frequent aortic valve opening	If contrast used, thrombus within inflow or outflow
High plasma free hemoglobin		Elevated right ventricular systolic pressure	
Hemoglobinuria			
Elevated bilirubin			

The use of medical therapy can be considered for patients:

- With asymptomatic hemolysis
- Who are poor candidates for surgical management
- In whom it would be advantageous to avoid surgery and instead expedite transplantation

The up-titration of anti-thrombotic therapy includes

- Addition of a second anti-platelet agent (clopidogrel, dipyridamole)
- Intravenous heparin (targeting PTT two to three times upper limit) or intravenous bivalirudin
- Fibrinolytics with intraventricular or systemic administration.

Right Heart Failure

Presentation of Right Heart Failure

Right heart failure (RHF) can present at any time after LVAD placement and frequently presents in the immediate post-operative period. It can be a temporary state that resolves with therapy or a chronic problem requiring regular management and recurrent hospitalizations after LVAD implantation. Approximately one third of LVAD patients will experience RHF.

Signs and symptoms of RHF are predominately those of recurrent HF and multiple laboratory abnormalities can develop (Table 8):

Table 8 Signs, symptoms and lab abnormalities with right heart failure

Fatigue	Dyspnea on exertion
Edema	Bloating
Early satiety	Decreased urine output
Ascites	Elevated jugular venous pressure
Elevated natriuretic peptide levels	Elevated creatinine and BUN
Elevated liver function tests	Elevated prothrombin time
Low albumin	

Prediction and Diagnostic Criteria

Numerous echocardiographic and hemodynamic (Table 9) variables have been associated with an increased risk of post-operative RHF and are also used in diagnosing RHF (Fig. 3) [6, 7].

Other non-echocardiographic and hemodynamic risk factors include:

- Female gender
- Non-ischemic cardiomyopathy
- Liver dysfunction
- Kidney dysfunction

Most criteria are derived from studies with small patient populations. No one criterion is sensitive or specific enough to predict or diagnose RHF, thus one should consider and incorporate multiple criteria for predicting and diagnosing RHF. Multiple risk scores for RHF have been developed that include many of the variables above but have not shown strong predictive performance outside of the population they have been derived in (Fig. 4).

Formal criteria suggested for defining RHF are listed in Table 10 [8].

Table 9 Features associated with post-operative right heart failure

Echocardiographic features	Hemodynamic features
Enlarged RV (ratio RV/LV > 0.75, but especially when RV is larger than LV)	Elevated CVP (>15 mmHg)
Bowing of the interventricular septum towards the LV	Elevated CVP to wedge pressure ratio (>0.63)
Low tricuspid annular planar systolic excursion (TAPSE) (<8 mm)	Low pulmonary artery pulsatility index (PAPi = PA systolic pressure—PA diastolic pressure/CVP; PAPi < 2.0 indicates increased risk)
Reduced RV fractional area change (<35%)	Elevated pulmonary vascular resistance (>4 woods units
Reduced RV strain (>−15.5%)	Low RV stroke work index (<300 mmHg ml/m^2)
Severe tricuspid regurgitation	

CVP—central venous pressure; LV—left ventricle; PA—pulmonary artery; RV—right ventricle

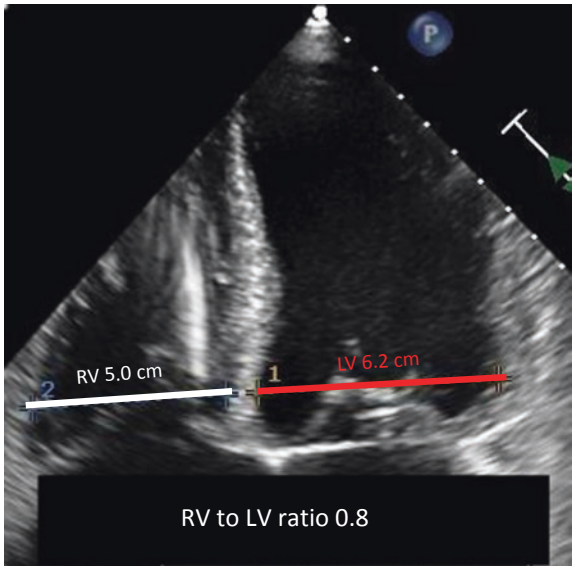

Fig. 3 Example of an echocardiogram from the apical four chamber view with substantial right ventricle (RV) dilation compared to left ventricle (LV) at a ratio > 0.75. Patient later experienced post-operative RHF after LVAD placement

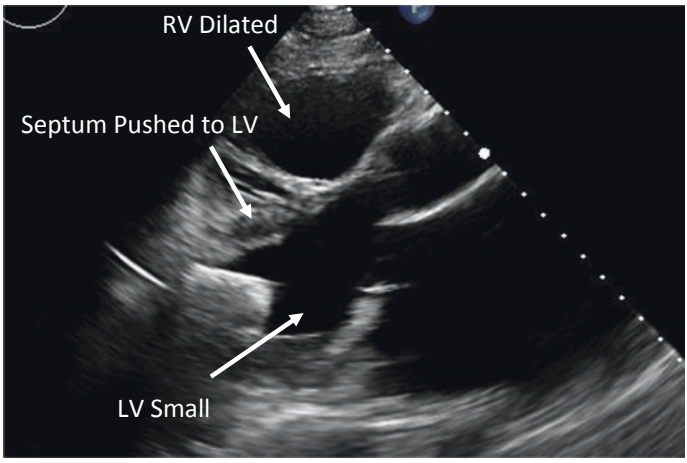

Fig. 4 Echocardiogram from parasternal long-axis view showing RHF after LVAD placement with a dilated right ventricle (RV) shifting the septum towards the left ventricle (LV) resulting in a small LV cavity. Patient's LVAD had to be run at low speed to prevent suction and RHF needed support with intravenous milrinone

Table 10 Criteria for defining right heart failure and severity

Elevated CVP reflected as either: • CVP > 16 mmHg • Dilated inferior vena cava without collapse on echocardiography • Elevated jugular venous pressure **And** signs of RHF reflected as either: • Edema • Ascites/hepatomegaly • Worsening liver or kidney function on labs
Grading
Mild • Prolonged post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators but not continued beyond post-operative day 7 after LVAD
Moderate • Post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators continued beyond post-operative day 7 but not beyond post-operative day 14 after LVAD
Severe • CVP greater than 16 mmHg **AND** • Prolonged post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators continued beyond post-operative day 14 after LVAD
Severe-acute • CVP greater than 16 mmHg **AND** • Need for mechanical right ventricular support **OR** death

CVP—central venous pressure

Differential

Mimics or causes of RHF both acutely and/or chronically include:

- Tamponade
- Inadequate LV support
- Pulmonary embolism
- Right ventricular (RV) myocardial infarction
- Arrhythmias

Management

Management of RHF is largely based on optimization of RV hemodynamics. Every effort should be made to optimize hemodynamics prior to LVAD implantation to reduce the risk of RHF. Pre-operative administration of oral phosphodiesterase-5 inhibitors has been associated with an increase in RHF post-LVAD [9]. There are no large randomized studies at this time for specific treatments or therapies to improve outcomes of RHF after LVAD. Management of RHF may vary in the acute post-operative setting and with chronic management. Therapies commonly used for both acute and chronic RHF include:

- Aggressive volume removal with diuretics and ultrafiltration if diuretics are inadequate
- Inotropic support with dobutamine, dopamine, milrinone, or levosimendan
- Inhaled pulmonary vasodilators including inhaled nitric oxide or epoprostenol
- For acute RHF after LVAD, early and planned use of mechanical RV support has better outcomes than late or emergent support [10].
- For chronic RHF, off-label use of oral phosphodiesterase-5 inhibitors are frequently administered with weak data of possible benefit, especially if hemodynamics suggest pulmonary hypertension. Digoxin can be empirically given for inotropic support.
- The ultimate therapy for chronic RHF is heart transplantation.

Bleeding

Presentation and Assessment

Bleeding is one of the most frequent LVAD complications occurring in one to two thirds of patients [1]. The most common cause is gastrointestinal, but other causes include epistaxis, bruising, and trauma related bleeding. Presenting symptoms and features of evaluation include:

- Active cutaneous bleeding, melena, hematemesis, epistaxis, fatigue, dizziness, syncope, HF
- Low mean arterial pressure (MAP), orthostatic symptoms, pallor
- Low hemoglobin, INR at goal or elevated, LDH may be elevated, elevated BUN
- Low flow on LVAD, low flow alarms, hematocrit is entered to calculate flow on HVAD and HM 3 so reprograming hematocrit will increase flow

Gastrointestinal bleeding frequently occurs from sites found in non-LVAD patients such ulcers, polyps, and hemorrhoids. Somewhat unique to LVAD patients is an increased frequency of bleeding from angiodysplasia. Arteriovenous malformations (AVMs) are thought to form from lack of pulsatile flow and an acquired von Willebrand disease (Figs. 5 and 6) [11]. Multiple risk factors have been identified for bleeding complications (Table 11).

Management

In the acute setting, therapy involves both pharmacologic and procedural interventions. Chronic management is determined by cause of bleeding, risk of recurrence and frequency of recurrence.

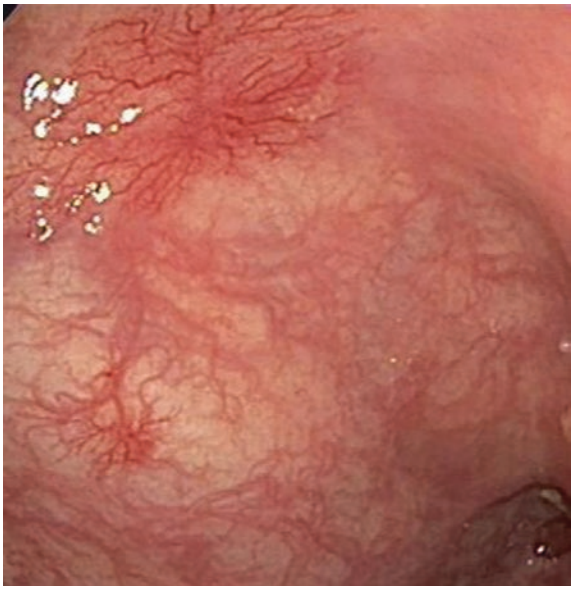

Fig. 5 AVMs in the colon of a patient with a HMII LVAD and recurrent blood loss

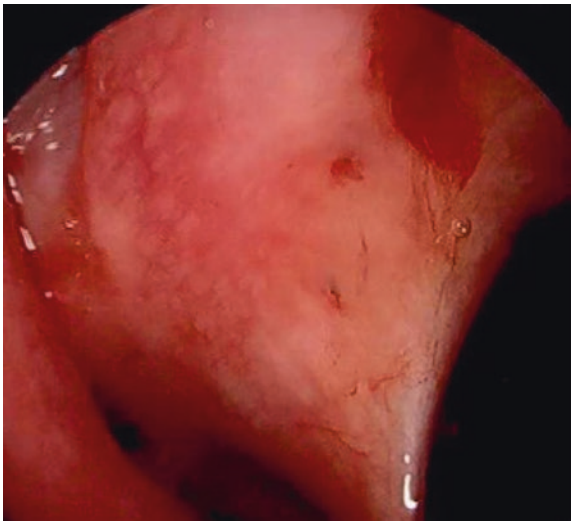

Fig. 6 Nasal AVM (top right of photo) in HVAD patient. Patient had profound epistaxis with repeated drops in hemoglobin until operative intervention where diffuse nasal AVMs were found requiring electrocautery

Table 11 Risk factors for bleeding in LVAD patients

Older patient age	Low pulsatility
History of gastrointestinal bleeding	Post-LVAD ejection fraction > 30%
Preceding coagulopathy	Post-implantation infection
Elevated creatinine	Low platelet count
RV dysfunction	

Potential interventions in the acute setting include:

- Hemodynamic stabilization with intravenous fluids and blood transfusions
- Withholding of antiplatelets and anticoagulants
- INR value and severity of bleeding should be carefully weighed against the risks of reversing anticoagulation. Administration of fresh frozen plasma could be considered with active life-threatening bleeding. Vitamin K is generally avoided as it does not acutely correct and may over-correct anticoagulation. Prothrombin complex concentrate should be given cautiously given its increased risk of thrombosis.
- Intravenous proton pump inhibitor
- Intravenous octreotide [12].
- Esophagogastroduodenoscopy and/or colonoscopy
- Capsule endoscopy (for diagnosis and identification of source)
- For severe uncontrolled or recurrent bleeding, surgical resection of bleeding bowel segment could be performed

Potential chronic therapies and measures after an episode of gastrointestinal bleeding or recurrent bleeding include:

- Adjusting LVAD speed to increase pulsatility and reduce sheer stress
- Lowering INR goal
- Stopping antiplatelets
- Chronic oral proton pump inhibitors
- Chronic octreotide (often administered in depot form) in the setting of AVMs [13].
- Studies suggest angiotensin blockade with angiotensin converting enzyme inhibitors or angiotensin receptor blockers reduces risk of gastrointestinal bleeding
- Thalidomide [14].
- Hormonal therapy with estrogen

Stroke

Background and Presentation

As with mechanical prosthetic valves, LVAD patients are at increased risk for both ischemic and hemorrhagic stroke given the thrombogenicity of the mechanical pump and necessity of anticoagulation. Almost 20% of LVAD patients will suffer a stroke within the first year after implantation, with slightly more than half being ischemic [1, 15]. Compounding risk is the presence of concomitant medical conditions that increase the risk of stroke such as atrial fibrillation, peripheral arterial disease, diabetes and hypertension. Additionally, it is believed that non-pulsatile flow alters cerebral vasculature potentially predisposing to stroke [16].

Table 12 Risk factors for stroke in LVAD patients

Systemic infection	Hypertension
Atrial fibrillation	Female gender
Anticoagulation levels	Duration of LVAD support
Low pulsatility	Prior stroke

Stroke symptoms in LVAD patients are the same as other patients. Neurologic deficits can vary and include focal weakness, sensory deficits, speech difficulties, vision loss, or loss of coordination. Symptoms may be less focal and include headache, confusion, or altered mental status. Thus, physicians should maintain a low threshold to evaluate for stroke in LVAD patients presenting with non-specific symptoms even if a neurologic deficit is not noticeable.

Risk factors for stroke are listed in Table 12. Two important risk factors are infection and hypertension. A concomitant systemic infection is one of the most common risk factors for stroke [15, 17]. Infections may promote a prothrombotic environment or become endocarditis with embolization. Hypertension has been repeatedly found to be a risk factor for stroke in LVAD patients, especially in HVAD patients [18]. Risk significantly increases when MAP is > 90 mmHg.

Assessment

Patient's with possible stroke symptoms should be rapidly assessed given the limited time available for possible intervention. Patients and their caregivers should be taught the F.A.S.T. acronym (Face drooping, Arm weakness, Speech difficulty, Time to call 911) for warning signs of stroke. Anytime stroke is a concern, neurology consultation should be immediately sought.

The preferred imaging modality for stroke is magnetic resonance imaging; however, this is prohibitive in LVAD patients [17]. Thus, diagnosis is based on history, physical exam, CT imaging, and vascular imaging. A CT scan should be obtained within 10 min of initial concern for stroke to differentiate hemorrhagic from ischemic stroke. In early ischemic strokes, CT head imaging will often be normal. Imaging is frequently repeated to assess for changes consistent with ischemic stroke, expansion of a hemorrhagic stroke, or to monitor for hemorrhagic conversion. CT angiography can evaluate for large vessel occlusions that might be intervenable upon. Digital subtraction angiography is usually only performed if endovascular intervention is performed; however, it may be necessary if there is concern for a mycotic aneurysm [17].

Evaluation for risk factors and sources of stroke should be sought. Given the association with concomitant infection, blood cultures should be drawn. This may lead to further evaluation for endocarditis. An echocardiogram should be obtained as this may visualize a thrombus or a vegetation of endocarditis (Fig. 7). Further testing may include carotid ultrasounds or transesophageal echocardiography based on evaluation.

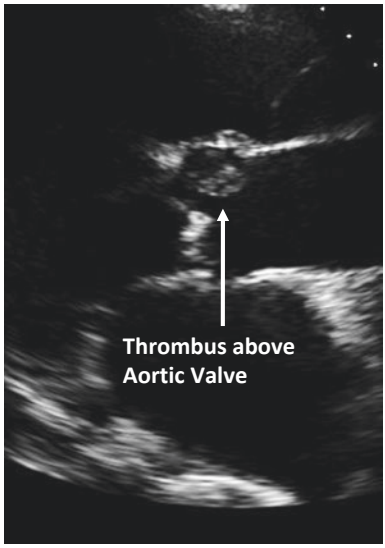

Fig. 7 Transthoracic echocardiogram showing a thrombus above the aortic valve and lack of aortic valve opening in an LVAD patient presenting with a stroke

Management of Ischemic Stroke

In non-LVAD patients, thrombolytic therapy with recombinant tissue plasminogen activator (rtTPA) is the treatment of choice if an ischemic stroke is detected early enough. However, rtTPA is frequently contraindicated in LVAD patients given the use of anticoagulation (contraindicated if INR > 1.7) and antiplatelet therapy that increase the risk of hemorrhagic complications. Additionally, there is a heightened risk of hemorrhagic conversion given the association of stroke and systemic infection in LVAD patients as well as other potential defects in the coagulation system of LVAD patients. Thus, use of rtTPA must be carefully weighed against these risks.

Mechanical thrombectomy offers an alternative for large vessel occlusion. This therapy has not been systematically studied in LVAD patients and case reports have reported variable outcomes. By avoiding systemic rtTPA, this could potentially minimize systemic bleeding risks; however, hemorrhagic conversion risk is similar and possibly higher than rtTPA [17]. The window for potential therapeutic benefit of mechanical thrombectomy is longer than rtTPA. Careful consideration and discussion with neurology should be performed when considering this treatment option.

Separate from these therapies, care is focused on supportive measures. Since most strokes in LVAD patients are presumed to be device related, risks of reversing or withholding anticoagulation should be weighed against risk for device thrombosis and possible recurrent ischemic stroke. Generally, anticoagulation should be held for the first 24 h to monitor for hemorrhagic conversion [17]. Anticoagulation may then be restarted 1 to 7 days after initial presentation based

on INR and clinical course. This decision should be individualized to a patient's risk for hemorrhage and clinical status.

Volume status should be optimized to avoid volume depletion, but also avoid fluid overload. Both hyper- and hypoglycemia should be corrected as necessary with goal of maintaining glucose in range of 80 to 180 mg/dL. In normal stroke management, permissive hypertension is allowed because of the loss of cerebral autoregulation; however, with continuous non-pulsatile LVAD flow, blood pressure often does not reach levels that would prompt treatment in normal stroke patients. Hypotension should be avoided and vasoactive agents may be needed to maintain cerebral perfusion.

Management of Hemorrhagic Stroke

An important initial distinction for management is determining if a hemorrhage is a primary process or the result of hemorrhagic conversion. Anticoagulation should often be reversed in hemorrhagic stroke; however, this must be weighed against the risk of device thrombosis. Also, if the initial stroke was ischemic with hemorrhagic conversion, reversal of anticoagulation may potentially lead to propagation of a device related thrombus. The decision to reverse anticoagulation needs to be individualized based on mechanism of hemorrhage, history of stroke or device thrombosis, current level of anticoagulation, and size of hemorrhage. Aggressive blood pressure reduction is usually pursued in hemorrhagic stroke, but because of continuous blood flow and altered blood pressure, the optimal blood pressure in an LVAD patient is unknown, but generally MAP is maintained at <90 mmHg.

For large hemorrhagic strokes with substantial vasogenic edema, there may be neurologic deficits from compression prompting neurosurgical evaluation for decompressive therapies. Studies are varied on benefits of decompressive surgeries and these procedures are even more challenging in LVAD patients given the bleeding risks from anticoagulation and need to minimize anticoagulation therapy for prolonged periods after performing such an operation. Requiring such therapies often portends a poor prognosis.

Long-Term Management

Following initial acute hospital management of stroke, care should focus on aggressive rehabilitation. For both ischemic and hemorrhagic stroke, goals of antiplatelet and anticoagulation therapy should be reassessed, and the target range of INR may need to be redefined. Blood pressure should be controlled to maintain MAP < 90 mmHg. Secondary prevention measures of lipid and glucose control have not been studied in LVAD patients but may improve outcomes depending on mechanism of stroke.

Arrhythmias

Presentation

Arrhythmias are a frequent complication in LVAD patients [19, 20]. Atrial arrhythmias and ventricular arrhythmias are estimated to occur in 20 to 50% of LVAD patients. Because of continuous flow with near full circulatory support provided, LVAD patients can be very tolerant to arrhythmias including ventricular arrhythmias (Fig. 8). Patients frequently present without symptoms or only vague and non-specific symptoms (Table 13). This requires clinicians to remain vigilant for arrhythmia detection before potential adverse consequences occur.

Risk Factors and Outcomes

Atrial arrhythmias are not well studied in LVAD patients, but the most frequent atrial arrhythmia is atrial fibrillation [19, 20]. Risk factors and outcomes are not well described for atrial arrhythmias, but the largest concern is thromboembolic risk with atrial fibrillation. The initial INR goal for LVAD patients is same for

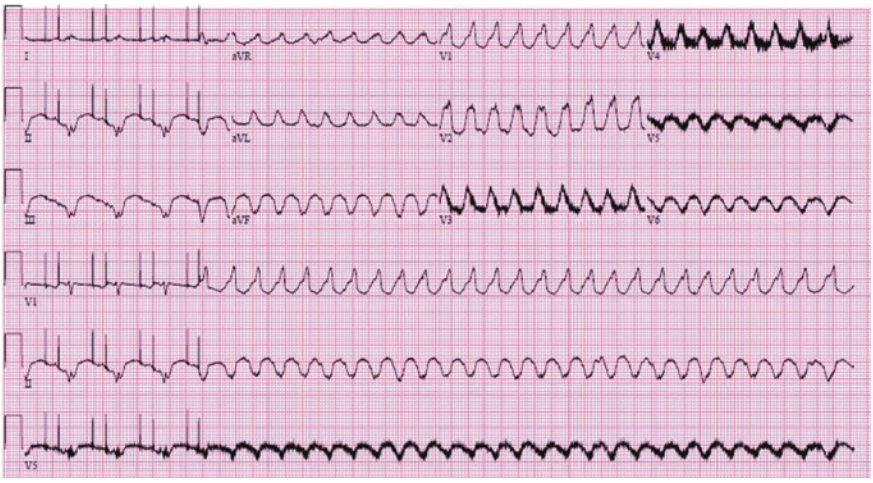

Fig. 8 Patient supported by LVAD is paced then goes into monomorphic ventricular tachycardia without loss of consciousness

Table 13 Symptoms from arrhythmias on LVAD support

Fatigue	Weakness
Palpitations	RHF
Pre-syncope	Syncope (rare)

atrial fibrillation, but a bleeding event may change the INR goal and thromboembolic risk may increase.

Ventricular arrhythmias most often occur early after LVAD implantation [20]. Risk factors include prior history of ventricular arrhythmias, lack of beta-blocker use, and potentially ischemic cardiomyopathy, though some studies report higher incidences with non-ischemic cardiomyopathy. One potential risk and source of early post-operative ventricular arrhythmias is scar from placement of the inflow cannula. Early post-operative ventricular arrhythmias have been variably associated with an increased morbidity and mortality, which likely depends on the status of the patient, RV, hemodynamic support, and clinical context.

Management

For any hemodynamically unstable arrhythmia, immediate cardioversion/defibrillation should be performed.

Management of atrial arrhythmias, mainly atrial fibrillation, focuses on rate or rhythm control and thromboembolic risk reduction. LVAD patients are usually anticoagulated to the same INR goal as atrial fibrillation. However, if a bleeding event occurs, INR goals may be lowered and the thromboembolic risk from atrial fibrillation may increase. Whether to pursue a rate or rhythm control strategy or any medical therapy at all depends on a patient's tolerance of the arrhythmia. Rhythm control should be sought for symptomatic patients with amiodarone, sotalol or dofetilide as preferred agents. Rate control with either carvedilol, metoprolol succinate, bisoprolol and/or digoxin can be used. For symptomatic patients unable to tolerate any medical therapy, AV node ablation may be necessary.

Ventricular arrhythmias are often initially managed with medical therapy including beta-blockers, amiodarone, mexiletine, sotalol or dofetilide. Early perioperative ventricular arrhythmias may resolve with sufficient time and healing. For medically refractory ventricular arrhythmias or those with significant hemodynamic impact, catheter ablation may be necessary [20]. Catheter ablation therapy has only been studied in case reports and series at specific centers. While results show efficacy in the short-term, long-term follow up studies are lacking.

Aortic Insufficiency

Presentation

Aortic insufficiency (AI) is a common complication after LVAD implantation. It is estimated that 1 in 4 patients will develop at least mild to moderate AI within one year of implantation [21]. With LVAD therapy, the heart is subjected to AI that is pancyclic, occurring throughout systole and diastole, in response to the constant positive transaortic pressure gradient. Risk factors for AI while under support are listed in Table 14 [21].

Table 14 Risk factors for aortic insufficiency

Persistently closed aortic valve	Excessive LV unloading
Prolonged duration of support	Small body surface area
Systemic hypertension	Female gender
Moderate mitral regurgitation	Older age
Larger aortic dimension at implantation	Cannulation site (at least 2 cm above the sino-tubular junction)
Anastomotic angle (≥ 90° transversally and between 60° and 120° in the coronal plane)	

Diagnosis

Transthoracic echocardiography (TTE) parameters (i.e. vena contracta, jet width/LVOT diameter, PISA) largely underestimate AI severity, because regurgitant flow occurs during the whole cardiac cycle (Fig. 9). However, TTE remains the gold-standard to detect AI.

Two novel echocardiographic parameters have been proposed for grading severity of AI [22]:

- *The outflow LVAD cannula systolic-to-diastolic peak velocity ratio (S/D ratio):* this value is inversely proportional to AR severity (significant AI is likely when S/D ratio is <5.0)
- *LVAD outflow cannula diastolic acceleration*, obtained by measuring the diastolic slope from the onset of diastolic to end-diastole (significant AI is when diastolic acceleration is >49.0 cm/s^2)

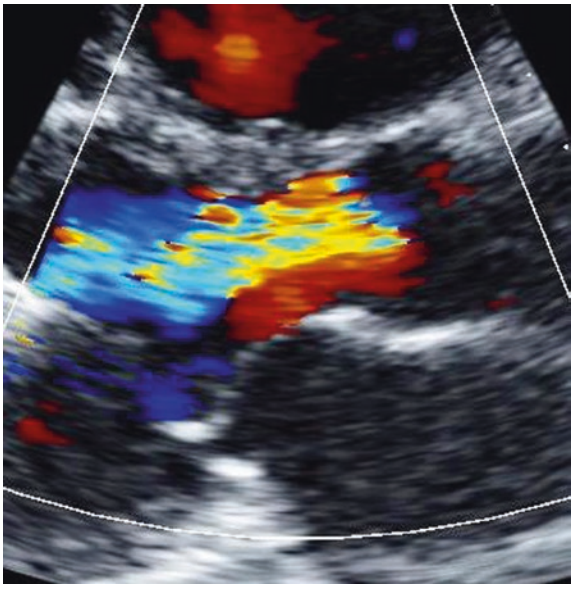

Fig. 9 Patient supported by HM3 LVAD with progressive heart failure symptoms found to have severe aortic insufficiency

Clinical Presentation

Patients may be asymptomatic or symptomatic [21]. Symptomatic patients frequently presents with recurrent HF and impaired end-organ perfusion. Asymptomatic patients may found:

- During routine TTE
- After addition of vasodilators which reduce afterload prompting less opening of aortic valve
- When diuretic therapy is given for hypervolemia leading to a decreased preload and native heart ejection and subsequently less aortic valve opening.

Management

There are no studies managing AI in asymptomatic LVAD patients; however, general recommendations include reducing LVAD speed to allow intermittent aortic valve opening and serial echocardiograms to monitor for progression [21]. For progressive AI that becomes symptomatic or hemodynamically significant management can be either medical, which only temporarily stabilizes the patient's status, or surgical with both open and percutaneous options available (Table 15) [21]. The benefits and risks of different surgical options are outlined in Table 16.

Tamponade

Presentation

Cardiac tamponade is a life-threatening complication following LVAD implantation that usually only occurs in the post-operative period [23]. Symptoms may include fatigue, dizziness, dyspnea, and chest pain. Signs include hypotension, elevated jugular venous pressure, pallor, cool extremities and decreased urine output.

Table 15 Medical and surgical options for aortic insufficiency

Medical · Escalating diuretics · Vasodilator therapy
Surgical · Over-sewing strategy (partial or complete) · Bioprosthetic replacement · Aortic valve ring annuloplasty
Percutaneous management · Transcatheter aortic valve implantation (TAVI) · Percutaneous occluder devices (PODs)

Table 16 Benefits and risks of different invasive approaches

Strategy	Technique	PROS	CONS
Surgical management	Partial over-sewing	Residual AI	20% incidence of moderate AI in 6 months
	Complete over-sewing	No residual AI	Higher mortality
	Bioprosthetic replacement	No residual AI	Only destination therapy Long term failure due to leaflet fusion
	Aortic valve ring annuloplasty	Reduces AI Landing zone for TAVI	Residual AI
Percutaneous management	Transcatheter aortic valve implantation	No residual AI	Risk of device migration Access site-related bleeding Vascular complication
	Percutaneous occluder device (PODs)	No residual AI	OFF label

LVAD parameters often show reduced flow, power and pulsatility. TTE is the diagnostic test of choice for diagnosing tamponade (Fig. 10).

Differential and Diagnosis

Few other conditions can mimic tamponade (Table 17) [23]. Given this narrow differential, chest radiography, TTE and invasive hemodynamic assessment should be performed rapidly. If initial tests are unrevealing, computed tomography for pulmonary embolus and assessment of inflow and outflow grafts should be considered. Usually TTE is adequate for diagnosing cardiac tamponade; however, in post-surgical patients, isolated effusions can occur (i.e. behind and compressing the left atrium) and transesophageal echocardiography (TEE) may be needed to identify the effusion and cause of tamponade.

Management

Tamponade is a surgical emergency and should prompt immediate return to the operating room for evacuation and determining the cause of tamponade. Pericardiocentesis can be performed as a temporizing measure for hemodynamic deterioration but is not definitive management.

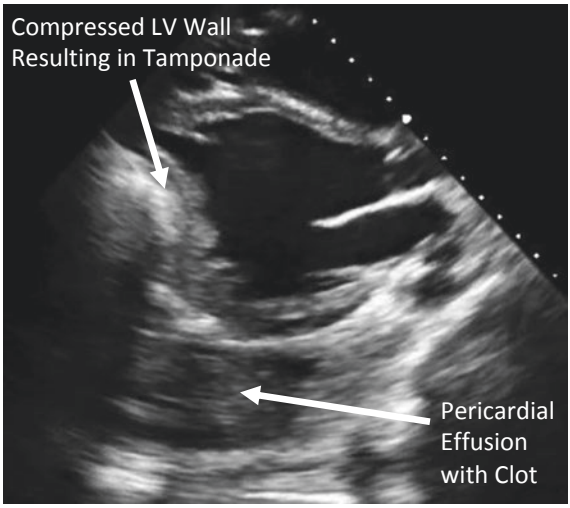

Fig. 10 Blood in pericardial space after LVAD implantation leads to LV compression and tamponade physiology requiring surgical evacuation

Table 17 Differential for cardiac tamponade

RHF	Cardiac tamponade
Pneumothorax	Pulmonary embolus
Inflow obstruction	Outflow obstruction

Infection

Presentation

LVAD patients are susceptible to community acquired infections but also have the unique risks of implanted hardware that can develop a chronic infection and externalization of the driveline that allows an entry point for infection. The International Society of Heart and Lung Transplantation (ISHLT) has divided infections into those specific to the VAD, VAD related, and non-VAD related (Table 18) [24]. LVAD related infections occur in 20–30% of patients within the first year after implantation. The most common VAD specific infections are driveline (Fig. 11) occurring in up to 50% of patients followed by bloodstream infections that may or may not be VAD related [24–26].

Presenting symptoms may be similar to a community acquired infection (i.e. fever and productive cough with pneumonia) or more indolent such as a change in odor or drainage from driveline, low-grade fever, malaise, or anorexia. Infection should be closely monitored for with routine evaluation of the driveline, and there should a low threshold to evaluate for infection in any patient presenting with symptoms concerning for infection or non-specific symptoms. Risk factors for LVAD specific infections are listed in Table 19 [25–27].

Table 18 Infection classification in VAD patients

VAD specific · Pump related · Pocket related · Driveline related
VAD related · Infective endocarditis · Bloodstream infections (may or may not be directly related to LVAD) · Mediastinitis
Non-VAD related · Pneumonia · Cholecystitis · Urinary tract infections

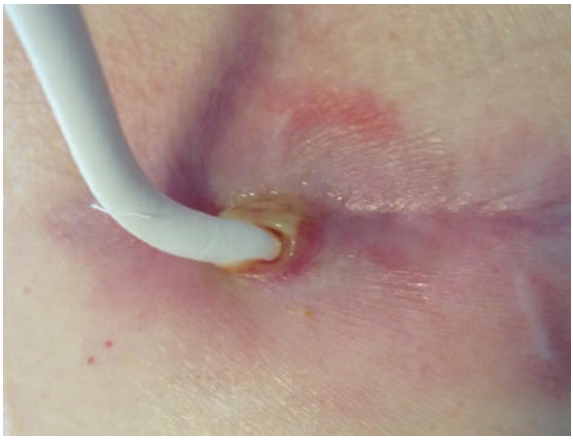

Fig. 11 Infected Driveline with Erythema and Purulent Discharge

Table 19 Risk factors for LVAD specific infections

Younger age
Higher BMI
Diabetes mellitus
Driveline site trauma
Exposed velour at driveline

Infectious Etiologies

Most VAD infections are bacterial in nature; however, fungal infections can occur in critically ill or immunosuppressed patients. The most common bacterial cause is gram-positive cocci including *Staphylococcus aureus* and coagulase-negative *Staphylococci*. Nosocomial gram-negative infections are the next most common bacteria and include *Pseudomonas, Enterobacter,* and *Serratia* [24, 26, 27]

Evaluation

A high index of suspicion should be maintained for a VAD related infection as symptoms and signs can be non-specific and patients are equally at risk for non-VAD infections as VAD related. A complete history and review of systems should be performed to find possible clues to an infection and/or cause. Physical examination should pay specific attention to surgical sites, the driveline exit site, and LVAD parameters. LVAD parameters may be abnormal from a non-VAD systemic infection causing vasodilation. All patients with suspected infection should have a white blood cell count, inflammatory markers (CRP, ESR, procalcitonin), and blood cultures sent. Blood cultures should be sent as 3 sets with a set at least 12 h separated similar to Duke Criteria for endocarditis, which have been adapted for determining a VAD-specific infection [24]. Additionally, urinalysis with culture, chest x-ray and possibly stool studies should be performed. Further testing and management are driven by the presumed cause of infection and results of cultures.

For patients with suspected driveline infection and negative blood cultures, testing is directed at evaluating the extent of driveline infection. The exit site should be thoroughly inspected for erythema, fluctuance and purulence. If pus is coming from the site, a sample should be sent for culture and examined for bacteria and fungus. Ultrasound imaging should be performed to evaluate for fluid collections around the driveline exit site and pump pockets, if accessible. CT imaging may also be used to evaluate possible fluid collections or abscesses. Based on culture and imaging findings, treatment approaches may vary [24].

When blood cultures are positive in a VAD patient, evaluation focuses on determining if this is a VAD specific infection. TTE, often followed by TEE, is performed to assess for vegetations related to the VAD or potentially other implanted devices (i.e. defibrillator). CT imaging is often performed to assess sources of infection that may or may not be VAD related (i.e. pneumonia, sternal wound infection, pump pocket fluid collection). Tagged white blood cell scans may be needed to help locate sources of infection but can return non-specific findings.

Treatment

Non-VAD related infections should be treated according to standard practice. Treatment of VAD related and specific infections should often be determined in conjunction with infectious disease consultation. General treatment recommendations are outlined in Table 20 [24, 26]. Of note, for many VAD related/specific infections, chronic suppressive antibiotic therapy may be needed.

Table 20 General treatment algorithms For VAD related/specific infections

Infection	Findings	Treatment
Localized driveline infection	Expanding erythema around driveline exit site, potentially purulent discharge	Two to four weeks of antimicrobial therapy. Chronic suppressive therapy NOT needed
Deep infection	Erythema at exit site, purulent discharge, possible fluctuance, ultrasound or CT findings of fluid/possible abscess	Two to four weeks of antimicrobial therapy Likely to need chronic suppressive therapy Surgical debridement may be needed
Pump/pocket infection	Sepsis, fluid collection/ abscess on imaging studies	Surgical debridement recommended Two to four weeks antimicrobial therapy followed by chronic suppressive therapy
Device infection or Bacteremia with presumed device infection	Sepsis, cultures meeting modified Duke's criteria for VAD infection per ISHLT guidelines	Treat as endocarditis, ≥6 weeks antibiotic therapy followed by chronic suppressive therapy Discuss surgical options, if any

Clinical Vignette: Conclusion

The patient was deemed too high surgical risk excluding option of device replacement. A continuous infusion of intravenous heparin was started and a second anti-platelet agent (dipyridamole 800 mg per day) was administered. Nevertheless, HVAD parameters continued to worsen (Flow > 10 L/min) and after 24 hours, the patient showed signs of cardiogenic shock (peripheral hypoperfusion, central venous pressure > 19 mmHg). Thus, the decision to perform fibrinolysis was made: fluoroscopy guided intraventricular thrombolysis was performed and Alteplase was administered (10 mg over 10 min every 15–20 min three times repeated a total of three times). After the third infusion, there was a complete resolution of adverse parameters with stable flows and power consumption. The patient was discharged on hospital day 15.

Key Points

- With an increasing number of LVADs implanted and prolonged use, complications are becoming increasingly prevalent.
- Pump thrombosis, although an uncommon complication, has substantial clinical implications and can lead to catastrophic pump failure or other complications such a stroke.

- Right heart failure can present anytime after LVAD implantation, but frequently presents in the immediate post-operative period.
- Bleeding can be quite frequent and occur up to two thirds of patients on LVAD support.
- LVAD patients are at increased risk for both ischemic and hemorrahgic stroke. Almost 20% of LVAD patients will suffer a stroke within the first year after implantation, although with new generation devices, this is less prevelant.
- Arrhythmias can occur in half of LVAD patients, ranging from atrial fibrillation to persistent ventricular tachycardia.
- Although LVAD patients are susceptible to community acquired infections, they are at unique risk of developing infection with implanted hardware and also infection at the exit site of driveline externalization.

Future Directions

While the newer generation of LVADs improve the hemocompatibility experienced with chronic hemodynamic support, complications continue to be of chief concern when managing patients and these devices. One of the exciting development in the next generation of devices may be eliminating the driveline exit site entirely. Both Abbott and Medtronic have dedicated enumerable resources to percutaneous battery charging, thereby eliminating the driveline all together. This development would improve the risk for infection and allow more mobility for LVAD patients.

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Section III
Devices for Stage C Heart Failure

Section Editor: Hao A. Tran

Long Term Hemodynamic Monitoring

Hao A. Tran

Clinical Vignette

A 62-year-old man with a history of ischemic cardiomyopathy (left ventricular ejection fraction, 35%) with biventricular pacemaker-internal cardioverter defibrillator, hypertension, and diabetes returned to clinic after his second heart failure readmission in the past six months. He reported shortness of breath with moderate exertional activity and that he did not respond to his diuretic regimen. He called the clinic to report of his symptoms and noted a weight gain of ten pounds over the past week. Compliant with his medications, he reported that his diet has not changed, and he thought he was doing well after the first hospitalization. His medications include carvedilol, sacubitril/valsartan, eplerenone, bumetanide and atorvastatin. None of medications have recently changed other than an increased dose of the diuretic at discharge. What can be offered to him to help in the management of the patient's heart failure and potentially decrease hospitalization rates?

Burden of Heart Failure Readmissions

Heart failure (HF) is characterized with a very high rate of hospital admission and readmission, resulting in substantial economic burden to the health care system. Moreover, the number of HF decompensation events predicts increased rates of morbidity and mortality, thereby increasing the rate of readmission [1–3] Currently, HF in the United States account for $30 billion a year and expected to exceed $70 billion annually by 2030 [4]. The great majority of costs of HF care

H. A. Tran (✉)
Division of Cardiology, Department of Internal Medicine, University of California, San Diego, La Jolla, CA 92037, USA
e-mail: hatran@health.ucsd.edu

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is attributable to inpatient hospitalization of acutely decompensated HF patients. Therefore, a reduction of HF hospitalization and readmissions substantially decrease costs.

Telemonitoring

The identification HF signs and symptoms along with weight changes has been shown historically to be unreliable in the prevention of HF readmissions, as many of these parameters appear late in clinical decompensation [5]. Moreover, following biomarkers such as B-type natriuretic peptide have not been shown to be helpful in preventing readmissions [6, 7]. Attention has be turned to improve communication with patients to monitor symptoms, blood pressure, heart rate, and weight changes to intensify management. These telemonitoring systems have had mixed results in reducing mortality and HF hospitalizations [8–13]. Two of the clinical trials are illustrated further below.

The multicenter randomized Tele-HF (Tele-monitoring to Improve Heart Failure Outcomes) trial evaluated 1,653 patients recently hospitalized for heart failure [9].

- Treatment group: daily telephone calls, interactive voice response system that collected information about symptoms and an electronic weight scale. All data was reviewed by the patients' providers and treatment was tailored to each individual.
- Endpoint: combined readmissions or death from any cause
- Results: after 180 days, there were no differences in outcomes between the treatment and control groups.

Noninvasive tele-monitoring of patients with heart failure was further investigated in the BEAT-HF (Better Effectiveness After Transition-Heart Failure) trial. 1,437 patients with acute decompensated HF were randomized to the intervention or control groups [11].

- Treatment group: combined health coaching telephone calls and telemonitoring, including daily electronic log of symptoms, blood pressure, heart rate, and weight. Centralized nurses conducted the review of telemonitoring data and calls to patients.
- Endpoint: readmission for any cause for 180 days after discharge. Secondary endpoints of all-cause readmission, all-cause mortality, and quality of life at 30 and 180 days.
- Results: after 180 days, there were no differences in outcomes between the treatment and control groups.

Cardiac Implantable Electronic Devices (CIEDs)

Physiologic parameters such as patient activity level, heart rate variability, and intrathoracic impedance have been reported with a high degree of fidelity with cardiac implantable electronic devices (CIEDs). These measurements have been shown to be more sensitive in predicting fluid congestion than daily weight monitoring [14]. Unfortunately, studies have not demonstrated significant benefit with clinical outcomes.

In the DOT-HF (Diagnostic Outcome Trial in Heart Failure), 335 patients with chronic heart failure with either an implantable cardioverter-defibrillator alone or with cardiac resynchronization therapy had monitoring tool for intrathoracic impedance available [15].

- Treatment group: patients were randomized to have the information available to physicians while patients with out of range reading experienced an audible alert.
- Endpoint: composite all-cause mortality and HF hospitalizations.
- Results: After 15 months, there were more significant endpoint events in the treatment group compared to the control group. Although the number of deaths was comparable, there were more HF hospitalizations and outpatient visits in the treatment arm.

The Shift to Intracardiac Pressure Monitoring

While the idea of remote monitoring and management is still believed to be beneficial, the failures of preceding trials are thought to attributed to the poor temporal correlation the type of data collected has with HF decompensation. In particular, typical symptoms and increased weight appear to occur later stages of decompensation and are poor surrogates for ventricular filling pressures. Studies of implanted intracardiac hemodynamic monitoring systems have deemed symptoms and weight change as unreliable [16]. Rather, the increases in ventricular filling pressures occur weeks prior to the watershed event of HF hospitalization. Therefore, interventions in response to intracardiac filling pressures may be early enough to thwart the cascade towards HF re-hospitalization.

The Right Ventricular Pressure Monitoring System

The Chronical IHM (Medtronic, Inc, Minneapolis, Minnesota) was the first right ventricular (RV) sensor introduced measuring RV systolic and diastolic pressures and heart rate. In seminal study, COMPASS-HF (Chronical Offers Management to

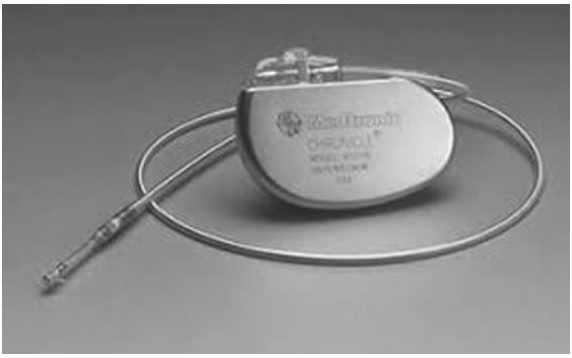

Fig. 1 Chronical IHM System (Permission will be obtained from Magalski et al. J Cardiac Fail 2002; 8(2):63–70)

Patients with Advanced Signs and Symptoms of Heart Failure), 274 patients with New York Heart Association (NYHA) functional class III and ambulatory class IV symptoms were randomized in a prospective, multicenter, single-blinded trial [17].

- Treatment group: every patient received the Chronical IHM monitoring device. Hemodynamic information from the monitor was available only to the patients' provider in the treatment arm.
- Endpoint: freedom from system-related complications, pressure-sensor failure and reduction in the rate of HF-related events (hospitalizations and emergency/urgent care visits requiring intravenous therapy)
- Results: although the treatment group had a 21% lower rate of all HF-related events compared to the control group, this number was not statistically significant (p 0.33). Therefore, the pressure guided management group did not significantly reduce total HF-related events when compared to optimal medical therapy (Fig. 1).

A retrospective analysis of the trial though, looking at the time to first HF hospitalization showed a 36% reduction ($p = 0.03$) in relative risk of HF-related hospitalization in the treatment group, which appeared to be powered by patients with NYHA Class III symptoms. Because of this finding, the idea of intracardiac pressure monitoring was not wholly abandoned.

The HeartPOD Left Atrial Pressure Monitoring System

The HeartPOD (Abbott, formerly St Jude Medical/Savacor, Inc) which directly measures left atrial pressure in ambulatory heart failure patients was used in the LAPTOP-HF (Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy). The device comprises of an implantable sensor lead and a subcutaneous antenna coil. The tip of the sensor is implanted trans-venously into the left atrium via the atrial septum. The prospective randomized controlled study evaluated the

safety and efficacy in ambulatory NYHA Class III patients with recent HF admission or elevated B-type natriuretic peptide [18].

Treatment Arm: patients randomized to the treatment arm had LAP measured twice daily.

Endpoints: freedom from major adverse cardiovascular and neurological events, and reduction of heart failure hospitalization.

Results: enrollment in the study was stopped early due to perceived excess implant related complications. Overall results were negative demonstrating no reduction in combined endpoints.

The Fidelity of Pulmonary Artery Measurements

More than half a century ago, invasive studies showed significant correlation between left atrial pressure (LAP), the pulmonary capillary wedge pressure (PCWP) and end-diastolic pulmonary artery pressure (PAPd) in the absence of high pulmonary vascular resistance [19–22]. This led to a new generation of implantable devices, taking advantage of the placement in the pulmonary arterial system.

It is important to note the limitations of these measurements. Pulmonary hypertension can observed in 25–83% of heart failure patients. The gradient between PAPd and mean PCWP, or the diastolic gradient, is less dependent upon blood flow, stroke volume and changes to PCWP, but will reflect changes in compliance and dispensability of the pulmonary arteries, therefore understanding the pulmonary vascular resistance is crucial prior to relying on the pulmonary arterial pressure as a surrogate for left sided filling pressure. Some studies have shown a high gradient (>5 mmHg) exist between the PAP and mean PCWP in half of patients with heart failure [23–26].

The CardioMEMS Pulmonary Artery Monitoring System

The most current and utilized device, the CardioMEMS HF System (Abbott, Sylmar, California), has taken the field of hemodynamic monitoring to new heights. The device is a wireless, battery-free, monitoring system lodged in the branch of the pulmonary artery. Pressure applied to the sensor registers a deflection of the pressure-sensitive surface resulting in a shift in resonant frequency. The recordings report systolic, diastolic, and mean pulmonary arterial pressures with concomitant readings of heart rate. Waveforms analyses are available to interrogate the fidelity of the pressure tracings and regularity of heart rhythm. In the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial, 550 patients received the device and were then randomized [27, 28].

Fig. 2 CardioMEMS HF System (from https://www.cardiovascular.abbott/us)

- Treatment arm: every patient received the CardioMEMS HF System monitoring device. Daily pulmonary artery pressure readings were available to the provider to augment standard of care.
- Endpoint: HF rehospitalization in 6 months.
- Results: in 6 months, treatment group had a relative risk reduction of 39% in HF-related hospitalizations compared to control group.

In addition, there was a significant reduction in pulmonary artery pressure and days alive out of the hospital with improved quality of life. Moreover, patients with preserved left ventricular ejection fraction > 40% had 46% lower HF-hospitalizations in the treatment group compared with the control group ($p < 0.0001$) [29]. Once extended to 18 months of follow-up, open access of pressures in the control group were available to the providers. Rates of admission for HF-related hospitalization in the former control group were reduced by 48% ($p < 0.0001$) compared with rates of admissions in the same group during the original trial [30].

These results lead the US Food and Drug Administration, in 2014, to approve the CardioMEMS HF System for patients with NYHA functional class III HF with recent HF hospitalization within 12 months prior to implant. Since then, the general use experience in 2,000 patients with at least 6 months of follow up reported an even greater reduction in pulmonary artery pressures compared to the CHAMPION clinical trial [31] (Figs. 2 and 3).

Other Pulmonary Artery Pressure Monitoring Systems

- Medtronic Reveal LINQ Insertable Cardiac Monitor device implanted with a small sensor (Minneapolis, Minnesota). Monitors pulmonary artery pressure, cardiac arrythmias, patient activity and other physiological trends.
- Endotronix (Woodridge, Illinois). Similar pulmonary artery pressure device to the CardioMEMS HF System but additive interface using the Cordella

Fig. 3 Endotronix and Cordella Monitoring Systems (from https://endotronix.com)

(Endotonix, Inc) remote monitoring system which includes a blood pressure cuff, weight scale, heart rate monitoring, pulse oximeter and patient portal tablet for direct communication with providers.

Remote Monitoring Reimbursement

Although robust reimbursement has been granted for remote monitoring device implantation, coverage is usually described in medical policies and is payer specific. Private insurance payers and the Centers for Medicare and Medicaid Services (CMS) may differ in terms of reimbursement for both the procedure and follow up monitoring. The reimbursement for transcatheter implantation of the wireless pulmonary artery pressures sensor for long term hemodynamic monitoring (deployment and calibration of the sensor along with the right heart catheterization) can be coded using common procedural technology (CPT) code 33289 (6.00 work relative value units, RVUs). Additionally, monthly reimbursement for pulmonary artery pressure recordings, interpretation(s), trend analysis, and report(s) by a physician or other qualified health care professional can be coded using CPT code 93264 (0.70 work RVU).

Case Conclusion

Our patient received the CardioMEMS HF system a month after the initiation of sacubitril/valsartan. While the patient has had titration of diuretics, our team was able to increase neurohormonal blocking agents for him over the last few months. The patient has yet to be admitted for heart failure decompensation.

Key Points

Increased intracardiac pressures causes worsening heart failure and may lead to hospitalization for decompensation. Non-invasive telemedicine and CIED-based management have not shown to reduce the risk of heart failure hospitalization.

- However, newer devices, such as the CardioMEMS HF system, allow moment-to-moment remote monitoring utilizing an implantable hemodynamic monitoring system.
- The CHAMPION trial demonstrated that using the CardioMEMS device, providers can reduce the rate of HF hospitalizations regardless of the ejection fraction.
- Newer and more advanced implantable monitoring systems are in development, and coupled with the constructions of workflow, therefore leading a revolution in management of chronic HF patients.

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Remote Monitoring for Cardiac Implantable Electronic Devices Used in Heart Failure

Uma N. Srivatsa, Connie Wright, and Xin Jian Zhang

Case Vignette

A 70 year old male presented with a history of stage C congestive heart failure (CHF) NYHA class III and was found to have non-ischemic cardiomyopathy low LVEF and wide QRS with left bundle branch block (QRS 158 ms) (Fig. 1a). After optimizing medical therapy, he received a biventricular (BiV) ICD (Fig. 1b). Subsequent remote monitoring alert showed inability of the device to test left ventricular lead auto-threshold and 80% BiV pacing (Fig. 1c). The patient was brought into the device clinic. Interrogation revealed high LV bipolar (tip- ring) threshold and loss of capture. Chest X-ray indicated partially dislodged LV lead position compared to the initial implant (Fig. 1d). The LV lead was reprogrammed to a LV tip to can configuration with successful capture and increased BiV pacing to 99% (Fig. 1e). Patient had considerably improved symptoms during follow up with an improved LVEF to 50% in the echocardiogram.

Introduction

Cardiac implantable electrical devices (CIED) are implanted in millions of Americans every year. These constitute permanent pacemakers (PPM), implantable cardioverter defibrillators (ICD), cardiac resynchronization devices (CRT) and implantable loop recorders (ILR). Following the positive results of the primary, secondary prevention, and heart failure studies, ICD implantations have significantly augmented in the past

U. N. Srivatsa (✉) · X. J. Zhang
UC Davis Medical Center, University of California, Davis, 4860 Y Street, Suite 2820, Sacramento, CA 95817, USA
e-mail: unsrivatsa@ucdavis.edu

C. Wright
University of California San Diego, San Diego, USA

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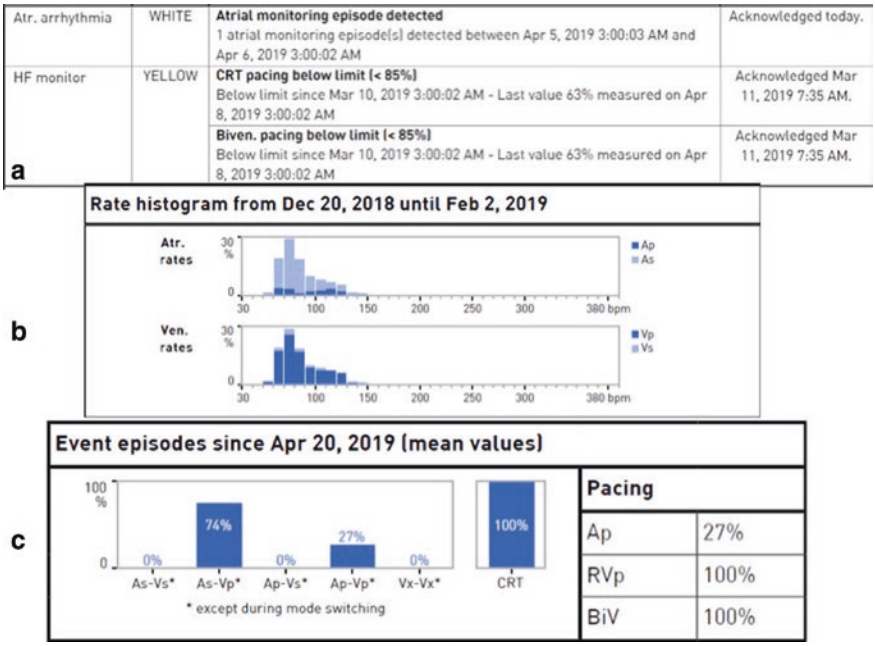

Fig. 1 Case Vignette

two decades [1–4]. While the ILR serves primarily as a diagnostic tool, the other devices have both diagnostic and therapeutic purposes. The rising volume of implantations has inundated the clinics and patients experience long wait times. In addition, with the conventional clinic model, crucial clinical and device related issues are only identified during such visits; any clinical or device related problem also frequently required urgent hospitalizations. With improved wireless access and internet utilization, the industry developed remote monitoring technology to make possible more frequent evaluations of the devices in the comfortable setting of the patient's home. Such remote systems provide physicians with critical device information such as battery life, programming or technical issues, and clinical data (e.g. a significant cardiac event). Such systems provide the added benefit of improved patient safety, as device failures and clinical events can occur between clinic appointments and may otherwise go undetected for months [5, 6]. In this chapter we will explore the remote monitoring technology, clinical utilization, case example of trouble shooting and the benefits for patient care specifically as related to heart failure patients.

Follow up of Patients After Device Implantation

Implantation of complex CIED systems constitutes only a fraction of the patient management; optimal follow up, troubleshooting, managing clinical problems as they arise play a valuable role in the follow up care. The goal of this device surveillance would be to:

- Tailor the device setting for individualized patient needs
- Manage patient's clinical condition and institute new medications as appropriate
- Manage evolution of clinical condition including a need for upgrade/downgrade to the device
- Monitor safety and extend longevity of the device
- Identify actionable device or lead related abnormalities
- Identify battery depletion and plan replacement
- Keep track of advisory or recalls.

The general guidelines for follow up of heart failure devices are listed in Table 1 [7]. Despite expert recommendations, about a quarter of the patients do not follow within a year of the implantation by either inpatient or remote visits, and only about a third of the patients have embraced remote monitoring an interrogation [8]. Some of the reasons of this lack of timely follow up could be access to care, inability to drive or clinical conditions prohibiting a visit to the healthcare facility. For this reason, remote monitoring was developed as a complementary tool to replace some of these clinic visits during the long-term phase of follow up while maintaining the annual clinical contact with the patient.

Remote Monitoring Technology: How It Works

Following the implementation of trans telephonic monitoring and inductive technologies *requiring active participation*, Biotronik, Inc. introduced automated encrypted remote monitoring in single chamber ICD system [9]. Since then, the technology has been implemented in all implantable devices. Other biomedical technology companies have also developed and implemented remote systems, including Medtronic (Carelink Network™), Boston Scientific (Latitude Patient Management system™), and Abbott Inc./St. Jude Medical (Merlin.net™)[5] which are widely utilized today. Embedded technologies have enabled the ability of the device to self-monitor its function and record arrhythmias and other parameters and communicate this to a database *without active participation* of the patient.

An essential component of remote monitoring is a home monitor or communicator. This is a device designed to automatically receive telemetry from a specific

Table 1 Recommended frequency of CIED monitoring

Time of follow up	Method of follow up
Within 72 h of implantation	In person
2–12 weeks post implantation	In person
Every 3–6 months	In person or remote
Annual until battery depletion	In person
Every 1–3 months at signs of battery depletion	In person or remote

Adapted from HRS/EHRA Expert Consensus on the Monitoring of Cardiovascular Implantable Electronic Devices (CIEDs). Heart Rhythm **5**(6): 907–925

CIED and transmit the encrypted data using telephone or internet technology do a remote secure monitoring center (Fig. 2). Symptomatic patients can also initiate interrogations in majority of these systems. The older technology utilized the Internet connection through the analog telephone line in a patient's home; currently mobile/portable unit connected via Cellular technology or Wi-Fi is widely used (Table 2). Cellular and internet technology has allowed patients to transmit information even while traveling. The transmitted information is reviewed by the healthcare personnel and is documented in the electronic medical records [6]. The database is searchable by serial number, model number, last name or date of birth. The data transmission can be preprogrammed to routinely occur at recurring intervals, as well as programmed to transmit any abnormal information as they occur; the latter can be set to website only alert, urgent (yellow alert), or emergent (red alert). The method of notification can also be preprogrammed on the website (e.g.) email, text, page or phone calls. The typical alerts programmed are listed in Table 3.

There is a distinction in the terminology between *remote interrogation* and *remote monitoring*. The former is a routine scheduled device interrogation that is performed at 3–6 month intervals automatically. Most information with the exception of manual pacing capture threshold is obtainable with this interrogation. Remote monitoring on the other hand is automated transmission of data based on pre-specified alerts listed in Table 2, and provides ability to rapidly detect abnormal device function or arrhythmias.

Clinical Benefits of Remote Monitoring

Remote monitoring cannot completely replace clinic visits because important information gathered from direct physical examination is not obtainable from remote appointments. Various clinical trials have been performed comparing clinic visits to remote monitoring using proprietary technologies in various healthcare settings [10–12] and have shown a benefit of remote monitoring over clinic visit including:

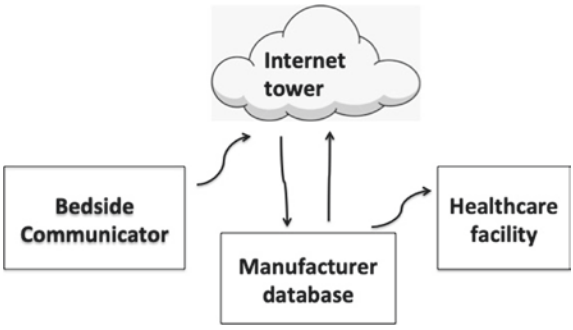

Fig. 2 Components of remote monitoring

Table 2 Remote monitoring systems

Manufacturer	Device to bedside transmitter	Bedside Transmitter to cloud database	Bedside transmitter	Hospital access to database	Transmission	Patient initiation
Biotronik	Radiofrequency-MICS	1.No landline 2.Cellular technology (T mobile) 3.No Ethernet or Wifi	Cardio Messenger International via cellular connectivity	SN, LN, MRN, DOB	Automatic	No Rivacor, Acticor- yes
Medtronic	1.Induction telemetry: Pacemakers: Advisa, Revo, Adapta, Versa, Sensia, Viva Biventricular pacer: consulta 2. Radiofrequency-MICS: ICD, BV ICD- Blue tooth: (Azure, Percepta) (encryption and verification algorithms for privacy)	1. No land line 2.Cell phone (Vodaphone) 3.Ethernet with adaptor 4.Wifi (Azure, Percepta)	MyCarelink: Ethernet with adaptor MyCarelink smart: Pacemakers using induction telemetry- to iphone or android- using blue tooth MyCarelink relay: Azure and Percepta- built in Wifi/cell phone MyCarelink heart: directly to patient iphone or ipad, android (Azure percepta)- through blue tooth- bypasses bedside transmitter International coverage based on cellular, internet, Wifi connectivity	SN, LN, MN	Manual- Advisa, Revo, Adapta, Enpulse, Versa, Sensia Others: automatic	Yes
Boston Scientific	Radiofrequency-MICS	Cellular phone (Vodaphone) Ethernet (Internet) Telephone line	Latitude NXT International coverage based on cellular, internet, connectivity Limited for SQ ICD	SN, LN, DOB, MN	Automatic Manual (SQ ICD)	Yes

(continued)

Table 2 (continued)

Manufacturer	Device to bedside transmitter	Bedside Transmitter to cloud database	Bedside transmitter	Hospital access to database	Transmission	Patient initiation
Abbott	1. Induction telemetry -Zephyr 2. Radiofrequency-MICS: all other devices-Bluetooth-(encryption and verification algorithms for privacy)-Implantable loop recorder- Confirm Rx	Landline Cellular phone (Verizon) Adaptor available for Ethernet Wifi	Merlin@home (Pacemaker and ICD) MyMerlin (implantable loop recorder) International coverage based on cellular, internet, Wifi connectivity	Last Name Serial number Date of birth	Automatic Manual: Zephyr (and older pacemakers) (needs specialized transmitter)	Yes

MICS: Medical Implant Communication system; SN: Serial number; MN- Model number; LN: Last name; MRN: Medical record number; DOB: date of birth; SQ- subcutaneous; ICD- implantable converter defibrillator; GSM: Global system for mobile communications

Table 3 Alerts programmed to trigger data transmission in remote monitoring system

Type of abnormality	
Device parameters:	· ICD therapy disabled · MRI mode ON · Battery depletion · Charge time limit reached · Device reset (altered pacing mode)
Lead parameters:	· Change in lead impedance, sensing, pacing threshold (out of programmed range) · Change in shock impedance (out of programmed range) · Percent of ventricular pacing (high in ICD; low in CRT) · Lead noise
Atrial arrhythmias:	· Frequent atrial arrhythmias (programmable) · Fast ventricular rate · Long atrial episode
Ventricular arrhythmias:	· VT/VF detected (untreated or treated) · Ineffective shock/therapy exhausted · ATP disabled
Heart failure monitor	· Mean ventricular rate · Mean PVC/hour · Heart failure indicator (e.g. weight gain, heart logic above programmed threshold)

- Adherence to follow up goals
- Earlier identification of clinical and device abnormalities with reduced time to diagnosis [13].
- Quality adjusted life year gained [14].
- Survival advantage in those who spent >75% time in remote monitoring versus none [15].
- Reduction in the volume of clinic visits by 50% while patients are monitored remotely [13].
- Reduced need for unscheduled hospital evaluations during remote monitoring while being safe [12].
- Cost advantage to remote monitoring [13]. The Multicenter Italian CareLink Evaluation demonstrated that remote appointments reduced costs to patients by almost €200 (euro) annually in direct costs (e.g. transportation, parking) and indirect costs (lost productivity), and approximately €1,200 over the device lifetime of 6 years [10].

Improving Utilization of Remote Monitoring

Though the patients followed remotely are more involved in their care because they can initiate contact with their clinic via the remote communicator at home, [16] there seems to be a low utilization rate of remote monitoring technology [17]. A prior study evaluated the cause of low remote monitoring utilization to

understand patient preferences regarding their device care in order to make device appointments more satisfactory to patients. Patients rated clinic visit with higher satisfaction due to better opportunities to ask questions, but there was no difference in perception of convenience, scheduling, or cost between the two groups. There was a 45% reduction of patients in work force after implantation of device; patients chose to retire or go on disability. Younger patients in the work force preferred remote monitoring for convenience than those who are retired or disabled [18]. Nevertheless this study emphasizes the need for communication with the patients, especially because the remote interrogation is automatic.

Ways to improve utilization of remote monitoring include:

- **Effective patient education**—The first step in effective utilization of remote monitoring involves effective patient instruction and education. It is important to instruct each patient enrolled in a CIED remote monitoring program the rationale for remote monitoring, proper utilization of remote monitoring and how the monitor actually collects and sends data. It is also important to inform the patient that the remote monitor does not take the place of routine clinic visits, it is used in conjunction with routine physician oversight and provides timely data between physician visits. Effective education includes:
  - How the monitor works—After the monitor is initially linked to the patient's implanted device, the monitor is placed near their bedside (or within 6 ft of where they most often sleep) as data is collected between the hours of 12 am to 3 am to avoid interruption of data transmission. This data is in most instances transmitted wirelessly through a cellular signal to the manufacturer's server which in turn is transmitted to the physician website.
  - Manual transmissions: In some instances a manual transmission is required, this process should be reviewed with the patients at time of enrollment. It is also important to review proper utilization of manual transmissions, for example transmission of data after ICD therapy, symptoms of AF or prolonged arrhythmia and syncope or near syncope. Manual transmissions are not recommended for symptoms such as headache and chest pain or such things as high blood pressure or orthostatic blood pressure changes.
  - Transmission schedules: Transmissions will occur every month or every 3 months depending on the type of CIED implanted. Instruct patient that the device makes a connection daily but it does not necessarily send a report for review, only data alerts and scheduled transmissions reports are sent to the provider.
  - Types of data collected with remote monitoring: It is important to stress that data is only reviewed when a data report or alert is received, it is not, in most cases, transmitted or reviewed daily and it may not be reviewed 24/7 as most clinics and offices do not have the personnel to monitor on a 24 h basis. It is important to make clear that the device remote monitor do not collect every abnormal beat/rhythm (i.e. palpitation, PVC, PAC), but rather it is a summation of data over a month or 3 month time period and it is dependent on the information or alerts the physician feels is significant.

- Patient Compliance—Alerts and notifications provide early detection of arrhythmia and device and lead malfunction. Often device therapies and medication effectiveness can be also be assessed through remote monitoring, but this information is all dependent on patient compliance. When a patient is noncompliant, important data regarding device and lead malfunction, battery longevity and recommended replacement, frequent, reoccurring arrhythmias go unnoticed and are often not detected for months or even years which may delay lifesaving treatments or even result in death. Some hospitals and physician offices have gone as far as drawing up a patient contract which is signed by the patient at enrollment and it delineates patient responsibilities and expectations and physician and staff responsibilities as well. Many practitioners have found this to be a very effective measure in insuring patient compliance.
- **Patient-specific, arrhythmia specific device programming/vendor website alerts and notifications**: It is important to evaluate each patient's indication for a device and any underlying cardiac arrhythmias when enrolling a patient in your CIED remote monitoring program. At time of implant or during the initial clinic visit, it is necessary to program the cardiac device to detect relevant alert criteria. This is important because these criteria are then used by the various vendor remote websites to generate alert notifications to you and your staff. Often is it necessary to adjust the vendor remote site notification criteria as well, otherwise one can be inundated by hundreds of irrelevant alerts per day if the practitioner does not consider both the device and monitoring website alert notification criteria, i.e. a patient is in persistent AF with an AF alert notification on, AF alert > 10 min. This one alert alone can generate numerous alert notifications per month which is not only time consuming but costly as it utilizes both staff and physician time to review massive amounts of irrelevant data, and this is time that could be used more effectively in your clinic or office.

Examples of notifications for consideration include:

- AF alerts—consider turning alert off for persistent AF, extend duration of AF if AF paroxysmal and patient is on an oral anticoagulant.
- Mode switch rates and criteria—consider increasing rate in patients who exercise or in younger patients with higher sinus rates.
- VT monitor zones and detection times—consider increasing detection rate criteria for both monitor zone and VT in younger patient populations and athletes who achieve higher than normal heart rates with exercise or activity.
- Heart rate and pause detection rates in ILR—consider lowest bradycardia rate in and acceptable pause duration in patient with an ILR implant, i.e. If the bradycardia detection is 40 bpm you may get hundreds of alerts for bradycardia during hours of sleep.
- **Patient and Provider communication**: It is important to set up a system to facilitate communication of results including device function, battery longevity and arrhythmia detection with the patient and provider, optimally this

can occur through use of the digital EMR i.e. Epic™ My Chart. Often a line of communication such as Epic™ In Basket is also necessary and helpful between the Device Nurse or Technicians and the provider as it provides a method to relay important alerts or findings from the staff to the Provider. If the physician does not establish some method of communication with staff, he will find he or she will be inundated with calls regarding device alerts and therapies and patient requests for monitoring results.

- **Educated and well trained staff members**: Key to any remote monitoring program is a highly educated, well trained staff. Staff should be well versed in device function, troubleshooting and report review as well as knowledgeable in heart rhythms and arrhythmia detection. Staff members can consist of EP lab or CV technicians and RN's as well as NP's but all should have some background and training in arrhythmia interpretation, CIED function, follow up and device programming. Often device manufacturers will provide device specific training and education and it is important to provide staff with any education opportunities offered by the manufacturers and their representatives, particularly when new products are introduced in the market place. Personnel who are highly trained in device function and programming and who are adept at communicating with physicians, staff members and patients are key to a well-functioning remote monitoring program and play an essential role in a successful Device and Remote Monitoring clinic.
- **Reimbursement and contracts**: It is important to make fees for remote monitoring reasonable and to contract with all insurance providers to insure adequate reimbursement for services provided and to insure patient compliance. In most cases, federal and state healthcare providers such as Medicare and Medicaid, and the majority of HMO insurers will cover all or the majority of cost associated with remote monitoring. Contracts with various insurance providers is necessary to receive reimbursement for patients not covered by government contracts or HMO's, otherwise patients may be billed at full cost which will lead ultimately lead to patient dissatisfaction and discontinuation of monitoring. It is important to inform patients with private healthcare coverage that there may be additional fees such as co-pays or facility fees that may not be covered by his or her insurance provider. If the patient feels the cost outweighs the value of the service they will often discontinue or unenroll from the program; therefore, it is important to make cost reasonable and contract with all insurance providers in your area.

How to Establish a Remote Monitoring Program

The basic components involved in a comprehensive remote monitoring program is shown in Fig. 3. The workflow starts at the time of implantation. The concept of remote monitoring needs to be addressed including the nature of access (wireless vs. landline). The majority of device manufacturers now provide cellular adapters

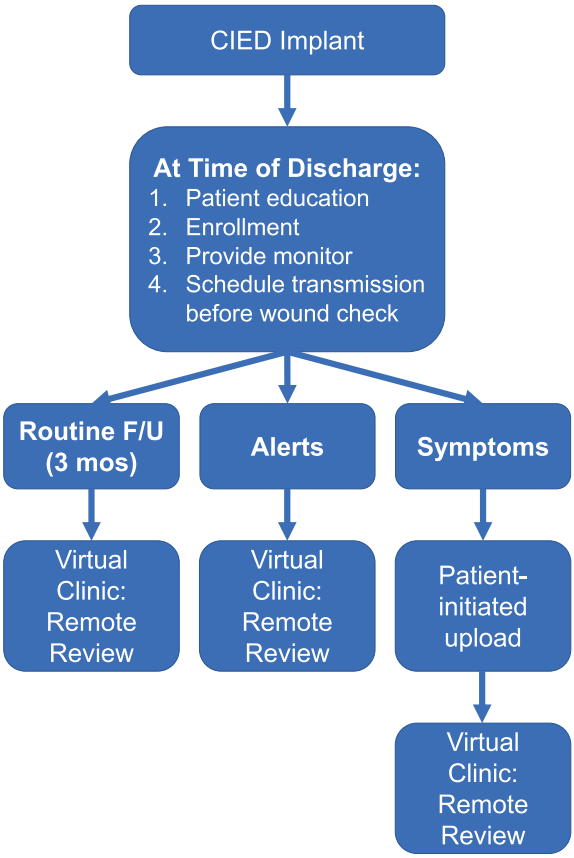

Fig. 3 Remote monitoring workflow

or have a cellular adapter built within the monitor so in most cases a landline is no longer necessary as it was years ago. Once the patient is given a device specific remote monitor transmitter a technician or device representative must enroll the patient into the manufacturer's remote monitoring database. This can be done at implant or in the clinic or office at the first follow up where appropriate instructions can be reviewed with the patient and family. A "pairing" of the device and monitor is often necessary to initiate the first transmission. Following the "pairing" of the device, patients receive the list of the "remote clinic" dates or "virtual" appointments and they are instructed that the device will download data automatically on those dates, most often while they are asleep, as long as the monitor is within 6 feet of their bed or sleeping area. Patients are also instructed to trigger a download if there are any alarms, worsening symptoms, or shocks and to apprise us of this download to enable our personnel to check the database. For Biotronik systems which does not allow patient triggering, they are advised to call the clinic for any abnormal symptoms or alarms, so that the clinic can initiate a download.

Trained personnel are key to the sustenance of the device surveillance program; the device downloads are received by trained device technicians, and reviewed by mid-level provider (nurse practitioner/Physician assistant). They are supervised by Clinical Cardiac electrophysiology (CCEP) certified physicians at our institution. If there are no CCEP trained physicians at the healthcare facility, then IBHRE certified physicians are recommended to supervise the device clinic [19]. Our device technologists are dedicated to the remote clinic; they rotate weekly to enable timely download and documentation. We found this to be an efficient way to monitor the patients given the diverse data repositories of different companies. Any urgent abnormalities are immediately communicated to the mid level personnel who in turn confer with the physician and contact the patient as clinically indicated. The recommended frequency of monitoring is based upon expert consensus [7, 19] and is listed in Table 1. However if there is a clinical need, patients can be interrogated more frequently.

Reimbursement

Remote monitoring and interrogation appears to be cost-effective. In November 2008, CMS approved an amended the set of codes in conjunction with HRS/American College of Cardiology/AMA to more accurately reflect the services of remote vs. in person clinic follow up of CIED. These codes recognize the role of allied personnel, and physician interpretation work value. To prevent over utilization, these codes may only be used every 90 days for ICD and pacemakers and 30 days for implantable loop recorders, regardless whether the transmission is for routine follow-up or patient-initiated transmission [20]. The CPT codes include:

- **Pacemaker: 93294**
- **ICD: 93295**
- **Implantable loop recorders: 93298**
- **Implantable physiologic monitor: 93297**

Legal Aspects and Security Considerations

It should be recognized that it is unclear who owns the data; patients do not have full access to complete information in the database. The health care institution or third party vendor following the patient assumes legal liability. Setting up a communication strategy is vital to the device clinic function and safe patient management. Documentation of any encounter is critical from a legal aspect, and whenever available, a EMR should be used. It is also important to instruct the

patient that there's no one watching their device 24/7, and reiterate the difference between automated or manual downloads.

Privacy and cybersecurity remains an important concern during remote monitoring. The patient data is transmitted via cloud to central data repository, which is accessed by the health care facility. The access is limited and password protected. In the United States, the security and privacy of protected health information has been addressed by state and federal laws, which include the Health Insurance Portability and Accountability Act of 1996 and the Health Information Technology for Economic and Clinical Health Act. The relationships between health care providers and organizations involved with RM are governed by a terms-of-use agreement between the CIED vendor and the health care provider [21]. It is also important to recognize patient privacy when the data is used for regulatory or research purposes.

The majority of the CIED systems (Table 2) are designed to communicate with external programmer in the Medical Implant Communication system (MICS) frequency (402–405 MHz). Some devices utilize the commercial blue tooth (2.45 GHz) frequency. Software radio based attacks can be designed to compromise patient safety and security [22]. Cyber attacks aim at stealing sensitive information and grant access to the IT system to alter programming. The biotechnology industry has created encryption and verification algorithms for privacy and safety. Although there is no evidence of security breach at this time, since patient perception of the integrity of such IT systems are critical to their care, recognition of malware, communications and utmost care in maintaining security remain a very important goal [23].

Pitfalls with Remote Monitoring

For the reasons discussed, remote monitoring is essential to any CIED program, but there are a few pitfalls that must be considered and addressed in order to create a successful remote monitoring program.

- Time intensive—Trained and efficient staff are needed to manage the volume of interrogation reports that are created from the routine remote interrogations, patient-activated transmissions and arrhythmia/lead alerts generated by enrolled patients.
- Reimbursement limits—Regardless of the nature of the transmission (routine, patient-activated and/or alerts), remote transmissions from ILRs or pacemakers/ICDs can only be billed every 31 days or 91 days, respectively.
- Liability—If remote interrogations are not reviewed in a timely or comprehensive manner, they can be a source of liability or malpractice

What Should the HF Physician Look for in a Remote Interrogation?

The large amount of arrhythmia and physiologic data collected by interrogation can be clinically valuable, but may be overwhelming for physicians especially as the data can be presented differently depending on the manufacturer. Nevertheless, a focused approach for the heart failure physician to interpret remote interrogations may be helpful and include focusing on the following categories:

1. Thoracic impedance (fluid accumulation decreases impedance, measured in ohms)
    a. Optivol™ (Medtronic), Corvue™ (Abbott), Heartlogic™ (Boston Scientific), impedance monitoring (Biotronik)
2. For CRT: LV pacing burden (Goal is 95%), effective LV pacing algorithms
3. Atrial fibrillation burden and ventricular rate histograms during AF
4. Ventricular arrhythmias and therapies
5. Premature ventricular contraction burden per 24 h (may need to divide total PVC count by amount of days since last cleared)
6. Heart rate variability
7. Device-specific HF toolboxes (such as Boston Scientific HeartLogic™ which integrates heart sounds, respiration, activity and night heart rate in addition to thoracic impedance).

Future Directions

Advances in remote technologies that are under development include:

- Smartphone apps for patients
- Bluetooth connectivity between smartphone and CIED
- Two-way communication between physician and patient's CIED
- Outsourcing management of remote monitoring to companies specializing in remote management.

Case Conclusion

The case presented exemplifies the need for monitoring to assess device function in the context of CHF. In our case, remote monitoring detected dislodgement of the LV lead by recognizing a drop in biventricular pacing burden and a higher pacing threshold in the programmed bipolar vector, as seen in Fig. 4. Changing the pacing vector enabled optimal biventricular pacing.

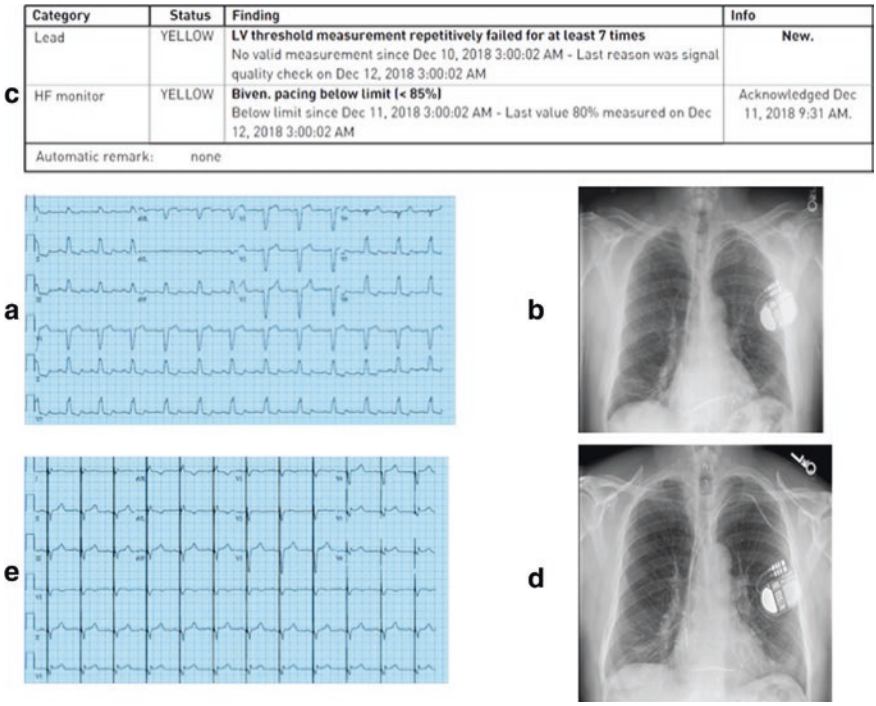

Fig. 4 Case Vignette **a** Baseline EKG with left bundle branch block; **b** Remote monitor report; **c** Post implant chest X ray; **d** Repeat chest Xray with LV lead dislodgement; **e** EKG with biventricular pacing after reprograming LV lead configuration

During device monitoring, non-response to CRT, and worsening cardiac function needs to be managed collaboratively with the heart failure team. Figure 5 indicates a non-responder patient with ischemic cardiomyopathy despite optimizing the CRT; his activity levels deteriorated on the remote device report, suggesting worsening CHF (Fig. 5a) and atrial fibrillation (AF) with controlled ventricular rates (Fig. 5b). He had non-sustained ventricular tachycardia (VT) and frequent increases optivol index (Fig. 5c). Evaluation of cardiac function revealed VO2 max 12 mg./kg/min, LVEF 10%, severely dilated LV and cardiac index of 1.6 L/m2. He underwent successful LVAD (Heartmate II) implantation with significant improvement in CHF symptoms and optivol index in the ensuing months (Fig. 5D). However he was noted to have VT requiring therapy (Fig. 5e) which is currently managed medically in our clinic. Rising optivol index is inverse of thoracic impedance; the latter reduces due to fluid accumulation in the chest cavity. An increased optivol index is an indicator of worsening heart failure and has been associated with frequent hospitalizations as noted in this patient. Though he had AF, his ventricle the rate was well controlled. He progressed from state C to stage D and ultimately underwent LVAD placement; thereafter the optivol index

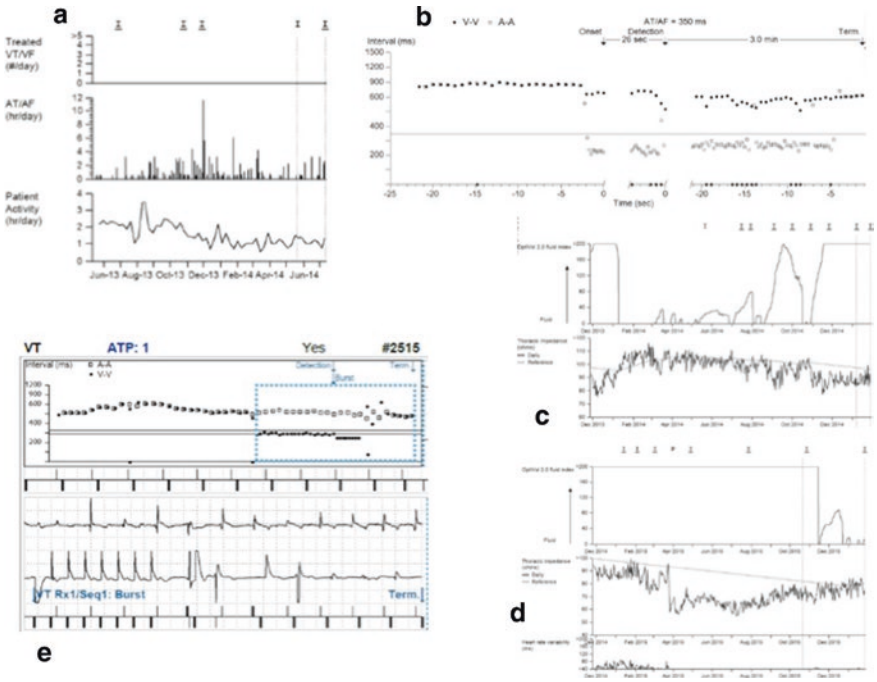

Fig. 5 Non responder with cardiac compass report. **a** Reduced patient activity; **b** Atrial fibrillation with controlled ventricular rate. Black dots indicate ventricular rate and open circles indicate atrial rate; **c** & **d**: Optivol Index and thoracic impedance before and after LVAD respectively; **e** Ventricular tachycardia with ATP therapy

considerably improved as did his clinical condition. The entirety of the device interrogation report including heart rate histogram, respiratory rate, patient activity, optivol index as well evaluation of arrhythmias are very valuable in managing patients with heart failure.

Key Points

- Remote interrogation (RI) is scheduled automatic download performed 3–6 months
- Remote monitoring (RM) is automated transmission of data based on pre-specified alerts
- Patients initiated download for clinical symptoms can occur
- Device, lead parameters, arrhythmia and heart failure indicators can be monitored

- RI and RM is cost effective, prevents frequent hospitalizations and improves survival
- Trained personnel dedicated to RM and RI and appropriate communication is key to success of the program
- Patient security and privacy is of paramount importance

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Section IV
Device Based Arrhythmia Management

Section Editor: Gordon Ho

Indications for the Implantable Cardioverter Defibrillator (ICD)

Hiro Kawata

Clinical Case

A 57-year-old male presented to an ER for chest pain and dizziness. He was found to have ST-elevation myocardial infarction in the ER. He developed ventricular fibrillation (VF) in the ER and required defibrillation. He was brought to a cath lab for an emergent coronary angiogram and percutaneous coronary intervention. A drug-eluting stent was placed in the proximal left anterior descending artery. Echocardiogram showed reduced Left ventricle (LV) systolic function with LVEF of 30%. Optimal medical therapy for coronary artery disease and heart failure was initiated. He was discharged with LIFEVEST. Three months later, a repeat echocardiogram showed LVEF of 35%. No sustained ventricular tachycardia (VT) was documented, and defibrillation therapy was not delivered from the vest. He is active and denies any symptoms currently (NYHA functional class I). EP was consulted for possible ICD implantation.

Introduction

The purpose of this chapter is to discuss practical aspects of ICD therapy, including indications, generator and lead selection.

H. Kawata (✉)
Oregon Heart & Vascular Institute, Peacehealth Sacred Heart Medical Center, 3311 RiverBend Drive, 3rd Floor, Springfield, OR 97477, USA
e-mail: hkawata@peacehealth.org

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Indications

ICD indications may be stratified by both ischemic versus non-ischemic cardiomyopathies and primary versus secondary prevention. Whereas secondary prevention is indicated for patients who have experienced sudden cardiac arrest or ventricular arrhythmias (VA), primary prevention is indicated for patients at risk for but has not experienced an event. The major guidelines for ICD implantation are listed below:

- 2012 ACCF/AHA/HRS Focused Update Incorporated Into the 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities [1]
- 2013 ACC/HRS/AHA/ASE/HFSA/SCA I/SCCT/SCMR Appropriate Use Criteria for ICD and CRT Therapy [2]
- 2014 HRS/ACC/AHA Expert Consensus Statement on the Use of Implantable Cardioverter-Defibrillator Therapy in Patients Who Are Not Included or Not Well Represented in Clinical Trials [3]
- 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: Executive Summary. A report form the ACC/AHA Task Force [4].

Ischemic Heart Disease

Secondary Prevention

Secondary prevention is defined as ICD placement in a patient with prior SCA, sustained VT, or syncope caused by VA.

Patients with cardiomyopathy who survived sudden cardiac death (SCD) or VT are at high risk for the future similar event. The evidence for an ICD for these patients has been well established [5–7]. According to the 2017 AHA/ACC/HRS guideline, secondary prevention indication of ICD for a patient with ischemic heart disease is summarized as below (Fig. 1). Published guidelines exclude cases in which there are completely reversible causes for SCA and VA. For example, an acute myocardial infarction can cause VA and the culprit lesion can be reversed with coronary revascularization. However, the risk of SCD and VA may remain in some patients, even after the revasculization.

Primary Prevention

Primary prevention is defined as ICD placement with the intention of preventing SCD in a patient who has not had sustained VT or CSA but who is at an increased risk for these events.

Patients who have had an MI resulting in reduced LVEF are at increased risk of SCD, most often due to a VT and VF. Multiple randomized trials in patients

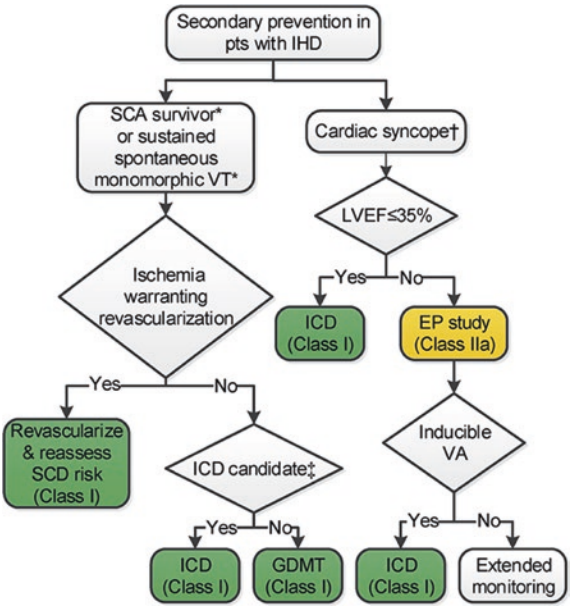

Fig. 1 Secondary prevention in patients with ischemic heart disease *Exclude reversible causes. †History consistent with an arrhythmic etiology for syncope. ‡ICD candidacy as determined by functional status, life expectancy, or patient preference. EP indicates electrophysiological; GDMT, guideline-directed management, and therapy; ICD, implantable cardioverter-defibrillator; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; pts, patients; SCA, sudden cardiac arrest; SCD, sudden cardiac death; and VT, ventricular tachycardia. *2017 AHA/ACC/HRS Guidelines for management of patients with ventricular arrhythmias and sudden cardiac death*

with ischemic heart disease have proved that ICD implantation reduces mortality over the long term [8, 9]. Interestingly, two randomized trials failed to prove the benefit of ICD implantation within 40 days after MI [10, 11]. The precise reasons for the ineffectiveness of ICD in the immediate post MI and post revascularization have not been elucidated well. Therefore, ICD implantation should be performed at least 40 days after MI. Considering the high risk of SCD in the first 40 days after acute MI, a wearable cardioverter-defibrillator (WCD) with reevaluation of cardiac function after 40 days is a reasonable option (Fig. 2). According to 2017 AHA/ACC/HRS guideline, primary prevention indication of ICD for a patient with ischemic heart disease is summarized as below.

Nonischemic Cardiomyopathy

Secondary Prevention

Secondary prevention indication of ICD for a patient with NICM is summarized (Fig. 3).

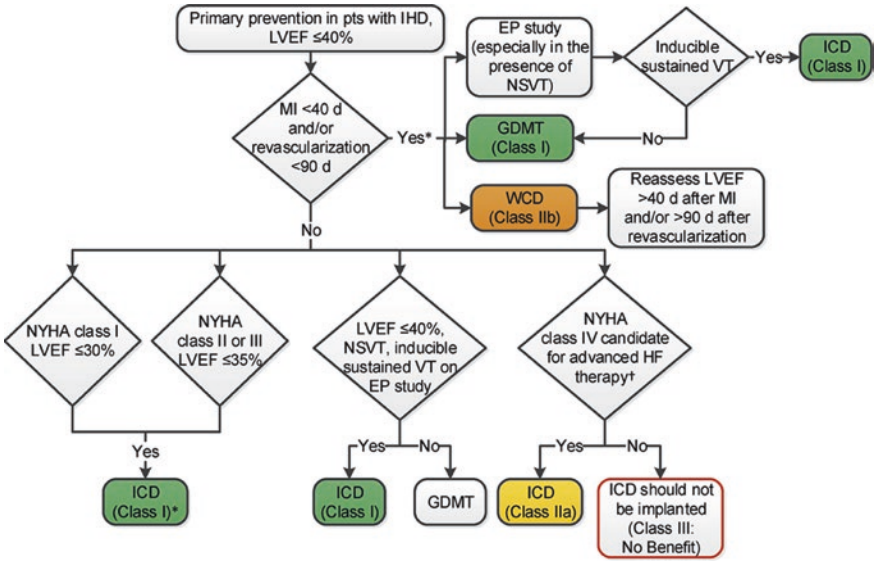

Fig. 2 Primary prevention in patients with ischemic heart disease *Scenarios exist for early ICD placement in select circumstances such as patients with a pacing indication or syncope. †Advanced HF therapy includes CRT, cardiac transplant, and LVAD thought due to VT. These are detailed elsewhere in an HRS/ACC/AHA expert consensus statement.[S7.1.2–24] CRT indicates cardiac resynchronization therapy; EP, electrophysiological; GDMT, guideline-directed management, and therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSVT, nonsustained ventricular tachycardia; NYHA, New York Heart Association; pts, patients; SCD, sudden cardiac death; VT, ventricular tachycardia; and WCD, wearable cardioverter-defibrillator. *2017 AHA/ACC/HRS Guidelines for management of patients ventricular arrhythmias and sudden cardiac death*

Primary Prevention

Compared to ischemic cardiomyopathy, the benefit of ICD remains controversial for primary prevention in patients with NICM (Fig. 4). In all patients with NICM, an adequate trial of guideline-directed management and therapy (GDMT) for at least 3 months prior to ICD implantation should be tried. Better adherence to GDMT may improve clinical outcomes and decrease the need for ICD therapy among patients with heart failure.

Over the past two decades, ICD implantation has been associated with significant reductions in the rate of SCD and total mortality in patients with ischemic cardiomyopathy. However, the evidence of benefit of ICD implantation for NICM has been weaker. The DEFINITE study randomized 458 patients with NICM and LVEF<36% into conventional medical therapy or ICD implantation. Arrhythmic mortality was significantly reduced by the ICD (Table 1) [12]. In SCD-HEFT (The Sudden Cardiac Death in Heart Failure Trial), the efficacy of ICD was compared

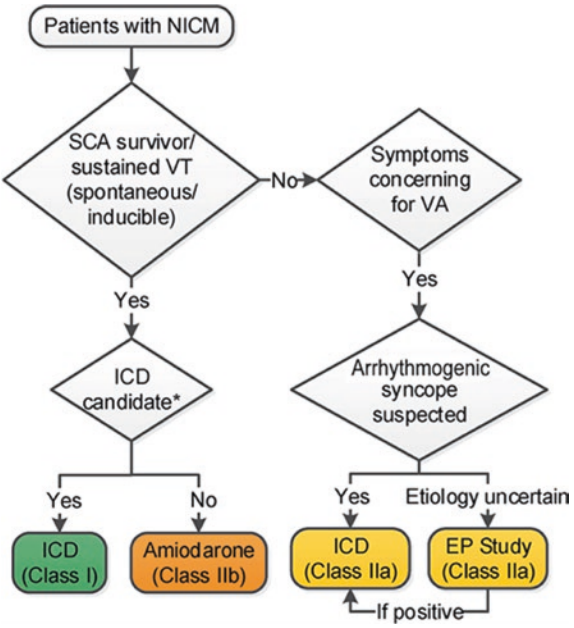

Fig. 3 Secondary prevention in patients with nonischemic cardiomyopathy

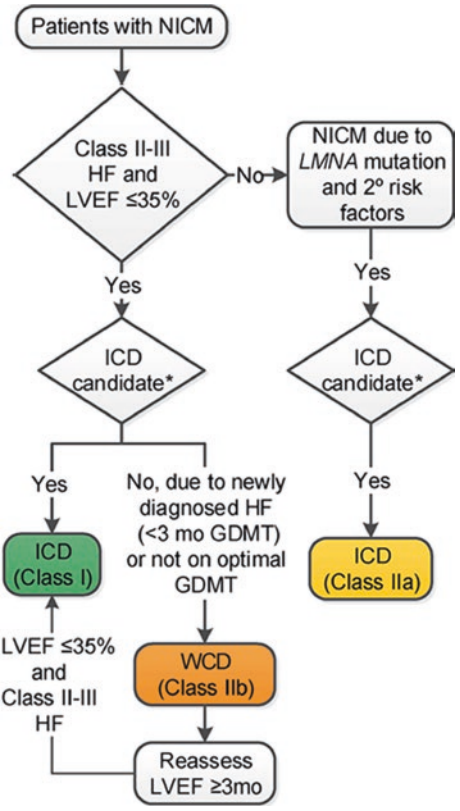

Fig. 4 Primary prevention in patients with nonischemic cardiomyopathy *2017 AHA/ ACC/HRS Guidelines for management of patients ventricular arrhythmias and sudden cardiac death*

Table 1 Landmark randomized control study in patients with NICM

Study	Control group	LVEF	Follow up (years)	ICD (N)	Control (N)	All cause mortality ICD versus control	
DEFINITE 2004	ICD versus medical therapy	<36%	2	229	229	7.9 versus 14.1%	HR 0.65; 95% CI, 0.40–1.06; P = 0.08
SCD-HeFT 2005	ICD versus amiodarone versus placebo	≤35%	3.8	829	847	22% (ICD) versus 28% (amio) versus 29% (placebo)	HR 0.77; 97.5% CI, 0.62–0.96; P = 0.007
DANISH 2016	ICD versus medical therapy	≤35%	5.6	556	560	23.4 versus 21.6%	HR 0.87; 95% CI, 0.68–1.12; P = 0.28

with amiodarone or placebo among patients with New York Heart Association (NYHA) class II or III congestive heart failure (CHF) and a left ventricular ejection fraction (LVEF) ≤35% [9]. The result showed a significant reduction in overall mortality in patients with ICD therapy compared to conventional medical therapies. The benefit of ICD was comparable between patients with IHD and NICM. However, the positive effect of ICD treatment was confined to patients in NYHA class II. More recently, a prospective randomized study, DANISH study was performed to attempt to answer the question [13]. Interestingly, the result of DANISH study was not consistent with the previous two large studies. The DANISH study includes 1,116 patients with NICM and were on optimal medical therapy for heart failure. The entry criteria include an LVEF ≤35%, NYHA class II or III and a pro-Brain N-terminal (pro-BNP) level >200 pg/ml. Patients were randomized to either ICD implantation or standard medical therapy. In this trial, ICD implantation was not associated with significantly lower long-term rate of death from any cause than usual clinical care. The annual mortality rate of the study was 3–4% and much lower than in other previous studies. This suggests that the improvement of medical therapy for heart failure over the decades lower the mortality of cardiomyopathy and decrease the benefit of ICD therapy. However, the high prevalence of CRT and GDMT in the DANISH trial likely reduced their statistical power for showing a significant difference in the primary outcome. All things considered, ICDs are useful to reduce total mortality and mortality from SCD in patients with NICM, although the benefits of an ICD on total mortality may be diminished in the setting of CRT and GDMT. In conclusion, for patients with NICM, current AHA/ACC/*HRS Guidelines* recommend ICD as primary prevention for those patients with an LVEF of ≤35%, NYHA class II or III, after 3 months of optimal GDMT for CHF. Future randomized studies may affect this indication.

Laminopathies are inherited cardiac disease caused by mutations in the Lamin A/C gene. A recent study showed that Life-threatening VAs are common in patients with LMNA mutations and significant cardiac conduction disorders, even if the left ventricular systolic function is preserved. [14] Therefore, in patients with laminopathies, ICD can be beneficial for those who have more than 2 risk factors (NSVT, LVEF<45%, nonmissense mutation, and male) (class IIa).

ICD System

The ICD system consists of a pulse generator (can) and one or two leads.

The pulse generator houses several essential components including,

1. battery to power the generator
2. high voltage capacitors and a charging circuit to provide the high voltage pulse to deliver the shock.

Defibrillator (Pulse Generator)

The ICD can is a sealed metal casing made of titanium (Fig. 5). The metallic casing protects the battery and electronic circuitry from damage caused by body tissue and external electromagnetic interference (EMI). The ICD can also be used as an active shocking electrode.

Lead Connector

ICD lead connectors and headers of the defibrillator have standardized design and ICD leads are compatible with defibrillators from different manufacturers. Most newly implanted ICD systems use the DF-4 lead connector system. Before DF-4 was approved, IS-1/DF-1 had been used (Fig. 6). In IS-1/DF-1 system, ICD lead terminals comprised an IS-1 pin for the pace-sense component and a DF-1 pin for each high-voltage coil. Thus, three ports were required for a defibrillation lead. In the DF-4 system, the pace/sense conductor and defibrillation coil conductor connect to a single, multi-interface connection pin. The advantages of the DF-4 system include decreased the smaller size of the device header, the shorter length of the lead and prevention of accidental reversal of high-voltage connections.

Fig. 5 Single chamber ICD with DF-4 lead connector system

Fig. 6 ICD with DF-4 (single chamber, left) and IS-1/DF-1 (dual chamber, right) lead connector system

Device Selection

Transvenous ICD Versus Subcutaneous ICD

To overcome the limitations of the transvenous ICD including lead-related complications, subcutaneous ICD (S-ICD) was developed. However, S-ICD can neither deliver anti-tachycardia pacing (ATP) to terminate VA nor continuous pacing during bradycardic events. Also, S-ICD is not indicated if the patient is anticipated to require CRT-D in the future, such as patients with LBBB. Most primary prevention ICD candidates do not require pacing therapy and considered suitable candidates for S-ICD. Inappropriate device shocks from S-ICD has been concerned

since they are released. The use of a conditional zone (rate plus discriminators) was associated with a significantly lower risk of inappropriate shocks for oversensing and supraventricular tachycardia [15]. Please see the chapter of S-ICD for a more detailed explanation.

Dual Chamber Versus Single Chamber

The decision whether to use a single or a dual chamber ICD has not been addressed in the randomized trials evaluating ICD efficacy. Most ICD patients do not have an indication for pacing and adding atrial lead is controversial. Theoretically, an atrial lead in a dual chamber ICD may improve rhythm discrimination over the single chamber ICD. However, adding the atrial lead will increase the cost and the rate of complications. Available data showed that dual chamber ICD did not lower the rates of inappropriate therapy or overall mortality. The dual chamber ICD is however associated with a higher rate of procedure-related complications and decreased longevity of the device [16–20]. Therefore, the routine use of dual chamber ICDs in patients without a pacing indication should be avoided, especially in young patients. Current guideline recommends single chamber ICD if the sole reason for the atrial lead is SVT discrimination.

> It is reasonable to choose single-chamber ICD therapy in preference to dual-chamber ICD therapy if the sole reason for the atrial lead is SVT discrimination, unless a known SVT exists that may enter the VT treatment zone, to reduce both lead-related complications and the cost of ICD therapy. (class IIa)

The Linox Smart DX lead (Biotronik, Berlin, Germany) is a 7.8 French single coil true bipolar lead, which contains 15 mm spaced pair of atrial ring electrodes mounted 15–17 cm from the tip of the lead (Fig. 7). This unique lead can provide atrial sensing in a single chamber ICD lead (VDD) without the risks and incremental cost of an additional atrial lead. The single lead pacing system (VDD) with the ability to sense atrial signals via floating atrial electrodes has been used since the 1980s. However, it has not been widely popular due to unreliable atrial sensing and concerns for the possible need for an atrial lead down the road. Compared to a previous VDD system, the DX ICD system uses an optimized atrial dipole spacing and improved atrial signal processing to offer more reliable atrial sensing. Usually, these atrial electrodes are floating and do not have direct contact with atrial tissue.

Those patients in whom dual chamber ICD is considered

- Patients who need dual chamber pacemaker
- Patients who need biventricular pacing (or biventricular pacing is anticipated)
- Patients with atrial tachycardia or atrial flutter (better discrimination)
- Patients in whom atrial pacing is useful (Long QT, hypertrophic cardiomyopathy).

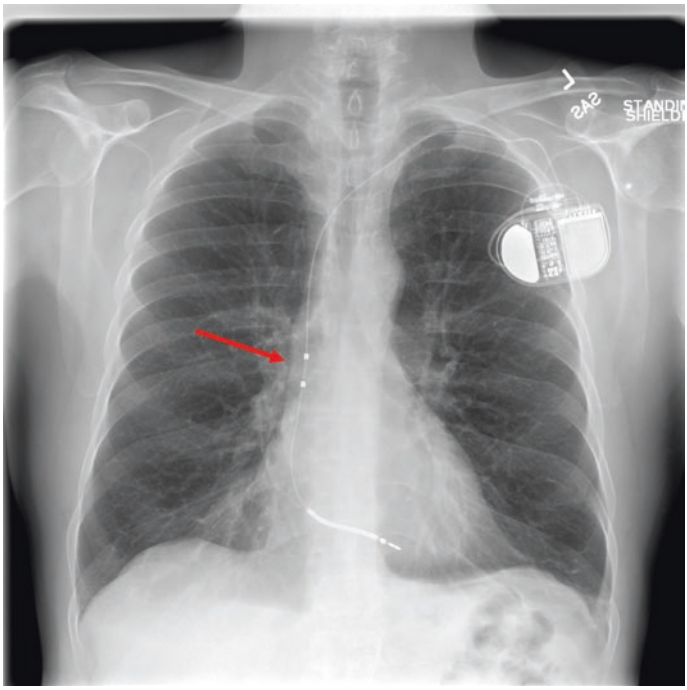

Fig. 7 The Linox Smart DX active fixation lead (Biotronik). The atrial signal sensed via these floating atrial electrodes

Single Coil Versus Dual Coil

All transvenous ICD lead has a distal shock coil in the RV. The dual-coil ICD lead with a shocking coil in the RV and supra vena cava (SVC) coil, had been widely used. The older ICD system did not have an active can as one of the defibrillation electrodes and the SVC coil was essential part of the ICD system. Having two coils (SVC and RV) in the ICD system can provide lower DFT. Previously DFT with dual-coil leads was considered to have significantly lower DFT compared to single-coil leads and the dual coil ICD was more commonly used. Today an active can system using the pulse generator as one of the electrodes and high energy device have become standard. These changes decrease the occurrence of high DFT and demand for the SVC coil has been decreased significantly. The SVC coil is also known to be potentially strongly adherent to the SVC wall and the risk of the SVC tear is increased during lead extraction. A recent study based on the National Cardiovascular Data Registry (NCDR) showed that the use of dual coil leads decreased from 85% in 2010 to 55% in 2015 [21]. Contemporary ICD system with a single-coil lead can achieve a low DFT (<5 J) with a safety margin of at least 10 J in most of the patients. The bottom line is that single-coil and dual-coil lead

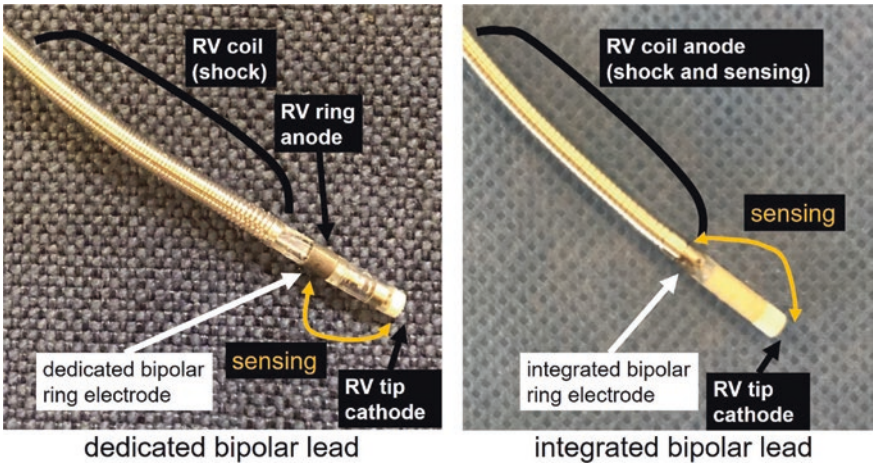

Fig. 8 Integrated bipolar lead and dedicated bipolar lead

systems provide effective defibrillation at comparable energy levels. Therefore, an additional SVC coil would not provide a significant benefit.

In patients with the right pectoral ICD system, right ventricular coil to can configuration may have less favourable efficacy. Therefore, some physicians use a dual coil lead system for those patients with the right pectoral ICD system. However, some studies did not show a significant difference in DFT between single and dual coil systems and a conclusion has not been reached regarding this issue.

Shock Polarity

The defibrillation function of the electrodes requires a relatively large surface area to defibrillate more myocardial mass. In addition, positioning of the lead is essential to maximize the density of current flow through the ventricular myocardium. Contemporary ICD systems take advantage of high voltage shock coil. This is a coil of wire that wrapped around the distal lead body, 5–6 cm in length and extends along with the ventricular lead as the primary defibrillation electrode (Fig. 8). The defibrillation shock is delivered by a dedicated lead, which may be a single coil (RV coil) or dual coil (RV and SVC). Single coil shocks can only be delivered between the RV coil and the pulse generator (can).

The shape of a defibrillation waveform can affect defibrillation efficacy significantly. Biphasic waveforms can lower the defibrillation energy significantly, compared to monophasic waveforms. In other words, biphasic waveforms require less energy and less damage to the heart, with a higher success rate. Thus, biphasic waveforms are used in all commercially available ICD devices.

The waveform has a polarity defined as that of the RV shock electrode. In the biphasic waveform, the polarity is defined as that of the first phase. An anodal shock corresponds at a shock with the right ventricular electrode as the anode in the first phase of a biphasic shock and as the cathode in the second phase. Most studies showed the superiority of anodal shock in biphasic defibrillation. Although, whether an anodal shock is really superior to cathodal shock is not concluded yet and anodal shock may be preferred. Currently, the nominal polarity setting is the right ventricle as the anode on Medtronic and Abbott ICDs and the cathode on Boston Scientific and Biotronik ICDs. The shock polarity is programmable and when you encounter with patients with high DFTs, reverse-shock polarity should be attempted. Since the DFT test is not routinely performed anymore, we always program at least one shock with reversed polarity in each zone, while others can maintain nominal polarity.

Integrated Bipolar Versus Dedicated (True) Bipolar

ICD leads use a bipolar configuration for sensing and this is referred to as "near field ventricular EGM". There are two different types of bipolar leads, dedicated (True) bipolar and integrated bipolar configuration (Fig. 8). Both configurations use the tip electrode as the cathode. The dedicated bipolar configuration uses a ring electrode as the anode and sensing occur between the tip electrode and a closely spaced dedicated ring. Therefore, the dedicated bipolar lead requires 1 more conductor than an integrated bipolar lead (The dedicated bipolar lead requires two conductors, versus one in the integrated bipolar lead). The dedicated bipolar has better sensing and pacing function (small antenna). Electrograms recorded between the tip and the RV coil are referred to as integrated bipolar electrograms because the RV coil integrates pace/sense and defibrillation functions. In the integrated bipolar configuration, a distal tip electrode is used for pacing/sensing and a distal coil is used for both pacing/sensing and defibrillation. The large antenna of the integrated bipolar configuration is more susceptible to oversensing of far-field potential, myopotential and EMI. R wave double-counting also happens more frequently with the integrated bipolar system. The integrated bipolar EGM records a greater amount of myocardial activation than the dedicated bipolar system. As a result, the total activation time is more likely to exceed the ventricular blanking period.

Although three is no difference between the dedicated and integrated leads regarding sensing of VF, dedicated bipolar is more commonly used. In general, the integrated bipolar often have larger R/T wave ratio, compared to the dedicated bipolar. T-wave oversensing is a potential reason for inappropriate shocks in patients with Brugada syndrome. A retrospective, multicenter study showed that the incidence of T-wave oversensing is significantly lower using an integrated lead system when compared with a dedicated bipolar lead system in patients with Brugada syndrome receiving ICDs [22]. This fact should be taken into consideration when we implant ICD for patients with Brugada syndrome.

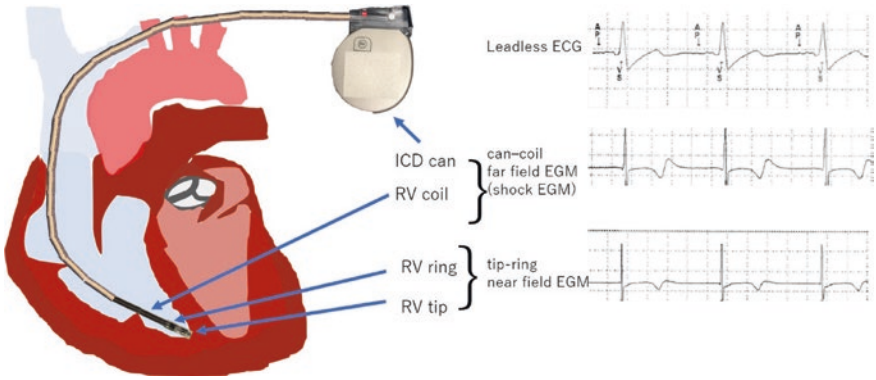

Fig. 9 ICD shock electrograms (near field and far field)

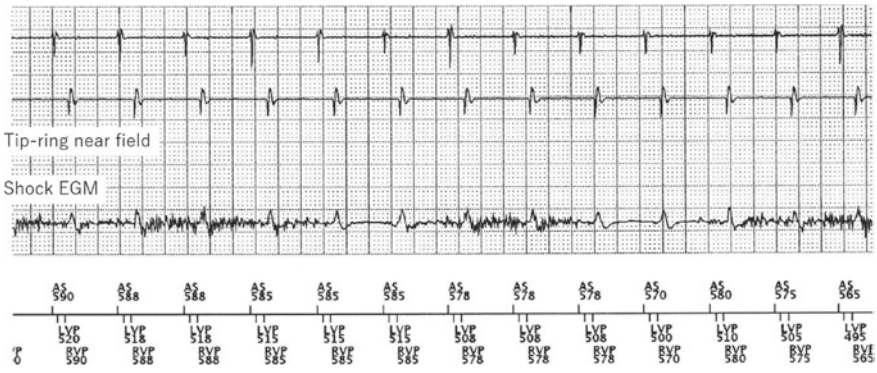

Fig. 10 An example of far field oversensing in ICD lead *This noncyclic noise was not detected on the near-field (the rate sensing electrode) recorded between the RV tip and ring electrodes, but rather on the far field EGM recorded between the distal or proximal coils and ICD pulse generator. This is likely from pectoral or diaphragmatic myopotentials*

In the Medtronic system, the RV sensing vector between true bipolar (RV tip to ring) and integrated bipolar (RV tip to RV coil) in the dedicated bipolar lead is programmable (RV Sense Polarity). As mentioned above, integrated bipolar often have larger R/T wave ratio, compared to true bipolar. Therefore this function can be a noninvasive option to troubleshoot T wave oversensing.

Considering the requirement of multiple leads implantation, the diameter of the ICD lead has been reduced. Current representative ICD leads size is 6.8 French to 8.6 French. The ICD has two primary electrograms + the shock (high-voltage) electrogram and the ventricular sensing electrogram (Fig. 9). The ICD shock electrogram (CAN to the distal coil) has much wider space between the electrodes compared with the ventricular sensing bipolar electrogram. The shock electrogram records a far-field signal and is more susceptible to oversensing problems (Fig. 10). Therefore, the ICD shock electrogram is not used for rate counting for

detection. The ICD shock electrogram is used as sensing electrograms for differentiating VT from SVT because they acquire ventricular activation signal from a much greater volume of the myocardium. Most of the cases, sensing electrograms have higher frequency content and sharper peaks than shock electrograms. When we analyse ventricular sensing, the shock electrogram is used as a double check on the sensing electrogram. Signals sensed on the sensing electrogram do not correspond to signals on the shock electrogram indicate oversensing. For a similar reason, true ventricular electrograms seen on the shock electrogram that is not associated with events on the marker channel indicate undersensing.

Case Conclusion

Two randomized trials failed to prove the benefit of ICD implantation within 40 days after MI [10, 11] Therefore, patients with recent MI should be reassessed for ICD implantation at least 40 days after MI. If those patients still have LVEF ≤35% and NYHA class II or III, ICD is indicated. ICD is also indicated in patients with LVEF ≤30% and NYHA class I. A recent study showed a high rate of LV function recovery among survivors of acute MI with an initial reduced LVEF ≤35%. [23] After percutaneous coronary revasculization, 57% of patients had LVEF recovery to >35% at 3 months post-MI.

In conclusion, this patient with LVEF 35% and NYHA class I do not meet indications for ICD at this point. Further evaluation should be performed to determine whether ICD is indicated in this patient.

Future Directions

More sophisticated sudden cardiac death risk stratification algorithms are being developed and tested to improve patient selection for ICD implantation, including machine learning techniques and computer modeling based on scar imaging.

Key Points

1. Two different ICDs are currently available; Transvenous ICD and subcutaneous ICD. The risk of lead-related complications, the rate of inappropriate therapy, and the device-specific limitations of S-ICD (incapability of ATP) should be taken into consideration on a case-by-case basis.
2. The evidence of secondary prevention of ICD has been established well.
3. Multiple studies also showed the benefit of ICD for primary prevention in patients with ischemic cardiomyopathy. Patients with ischemic

cardiomyopathy, LVEF ≤35% and CHF with NYHA class II or III, ICD is recommended for primary prevention of SCD. Likewise, patients with ischemic cardiomyopathy, LVEF ≤30% and NYHA class I, ICD is recommended. Patients should be evaluated at least 40 days after MI and more than 3 months following coronary revascularization.

4. For patients with nonischemic dilated cardiomyopathy, LVEF ≤35%, and CHF with NYHA class II or III, we recommend ICD therapy for primary prevention of SCD on top of optimal medical therapy
5. Most ICD patients do not have an indication for pacing and adding atrial lead is controversial. Therefore, the routine use of dual chamber ICDs in patients without a pacing indication should be avoided, especially in young patients.
6. Single-coil defibrillation leads (versus dual-coil) should be used in most patients receiving an ICD, especially in young patients.
7. ICD shock electrogram (CAN to the distal coil) has much wider space between compared with the integrated or dedicated bipolar electrogram and is more susceptible to oversensing problems. Therefore, the ICD shock electrogram is not used for rate counting for detection.

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Implant Considerations for the Implantable Cardioverter Defibrillator

Hiro Kawata

Clinical Case

A 49-year-old female with nonischemic cardiomyopathy and recent ICD implantation (10 days before) who presented to a hospital with a complaint of chest pain that started the night before described as heavy constant and with intermittent sharp pain. The pain got worse when she sat up and better when she lay down.

Introduction

The purpose of this chapter is to discuss the practical aspect of the ICD implantation technique and perioperative complications.

Implantation of ICD

Preparation for ICD Implantation

Management of Anticoagulation

Major or minor bleeding is a common complication after ICD implantation, which increases the risk of device-related infection [1, 2]. A substantial number of patients takes anticoagulant before an ICD implantation. Since the risk of

H. Kawata (✉)
Oregon Heart & Vascular Institute, Peacehealth Sacred Heart Medical Center, 3311 RiverBend Drive, 3rd Floor, Springfield, OR 97477, USA
e-mail: hkawata@peacehealth.org

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discontinuing anticoagulation therapy vary among patients, the perioperative management of anticoagulation therapy should be individualized.

1. Warfarin

Considering the results of randomized studies, we recommend the continuation of warfarin rather than a heparin bridging [3]. For patients who are taking warfarin and have a low risk of thromboembolism, either interrupted or continued warfarin may be used, because currently there is no evidence to clearly support either strategy. When the ICD implantation is performed without interruption of warfarin, the INR should be checked 5–7 days prior to the procedure for possible dose adjustment. And then the INR should be checked on the day of the procedure. The INR on the procedure day preferably should be $\leq$3.0 (except for patients who needs higher INR for mechanical mitral valve).

Current consensus recommendation was shown in Table 1.

2. Factor Xa inhibitors and direct thrombin inhibitor

The Bruise control-2 study randomly assigned patients with atrial fibrillation and CHA2DS2-VASc score $\geq$2, to continued versus interrupted DOAC (direct oral anticoagulant such as dabigatran, rivaroxaban, or apixaban) [5]. The result showed that continuation of DOAC was not associated with any major perioperative bleeding events. This result suggests it is safe to perform ICD implantations without

Table 1 Device implantation in patients receiving vitamin K antagonists (VKA): consensus recommendation

In the following patient groups with AF, it is recommended to perform device surgery without interruption of VKA
(i) Patients with non-valvular AF and a CHA_2DS_2-VASc score of $\geq$3
(ii) Patients with a CHA_2DS_2-VASc score of 2 due to stroke or TIA within 3 months
(iii) Patients with AF planned for cardioversion or defibrillation testing at device implantation
(iv) Patients with AF and rheumatic valvular heart disease
In the following patient groups with prosthetic heart valves, it is recommended to perform device surgery without interruption of VKA
(i) Prosthetic mitral valve
(ii) Caged ball or tilting disc aortic valve
(iii) Bileaflet aortic valve prosthesis and AF and a CHA_2DS_2-VASc score of $\geq$2
In patients with severe thrombophilia, it is recommended to perform device surgery without interruption of VKA
In patients with recent venous thromboembolism (within 3 months), it is recommended to perform device surgery without interruption of VKA
The INR on the day of surgery should be under the upper limit of the prescribed therapeutic range for the patients. (usually $\leq$3, $\leq$3.5 for some patients with prostehtic valves)
In patients with an annual risk of thromboembolism events $<$5% either perform surgery without interruption of VKA or interrupt VKA 3–4 days before surgery, no heparin bridging is recommended
Interruption of VKA and bridging with an unfractionated heparin or low molecular weight heparin should be avoided
Europace. 2015 Aug; 17(8):1197–214 [4]

interruption of NOAC therapy. For patients with a higher risk for bleeding complications, it might be reasonable to hold DOAC 48 h before the implantation. Bridging with heparin, subpectoral implantation, an upgrade procedure, and older patients are known as risk factors for bleeding complications.

Assessment of Axillary Vein

Subclavian venous occlusion is relatively common following cardiac device implant (10–12%) (Fig. 1). A study showed about 50% of patients with existing pacing or ICD systems had >50% stenosis [6]. In addition, complete occlusion of the subclavian/axillary or innominate vein occurred in 26% of patients. Although

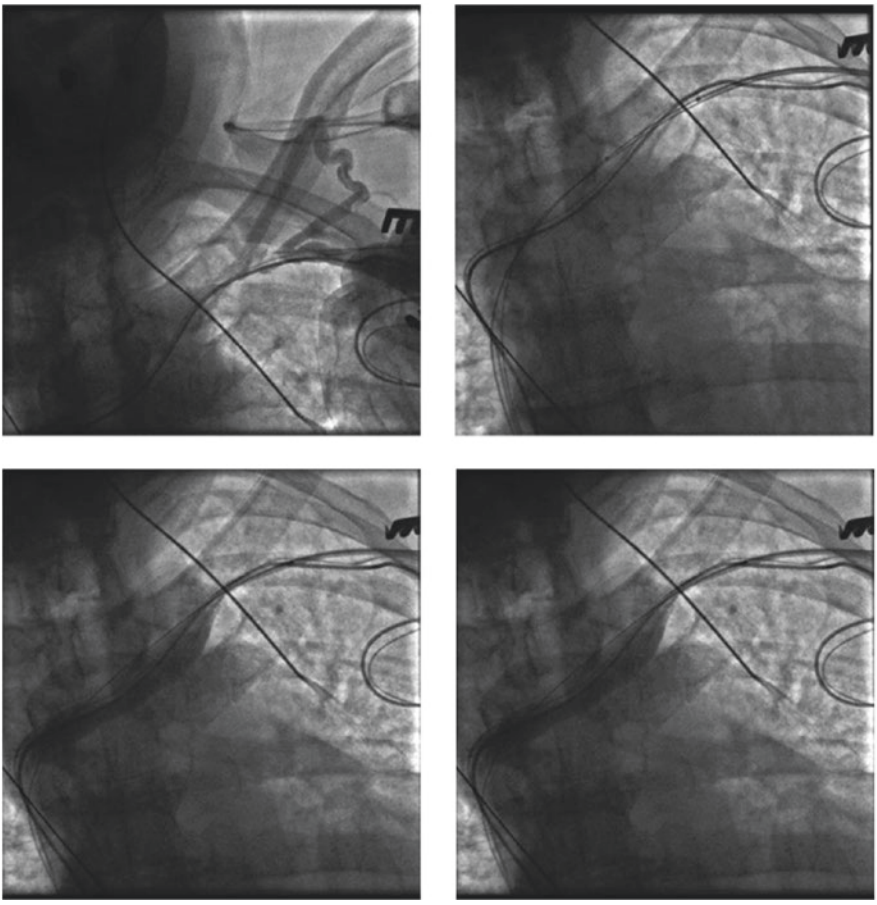

Fig. 1 Chronic total occlusion of the left subclavian vein at pacemaker lead site with prominent collateral (left upper). Venoplasty using 6 mm x 40 mm balloon (right upper). Venography after the venoplasty (left lower)

the association of venous stenosis and the number of leads has been controversial, some studies showed a high incidence of venous stenosis in patients with multiple leads, procedures, and the sum of lead diameters implanted. Venous stenosis and thrombosis are usually asymptomatic due to the formation of collaterals veins. Ipsilateral contrast venography of the axillary and subclavian vein can specify the exact location and length of the stenosis and occlusion. Therefore, I would recommend contrast venography when you need to add pacemaker or ICD lead in patients with cardiac devices, such as upgrade cases or lead revisions.

Different approaches can be taken for the venous stenosis, including contralateral leads implantation with tunnelling, recanalization with or without lead extraction and venoplasty (Fig. 1). The decision making depends on individual anatomical considerations, physician's experience, and available resources.

Implantation Techniques

Most CIED implantations are performed with local anesthesia and sedation. Efficacy of prophylactic antibiotics has been reported [7]. Prophylactic antibiotics should be given within 1 hour prior to the procedure.

Position of the ICD Can (Pulse Generator)

The contemporary ICD can is small enough to be implanted in the pectoral region of the anterior chest wall subcutaneously. Subpectoral implantation of ICD can be beneficial for elderly, lean patients or young patients who request better cosmetic results. Subpectoral implantation carries a higher risk for bleeding complications and this procedure should not be performed routinely.

In general, ICD is implanted patients' non-*dominant* side. The skin incision is usually made in the left or right infraclavicular area. The location of the incision depends on the vascular access approach. The length of skin incision is about 3–5 cm and carried down to the subcutaneous tissue. The dissection is extended to the fascia of the pectoral major muscle with electrocauterization, blunt dissection, or both.

For a cephalic vein cutdown, in order to identify the vein, an incision in the deltopectoral groove may be preferred. When axillary vein puncture is performed under fluoroscopic guidance, the incision should be guided fluoroscopically by inspection of anatomical landmark including the clavicle and ribs.

I always perform axillary vein puncture under ultrasound guidance. In my practice, axillary vein puncture is performed before the skin incision (Fig. 2). After obtaining axillary vein access, the skin incision is made just below the puncture site of the skin (Fig. 3). The medial edge of the incision is placed at the 2–3 cm medial side of the puncture (depends on the thickness of the subcutaneous tissue). In order to suture the leads on the fascia without extensive stress, you should have adequate space around the puncture site.

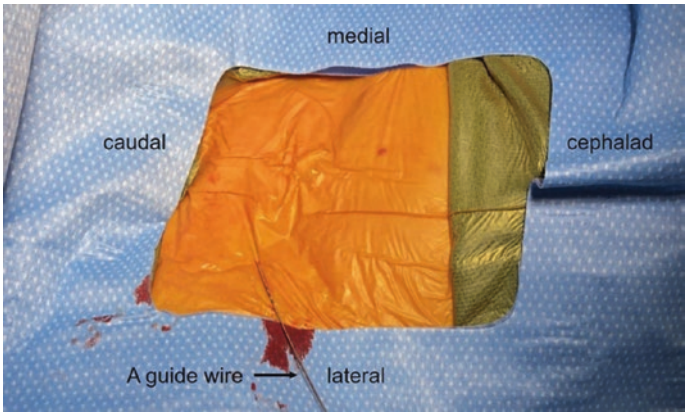

Fig. 2 Micro puncture wire insertion before skin incision on the left infraclavicular area

Venous Puncture

Various approaches for the venous access was summarized as below.

Various Approaches for Venous Access

- Direct cutdown on the axillary vein
- Subclavian vein puncture under fluoroscopic guidance
- Lateral Axillary vein puncture under fluoroscopic guidance with or without contrast venography
- Medial axillary vein puncture under fluoroscopic guidance with or without contrast venography
- Ultrasound guidance axillary vein puncture.

The incidence of pneumothorax during pacemaker or ICD implantation is reported to be about 0.5–1%. The risk is lowered by identifying the exact location of the vein with cephalic vein cut down, contrast venography or ultrasound guidance. The cephalic vein is smaller than the axillary vein and to implant all leads with cephalic vein cut down technique might not be easy, especially for CRT devices [8]. Even after contrast venography, the puncture under fluoroscopy can be unsuccessful due to severe venous spasm or marked collapse.

A 5 Fr micropuncture needle is should be utilized to minimize the risk of complications. If you puncture the vein at a steep angle, you end up giving excessive stress when you suture the leads. Therefore, the needle should be advanced the vein at a 30–45 degree angle. **I strongly believe axillary vein puncture under ultrasound is the safest and the most reliable method.** Ultrasound image shows you the exact location of axillary vein, axillary artery and lung and the incidence of pneumothorax or arterial puncture is extremely low (Fig. 4). In addition,

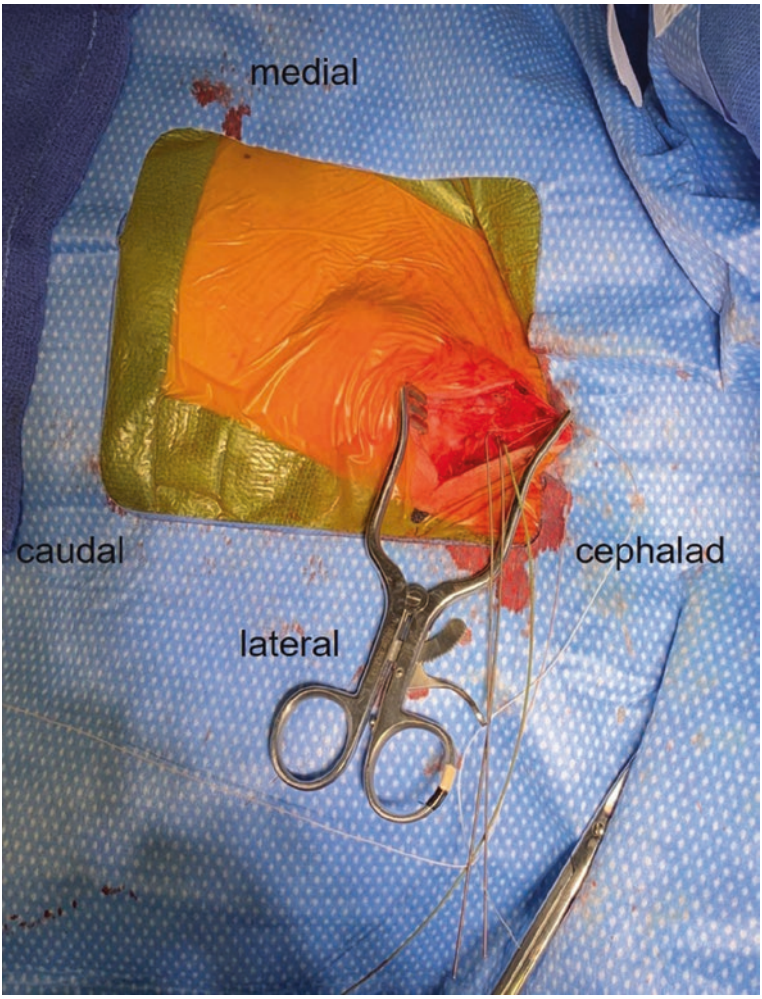

Fig. 3 After the skin incision

contrast venography is not needed in axillary venous puncture under ultrasound guidance. As I mentioned already, I believe the incision site should be determined by the puncture site and I do perform axillary vein puncture first, followed by skin incision. This manner helps us to avoid having excessive tension on the leads when we house the ICD and the leads in the pocket. Ultrasound may not show you a clear image of the axillary vein in obese patients. The distal part of the subclavian vein and the axillary vein lie below and in front of the subclavian and axillary artery. Therefore, most of the cases, you still be able to estimate the location of the vein using the axillary arterial pulse. For those patients with thick fat tissue, you may need to make the skin incision and the pocket first. Once you make the skin incision and the pocket, the ultrasound probe on the pectoralis major will show you a clearer image of the axillary vein (Fig. 5).

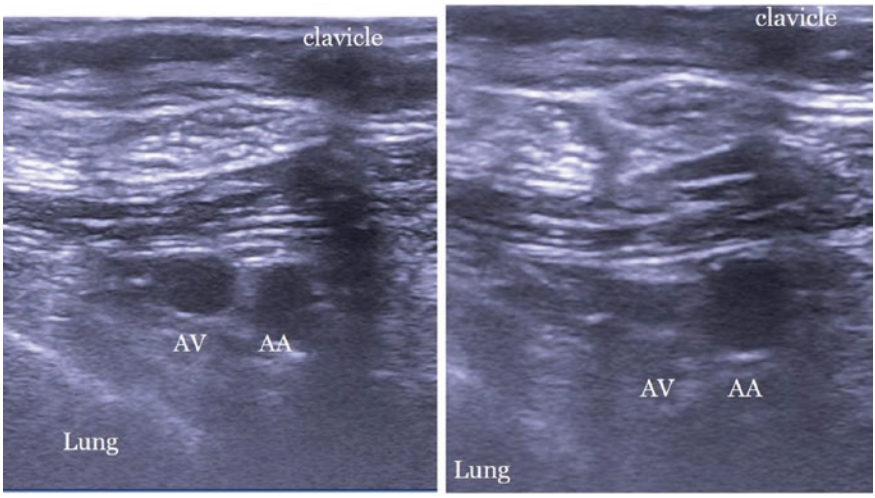

Fig. 4 Ultrasound image during left axillary venous puncture. The axillary vein (AV) runs along the medial side of the axillary artery (AA) and is collapsible. Left : Ultrasound image of the puncture site (about two fingers below the deltopectoral triangle). Right : Ultrasound image of the same area during compression with the probe. The axillary vein is collapsed while the axillary artery maintains the circular shape

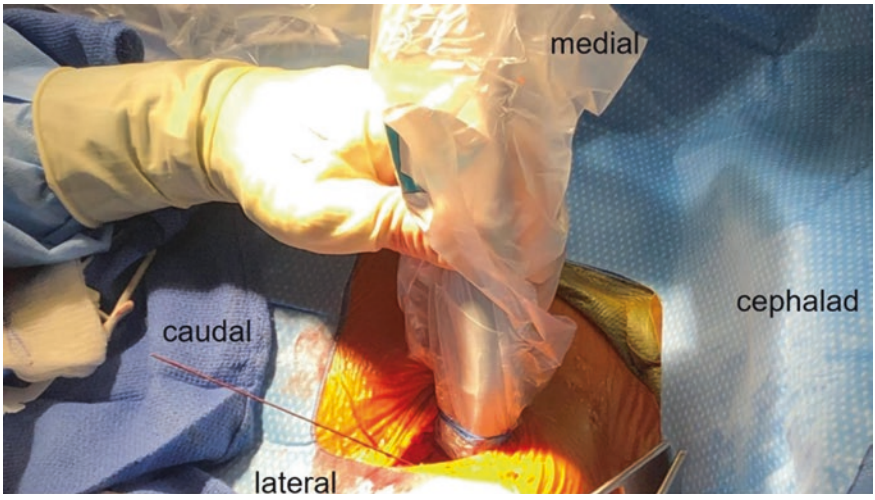

Fig. 5 Ultrasound probe placed in the pocket

The risk of pneumothorax and clavicular crush syndrome (Fig. 6) is high in conventional subclavian vein puncture; thus, more lateral puncture in the axillary vein with or without contrast venography is preferred.

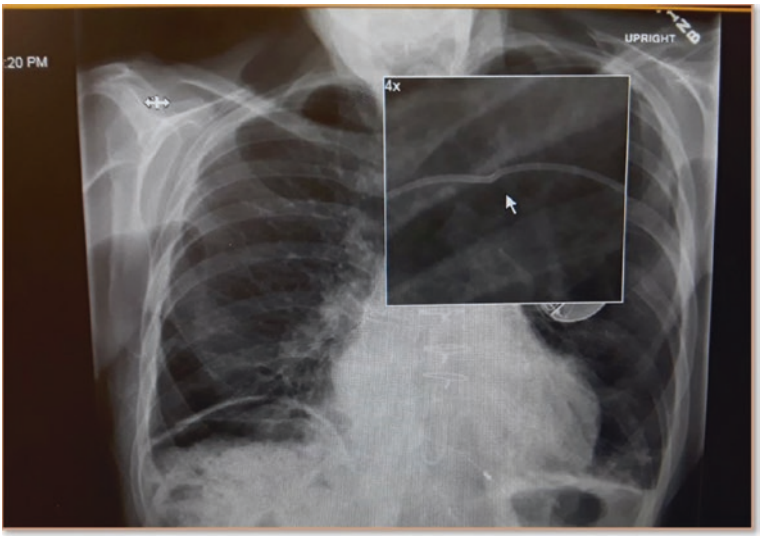

Fig. 6 Clavicular crush due to medial venous puncture in subclavian vein

If the fluoroscopic guided puncture is pursued, an extrathoracic axillary vein puncture is the preferred method to avoid pneumothorax. Although often aided by venography, implanting physicians performing ICD implantation may attempt blind access based solely on radiographic landmarks, such as the ribs and ribcage. The most common radiographic position of the axillary vein was over the third rib [9]. Understanding anatomical characteristics that may predict the cranial-caudal position of the axillary vein could shorten procedure time and reduce the risk of complications. There are two different approaches for extrathoracic axillary vein puncture, medial and lateral axillary vein puncture. In the medial axillary vein puncture method, the tip of the needle is aimed at the 1st rib. You should never cross the medial border of the 1st rib to avoid pneumothorax. In lateral vein puncture, the edge of rib cage formed by the 2nd and 3rd ribs will be the anatomical target for the tip of the needle. In this method, as far as the tip of the puncture needle is lateral to the medial border of the 2nd or 3rd rib, the chance of pneumothorax is very low (Fig. 7). In obese patients, you need to start puncture of the needle more lateral. Otherwise, you might end up having vertical angle of the leads to reach the vein before the tip of the needle crossing the medial border of the rib. It is cumbersome to tie suture sleeve onto the fascia when the leads are inserted vertically.

Placement of Atrial and Ventricular Leads

Right ventricular (RV) lead can be placed RV apex (RVA), RV mid septum or RV outflow tract (RVOT). RVOT septal area is close to a physiological conduction system and pacing from RVOT would produce more physiological ventricular

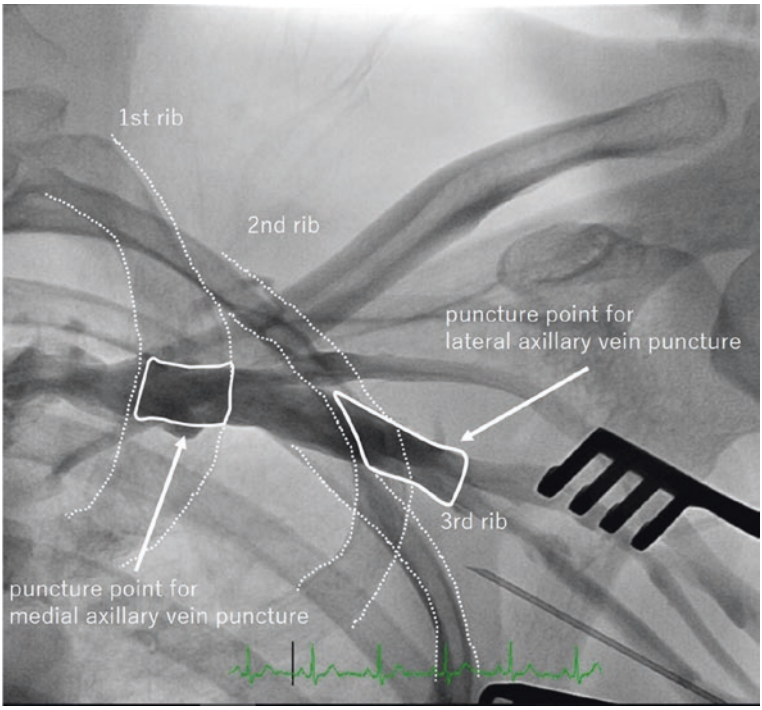

Fig. 7 Contrast venography of the axillary vein. (Contrast venography of the left axillary and subclavian vein. An anteroposterior fluoroscopic projection of an axillary venogram of a subject undergoing ICD lead implantation. The most common radiographic position of the lateral axillary vein was over the third rib)

activation through rapid conduction. Some studies showed long term RVOT pacing was associated with the better index for LV structure and function, compared with RVA pacing [10, 11]. However, there are conflicting results regarding this question [12]. To avoid the risk of cardiac perforation, I believe, an RV lead at least should be implanted to the septal side. In order to position an RV lead on the septal side, a stylet needs to be shaped in order to guide the lead. **The stylet guiding the lead to the septum requires two curves.** The first large curve facilitates crossing the tricuspid valve and the small curve at the end makes the lead point towards septum instead of the free wall (Fig. 8). For RVOT There is commercially available preshaped stylet from Abbott (Mond stylet). The final position of the lead should be confirmed with fluoroscopy. The LAO projection will reveal if the tip of the lead is directing to the septum or free wall. To avoid cardiac perforation by the ICD lead, you should not push hard the lead with the stylet advanced all the way to the tip (Fig. 9).

The bipolar endocardial signal of the RV lead should be $\geq$5 mV. Right atrial lead is placed in right atrial appendage using either active fixation or passive fixation lead. Bipolar endocardial signal of the RA lead should be $\geq$2.0 mV.

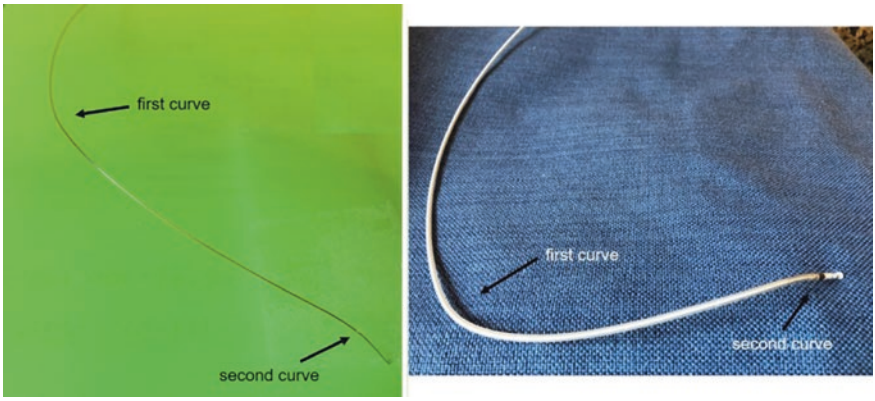

Fig. 8 A curved stylet for RV septal lead placement and an ICD lead with the stylet. To achieve RVOT septal pacing, the first curve needs to be tighter

Fig. 9 The tip of ICD lead with and without stylet. (The tip of ICD lead is very stiff when the stylet is advanced all the way in. All tension is delivered to the tip of the lead and the transparent cellophane can be perforated easily (left). The tip of ICD lead is relatively floppy if a stylet is in the middle of the lead. (middle and right))

Lead Connection, ICD Generator Placement, and Wound Closure

After the leads have been properly positioned and tested, the ICD pocket is irrigated with antimicrobial solution, and the ICD generator is connected securely to the leads.

The device migration may be associated with multiple potential factors, including the size of the pocket, the weight of the device and gravity, the fat tissue in

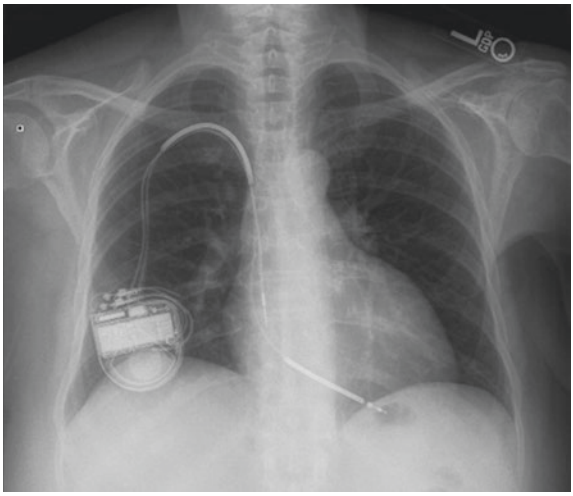

Fig. 10 Migration of ICD generator and dislodgement of RA and RV leads in an obese female patient. (Migration of ICD generator and dislodgement of RA and RV leads in an obese female patient)

the subcutaneous layer, the slack and whether the device is sutured or anchored on the pectoral muscle. ICD generators are heavier than pacemakers and the risk of device migration is higher, especially in obese female patients [13] (Fig. 10). I secure ICD generators to underlying pectoral muscle with a nonabsorbable suture to prevent migration in those high-risk patients.

After hemostasis is confirmed, a final survey with fluoroscopy before the closure of the incision is recommended to confirm appropriate lead positioning.

Defibrillation Threshold (DFT) Testing

The goal of defibrillation is to use the minimum amount of energy required to overcome the threshold of defibrillation. Excessive energy can cause myocardial injury and cardiac arrhythmias. The defibrillation threshold (DFT) is the minimum amount of energy required to reliably defibrillate the heart when it is experiencing a hemodynamically unstable VF or VT. By knowing the DFT, the physicians can be sure that the ICD is programmed to deliver energy that is sufficient enough to defibrillate ventricular arrhythmias. Another reason for the DFT testing is to confirm the reliable sensing, detection, and redetection of VF. The DFT does not exhibit a constant value because defibrillation requirements vary as a result of many influencing factors. In fact, a clinical measurement of DFT has only fair reproducibility.

Defibrillation Threshold (DFT) Testing in Clinical Practice

DFT had been considered an integral part of ICD implantation for many years. This has traditionally been done by VF induction and termination through the

device or, less commonly applied, through the upper limit of vulnerability (ULV) testing. The DFT testing usually starts by programming a ventricular sensitivity of 1.2 mV, which is higher than the nominal setting of 0.3mv (less sensitive). Defibrillation from ICD might be unsuccessful and external defibrillation pads are placed before the implantation procedure begins. Testing is done with the device in the surgical pocket and with leads connected. Electrical activity during VF is lower than that during VT. VF, not fast VT has to be induced for the testing. The method of VF induction depends upon the manufacturer and the capabilities of the device and programmer. VF is induced by rapid pacing, direct current, or T-wave shocks. Given the probabilistic nature of DFT, DFT testing requires multiple shocks to determine with precision. During DFT testing, VF is induced one or more times, and each episode of VF is defibrillated at one or more shock energies. In patient-specific testing, the success or failure of the first test shock usually determines the programmed strength of the next test shock:

There are two common methods for DFT testing, "the safety margin protocol" and "the step-down protocols". In both protocols, the first shock is programmed at least 10 J below the maximal output of the ICD. A safety-margin protocol is preferred when the principal goal is to minimize the risks of shocks, fibrillation, and defibrillation testing. After the safety margin testing, the first shock usually is programmed to maximum output. While DFT testing requires induction of VF, ULV does not. ULV is the stimulus strength above which VF cannot be induced even when the stimulus occurs during the vulnerable period of the cardiac cycle. It correlates closely with the minimum shock energy that defibrillates reliably. Testing the ULV has been used as an alternative to standard DFT testing as a way to estimate DFT without inducing VF. ULV testing provides an accurate estimate of the probability of defibrillation success and is more reproducible than DFT testing. If shock was applied during a certain period of time of a regular cardiac cycle, VF can be induced. This period is called a "vulnerable period". This period is simultaneous with the T wave in the ECG (Fig. 11). To successfully defibrillate, the shock strength must reach or exceed the upper limit of vulnerability. A shock on the vulnerable period of the T wave can only induce VF if the energy is smaller than a critical value. If higher energy is delivered, VF will not be induced. It correlates closely with the minimum shock energy that defibrillates reliably. The measurement of ULV is performed in regular rhythm (usually during right ventricular pacing at 120–150 beats per minute) providing an estimate of the minimum shock strength required for reliable defibrillation. The first shock is delivered on top of the T wave. If VF is not induced, the next shock will be delivered 20 ms before or after the top of the T wave. If you only need to determine a safety margin, the shock strength should be 5–10 J below the maximum output of the device. For example, if VF is not induced by the 20 J shock, the ICD shock can be programmed at 30 J (more than 10 J safety margin). The ULV is more reproducible than the DFT and can provide an accurate patient-specific safety margin with fewer episodes of VF. Thus, the ULV testing has been used as a surrogate for the DFT testing, especially patients with high risk for DFT.

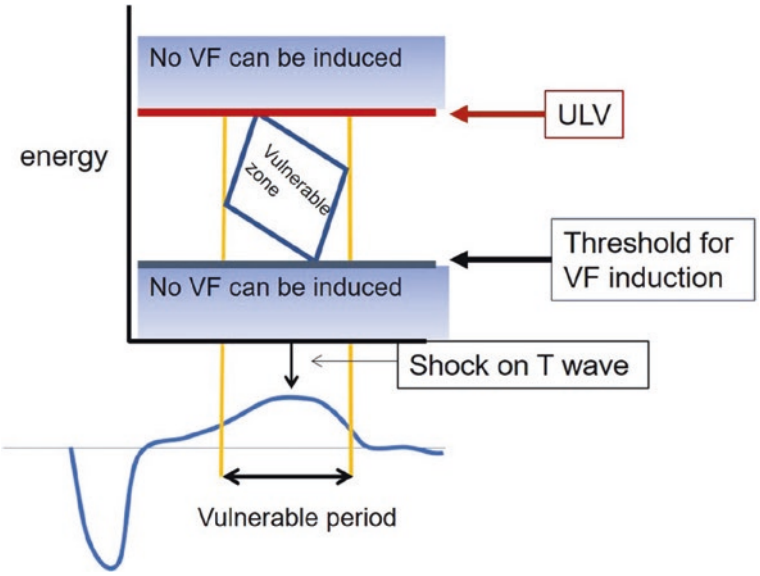

Fig. 11 Upper limit of vulnerability to assess defibrillation efficacy

Since the initial emergence of ICD systems, significant advancements in technology have occurred. Contemporary ICD systems take advantage of biphasic waveforms, active can technology and high energy shocks of 35 J-40 J. These changes raised the question for routine DFT testing during the ICD implantation. Multiple studies showed that ICD implantation without DFT testing was not inferior to ICD implantation with DFT testing in left-sided ICD implants. Current guidelines concluded that for patients undergoing initial left pectoral transvenous ICD implantation, not performing DFT testing is acceptable (where appropriate sensing, pacing, and impedance values are obtained with fluoroscopically well-positioned RV leads). However, for patients undergoing right pectoral ICD implantation, DFT is still recommended. (Class IIa).

A multi-national Consensus Statement on DFT Testing was shown below (Table 2).

Right Pectoral Implantation

Right side implantation should be considered in left-handed patients or other special circumstances such as violinists or hunters using the left shoulder. Patients with special anatomy such as persistent left superior vena cava, venous occlusion, and history of left-sided breast cancer (may need radiation therapy) are also candidates for right side ICD implantation. Arguably, in right pectoral devices with

Table 2 Intraprocedural testing of defibrillation efficacy recommendations class of recommendation {Wilkoff, 2016#5624}

1. Defibrillation efficacy testing is recommended in patients undergoing a subcutaneous ICD implantation (Class I recommendation)
2. It is reasonable to omit defibrillation efficacy testing in patients undergoing initial left pectoral transvenous ICD implantation procedures where appropriate sensing, pacing, and impedance values are obtained with fluoroscopically well-positioned RV leads (Class IIa recommendation)
3. Defibrillation efficacy testing is reasonable in patients undergoing a right pectoral transvenous ICD implantation or ICD pulse generator changes (Class IIa recommendation)
4. Defibrillation efficacy testing at the time of implantation of a transvenous ICD should not be performed on patients with a documented non-chronic cardiac thrombus, atrial fibrillation or atrial flutter without adequate systemic anticoagulation, critical aortic stenosis, unstable CAD, recent stroke or TIA, hemodynamic instability, or other known morbidities associated with poor outcomes (Class III–Harm)

a less favourable right ventricular coil-to-can configuration, an SVC coil may be used to decrease DFT. In fact, the right side implantation is reported to have high DFT compared with left side implantation. As we discussed already, DFT testing may be considered at the end of the case and if high DFT is confirmed, additional defibrillation coil in the azygous vein may be useful.

Complications

Although the definition of complications is not consistent among studies, complication risks after ICD implantation have been reported to be 3–9% (Table 3) [14–16]. These data were abstracted from the National Cardiovascular Data Registry (NCDR). However, a study suggested that there should be significant underreporting of complications in these registry data. In fact, most data from a randomized controlled study or other registry showed higher complication rate. Perioperative mortality with transvenous ICD implantation is rare and peri-procedural mortality has been reported to be from 0. to 0.4%. Cardiac perforation is a rare complication but can cause fatal consequences. According to the study based on the NCDR registry, the occurrence of cardiac perforation was reported as 0.14%. After multivariable adjustment, older age, female sex, left bundle branch block, worsened heart failure class, higher left ventricular ejection fraction, and non–single-chamber ICD implant was associated with a greater odd of perforation. Another study from the NCDR showed the occurrence of complications within 90 days of ICD implantation was associated with an increased risk of all-cause mortality and all-cause mortality or hospitalization at 1 and 3 years [17] (Fig. 12). Using the NCDR ICD registry, the following risk score model was also reported (Table 4) [18].

Table 3 The occurrence of most common complication, by ICD type

Type of complication	Occurrence			
	Overall	Single chamber	Dual chamber	CRT-D
All complications	3.08%	1.88%	2.89%	4.13–4.47%
Lead dislodgement	1.02%	0.47%	0.90%	1.53%
Hematoma	0.86%	0.58%	0.77%	0.68–1.15%
Pneumothorax	0.44%	0.34%	0.46%	0.49–1.05%
Cardiac perforation	0.14%	Not available	Not available	Not available
Cardiac arrest/death	0.29%	0.23%	0.29%	0.34–0.66%
Circulation. 2012 125(1):57–64, Circ Cardiovasc Qual Outcomes. 2013; 6(5):582–90				

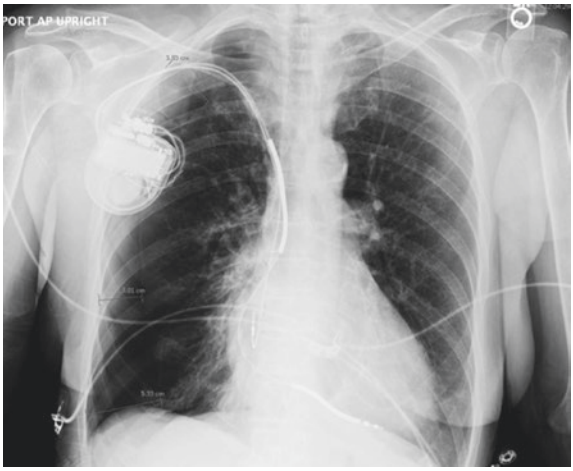

Fig. 12 Large pneumothorax after right side ICD implantation

Follow up After Implantation

After ICD implantation, we do a wound check in 1–2 weeks after the initial implantation. If patients are stable, we schedule 3 months follow up thereafter. These follow up may be in person or remote. Please refer the chapter on remote monitoring. However, we schedule in-person follow up at least once a year. If there is any concern (i.e. unstable parameters of the device, device nearing end of the battery), we would see those patients more frequently.

When a patient receives one or multiple ICD shocks, those episodes should be reviewed in person or remotely. Patients who receive a single ICD shock associated with any symptom including loss of consciousness, dizziness, chest pain, and shortness of breath should be evaluated as soon as possible. In most cases, these patients need certain interventions to prevent subsequent ICD therapy.

Table 4 The risk score model based on the NCDR ICD registry

Risk factors	Risk score
Age ≥ 70	1
Female sex	2
Atrial fibrillation or flutter	1
Previous valvular surgery	3
Previous ICD–Reimplantation for reason other than end of battery life	6
Chronic lung disease	2
BUN level > 30	2
ICD type: dual chamber	2
ICD type: biventricular	4
NYHA class III	1
NYHA class IV	3
Admission not for ICD implantation	3
The risk of any in-hospital complication increased from 0.6% among patients with a score of ≤ 5 (8.4% of the population) to 8.4% among patients with ≥ 19 risk points (3.9% of the population).	
Circulation. 2011;123:2069–2076	

Patients who receive a single ICD shock without any symptoms can be followed at the device clinic within 1–2 days. Inappropriate ICD shocks are common and associated with a high risk of all-cause mortality. Therefore every effort should be made to avoid inappropriate ICD shocks. Multiple appropriate ICD shocks can be induced by electrolyte abnormality, worsening heart failure exacerbation, and worsening coronary ischemia. These patients will need urgent evaluation and underlying causes should be addressed.

Case Conclusion

When she was brought to the ER, she was hypotensive and required hemodynamic support with inotropes. A CT chest showed 1.5 cm pericardial effusion. An echocardiogram also revealed moderate pericardial effusion (Fig. 13). She was admitted to the hospital for urgent lead removal and pericardiocentesis. Fatal complications can happen even in a simple ICD implantation procedure. Implanting physicians should make every effort to reduce the risk of all complications.

Future Directions

- New subcutaneous ICD technologies, such as the Boston Scientific SubQ ICD and extravascular ICD String, continue to be improved and developed to avoid the complications and device malfunction that may be associated with intravascular and intracardiac ICD implantation.

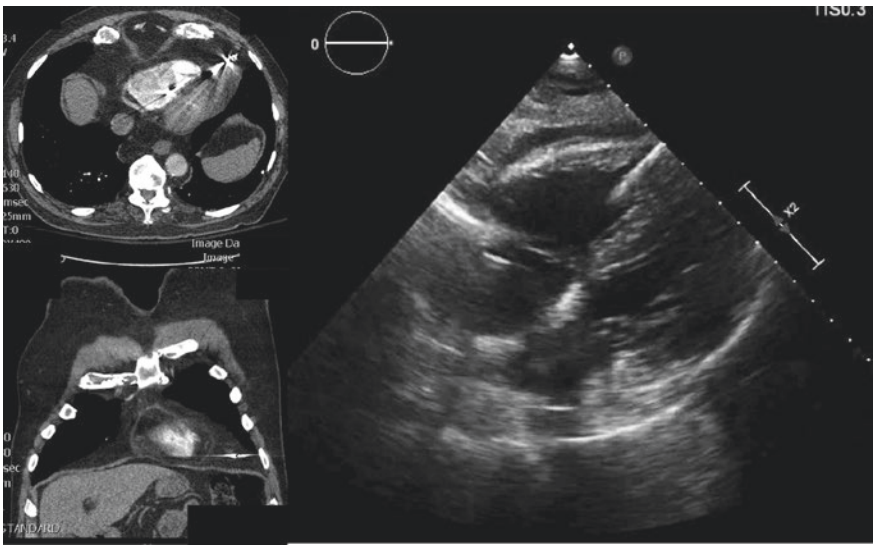

Fig. 13 A moderate size pericardial effusion observed in the CT and echocardiography

- Improved battery technologies, including rechargeable inductive battery technologies, are under development.

Key Points

1. In most patients, interruption of anticoagulation (either warfarin or DOACs) would not be necessary for the ICD implantation. However, the risk and the benefit of interruption of anticoagulants should be assessed according to each patients' risk.
2. Bridging with low molecular weight heparin (LMWH) or unfractionated heparin should be avoided due to the higher chance of hematoma formation.
3. Subclavian puncture under ultrasound guidance is the preferred approach to avoid pneumothorax and contrast usage, especially patients with chronic kidney disease.
4. Subclavian venous occlusion is relatively common following cardiac device implants. Contrast venography before the procedure may be useful to make a detailed plan.
5. For patients undergoing initial left pectoral transvenous ICD implantation, it is reasonable to omit DFT testing when appropriate sensing, pacing, and impedance values are obtained with fluoroscopically well-positioned RV leads.
6. In general, the risk of ICD complications is small. However, lethal complications can occur and implanting physicians should know the risk factors for those complications.

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Implantable Cardioverter Defibrillator Programming and Troubleshooting

Chin Lee, Kunal Shah, Sanjay Shah, and Farshad Raissi

Clinical Case

A 60 year old patient with history of syncope, non-ischemic cardiomyopathy and frequent premature ventricular contractions (PVCs) and nonsustained ventricular tachycardia on Holter monitoring and recently implanted primary prevention implantable cardioverter-defibrillator (ICD) presented with 3 ICD shocks. Figure 1 showed the electrogram (EGM) during two of the shock events. The cardiology service was consulted for management of ventricular tachycardia and possible PVC ablation.

When managing a patient with ICD shock, one must first carefully examine the ICD EGMs. This is essential and can help one determine if the shock is appropriately administered due to true ventricular arrhythmia. In addition, the patient's evaluation should encompass obtaining careful clinical history, physical exam, remote device telemetry data and other cardiac imaging and electrocardiographic recordings.

C. Lee · K. Shah · F. Raissi (✉)
University of California San Diego, 9452 Medical Center Dr, 3rd Floor Rm 3E-507, La Jolla, CA 92037, USA
e-mail: fraissi@health.ucsd.edu

S. Shah
University of Arkansas Veterans Administration Healthcare System, Fayetteville, AR 72701, USA

U. Birgersdotter-Green and E. Adler (eds.), *Case-Based Device Therapy for Heart Failure*, https://doi.org/10.1007/978-3-030-70038-6_12

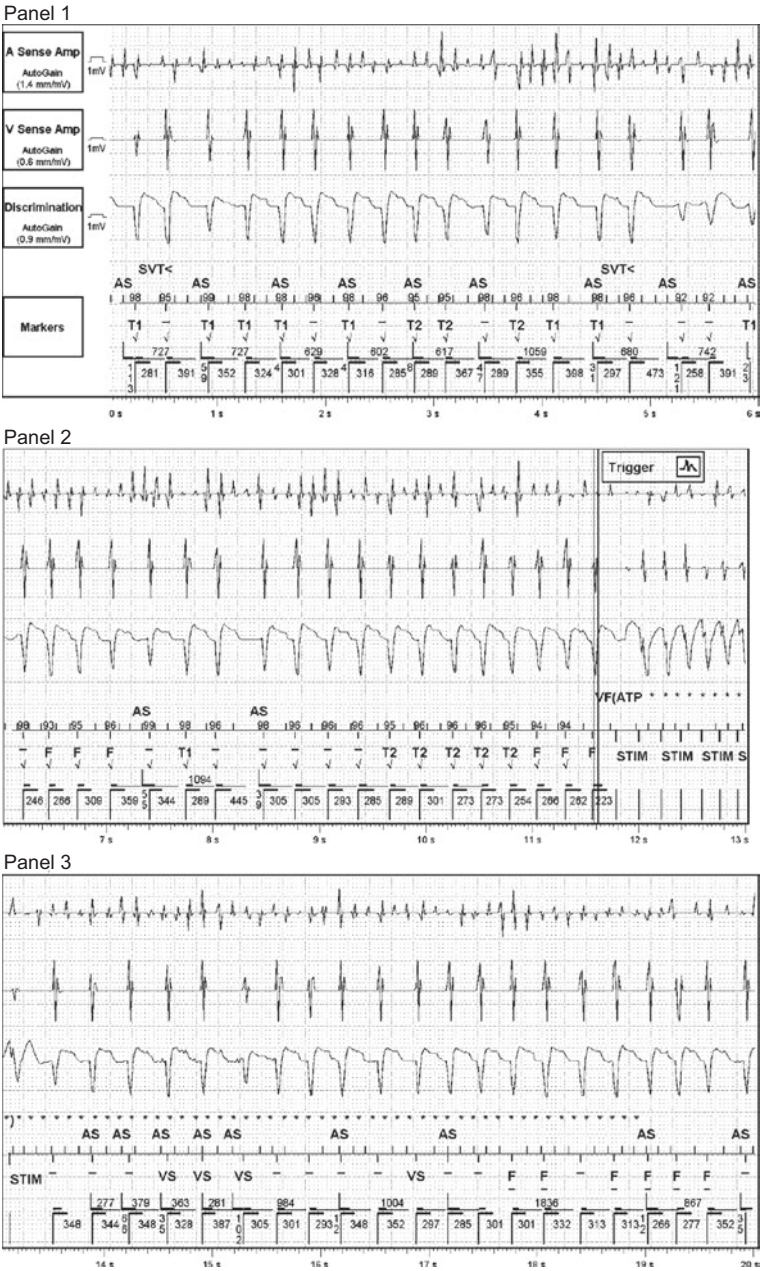

Fig. 1 Panel 1–5

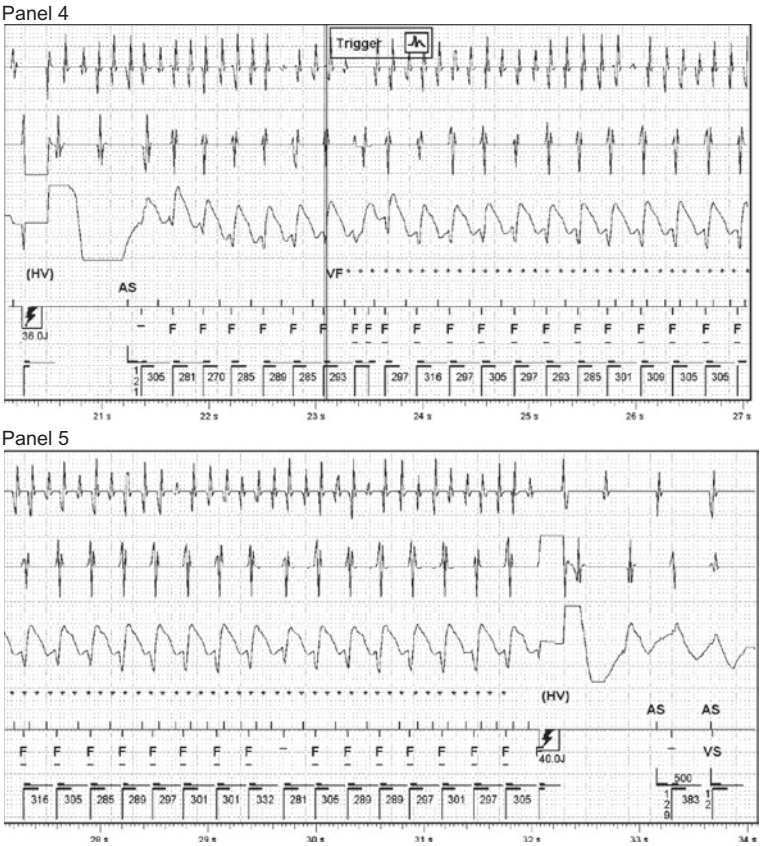

Fig. 1 (continued)

Basic Programming of the Pacemaker Function for Defibrillator

The principles of pacing for bradycardia or atrioventricular (AV) block carry over to the realm of defibrillators. All modern ICDs have the full suite of pacing capabilities that allows maintenance of AV synchrony if have dual chamber leads (both right atrial and right ventricular lead) implanted, or provide just back up pacing if have single right ventricular (RV) lead. When possible, the reduction of RV pacing is beneficial to reduce adverse remodeling, dyssynchrony and improve clinical outcomes [1].

ICD Shocks and Inappropriate Shocks

ICDs improve patients' survival with timely and effective delivery of high-voltage discharge for arrhythmias which can potentially result in sudden cardiac death. These arrhythmias include incessant or repetitive ventricular tachycardia (VT) or ventricular fibrillation (VF). ICD shocks for reasons other than these fatal ventricular arrhythmias are deemed inappropriate. These etiologies include supraventricular tachycardias (atrial fibrillation, atrial flutter or sinus tachycardia), T-wave or P-wave oversensing, electrical noise and electromagnetic interferences (see below for details).

Approximately 10–20% of patients with ICDs may experience inappropriate ICD shocks [2–4]. Inappropriate shocks can result in several issues, such as increased mortality, increased hospitalizations, and long-lasting fear and trauma from ICD treatments.

Defibrillator Anti-tachycardia Detection and Therapy Setting

All ICDs rely on detection criteria to determine if therapy will be administered. The arrhythmia must exceed the heart rate and duration (expressed as number of beats or time intervals in seconds) criteria to trigger anti-tachycardia therapy, which includes, anti-tachycardia pacing (ATP) and defibrillation. The goal of programming is to minimize unnecessary therapy and shocks by allowing non-sustained arrhythmias to terminate spontaneously, while not compromise patient safety. In PREPARE and MADIT-RIT trials (Table 1), programming strategies to prolong arrhythmia detection time and to deliver therapy at higher rates have shown to reduce shocks and are associated with lower all-cause mortality [5–7]. In the most recent 2019 h focused update on optimal ICD programming and testing guideline (Table 1), similar strategies have been recommended for device programming [8].

ICD Criteria to Minimize Inappropriate Shocks

One of the common causes of inappropriate shocks is supraventricular tachycardia (SVT) with rapid ventricular response triggering the rate and duration criteria for therapy. Dual chamber systems can significantly minimize inappropriate shocks [9]. There are different SVT discriminators employed by ICDs to differentiate SVT from VT:

Table 1 Summarize the detection, therapy, and SVT discriminator setting recommended by the 2019 focused update to the 2015 expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing

Detection	Abbott	Biotronik	Boston Scientific		Medtronic	MADIT-RIT		PREPARE
No VT History	VF: 30 intervals, 240 or 250 BPM VT2: 30 intervals, 187 BPM VT: Monitor zone	VF: 30 of 40 intervals, 231 BPM VT2: 30 intervals, 188 BPM VT1: Monitor zone	*Delayed Therapy Option:* VF: 8 of 10 intervals plus 5-seconds duration, 250 BPM VT: 8 of 10 intervals plus 12-seconds duration, 185 BPM VT1: Monitor zone	*High-Rate Therapy Option:* VF: 8 of 10 intervals plus 2.5-seconds duration, 200 BPM VT1: Monitor zone	VF: 30 of 40 intervals, 188 BPM** FVT: Off VT: Off VT Monitor: User discretion	Delayed Therapy Option: VF: 2.5-second monitoring, 250 BPM VT: 12-second monitirng, 200 BPM VT1: 60-second monitoring, 170 BPM	High-Rate Therapy Option: VF: 2.5-seconds monitoring duration, 200 BPM VT1: Monitor zone	VF: 30 of 40 beats, 250 BPM FVT: 30 of 40 beats, 182 BPM VT: Monitor zone
VT cycle length is known	VF: 30 intervals, 240 or 250 BPM VT2: 30 intervals, 187 BPM, or 10-20 BPM less than VT rate VT: Therapy at 10-20 bpm less than VT rate or monitor zone	VF: 24 of 30 intervals, 231 BPM VT2: 30 intervals, 188 BPM, or 10-20 BPM less than VT rate VT1: Therapy at 10-20 BPM less than VT rate	VF: 5-seconds duration, 250 BPM VT: 12-seconds duration, 185 BPM, or 10-20 BPM less than VT rate VT1: Monitor zone, or therapy at >=12-second duration, 10-20 BPM less than VT rate		VF: 30 of 40 intervals, 188 BPM FVT: Off VT: 24 intervals, 10-20 BPM less than VT rate VT Monitor: User discretion			
					**Consider MADIT-RIT detection setting (delayed therapy or high-rate therapy option).			

Therapy	Abbott	Biotronik	Boston Scientific	Medtronic	MADIT-RIT	PREPARE
	VF: ATP while charging, 8 pulses at 85% of VT cycle length (15% faster than the VT). 1st shock 4-6 J below max output; all other shocks at max output. VT2: ATP >=1 burst with 8 pulses at 85% of VT cycle length. All shocks at max output like VF zone. VT: Favor more ATP than VT2 zone	VF: ATP 1x burst of 8 pulses at 88% of VT cycle length. Max output shocks. VT2: TP >=1 burst with 8 pulses at 88% of VT cycle length. All shocks at max output like VF zone. VT1: Monitor zone or therapy as VT2 but favors more ATP.	VF: QuickConvert ON to 300 BPM (if available). All shocks at max output. VT: ATP with >=1 bursts, 8 pulses at 84% of VT cycle length. All shocks at max output. VT1: therapy as VT but favors more ATP.	VF: ATP before charging; Max output shocks. VT: ATP with >=1 bursts, 8 pulses at 88% of VT cycle length. All shocks at max output.	VF: QuickConvert ON. ATP and All shocks at max output. VT: ATP with all shocks at max output. VT1: therapy as VT but favors more ATP.	VF: All shocks at max output FVT: ATP with 1 burst, 8 pulses at 88% of VT cycle length. All shocks at max output. VT: Monitor zone

SVT Discriminators	Abbott	Biotronik	Boston Scientific	Medtronic	MADIT-RIT	PREPARE
Single Chamber ICD	Far-field morphology: ON, 90%, 3 of 10 intervals All others: Passive	MorphMatch: ON * Onset: OFF Stability: OFF Sustained VT Timer: OFF	Rhythm ID (morphology and timing): ON	Wavelet (morphology): ON Limit: 260 ms(230 bpm) Stability: OFF Onset: OFF	Rhythm ID: ON	Morphology: ON Consider other SVT discriminators
Dual Chamber ICD/CRT-D	Far-field morphology: ON, 90%, 3 of 10 intervals Arrythmia Onset: On Interval Stability: On SVT Upper Limit: 230 bpm SVT Discrimination Timeout: OFF VT Therapy Timeout: OFF CRT: Template Auto Update 30 days and Template pacing hysteresis ON	SMART: ON (default settings or adapted to known VT)	ICD: Rhythm ID (morphology and timing): ON CRT-D: Onset/Stability: ON or RhythmID: ON Sustained Rate Duration: OFF SVT Discrimination available only up to 230 bpm	PR Logic: ON (after lead stable for 3 months) Wavelet (morphology): ON Limit: 260 ms(230 bpm) Stability: OFF Onset: OFF		Morphology: ON Consider other SVT discriminators
		* If Narrow QRS and sufficient far field amplitude, if not then Onset: 20% and Stability: 48 ms				

Adoped from Stiles et al. 2019 HRS/EHRA/APHRS/LAHRS focused update to 2015 expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. J Arrhythm. 2019 May 14;35(3):485-493.

PREPARE Trial: J Am Coll Cardiol. 2008 Aug 12;52(7):541-50.

MADIT-RIT: N Engl J Med. 2012 Dec 13;367(24):2275-83.

– **AV dissociation (only available in dual chamber systems, or Biotronik DX system with atrial sensing in a single RV lead ICD)**—this discriminator compares the A:V relationship during tachycardia, and common SVT such as atrial fibrillation (AF) or atrial flutter (AFL) often have A>V. AV dissociation is not a fault-proof algorithm. In VT with 1:1 retrograde conduction (A=V), or in "dual tachycardia" where SVT such as atrial fibrillation can occur simultaneously with VT leading to difficulty classifying the arrhythmia. It has been estimated that over half of all ICD patients may develop atrial fibrillations, and therefore, it is always important to review the interrogation tracing for SVT as a cause of inappropriate shocks [10].
– **Morphology**—ventricular EGM is templated during sinus rhythm and often automatically updated. The morphology template is used for comparison during tachycardia. During ventricular arrhythmia, the ventricular EGM will be different from the template in sinus rhythm, and help categorize the tachycardia as ventricular arrhythmia. Some of the challenges to morphology discriminator are conditions that can alter baseline ventricular EGM morphology. For instance, SVT with aberrancy, distortion from myopotentials [11], and errors in EGM alignment [12], are all conditions that would alter the ventricular EGM morphology.
– **Interval Stability**—monitor for irregularity during tachycardia to differentiate SVT such as atrial fibrillation (common coexisting arrhythmia and cause of inappropriate shock) from ventricular arrhythmia.
– **Onset**—physiologic sinus tachycardia would have gradual onset in rate as patient increases exertion level as compared to ventricular arrhythmia with sudden onset in tachycardia.

Management of ICD Shocks

When ICD shock occurs, one must determine if the therapy is appropriate by determining if a true VT has occurred. ICD will deliver anti-tachycardia therapy for any arrhythmia that meet the detection criteria. The most common cause of inappropriate shocks is SVT. Thus, the first step for caring for a patient with ICD shock is to determine whether a true VT had occurred.

The following algorithm (Fig. 2) provides a basic framework for analyzing stored EGM in both single and dual chamber ICD [13]. In dual chamber device, by analyzing the atrial and ventricular relationship provider can often determine if an event was due to VT. When analyzing the EGM, if the ventricular rate is greater than the atrial rate (V>A), it is most likely VT. If the atrial rate is greater than the ventricular rate (A>V), then it is likely SVT. However, one should also consider dual tachycardia. For VT, the EGM should show a tachycardia event in the VT zone with a stable V-V interval with no relation to the atrial EGM (AV dissociation) [14]. An exception to AV dissociation rule is when patients maintained 1:1 V to A conduction during VT, which can occur in up to 26% of patient [15]. In situations where the atrial rate and ventricular rate are approximately equal, clues

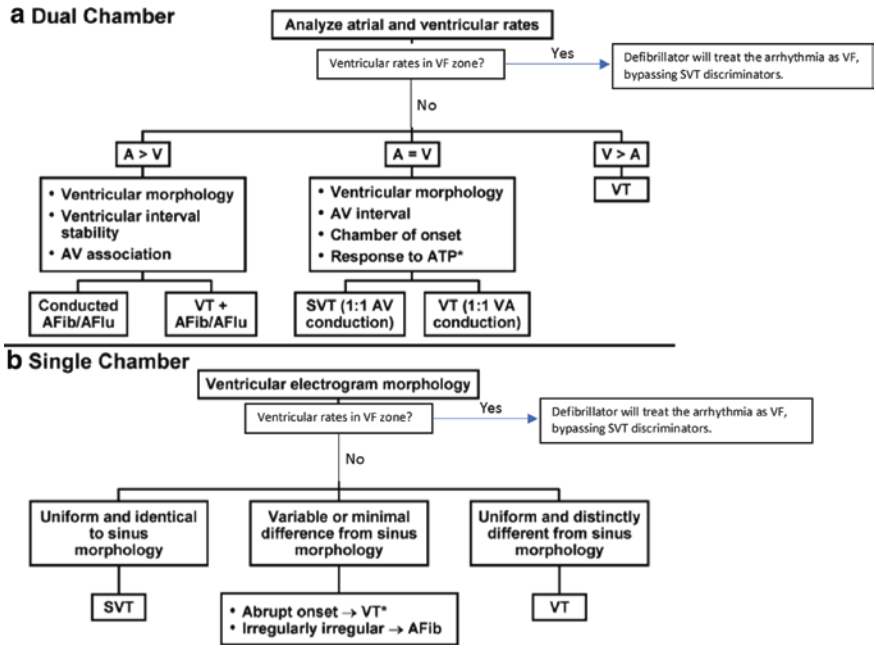

Fig. 2 Basic algorithm for analyzing ICD shocks. (Modified from Swerdlow et al. PACE 2005;28:1322–1346)

suggesting SVT include a stable V-V interval, a stable A-A interval, and a stable A-V interval. In situations where VT with 1:1 retrograde conduction occur, one can analyze the EGM to assess if changes in the V-V interval drives changes in the A-A interval, or vice versa [16]. In single chamber device, determining SVT from VT is more difficult because only ventricular events are stored and must rely on the SVT discriminators (morphology, interval stability, and sudden onset) previously discussed (Fig. 2).

Any arrhythmia which meets the VF zone heart rate and duration criteria will be labeled as VF and SVT discriminators are bypassed to minimize delay in therapy given the hemodynamic compromise during VF, or other rapid tachyarrhythmia.

Common Causes of Inappropriate ICD Shocks

Majority of inappropriate shocks are due to atrial arrhythmias meeting ventricular tachyarrhythmia zone therapy criteria. Although less common, the device may also be oversensing intracardiac/extracardiac signals, such as noise from lead failure, diaphragmatic myopotential (seen in unipolar sensing), or T-wave oversensing. The following table reviews the common causes of inappropriate shocks.

Arrhythmias	
Atrial arrhythmias (e.g. atrial fibrillation, atrial flutter, atrial tachycardia, other SVTs)	1. Consider increasing medical therapy for rate control (e.g. beta blocker, calcium channel blocker) 2. In patient with atrial fibrillation or atrial flutter, consider rhythm control strategy (e.g. EP study and ablation) or AV node ablation, if unable to control the ventricular rate 3. Consider increasing the VT zone rates and/or programming a prolonged delay in therapy
Sinus tachycardia	1. Enable and optimize SVT discrimination (re-template ventricular morphology, gradual onset in heart rate with sinus tachycardia) 2. Check the VT detection rate, which may be set too low
Oversensing Intracardiac Signals	
Noise from lead failure (insulation break, lead fracture, loose set screws, header-connection problem)	1. Erratic noise or artifacts on EGM. Typically, there is a high frequency signal on the ventricular channel with no relation to the cardiac cycle leading to inappropriate classification of the non-physiologic short V-V interval noise as a ventricular arrhythmia 2. Common to see abrupt changes in lead impedance (high impedance with fracture; low impedance with insulation break) 3. Pacing with failure to capture 4. Can manually manipulate the pocket during device interrogation to see if this high frequency signal is reproduced 5. Obtain 2 view chest x-ray to check for lead fracture 6. Disable anti-tachycardia therapy. Consider wearable defibrillator (e.g. LifeVest) while waiting for lead revision if patient is high-risk for ventricular arrhythmia 7. Consider lead extraction and/or revision
T-wave oversensing	1. T-wave oversensing is caused by relative large T wave to R wave amplitude, resulting in double counting of each beat (counting QRS and T as two separate beats) and may lead to ICD falsely classifying a sinus rhythm or SVT as ventricular arrhythmia 2. Update template of ventricular EGM 3. Use different ventricular sensing vectors to get larger R waves allowing for elimination of T-wave oversensing 4. If the R/T ratio is large (R wave amplitude is larger than T wave), can use programming to minimize T wave oversensing using manufacturer oversensing attenuation algorithm including morphology discriminators, T-wave blank period, and high-pass filtering 5. Program to lower the sensitivity could be attempted. Avoid extreme adjustments (>0.6 mV) because could lead to under detection of true ventricular tachyarrhythmias 6. If above fail, consider reposition of the ICD lead

Arrhythmias	
P-wave oversensing (oversensing far-field atrial signal)	1. P-wave oversensing is a rare cause of inappropriate shocks. Oversensing of the P waves as R waves due to far-field signal can lead to inappropriate ventricular tachyarrhythmia detection and therapy. This often occurs when the patient is in atrial tachyarrhythmias (e.g. atrial fibrillation or flutter) [13] 2. It has been described in placement of RV lead in the coronary sinus [17], and in integrated bipolar ICD lead with the ventricular coil (sensing coil) at close proximity to the tricuspid valve annulus due to dislodgement [18] 3. Obtain 2 view PA-lateral chest x-ray to check for ICD lead position. 4. If the ICD lead did not appear to have been dislodged or misplaced in the coronary sinus, can try to program to reduce ventricular sensitivity. If with reduced ventricular sensitivity and the device cannot reliably detect ventricular arrhythmia, then should plan for ICD lead revision [13] 5. In cases with lead misplacement to coronary sinus or lead dislodgement, plan for ICD lead revision
Oversensing Extracardiac Signal	
Myopotential (skeletal muscle or diaphragmatic oversensing)	1. Often seen when using unipolar sensing on the RV lead, which is sometimes employed if has low R wave sensing with bipolar configuration. Myopotentials have high frequency pattern on EGM and may be misinterpreted as ventricular arrhythmias 2. If suspect diaphragmatic oversensing, may try to reproduce the phenomena by exaggerating diaphragmatic motion including deep inspiration, harsh coughing, or Valsalva maneuver 3. If suspect skeletal muscle oversensing, reproduce with isometric exercises of the upper extremities and torso [19] 4. Change the sensing vector and employ bipolar sensing to prevent oversensing (assuming have adequate R wave sensing in bipolar mode)
Electromagnetic interference (e.g. welding)	1. Avoid source of electromagnetic interference 2. If patient is unable to avoid the EMI (e.g. career welder), take precaution to limit EMI by using lower welding current (160 Amps) or nonelectric welding. Maintain a distance from the welding machine for more than 2 feet from the device pocket, attach the ground clamp to the metal as near as possible to the point of welding, and allow at least 5 to 10 s between welding bursts. Nonconductive gloves should be worn by the operator [20]

Subcutaneous ICD

Subcutaneous ICD (S-ICD) behaves similarly as a single lead transvenous ICD and have arrhythmia discriminators employed to minimize inappropriate shock (for more details see Chap. 13). S-ICD relies on template morphology during sinus rhythm to compare with during tachyarrhythmia. S-ICD also has a heart rate zone and duration criteria to satisfy prior to categorizing an arrhythmia as ventricular tachyarrhythmia. Gold et al. have shown that "dual zone programming" utilizing the arrhythmia discriminators can reduce inappropriate shock rate from 12 to 6.4% [21]. More so than transvenous system, S-ICDs have a high rate of inappropriate shocks (73% of cases) due to T-wave oversensing [22]. Pre-implant screening involves identifying candidates with appropriate QRS to T wave ratio in supine and upright positions on selectable vectors. Despite screening, T-wave morphology may change with exercise or changes in position that lead to T-wave oversensing (double-counting T waves as QRS).

Evaluation for T-wave oversensing involve trying different vectors to try to maximize R/T wave ratio. Treadmill exercise evaluation is also reasonable especially if prior inappropriate shocks occur during exercise given how T wave morphology can change with exertion. If reprogramming fail, then may need to consider revise the position of the S-ICD lead and/or generator for better R-wave detection relative to T-wave. Alternatively, changing to a transvenous ICD system can also be considered [20].

Case Conclusion

The patient's device interrogation revealed new-onset atrial fibrillation with rapid ventricular response. Careful examination of ICD EGMs showed that the ventricular arrhythmia was first labeled an SVT by the device (Fig. 1, panel 1). However, as the ventricular rate was accelerated after delivery of ATPs, it is labeled as VF as it met the VF zone heart rate and duration criteria, and hence committing the device to treat it as VF. When this occurred, SVT discriminators were bypassed and shocks were administered (Fig. 1, Panels 2–4). The first ICD discharge did not resolve the tachycardia. However, the second ICD discharge temporarily terminated atrial fibrillation and rapid ventricular response (Fig. 1, Panel 5).

Patient was admitted for management of new-onset atrial fibrillation with rapid ventricular response, acute heart failure exacerbation, and inappropriate shocks. After diuresis and management of his heart failure, he was converted back into sinus rhythm with IV amiodarone and started on antiarrhythmic drug and beta blocker for aggressive rhythm management and rate control. His ICD settings were also reprogrammed for higher VF zone detection rate and updated ventricular morphology templates.

Key Points

- The common cause of inappropriate shocks is SVT with rapid ventricular response.
- Any arrhythmia which results in rapid ventricular rate meeting the VF zone heart rate and duration criteria will be labeled as VF and SVT discriminators are bypassed to minimize delay in therapy.
- ICD out-of-box nominal settings are often conservative with the heart rate criteria and can lead to inappropriate shocks. Results from MADIT-RIT trial have shown that programming strategies to prolonged arrhythmia detection time and delivery therapy at higher heart rates have shown to reduce shocks without compromising safety, and are associated with lower all-cause mortality.
- Inappropriate shocks can be mostly managed with addition of medical therapy, reprogramming ICD settings, and on occasions catheter-based ablative treatment of SVTs.
- Infrequently, lead extraction and/or revision are required to resolve inappropriate shocks.

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Use of the Subcutaneous Implantable Cardioverter Defibrillator in Patients with Heart Failure

Paul S. Bibby, Walid Barake, and Siva K. Mulpuru

Case Vignette

A seventy-two-year-old male with a history of dilated cardiomyopathy, paroxysmal atrial fibrillation, with previous atrial fibrillation and ventricular tachycardia ablations presents to the clinic with complaints of subcutaneous implantable cardioverter-defibrillator (S-ICD) shocks. Interrogation of the device shows a normally functioning defibrillator (SQ-RX 1010, Boston Scientific, Natick, MA) with appropriate stable lead impedance status. The device is currently programmed in the secondary sensing configuration (Fig. 1). Conditional shock zone was programmed to start at 190 beats per minute (bpm), and shock zone was programmed at 220 bpm. The device interrogation reveals one treated episode since the last follow-up. The presenting electrogram shows a regular sensed rhythm at 70 beats per minute with intermittent PVC's (Fig. 2). Upon review of the shock episode, it appears that the patient was shocked due to T-wave oversensing (TWOS), not due to a true ventricular arrhythmia. Some key observations in Fig. 3 include delivery of S-ICD shock; programmed sensing vector, programmed detection zones and the rhythm at the time of the shock appears to be atrial fibrillation around 120 bpm with TWOS leading to double counting of the QRS complexes and inappropriate S-ICD therapy. However, his current rhythm in clinic was regular and most likely sinus rhythm. It is possible the shock from his device cardioverted the patient out of atrial fibrillation and into sinus rhythm.

P. S. Bibby
Heart Rhythm Services, Mayo Clinic, Phoenix, AZ, USA

W. Barake · S. K. Mulpuru (✉)
Heart Rhythm Services, Mayo Clinic, 200, 1st Street SW, Rochester, MN, USA
e-mail: Mulpuru.siva@mayo.edu

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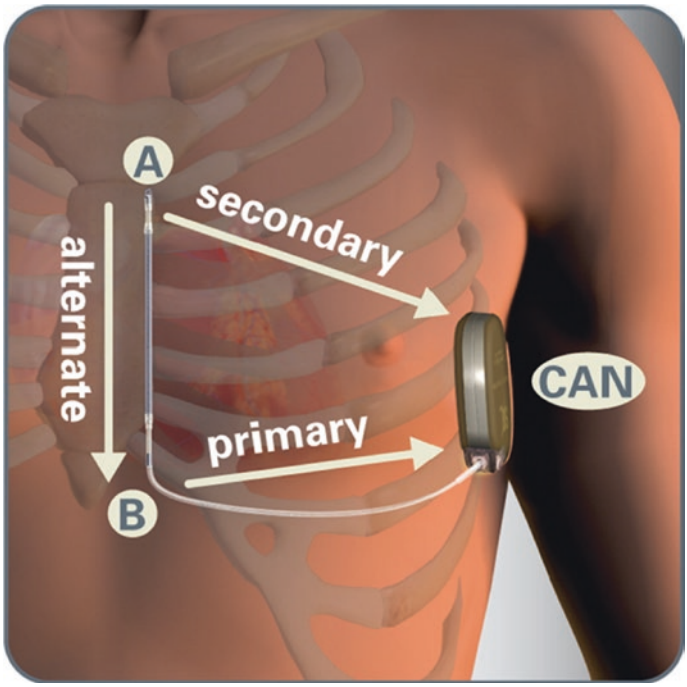


Fig. 1 The can of the SICD system is placed laterally on the chest wall. The lead is tunneled in the subcutaneous plane. There are three sensing vectors, as illustrated in the figure

Introduction to Subcutaneous Implantable Defibrillators

The S-ICD system is a defibrillator that is implanted under the skin and provides an electric shock for the treatment of ventricular tachyarrhythmias. The leads are totally extravascular in the S-ICD system. The advantages of the S-ICD system include minimal risk of vascular damage, thrombosis, tricuspid valve dysfunction, and systemic infection. As the system is totally extravascular the risks associated with removal are minor compared to ones associated with transvenous lead extraction. The system can also be implanted in patients with vascular issues such as occluded veins, hemodialysis sites, or congenital abnormalities. There are certain limitations of the S-ICD system. These include inability to pace for bradyarrhythmias or cardiac resynchronization therapy, inability to deliver anti-tachycardia pacing for tachyarrhythmias and delivery of inappropriate shocks due changes in sensed electrogram.

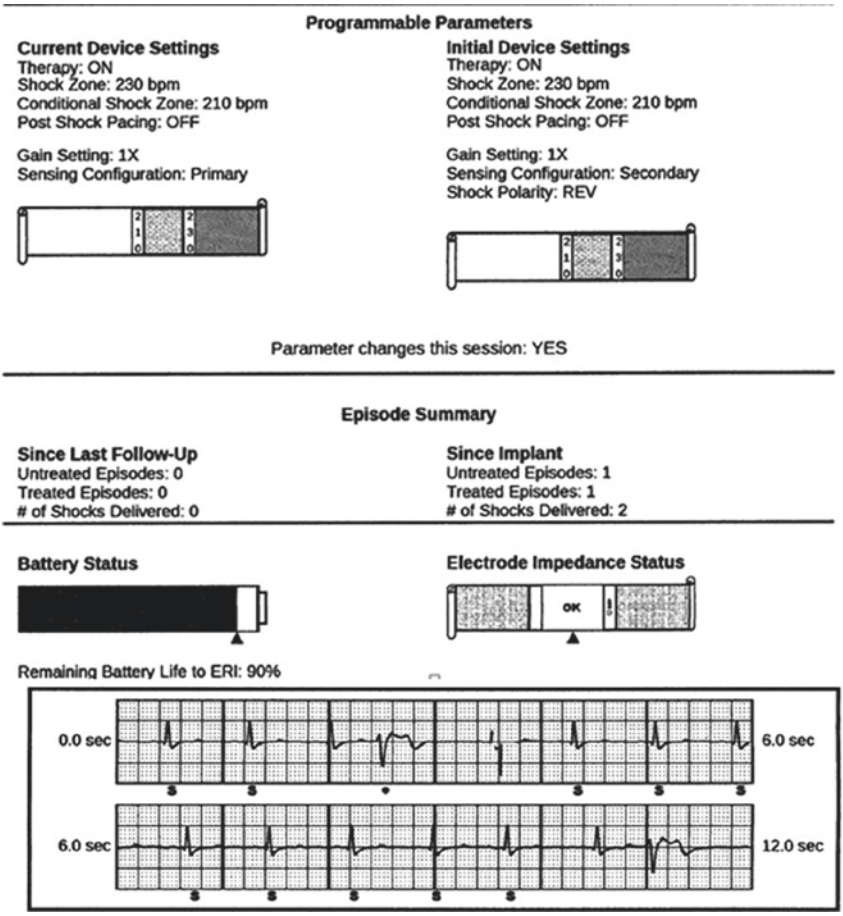


Fig. 2 The top panel shows the programmed setting on the device. The bottom panel shows the episode summary for the shock and the sensed electrograms. There was one treated episode during which two shocks were delivered

Historical Perspective

The first investigational device exemption (IDE) study patient was enrolled in 2010. Cameron Health, Inc., was acquired by Boston Scientific and the SQ-RX 1010 S-ICD device received FDA approval for use in the United States in the year 2012. The current version of S-ICD is approximately twenty percent smaller than the previous SQ-RX 1010 model, and it has better battery longevity, MRI conditional labeling in a 1.5 T environment, home monitoring with Latitude NXT, and an atrial fibrillation detection algorithm.

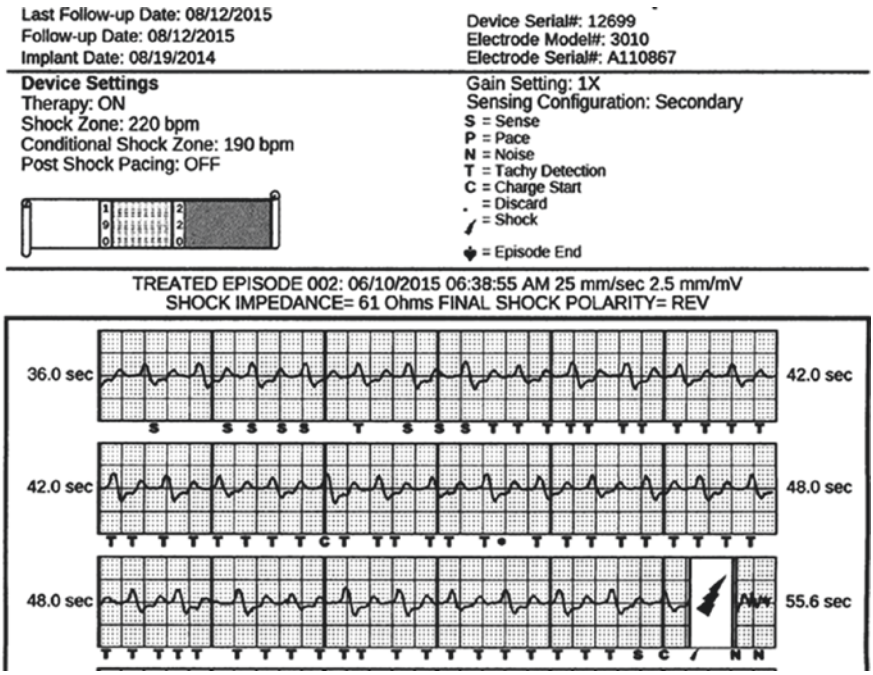


Fig. 3 Electrograms during the episode reveal T wave over sensing and delivery of inappropriate therapy. The panels reveal more markers than QRS complexes

Basic Information

The S-ICD system delivers up to eighty-joule shocks to treat tachyarrhythmias. The newer Boston Scientific Emblem platform devices have atrial fibrillation detection algorithms and can detect overall burden of atrial fibrillation in addition to ventricular arrhythmia burden. The following are the main features of the current generation device.

- The battery can last approximately five to seven years and they can deliver up to one-hundred shocks per device [1].
- It is safe to perform CPR on a patient while these devices are delivering therapies.
- A magnet placed over the device will suspend ICD therapies, and the device will beep while the magnet is placed over the device for the first sixty seconds. The device does have an auditory alert when it reaches its elective replacement indicator, or if detects a prolonged charge time, failed device integrity check, irregular battery depletion, or impedances out of range.
- The current generation of the device MRI conditional; however, the MRI magnet field can render the auditory alert tones inoperable, so the benefits of the MRI scan should be considered vs. the risks of disabling the auditory alert. The

S-ICD device has three different sensing configurations. The device detects arrhythmias based upon an X/Y criterion (typically 18/24 for initial detection of arrhythmia and 14/24 for redetection).

- The S-ICD can deliver post-shock pacing for up to thirty seconds at fifty beats per minute and can store up to forty-five arrhythmia episodes for review.
- Similar to trans-venous implantable cardioverter-defibrillator (TV-ICD), the S-ICD involves a pulse generator (device) and a shocking lead/electrode (Fig. 1). The pulse generator is implanted subcutaneously in the left lateral mid-axillary line. The lead, comprising an 8 cm shocking coil, is tunneled subcutaneously along the left parasternal border [2, 3]. The lead also contains proximal and distal sensing electrodes positioned on each side of the shocking coil.
- The S-ICD delivers up to 80 Joule-shock for defibrillation of ventricular dysrhythmias. For the same arrhythmia episode, the S-ICD delivers up to a maximum of 5 shocks. Following the initial shock, the polarity reverses between the electrodes in subsequent shocks. The device will provide demand pacing at 50 beats per minute (bpm) following defibrillation if ventricular asystole of 3.5 s or more is detected.
- Unlike TV-ICDs that sense using closely spaced electrodes, the S-ICD detects the rhythm using two widely spaced electrodes or one of the sensing electrodes and the generator. Thus, the electrograms generated are morphologically similar to the surface electrocardiograms (ECG) with distinct QRS-T morphology. The pulse generator, acting as an optional sensing electrode, in addition to the sensing electrodes allow for three sensing vectors.
- Upon implantation, the device will automatically recommend the optimal vector to distinguish the QRS complex from the T wave and avoid double counting. The vector can be selected manually, as well. The sensing algorithm of cardiac events encompasses three different phases: 1-Detection phase, 2-Certification phase, and 3-Decision phase [3–5].

Indications and Current Evidence of Subcutaneous Implantable Cardioverter-Defibrillators

Subcutaneous implantable cardioverter-defibrillator (S-ICD) is not the best choice for every patient requiring an ICD (Table 1). Although S-ICDs address the need for vascular access and high infection risk, they have limitations and are contraindicated in some individuals. At large, S-ICD should be avoided in the following scenarios (Fig. 4):

– Anticipated need for bradycardia pacing
– Anticipated need for anti-tachycardia pacing (ATP) /known ventricular tachycardia
– Need for cardiac resynchronization therapy
– Ineligible patients based on pre-implantation surface ECG screening.

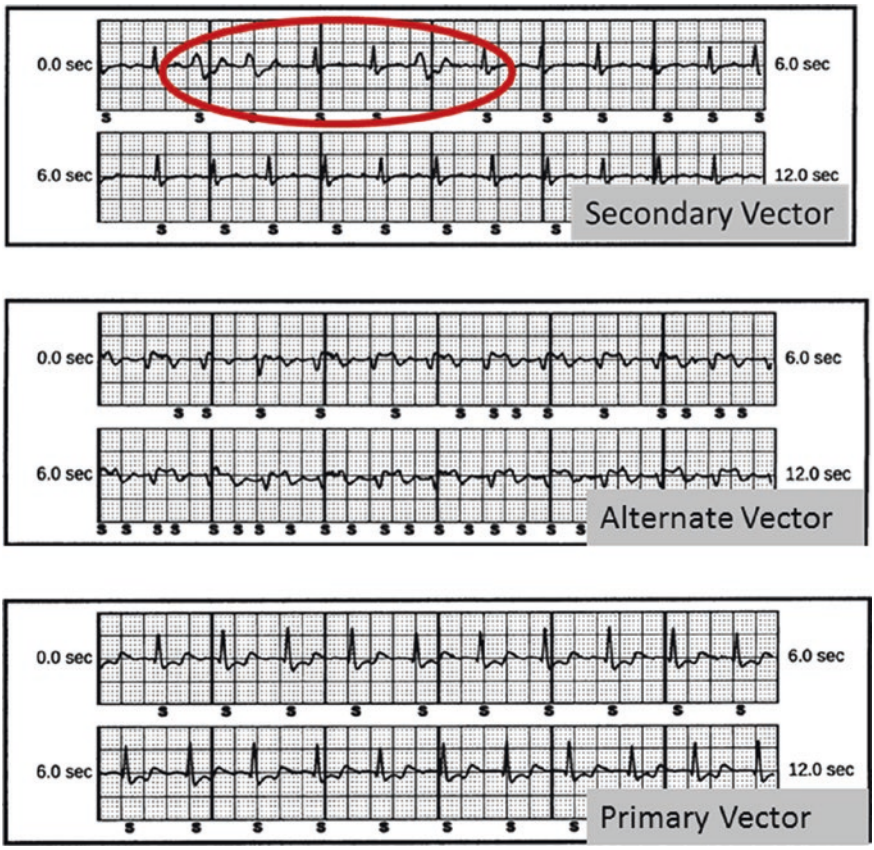


Fig. 4 The top panel reveals intermittent wide-complex beats. LBBB developed during wide exercise (middle strip resulting in persistent wide complex rhythm and T wave oversensing). T wave oversensing was not noted in the primary sensing configuration (bottom panel)

Table 1 Appropriate indications and contraindications for SICD therapy

Appropriate candidate for S-ICD	Inappropriate candidate for S-ICD
Poor venous access	Need for bradycardia pacing
Dialysis patients	Need for cardiac resynchronization
Immunosuppression	Known VT (need for anti-tachycardia pacing)
Prior device system infection	Failed ECG screening
History of lead failure	High risk for inappropriate shocks
Younger patients	
Primary prevention	
History of endocarditis	
Life expectancy >1 year	
Prosthetic valve or chronic vascular catheters	

As per the 2017 AHA/ACC/HRS guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death [6], S-ICDs are to be considered in the following circumstances:

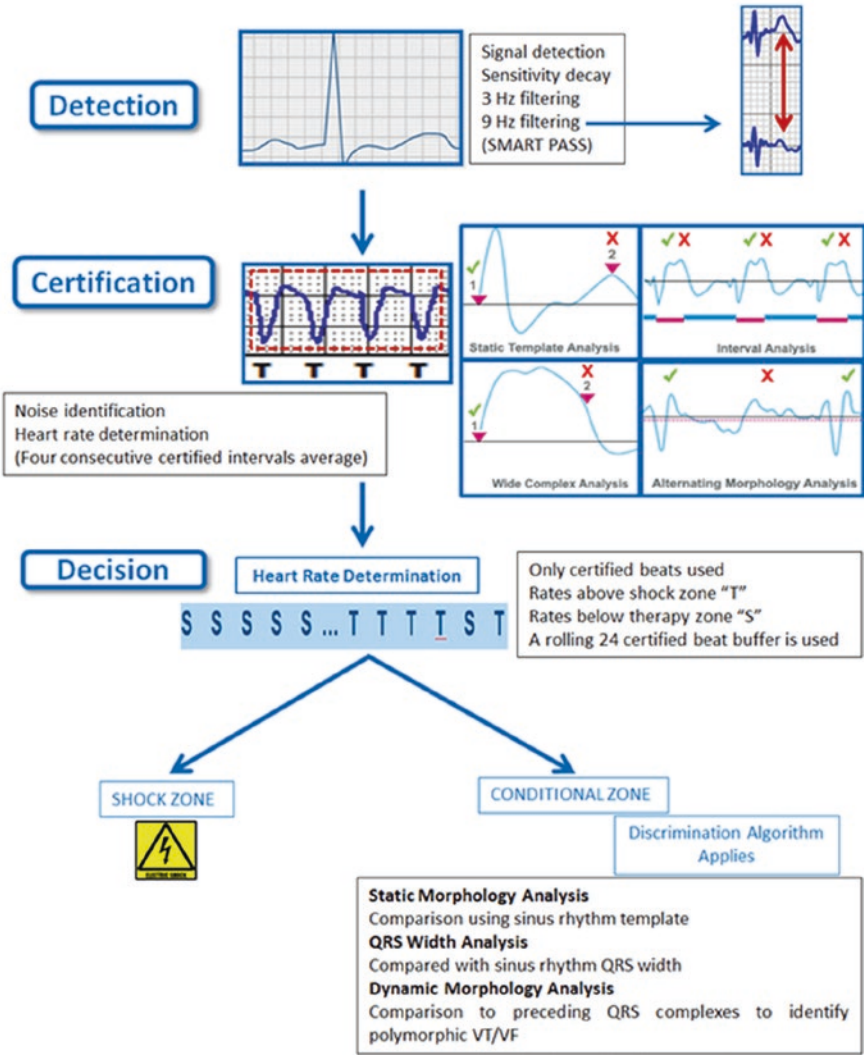
– Young patients with a desire to avoid long term chronic transvenous leads
– Patients with inadequate vascular access
– Individuals are at high risk for infection or have indwelling venous catheters
– Patients in whom pacing for bradycardia, ATP or CRT is neither needed nor anticipated

Several baseline clinical characteristics are useful in the selection of patients suitable for S-ICD implantation. Substantial predictors for the inappropriateness of S-ICD have been identified in retrospective cohorts such as secondary prevention indication, severe heart failure and prolonged QRS duration [7].

In the absence of randomized data to guide the selection of S-ICD over TV-ICD, the S-ICD remains currently a class I recommendation for patients at high risk for infection or without adequate venous access, in the absence of an indication for pacing or ATP as per the 2017 AHA/ACC/HRS guidelines. Several clinical, demographic and procedural characteristics are to be considered when selecting appropriate patients for S-ICD implantation (Table 1).

Screening

A screening ECG tool was developed to assess the appropriateness of S-ICD before device implantation. This tool helps identify patients at risk for inappropriate shocks due to T-wave over-sensing errors (Figs. 5 and 6). It detects patients who have relatively large or late T-waves using all three vectors by simulating the device sensing vectors. This ECG screening tool is completed using the Boston Scientific Latitude Programming System. Three ECG leads are placed on the patient, and the ECG electrode LL should be placed in a lateral location at the fifth intercostal space along the mid-axillary line, representing the intended location of the implanted pulse generator. The ECG electrode LA should be placed one centimeter left lateral of the xiphoid midline to represent the intended location of the proximal sensing electrode. The ECG electrode RA should be placed approximately fourteen centimeters superior to the ECG electrode LA to represent the position of the distal sensing tip of the electrode. It is important to use new surface electrodes to get a clean ECG signal during this testing. The screening should be completed with the patient in a supine position and sitting or standing positions. Some clinics even obtain baseline exercise testing to make sure there are no significant changes to the T-waves during exercise that would lead to inappropriate ICD therapies. It is estimated that up to 15% of patients are ineligible for an S-ICD due to susceptibility to T-wave over-sensing. A scoring system (PRAETORIAN score) was developed as well and is based on clinical and computer modeling determinants that influence the defibrillation threshold (DFT):


Detection
Signal detection
Sensitivity decay
3 Hz filtering
9 Hz filtering
(SMART PASS)
Certification
Static Template Analysis
Interval Analysis
Wide Complex Analysis
Alternating Morphology Analysis
Noise identification
Heart rate determination
(Four consecutive certified intervals average)
Decision
Heart Rate Determination
S S S S S ... T T T T S T
Only certified beats used
Rates above shock zone "T"
Rates below therapy zone "S"
A rolling 24 certified beat buffer is used
SHOCK ZONE
CONDITIONAL ZONE
Discrimination Algorithm Applies
Static Morphology Analysis
Comparison using sinus rhythm template
QRS Width Analysis
Compared with sinus rhythm QRS width
Dynamic Morphology Analysis
Comparison to preceding QRS complexes to identify polymorphic VT/VF

◀ **Fig. 5** The figure illustrates the SICD detection, discrimination and therapy delivery algorithm. The detection phase includes signal filtering with a bandpass and notch filters. The notch filter is programmed based on the time zone selected. A SMART pass filter may be activated during set up. This filter uses a 9-Hz high pass filter to reduce the amplitude of low-frequency signals (such as T waves). This SMART pass filter is only applied for sensing QRS for event rate determination, hence does not affect the QRS morphology. Similar to the sensing process used by the TV-ICDs, the QRS is sensed and predetermined blanking periods followed by sensitivity decays are activated to avoid T-wave over-sensing. The sensitivity decay, however tracks three different patterns - one for slow heart rates, one for the conditional tachycardia zone, and another for the shock zone, with increasing sensitivity to avoid VF under-sensing. The sensing threshold is adapted based on the two preceding QRS complexes amplitude. The device uses a low sensing floor of 0.08 mV and a low high-pass filter of 3 Hz that cannot be changed to ensure VF detection. The certification phase then uses the illustrated algorithms to distinguish QRS components from electromagnetic interference, myopotentials, T waves, and R-wave double counting. Finally, the decision phase is where the rhythm is analyzed using the certified beats for heart rate calculation. If the heart rate falls in the shock zone, defibrillation shock will be delivered. If the rate falls in the conditional zone, discrimination morphology analyses will be applied prior to final shock decision

sub-coil fat, sub-generator fat, and anterior positioning of the device pulse generator, as shown in Fig. 7, taken from Quast et al., Heart Rhythm, 2018.

This score was evaluated and validated in 321 patients using those elements on the postoperative chest radiographs. The score has three groups: 30–<90 points—low risk, 90–<150 points—intermediate risk, and >150 points representing a high

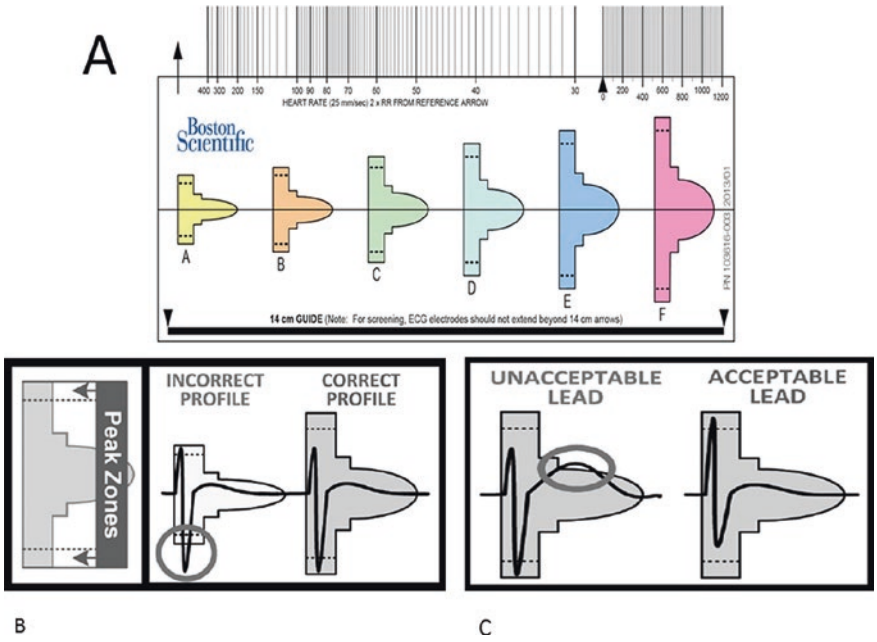


Fig. 6 The automated ECG screening tool for SICD system (reproduced with permission from Boston Scientific)

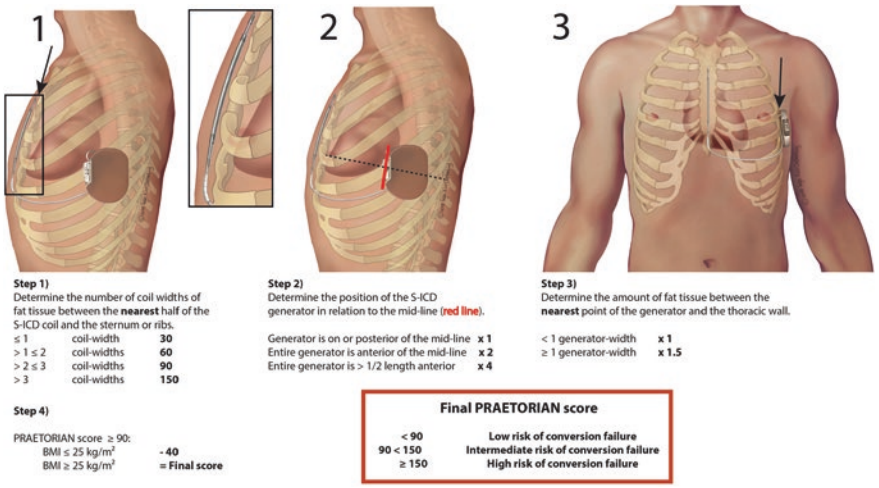


Fig. 7 PRAETORIAN risk score to predict defibrillation failure (Quast et al. Heart Rhythm, 2018)

risk of DFT testing failure. The positive predictive value for an intermediate or high PRAETORIAN score for a failed conversion test was 51%, while a low PRAETORIAN score predicted a successful conversion in 99.8% of patients.

Implant techniques: The S ICD implant procedure can be performed in the electrophysiology laboratory or in the operating room. The procedure can be performed with regional anesthesia techniques, monitored anesthesia care, or under general anesthesia (Fig. 8). Adequate light source through a headlamp or through a source mounted on retractor is required for optimal hemostasis in patients who require larger later pocket. Meticulous skin preparation is required has the implant side is most often close to the axilla. The hair should be clipped rather than shaved to minimize the risk of infection. The patient is placed in a supine position on the operating table with the arm extended up to 60° and secured to an arm board. Care should be taken not to hyperextend the arm to prevent brachial plexus injury. Certain implanters place support below the left scapula to turn the chest more towards the right side. Fluoroscopic images in AP position may change when supports are used below the scapula. Surgical markings may be helpful and can be done with fluroscopy prior to draping. Many operators include a wide area under the drape that incorporates the sternal region, subcostal region near the xiphoid process and the lateral chest wall including the skin over the fold of the latissimus dorsi muscle in the operating field. Draping is commonly performed from mid-sternal to posterior axillary line and from clavicle region to region below the xiphoid process. When the S ICD was introduced in the market a three incision technique was commonly used. Later on a two-incision technique quickly became popular.

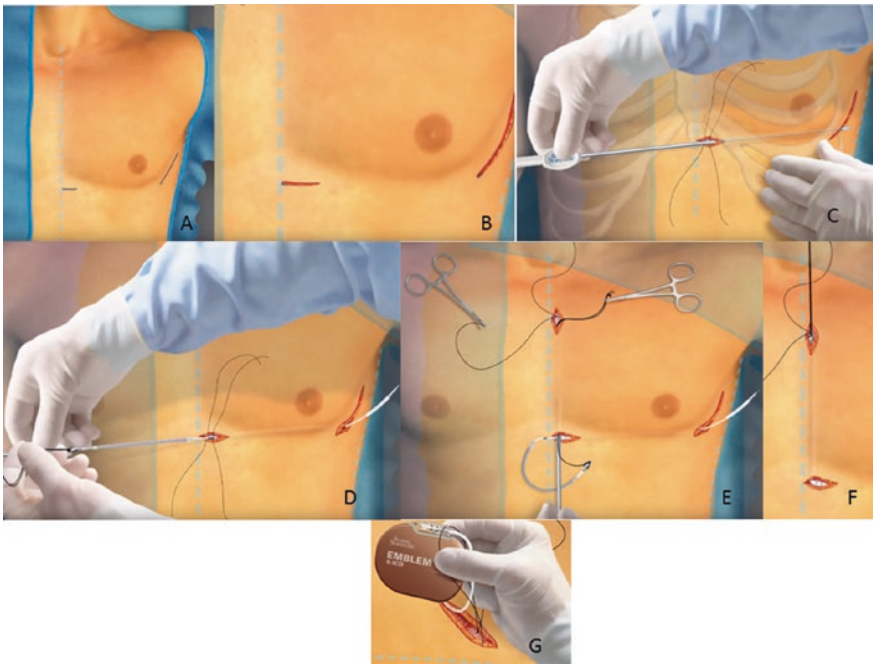


Fig. 8 Procedural steps for implantation of the SICD system: The patient is prepped and draped and the potential incision sites are marked (**A**). The incisions are taken down and the pockets are made at the fascial plane (**B**). The lead is tunneled from the lateral pocket to the medial lower pocket and is secured using sutures (Panels **C** and **D**). The lead tip is then tunneled to the superior pocket and secured with sutures (Panels **E** and **F**). The device is connected to the lead, and then the pocket is closed in layers (Panel **G**). Above figures reproduced with permission from Boston scientific

The skin is anesthetized using a local anesthetic medication. A 5–7 cm long curved incision is made along with the 5th or 6th intercostal space. Meticulous dissection should be performed to avoid cutting any muscle and to secure adequate hemostasis. Using retractors the plane between serratus anterior and latissimus dorsi should be localized. Care should be taken to create a pocket as posteriorly as feasible. Long thoracic nerve courses over the serratus anterior muscle and potentially can be damaged during the dissection process. A second pocket is created horizontally at the level of the xiphoid process. The lead is then connected to the tunneling tool and is tunneled from the medial pocket to the lateral pocket. The lead is secured to the fascia in the medial pocket using nonabsorbable sutures. Then the tunneling tool is advanced in the left parasternal region with a peel-away sheath on it. Once the tool reaches an adequate position the tool is removed and the lead inserted through the sheath. The sheath is peeled away while advancing the lead forward. In obese individuals a third pocket is created near the clavicle to secure the tip of the lead to the fascia. The device is connected to the lead and placed in the pocket.

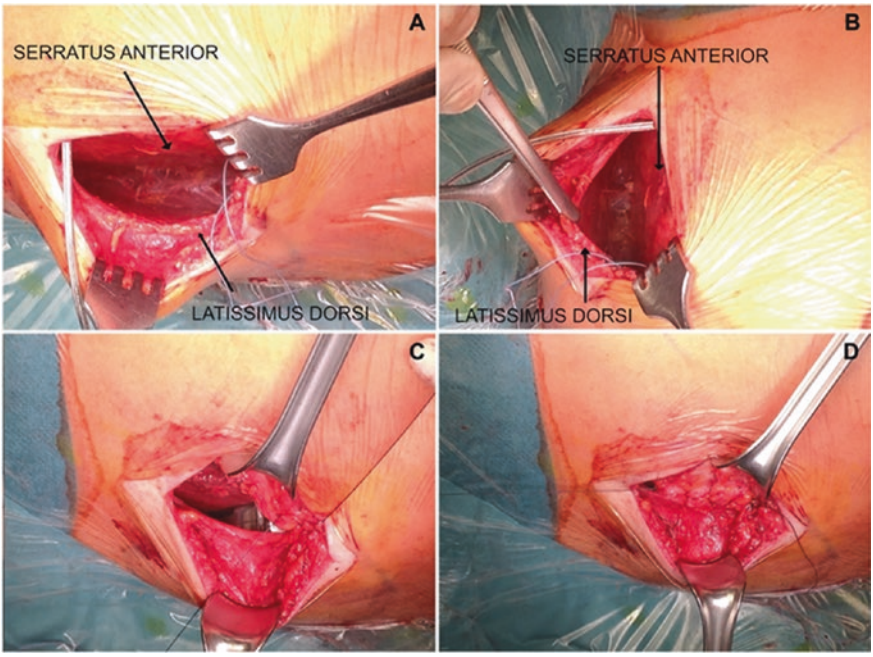


Fig. 9 Reproduced with permission (Pacing and Cardiac Electrophysiology, Wiley). The device is placed in the plane between the latissimus dorsi and the serratus anterior muscle. The plane is closed with interrupted sutures

Most operators secure the device with non-absorbable sutures to prevent migration. The muscular pane is closed using absorbable sutures. There are two main implantation techniques: standard and intramuscular generator placement. Standard implant technique involves creating a device pocket at the fifth intercostal space between the mid and anterior axillary lines. The incision is made along the inframammary crease at the anterior edge of the latissimus dorsi. The subcutaneous tissue is dissected directly down to the muscular fascia to create the pocket. In the intramuscular implantation technique, the generator is commonly placed in a muscular plane bounded posteriorly by serratus anterior muscle and anteriorly by the latissimus dorsi muscle (Fig. 9). In both techniques, the generator is placed as posterior as possible to provide the most optimal defibrillation vector with the anterior sternal lead in order to encompass as much myocardium as possible. All the pockets are flushed with saline solution, and the skin over the lead course is milked to express any air bubbles to improve conduction. Nonphysiological signals can be seen on telemetry in patients with air bubbles over the lead. Long-acting local anesthetic (liposomal bupivacaine) may be injected in the tissues to minimize patient discomfort. The first layer of pocket is closed, and sensing tests are performed. The outer layers are closed with sutured or with medical adhesive.

Foam adhesive dressings with silver impregnation have been used to promote wound healing and to minimize the chance of infection. Post-operative wound management education is important for pain control and adequate healing.

Defibrillator Threshold Testing

DFT testing is required for all SICD implantations at the end of the procedure to ensure effective implantation. A DFT testing protocol is provided courtesy of Boston Scientific in Fig. 10. A high-frequency current is used to induce ventricular fibrillation. Care should be taken not to impede the contraction of shoulder muscles during DFT testing. Rare cases of shoulder dislocation have been reported [8]. Conversion of VF with 65 J shock is considered a success. If 2 or more shocks are unsuccessful the lead and or the generator position are altered to achieve an acceptable threshold. An alternative to full DFT testing in select patients is use of a 10 J command shock to test the lead impedance. An impedance of <100 ohms can be considered more likely to deliver a successful shock for VF.

What To Do When You Have a High DFT

- Air in the pocket and around the lead significantly increases impedance. If air is present, it is important to **repeat flushing & massage**.
- Perform DFT testing with at least the first layer of incisions closed.
- Check impedance. If >100 ohms consider revising lead location. Do fluroscopy to determine coil location.
- Anesthesia and anti-arrhythmic medications (amiodarone) may affect DFT
- Verify terminal pin insertion into header (rare instances)
- Change polarity of the shock waveform (standard to reverse) and repeat induction @ current output or higher.
- Consider changing generator location; depth and/or not posterior enough. The vector from lead to can should include as much of the ventricles as possible.

Follow Up Considerations

Team-based management after device implant is essential for optimal outcomes with S-ICD. Appropriate device programming, patient education, enrollment in remote monitoring and follow up are various components of the management plan. Common solutions to troubleshooting are listed in Table 2. Follow up care is listed in Fig. 10.

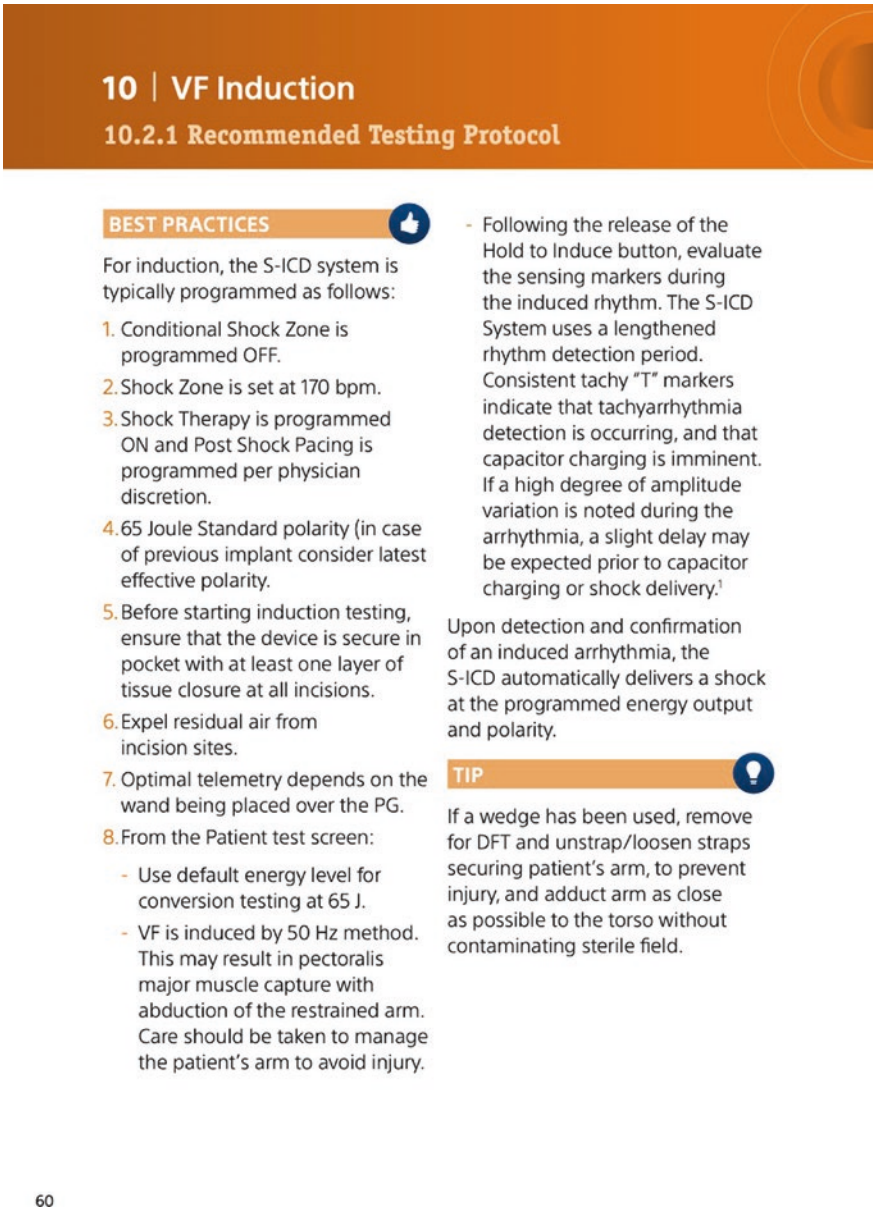


Fig. 10 Recommended DFT Testing Protocol. Content provided courtesy of Boston Scientific.

Table 2 Variable S-ICD potential issues and suggested troubleshooting actions

Challenge	Best handled
Over-sensing (P-R-T waves) /Inappropriate shocks	ECG screening of S-ICD Candidates Optimization of sensing vectors Discrimination (conditional) zone programming
Device migration or erosion	Intermuscular plane placement Secure the device with two sutures Device extraction, revision or replacement
Lead dislodgement or migration	Prevention by the use of suture sleeves (anchoring the proximal parasternal lead segment) Lead /device revision
Interference with ventricular assist device (VAD)	Use of alternate vector (automatic or manual) Device revision
Loss of beeping tones	Close follow-up (every 3 months) Generator replacement

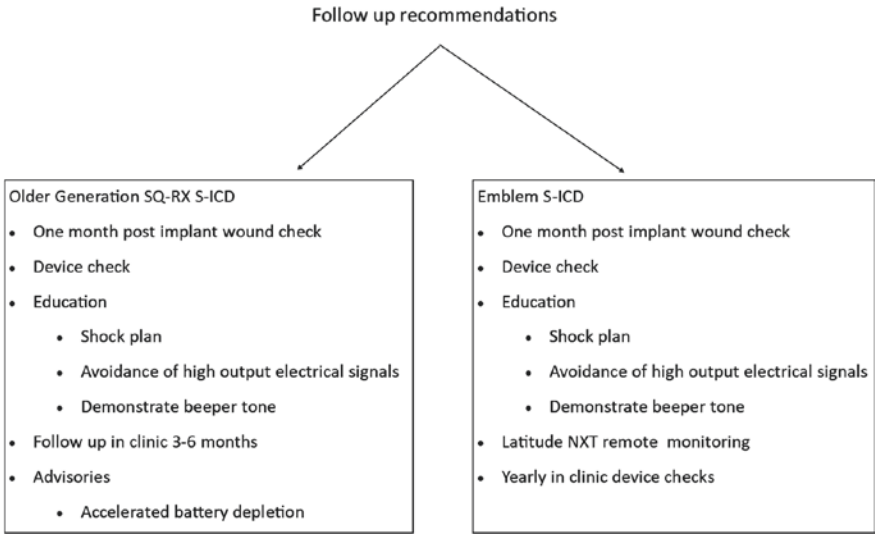


Fig. 11 Suggested follow up care of S-ICD after the initial implant porcedure

Special Situations

Congenital Heart Disease: Patients with adult congenital heart disease pose special challenges for defibrillator implantation. Many of them may have intracardiac shunts or limited vascular access that limits traditional device implants. The position of the cardiac chambers in the chest may be different. ECG screen should be

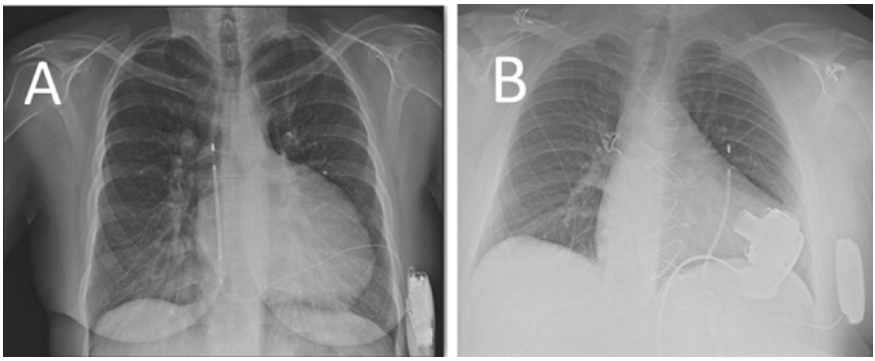


Fig. 12 Panel **A** shows the placement of the lead in the right parasternal region in a patient with congenital heart disease. Panel **B** shows SICD use in a patient with left ventricular assist device (Heartmate 3)

considered with leads placed on the right side of the sternum in patients who fail traditional screening (Fig. 10 panel A).

Left ventricular assist devices: The use of LVAD therapy in patients with SICD has been reported in the literature. Some patients required inactivation of the ICD due to EMI from the LVAD or R wave attenuation due to heart and chest wall geometry changes after LVAD surgery. Inappropriate shocks are also reported due to EMI, and in some patients, change in sensing vector was able to prevent inappropriate detection and therapies (Fig. 10 panel B).

SICD and Leadless pacemaker combination: Case reports of patients with combined leadless pacemakers and SICDs are reported in the literature. To date, the modular system with bidirectional communication between devices is not yet available for commercial use although animal studies and initial human experience has been reported. When combined, the pacing output should below not to interfere with VF/VT detection, and the SICD testing should be performed in the most sensitive configuration.

Case Follow up: An exercise stress test was performed to evaluate sensing at faster rates on a treadmill while the detection and therapies were programmed off. The patient developed rate-dependent bundle branch block leading to inappropriate TWOS in the alternate and secondary sensing configurations (Fig. 4). There were no TWOS in primary sensing configuration. The sensing configuration was changed to the primary sensing configuration. The rates of conditional shock zone and shock zone were increased from 190 bpm to 210 bom and 220 bpm to 230 bom respectively. The patient remains shock free since optimal programming of the device (Table 3).

Future Directions

- Improvements in SICD device technologies continue to be developed to reduce SICD device footprint, and may also include introduction of a dual coil lead to allow decreased electrical output.

Table 3 Summary of important studies for S-ICD

Clinical studies	Results
Systematic review [9]	Successful defibrillation 96% Inappropriate shocks 4%
Observational registry [10]	Complication-free rates of 92% at 360 days 8% inappropriate shocks at one year
Post approval study [11]	99% successful defibrillation at implant 96.2% -30 day complication rate
RCT S-ICD versus TV-ICD [2]	As effective as TV-ICD but required higher energy
Predictive score for defibrilation suceess [12]	Increase in DFTs if More fat between • Coil to sternum • Generator to ribcage Anterior canposition
S-ICD patients requiring extraction	5.6% due to refractory sensing issues All patients passed initial screen
Ongoing Studies	
PRAETORIAN [13]	S-ICD versus TV-ICD
ATLAS S-ICD [14]	S-ICD versus TV-ICD in younger patients at higher risk of device complications
UNTOUCHED [15]	S-ICD for primary prevention. Inappropriate shocks will be compared to TV-ICD patients in MADIT-RIT

- Integration with leadless pacing technologies to provide anti-tachycardic pacing to terminate ventricular tachcyardia are under development.
- Alternative extra-vascular ICDs with sub-sternal lead placement enabling a smaller device footprint and ATP delivery are being developed and tested.

Key Points:

- The development of a totally extravascular defibrillator system is a new advance in the last decade.
- The device relies on surface electrogram for sensing and detection of tachyarrhythmias. Special algorithms have been developed for discrimination.
- Lacks of bradycardia pacing and anti-tachycardia pacing therapies are the potential drawbacks of the system.
- Implantation techniques are pretty straightforward, and the development of intermuscular technique is a new advance that markedly increased patient comfort.
- In a small group of patients with oversensing that cannot be corrected by traditional programming extraction of the system may be required.

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How to Identify and Manage Complications from Cardiac Implantable Electronic Devices

Lalit Wadhwani, Arif Albulushi, and Faris Khan

Case Vignette

Fifty three year old female with history of hypertension, chronic renal impairment, and complete heart block status post dual chamber permanent pacemaker placement who presented with 1 week history of fever, malaise and failure to thrive. Initial work up with an echo showed a possible new vegetation on her right ventricular pacemaker lead and blood culture came back positive for gram positive cocci. Cardiac Electrophysiology team was consulted for cardiac implantable electronic device infection and possible device extraction.

Introduction

Cardiac implantable electronic device (CIED) is a universal term used for any implantable cardiovascular device that interacts with the inherent electrical cardiac conduction system. It encompasses a myriad of devices including permanent pacemaker (PPM), implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT). It has been estimated that more than 1.5 million CIEDs are implanted worldwide each year [1]. Out of these, about 350,000 devices are implanted each year in the United States alone.

All CIEDs were implanted utilizing the trans-venous route until 2012, when the first subcutaneous implantable cardioverter defibrillator (SICD) was approved by

L. Wadhwani
NYU Langone Health, New York, NY, USA

A. Albulushi · F. Khan (✉)
Division of Cardiology, University of Nebraska Medical Center, 42nd and Emile, Omaha, NE 68198, USA
e-mail: fariskhan@gmail.com

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the US Food and Drug Administration (FDA). A new dimension was added to the trans-venous implantation of CIEDs with the advent of leadless pacemaker system and its FDA approval in 2016.

Incidence of Complications

Numerous studies showed that CIED complications can be acute, subacute or chronic [2] as summarized in Table 1. Similarly, other studies reported major complication rates ranging between 2.6 and 4.8% while minor complications range between 2.3 and 5.3% [3–5].

Risk Factors

Several risk factors can potentially predict the possibility of CIED implantation related complications [6, 7]. The common risk factors are:

- Age greater than 75 years
- Female gender
- Chronic lung disease
- Body mass index (BMI) less than 18.5

Table 1 Cardiac implantable electronic device complications

Immediate Complications
– Pocket hematoma – Inadvertent Arterial access – Bleeding – Pneumothorax – Vascular injury due to placement of wire/sheaths – In appropriate lead implant position (RV lead in MCV, RV lead in LV (if arterial stick that goes un recognized) CS lead implant in poor location) – Lead dislodgement – Pericardial effusion
Sub-acute Complications
– Lead dislodgement requiring repositioning of lead – Pericardial effusion – localized discomfort at the CIED implant site (SICD specially and trans venous occasionally)
Long-term Complications
– Pocket skin erosion and infection – Twiddler's syndrome – Complication during lead extraction (vascular tear, myocardial perforation, leads remnants, bleeding) – Localized discomfort (SICD specially and transvenous occasionally)

- Hypertension
- Left bundle branch block on EKG
- Continued warfarin use or other anticoagulants.

Based on the timing, complications associated with CIED implantation may be divided into three categories:

- Immediate—Complications during the procedure.
- Subacute—Complications within 48 h after the procedure.
- Long-term—Complications days to weeks after the procedure.

A. **Immediate Complications**

Immediate complications occur during the procedure and although some of these complications may be managed expectantly, many require active intervention. The list of these complications is extensive and includes excessive bleeding, vascular injury, pneumothorax, hemothorax, venous obstruction, lead malposition, cardiac perforation, cardiac tamponade and valve injury. As is expected, the risk of complications is higher with physicians whose implant volume is lower. A study based on the Ontario database suggested that complication rates were significantly higher if the implanter volume was < 60 devices/year compared to implanters with a volume of >120 devices/year [4]. Some of the immediate complications are discussed below.

A.1. Pneumothorax

1. Occurs from inadvertent puncture of the pleural cavity or lung parenchyma while obtaining venous access (Fig. 1)
2. Even though it is rare, it can be a potentially life threatening complication [3, 6]
3. It is more common in women than men, as shown in the MADIT-CRT trial [8]
4. It may present as pneumothorax, hemothorax, hydro-pneumothorax and tension pneumothorax.
5. Sudden onset of shortness of breath and chest pain should raise clinical suspicion for pneumothorax.

How to avoid it:

1. Cephalic vein cut-down technique is better than contrast guided extrathoracic approach [9]
2. Axillary stick rather than subclavian
3. Peripheral IV contrast injection
4. Ultrasound guidance while obtain intra venous access.

Treatment:

Small (1 cm or less air rim) and asymptomatic pneumothorax can be managed with close observation. However, large pneumothorax, hemothorax or tension pneumothorax may require chest tube placement.

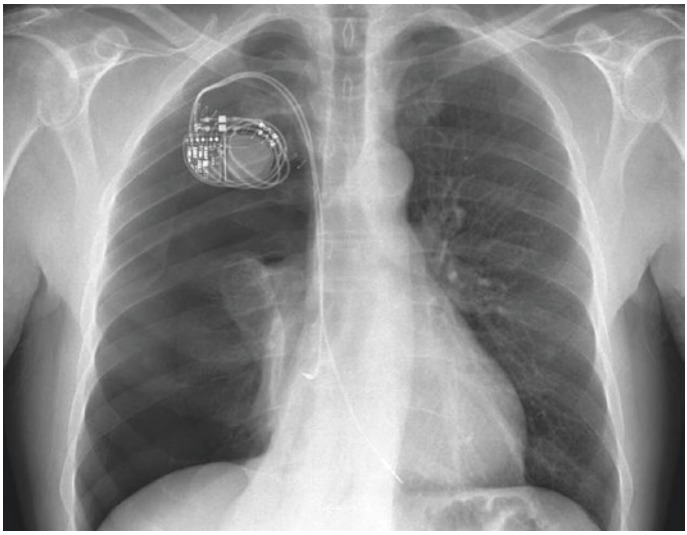

Fig. 1 Pneumothorax. (With permission to use from Ulrika Birgersdotter-Green, MD; University of California San Diego)

A.2. Cardiac perforation and tamponade

1. Although rare, it is the most significant complication of CIED implantation [2, 3, 7]
2. It may present as acute tamponade or may have a subacute presentation with chest pain and shortness of breath due to a small to moderate pericardial effusion
3. Some of the risk factors for developing cardiac perforation include temporary pacemaker wire use, steroids use and helical screw in leads use [10]
4. A sudden drop of blood pressure during the procedure, especially after implantation of a lead is usually the first sign of development of cardiac tamponade
5. An important sign of lead perforation without clinically significant effusion is increase in the lead threshold and impedance compared to the baseline values.

How to diagnose it:

Chest x-ray (CXR) shows presence of lead tip outside the cardiac silhouette, transthoracic echocardiography (TTE) assess the extent of pericardial effusion and computed tomography (CT) scan (Fig. 2) has a better diagnostic yield for cardiac perforation with a pacemaker or an ICD lead [11, 12]

How to avoid it:

1. Avoiding over rotation of helix when it is fully extended
2. Careful use of lead stylet and probing with soft tip during lead positioning.
3. Use multiple fluoroscopic views for lead location.

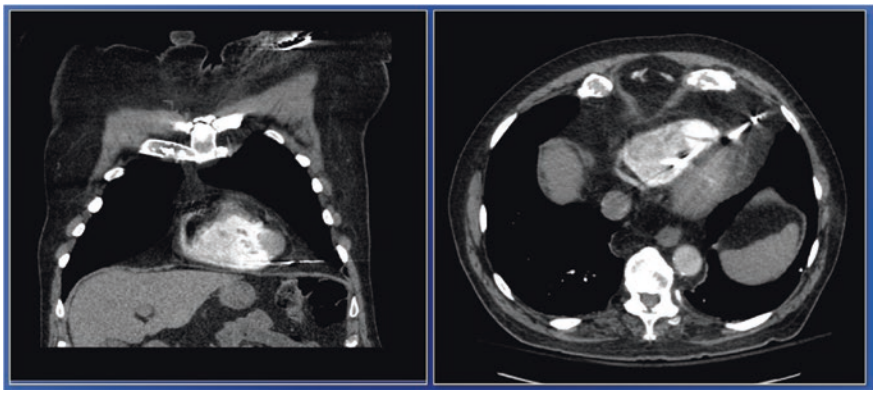

Fig. 2 RV lead perforation. (With permission to use from Ulrika Birgersdotter-Green, MD; University of California San Diego)

Treatment:

Lead perforation can be a surgical emergency and may require immediate action in the form of pericardiocentesis versus open surgical repair if the bleeding does not stop.

A.3. Loose Set Screw

1. Loose set screw may be documented as noise, fluctuating lead impedance, pocket stimulation during pacing, inappropriate mode switches and inappropriate shocks
2. The time frame, in general, is shortly after the procedure (hours–days).

How to avoid it:

1. It can be avoided by visualizing the terminal pin's position on fluoroscopy, by appropriately tightening set screw and by doing a tug test.

A.4. Coronary Sinus (CS) Dissection

1. This complication is specifically associated with cardiac resynchronization therapy (CRT) however, it is a rare complication [13]
2. It may occur during wire manipulation or sheath introduction into the CS.

Diagnosis:

1. Monitoring of vital signs, fluoroscopy of the cardiac silhouette and use of echo should aid in the diagnosis.
2. A more distal dissection of a smaller branch can be demonstrated by staining of contrast outside the lumen. This, in general, is not associated with any hemodynamic consequences but will likely preclude placement of a lead in this location
3. Careful use of balloon and guide sheaths while in the CS.

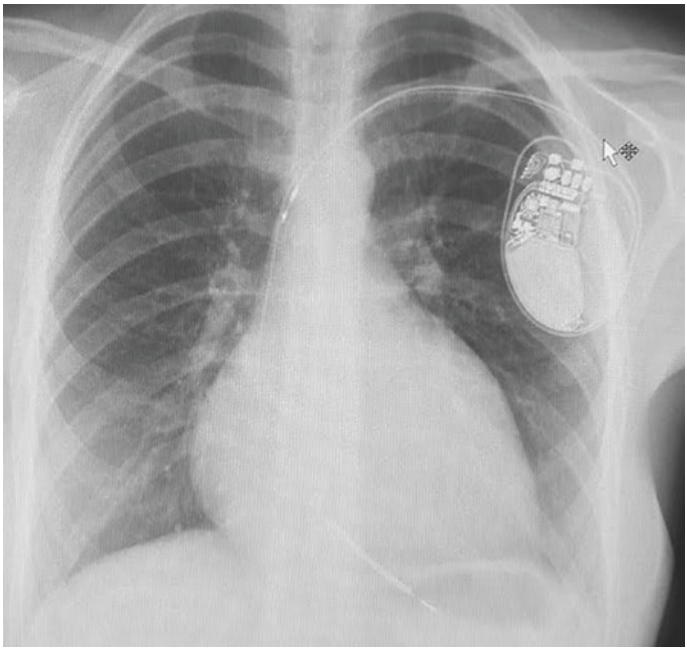

Fig. 3 Atrial lead dislodgement

Treatment:

In general, it is well tolerated in most of the cases without any clinical or angiographic adverse outcome [14] and may not require any active intervention except close monitoring.

B. **Subacute Complications**

Subacute complications occur within 48 h of CIED implantation and are usually noticed prior to hospital discharge. These include lead dislodgement, pocket hematoma, localized discomfort and subacute presentation of pericardial effusion. Lead dislodgements almost always require repeat surgical intervention but rest of the subacute complications may be managed expectantly.

B.1. Lead dislodgement

1. A small proportion of leads get dislodged due to cardiac contraction, rotation and translocation.
2. Most lead dislodgements occur within the first 24–48 h after device implantation
3. Acute lead dislodgement occurs more commonly with CRT-D devices [15]
4. Common risk factors associated with acute dislodgement include older age, female sex, more advanced heart failure, and a greater number of comorbidities.

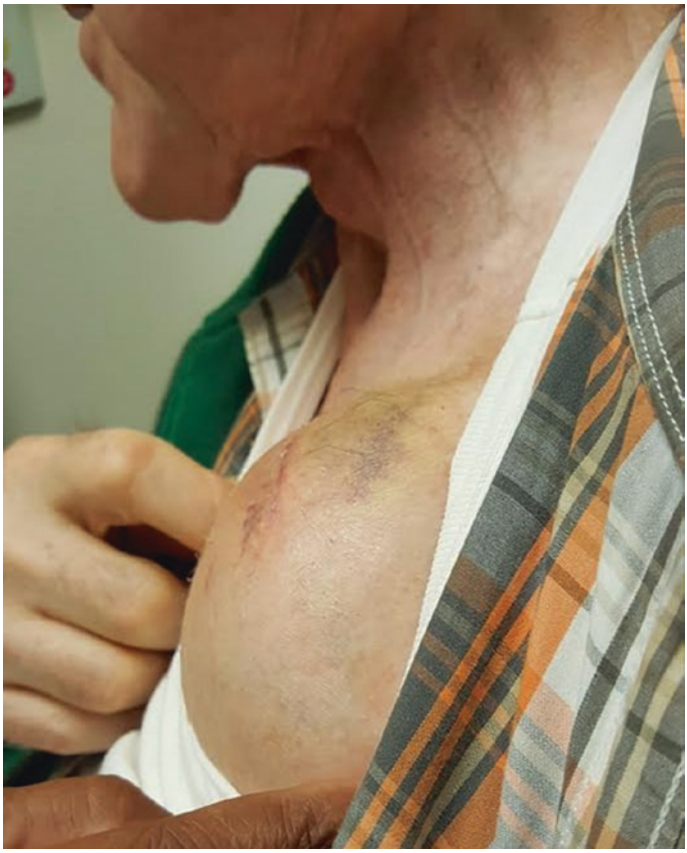

Fig. 4 Pocket hematoma

5. Sudden change in lead sensing and pacing threshold associated with change in the lead position on CXR clinches the diagnosis of lead dislodgement (Fig. 3)
6. Rate of dislodgement of leadless pacemakers is much lower than that of traditional pacemakers [16].

How to avoid Right Atrial (RA) or Right Ventricular (RV) lead dislodgement:

1. Atrial lead should be preferentially placed in RA appendage
2. Apically placed RV lead has a less chance of dislodgement than implantation on mid RV septum.
3. By retaining stylet during lead placement, the active helix can be deployed properly and this reducing the risk of lead dislodgement.
4. Atrial lead stability testing should be performed after implantation.
5. Ensuring adequate lead slack at end of procedure
6. Properly suturing lead to pectoral muscle.
7. Consider suturing device to pectoral muscle to avoid its migration.
8. Clear patient instructions regarding post procedure activity restrictions.

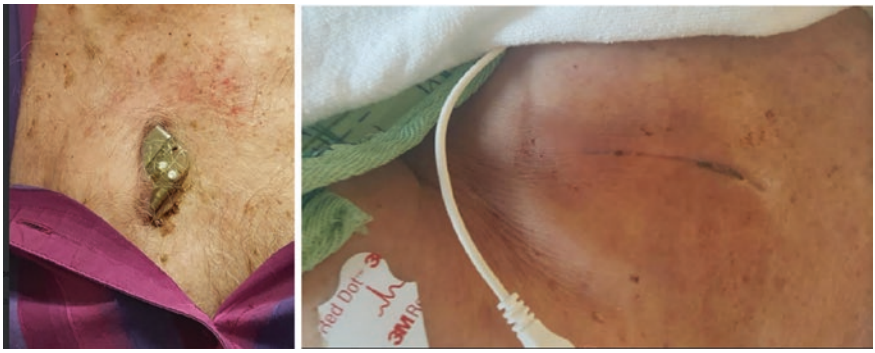

Fig. 5 CIED infection with skin erosion (left) and skin erythema (right)

How to avoid Left Ventricular (LV)/CS lead dislodgement:

1. Obtain a separate stick for LV lead reduces the risk of its dislodgement.
2. If the lead pulls back when you remove the guide sheath consider a different lead type or location.
3. Quadripolar leads may allow for more apical location of distal tip thu]s stabilizing the lead position.

B.2. Pocket hematoma

1. It is comparatively common complication after CIED implantation [12]
2. It is more common in patients who are on anticoagulation and/or dual antiplatelet therapy
3. Previous studies shown rate of device hematoma is less with continued warfarin in comparison to heparin bridging strategy [17, 18]
4. It can cause significant pain and discomfort but most of them resolve spontaneously without any surgical intervention (Fig. 4)
5. It is important to NOT aspirate hematoma for diagnosis since it can lead to pocket infection.

How to avoid it:

1. One should know anticoagulation status before, during and after the procedure.
2. Meticulous attention should be paid to secure hemostasis during the procedure, including figure of 8 stitch or purse string suture around insertion site, if indicated.
3. Thrombin injection in the pocket, if indicated.

Treatment:

1. Hematoma evacuation is needed in the cases where the size is very large, and the incision integrity is compromised.
2. Hemoglobin and hematocrit may need to be checked and transfusion may be required if there is a significant drop of hemoglobin level.

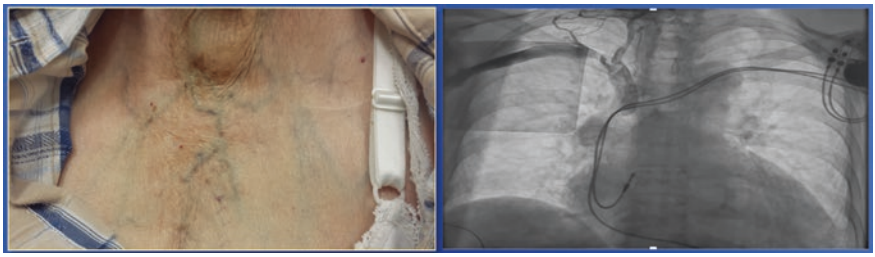

Fig. 6 Venous Occlusion. (With permission to use from Ulrika Birgersdotter-Green, MD; University of California San Diego)

3. Pressure dressing with pocket compression device can also be used.
4. If patient develops hematoma, one can consider antibiotic coverage if the risk of infection is high.

C. **Long term Complications**

Complications after CIED implantation may occur any time after the implant. Complications that occur weeks to months, and sometimes even years after device implantation include persistent localized discomfort at the site of implantation especially with the relatively large subcutaneous ICDs, twiddler's syndrome, pocket erosion, pocket infection, stitch abscess, bacteremia and infective endocarditis. These complications are rarely managed conservatively and almost always require surgical intervention.

C.1. CIED Infections

1. It is one of the most dreaded complications as it is associated with high morbidity and mortality.
2. Patient will usually present with tachycardia, fever, elevated white blood cell count, elevated procalcitonin and/or positive blood cultures (Fig. 5)
3. Most of these infections are bacterial in nature.
4. The infection risk is the highest in the first 6–12 months after implantation
5. The risk of infection is higher in CRT compared to ICD or PPM implantation.
6. Major risk factors of CIED infection include diabetes, hemodialysis, hematoma formation, corticosteroid use, chronic skin disease and temporary pacemaker wire [19].

Diagnosis:

1. Ultrasound can be used for assessment of pocket infection. In addition, radionuclide imaging (^{18}F-FDG PET/CT or WBC SPECT/CT) can also be used for detecting CIED infection however, most of the diagnosis are made on clinical judgement.

How to avoid CIED infection:

1. Always perform your procedure in a sterile environment.
2. Use prophylactic antibiotics at the start of the procedure before skin incision is made.
3. Keep the procedure duration short, if possible.
4. Follow the precautions to avoid hematoma formation
5. For high risk patients consider the use of an absorbable antibacterial envelope as it has shown to be beneficial in WRAP-IT trial [19].

C.2. Venous obstruction

1. Risk factors for venous obstructions include but are not limited to upgrade of an existing device with placement of additional lead; device and/or lead infection, use of hormone replacement therapy, dual coil ICD leads, prior history of deep vein thrombosis and presence of temporary trans venous pacing lead [20, 21]
2. It can potentially make future device implantation/upgrade quite challenging, rendering it even impossible at times.
3. The most common site of obstruction was peripheral subclavian/distal innominate veins [22]
4. Presence of prominent and dilated veins over the pacemaker pocket can sometimes be seen in patients with venous obstruction (Fig. 6).

How to avoid it:

1. Contrast venography should be considered prior to CIED implant in patients with any risk factors as described above.
2. Monitor for signs of arm swelling after device implantation procedure.

Diagnoses:

Doppler ultra sound can be used to assess for deep vein thrombosis and venous obstruction.

Treatment:

1. Patient may require oral anticoagulation.
2. In patients with peripheral venous obstruction, device may need to be implanted on the contralateral site.
3. In cases with central obstruction or in patients who can't undergo device implantation on the contralateral site, venoplasty should be considered.

Leadless Pacing Complications

The introduction of leadless pacemaker systems have certainly reduced the risks of several pocket and lead related CIED complications however, there is a risk for access site related complications such as hematoma or pseudo aneurysm. Other

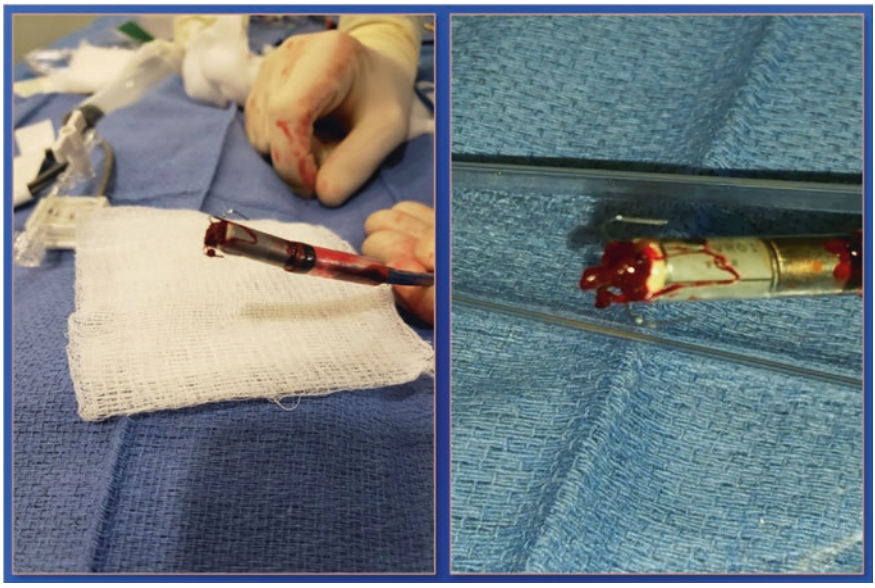

Fig. 7 Leadless Pacer Clot. (With permission to use from Ulrika Birgersdotter-Green, MD; University of California San Diego)

complications may include vascular injury, clot formation (Fig. 7) or right ventricular perforation leading to pericardial temponade.

Possible predictors of lead less pacemaker implantation complication include:

- Old age
- Female gender
- Low BMI and
- Chronic lung disease [22].

How to avoid it:

1. Obtain venous access using ultrasound guidance
2. Flush the delivery sheath with heparinized solution to avoid clot formation
3. Use contrast and different fluoroscopy views to confirm appropriate implant location
4. Use septal rather than apical device location to reduce the risk of perforation
5. Physician's proctoring during device implantation until adequate skills have been acquired to perform the procedure independently

Key Points:

1. CIED implantation can be associated with complications like any other procedure
2. The complications can be either major or minor

3. These complications are divided into immediate (during the procedure), subacute (within 48 h post op) or long term (days-weeks post op) complications
4. Most commonly reported complications include lead dislodgement, lead malfunction, pocket hematoma, pneumothorax and incision/device infection
5. Major risk factors for developing these complications include age greater than 75 years, female gender, chronic lung disease, body mass index less than 18.5, hypertension, left bundle branch block on EKG and continued warfarin use
6. It is very important to recognize these complications in a timely fashion
7. Use current guidelines and local expertise to manage each complication as indicated.

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Management of Implantable Cardioverter Defibrillators in Patients with a Left Ventricular Assist Device

Oscar Braun

Case Vignette

A 50-year old man with no medical history presented with a viral illness, fulminant myocarditis and cardiogenic shock. He required an urgent Heartmate III left ventricular assist device (LVAD) implantation 3 weeks later. During his entire hospital course, the patient did not have any significant ventricular arrhythmias. Two weeks after the LVAD implantation the decision was made to implant a primary prevention ICD. The procedure was complicated by a large pneumothorax that progressed into a hemothorax requiring an acute thoracotomy with evacuation of blood. After an extended hospital stay, the patient was eventually discharged to a rehabilitation facility without any reported ICD therapies.

ICD Indications In Patients With LVADs

Approximately 80% of patients have an ICD present prior to LVAD implantation [1]. In patients who undergo LVAD implantation without an existing ICD, there are limited data advising whether to implant an ICD [2]. In the 2017 Guidelines for Management of Patients with Ventricular Arrhythmias, it is a Class IIa recommendation that an ICD can be beneficial in LVAD patients with sustained VAs [3]. On the other hand, the 2013 International Society for Heart and Lung Transplantation (ISHLT) guidelines recommend routine placement of an ICD for patients who did not have an ICD before LVAD implantation (Class IIa) [4]. These recommendations are based on retrospective studies, and no randomized trial has ever been performed to evaluate the clinical benefit of ICD implantation in patients with LVADs.

O. Braun (✉)
Department of Cardiology, Clinical Sciences, Lund University and Skåne University Hospital, Lund, Sweden
e-mail: oscar.braun@med.lu.se

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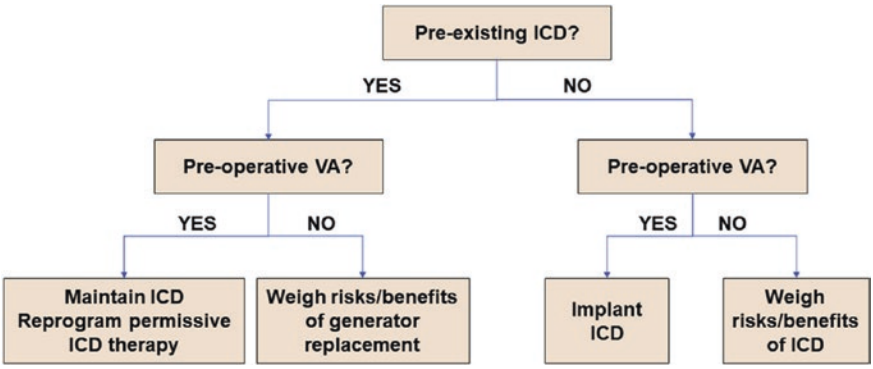

Fig. 1 Suggested algorithm to guide implantable cardioverter-defibrillator implantation in LVAD patients. Adapted from Ho et al., JACC-EP 2018, permission obtained to use

Several retrospective studies have investigated the association between ICDs and mortality in LVAD patients with conflicting results. In earlier studies that included pulsatile LVADs the presence of an ICD was associated with a survival benefit after LVAD implantation [5, 6]. However, more recent single center retrospective studies of patients with CF-LVADs haven't suggested a survival benefit with an ICD [5–8]. Recently two large propensity-matched registry studies from the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) and the United Network for Organ Sharing (UNOS) registry respectively including over 5400 patients has further confirmed these findings of an absence of association between an ICD and mortality [1, 9]. A recent meta-analysis further confirmed the lack of signal for a survival benefit with an ICD during CF-LVAD treatment [10].

In conclusion, based on recent guidelines and available retrospective data, it appears that patients with pre-LVAD or post-LVAD VAs may benefit from an implanted ICD, whereas an ICD may not always be needed in patients with no history of VAs (Fig. 1), although randomized studies are clearly needed.

Generator Replacement After LVAD Implantation.

No studies have evaluated the necessity of ICD generator replacement in patients with a LVAD who reach elective replacement indicator status. The benefits of ICD therapy must be weighed against risks of generator replacement, including infection which occurs in up to 7% of LVAD patients [11]. In a study of 247 LVAD patients, 3% developed cardiac implantable electronic device (CIED) infections [12]. One-half of these patients (n = 3) developed a pocket infection without bacteremia, and were all preceded by a generator replacement. The other half (n = 3) had bacteremia. All patients underwent complete CIED removal. Despite chronic suppressive antibiotic therapy in the patients with bacteremia, 1 patient required LVAD

exchange and 1 patient died from infection-related complications. This small study suggests that patients with isolated pocket infection had a good outcome with only CIED removal, but patients with bacteremia had a worse outcome. Another study reproduced these findings and reported 6 patients with CIED infections, of which 5 patients presented with bacteremia [13]. These patients experienced recurrent bacteremia despite complete CIED removal. The majority of these patients (n 4) eventually died due to infection- related complications including 1 patient who underwent LVAD exchange. These studies suggest that it is difficult to clear bacteremia in the presence of a LVAD despite complete CIED removal. More studies are needed to assess whether LVAD exchange may improve the outcome in these patients.

Given the high burden of post-LVAD VAs and associated complications, it is probably reasonable to pursue generator change in all secondary prevention patients or those with pacemaker indications [4]. However, patients without prior VAs and who do not experience post-operative VA may not benefit from generator replacement at elective replacement indicator, although there are no studies addressing this issue.

Use of Subcutaneous ICDS in LVAD Patients

The use of a subcutaneous (sub-Q) ICD may be an attractive option in selected patients with higher risk of bloodstream infections or who have limited venous access, but this comes with some limitations for patients with LVADs. Although there have been 2 case reports of successful use of sub-Q ICDs with the HMII and HVAD [14, 15], there has also been 1 report of electromagnetic interference (EMI) with an HVAD [16], 1 report of R-wave sensing problems [17], and 1 report where the sub-Q ICD was in the field of the minimally invasive mini-thoracotomy approach for LVAD implantation [18], the latter 2 requiring switching to a transvenous ICD system. In addition, implantation of LVADs has been shown to significantly alter the surface ECG, especially the R:T ratio in leads I, II and aVF. Since these leads correlate to the leads used by sub-Q-ICDs careful electrogram screening is necessary when considering implantation in a patient with a LVAD [19].

Furthermore, thorough interrogation of a pre-existing sub-Q ICD is necessary post-LVAD implantation. Further studies of device interactions are needed before recommending this to a more general population.

ICD Troubleshooting After LVAD Implantation

After LVAD implantation, device interference has been reported with all generations of ICDs. Device interference can manifest as a loss of telemetry with the programmer or with EMI leading to inappropriate ICD therapies. Two retrospective studies [20, 21] and case reports [22–26] of HMII patients have reported

interactions with older-generation St. Jude Medical and Sorin ICDs, with an incidence of approximately 2 to 17% of all patients before 2012. More recently, there have been case reports of loss of telemetry in 2 patients with the HM3 in combination with current- generation Biotronik (Ilesto and Iforia) and Sorin ICDs [27, 28]. Both cases were successfully temporarily resolved using maneuvers to minimize interference during interrogation. These techniques involve creating a metal insulation shield between the LVAD and the programmer [24, 26, 29]. Examples of insulation contraptions include cast iron frying pans. Table 1 shows the ICD models that have been reported to Thoratec/Abbott, the manufacturer of the HeartMate devices.

Inappropriate ICD shocks due to EMI rarely occur but have been reported. In a retrospective study of 44 LVAD patients, 1 patient (2%) experienced 5 inappropriate shocks due to EMI (detected at 250 beats/min) from a Boston Scientific ICD. EMI may be minimized by adjusting the RV sensing threshold and extending detection intervals.

It is important to note that oversensing can occur due to EMI from LVAD and cause inhibition of pacing. In a patient with a history of complete heart block s/p Abbott CRT-D who underwent a HeartMate III implantation, it was noted that he had ventricular pauses due to inhibition of pacing. Interrogation showed that he had oversensing which inhibited Bi-V pacing (Fig. 2a). Although the EMI was very low amplitude, a feature called Low Frequency Attenuation Filter was turned on nominally on this Abbott CRT-D. The purpose of this filter is to minimize T-wave oversensing by amplifying R waves and diminishing T waves. As a result, the EMI was amplified. In this case, turning off the LFA filter prevented further oversensing (Fig. 2b) and resolved inhibition of pacing and heart block.

Significant changes in lead function have also been reported after LVAD implantation with mixed clinical implications. Several studies report significant reductions in RV sensing amplitude and increases in capture thresholds and defibrillation thresholds [21, 30, 31]. These changes continued to persist beyond 30 days postoperatively and led to an intervention in approximately 20% of patients. Undersensing of clinical VT due to a decrease in lead sensing was noted in up to 5% of patients and required RV lead revisions. Unsuccessful shocks occurred in up to 9% of patients, and high defibrillation thresholds requiring sub-Q array implantation occurred in up to 7% of patients. There were rare occurrences of direct lead damage, including 1 RV lead fracture and 1 dislodged epicardial LV lead. Given significant persistent changes in RV lead parameters after LVAD implantation, it is imperative to perform ICD interrogation postoperatively to monitor for EMI, RV lead undersensing, and inappropriate or ineffective ICD therapies.

Programming ICD Therapy Zones.

In large randomized ICD trials of non-LVAD patients comparing less-aggressive ICD programming versus conventional programming, the conventional ICD programming patients received more shocks and had a significant increase in mortality, suggesting

Table 1 ICD models with reported interactions with LVAD implantation

Heartmate II™ LVAD reported ICD experience	
Manufacturer	Model No.
Abbott	Atlas™ model V193
Abbott	Atlas™ model V-242
Abbott	Atlas™ model V-243
Abbott	Atlas™ model V-366
Abbott	Atlas-HF™ model V-340
Abbott	Atlas-HF™ model V-341
Abbott	Atlas-HF™ model V-343
Abbott	Atlas™ VR model V-199
Abbott	Current™ DR RF 2207-36
Abbott	Current™ RF VR 1207-36
Abbott	Epic™ HF CRT-D model V-337
Abbott	Epic™ HF CRT-D model V-338
Abbott	Epic™ HF model V-350
Abbott	Epic™ Plus VR model V-196
Abbott	Integrity™SR model 5142
Abbott	Photon™ Micron DR model V-232
Abbott	Promote™ RF CRT-D model 3207-36
Abbott	Quadra Assura MP model 3371-40QC
Abbott	SN model V-235
Abbott	Unify Quadra model 3251 40Q
Sorin Group	Alto 2 model 624
Sorin Group	Paradigm
Heartmate 3™ LVAD reported ICD experience	
Biotronik	Iforia 5-HF-t
Biotronik	Iforia 5-VR-T
Biotronik	Iforia CRT-D
Biotronik	Ilestro 7-VR-T DX
Biotronik	Ilestro 7-HFT-RF
ELA Medical (Sorin)	Paradyme RF CRT-D9750

an association with ICD shocks and higher mortality [32–35]. Given that VAs are usually not immediately hemodynamically compromising in patients with LVAD support, an optimal ICD programming strategy might be to maximize detection times and rate zones and to enable anti-tachycardia pacing (ATP) to minimize ICD shocks.

A recent small trial randomized 83 patients to conventional ICD programming compared to ultraconservative programming which included:

(1) VT zone at 180 beats/min with maximal detection time at 33 s, 3 to 8 rounds of ATP and shocks; and (2) VF zone at 220 to 240 beats/min with maximal detection time of 15 to 32 s and shock therapy, with variations depending on the manufacturer [36].

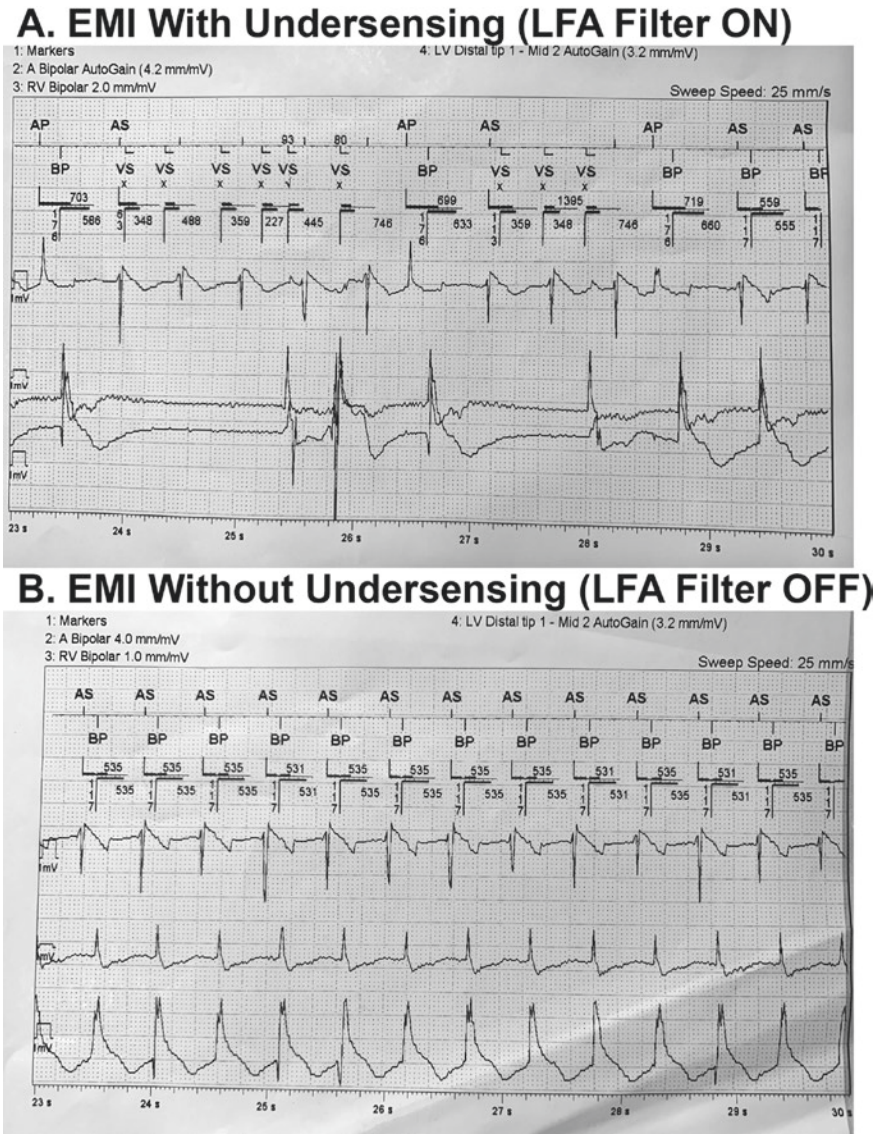

Fig. 2 Electromagnetic interference (EMI) caused by LVAD. **A** Oversensing due to EMI, aggravated by low frequency attenuation (LFA) filter that is used to decrease T-wave oversensing, but accentuates R waves. **B** EMI oversensing eliminated by turning off LFA filter

Although there was a trend towards less ICD shocks in the ultraconservative group, the results did not reach statistical significance with a median follow-up of 11 months. As the authors admit, the study may have been underpowered to show a significant effect. Additionally, conventional programming was noted to

be already relatively conservative and most of the shocks were for VF. Another limitation faced by the authors was the restricted range of programming allowed by the device firmware and the inability to extend detection times longer. Nevertheless, as the first randomized trial assessing conservative ICD programming, an important finding was that conservative programming was not associated with adverse events such as mortality or cardiovascular-related hospitalizations, which suggests that this programming strategy could safely be implemented. However, larger multicenter studies with longer follow-up must be conducted to fully evaluate the effect of these programming strategies.

Case Conclusion

Our patient slowly recovered his heart function with optimal medical therapy and LV unloading. After 3 years, he had improved to a point that his LVAD could be explanted. Repeat echo 1 year after LVAD explantation showed a nearly recovered ejection fraction at 45%. The ICD was still in place but never detected nor treated any significant arrhythmias. This case illustrates the controversy of ICD implantation, particularly for primary prevention. This patient did not require ICD therapy but experienced increased risks of complications such as bleeding contributed by LVAD-associated anticoagulation and coagulopathy.

Key-Points

- There is conflicting evidence from retrospective studies studying the benefit of ICDs in patients with LVADs
- Patients with pre-LVAD or post-LVAD VAs may benefit from an implanted ICD, whereas an ICD may not always be needed in patients with no history of VAs
- ICD generator change should probably be performed for secondary prevention ICD patients or those with pacemaker indications
- The use of subcutaneous ICDs can be an alternative mode of ICD therapy but there are risks including electromagnetic interference and sensing problems
- Lead and device malfunction may occur post-operatively after LVAD implantation such as EMI, RV lead undersensing, and inappropriate or ineffective ICD therapies, and I tis important to perform post-operative ICD interrogation.
- In LVAD patients who may experience hemodynamically tolerated VAs, conservative ICD programming is reasonable unless patients are at high risk for RV failure.

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Indications and Use of the Wearable Cardioverter-Defibrillator

Michael Eskander MD and David Krummen MD

Clinical Case

A 62 year old male with nonischemic cardiomyopathy was admitted to the intensive care unit for pneumonia, atrial fibrillation with rapid ventricular response, and decompensated congestive heart failure. He was started on antibiotics, atrioventricular nodal blocking medications, anticoagulation, and intravenous diuretics. Serial electrocardiograms and cardiac biomarkers showed no evidence of acute myocardial infarction. Telemetry monitoring revealed frequent ventricular ectopy, with runs of nonsustained ventricular tachycardia. A transthoracic echocardiogram demonstrated a severely depressed left ventricular ejection fraction of 20% (normal 55–65%), decreased from a prior value of 50%. Concerned about his risk for sudden cardiac death, his inpatient team requested cardiology consultation regarding the patient's eligibility for a wearable cardioverter-defibrillator (WCD).

Introduction

Ventricular tachycardia (VT) and ventricular fibrillation (VF) are responsible for the majority of cases of sudden death (SCD) [1], affecting approximately 3 million patients annually worldwide. While the implantable cardioverter-defibrillation (ICD) provides definitive protection from sustained ventricular arrhythmias [2], many patients are ineligible for ICD therapy for a number of reasons including recency of heart failure diagnosis, the presence of an infection, or other factors.

M. Eskander · D. Krummen (✉)
University of California San Diego and VA San Diego Healthcare System, 3350 La Jolla Village Drive, Cardiology Section 111A, San Diego, CA 92161, USA
e-mail: dkrummen@ucsd.edu

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An alternative to the ICD, the wearable cardioverter-defibrillator (WCD) is a self-contained, external vest able to automatically detect ventricular arrhythmias and deliver lifesaving defibrillation. The purpose of this chapter is to discuss the technology, review patients who may benefit from WCD therapy, and discuss the current state of medical knowledge regarding use of the WCD.

The Wearable Cardioverter-Defibrillator

The WCD consists of two shoulder harnesses and a belt which allow positioning of 2 back and 1 anterior chest defibrillation pads, 4 sensing electrodes in the belt, and a portable battery/monitoring unit which is attached by wires and may be attached to the belt or the patient's clothing (Fig. 1). The harnesses and belt are user-adjustable, intended to fit relatively snugly to the torso.

WCD Functioning

During normal functioning, the 4 belt electrodes monitor the patient's heart rhythm continuously. Rhythm analysis is performed in real time by a microprocessor in the battery/monitoring unit. The monitoring electrodes are held in position by tension from the elastic belt and provide two surface electrogram leads [3]. Arrhythmia detection is programmable to accommodate different expected rate of normal rhythms versus VT/VF. Proper fitting must be confirmed with appropriate electrode-skin contact to avoid noise and frequent device alarms.

Detection of arrhythmia is based on programmed rate and morphology criteria. If VT or VF are detected, the WCD initiates a sequence of programmed actions. These include escalating audible tones, vibration against the wearer's chest, and a spoken warning of impending shock to the wearer and bystanders nearby. If no response is received by the WCD, a blue conductive gel is released from the defibrillator electrodes, and up to 5 biphasic shocks are delivered at preprogrammed energy levels. Alternatively, the patient may silence the audible warnings and delay therapy by holding the response button.

Gaps in ICD Eligibility and SCD Risk

Presently, a gap exists between the time patients are diagnosed with conditions associated with risk of sudden death and their eligibility for ICD implantation. This gap stems from the results of the DINAMIT [4] and IRIS [5] trials enrolling patients with myocardial infarction with a left ventricular ejection fraction (EF) $\leq$35%. Patients were randomized to an early ICD (6–40 days) versus medical therapy. Both trials showed no improvement in mortality with early ICD implantation despite a reduction

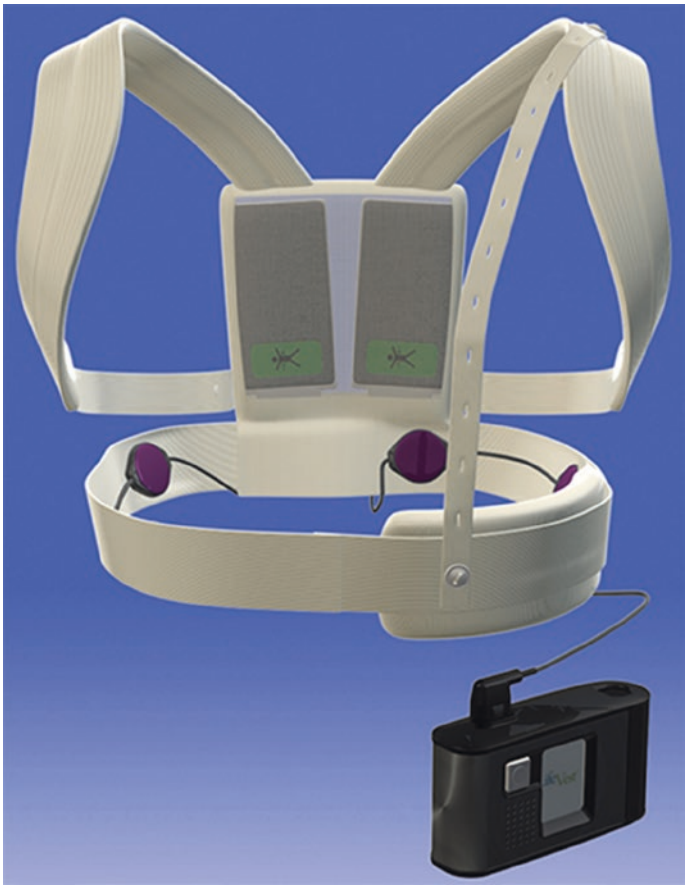

Fig. 1 The wearable cardioverter-defibrillator is shown, including the shoulder harnesses, belt, electrodes, and detachable battery pack/monitoring unit (Lifevest, Zoll Medical Corp.)

in arrhythmic deaths; there was a higher risk of nonarrhythmic deaths during this early period, resulting in similar overall mortality rates [4, 5]. Unfortunately, SCD risk was highest in the first 30 days at 1.4–2.3% per month in the same population with myocardial infarction and left ventricular dysfunction, heart failure, or both [6].

A similar gap exists in individuals with left ventricular dysfunction early after revascularization. This is largely based on characteristics of individuals with ischemic cardiomyopathy receiving ICD implantation for primary prevention of SCD in MADIT and CABG-Patch trials [7, 8]. While professional societies do not exclude ICD implantation for these individuals, Centers for Medicare and Medicaid Service (CMS) excludes coverage for primary prevention ICD for individuals with revascularization within the past 90 days. More recent investigation of the National Cardiovascular Data Registry by Weintraub et al. continues to illustrate a higher rate of 30-day mortality of 3% in individuals with left ventricular dysfunction and recent percutaneous coronary intervention [9].

Additionally, there are patients who meet indication for ICD implantation though device implantation must be delayed or interrupted due to comorbid conditions such as device infection, vascular access, or recent surgical procedure. These patients remain at risk for SCD. For these groups, the WCD remains an option for mitigating SCD risk.

Eligible Patients

Current expert consensus documents recognize the following situations for which WCD therapy may be useful (Table 1) [10]. In general, WCD may be useful when ICD is indicated though device implant must be deferred or interrupted due to patient factors, ongoing assessment of left ventricular function while awaiting response to guideline-directed medical therapy, or as a bridge to ICD implant due to national coverage requirements.

WCD Therapy Rate and Effectiveness

The US post market study reported outcomes from 8453 patients prescribed WCD after MI. Overall, there were 146 VT/VF events occurred in 133 patients (1.6% of the enrolled population). Overall shock success was 82%, with 91% immediate survival. Notably, there was a difference in shock success rate between patients with

Table 1 Indications for WCD use

Indications for WCD use	Class	Level of evidence
Use of WCDs is reasonable when there is a clear indication for an implanted/permanent device accompanied by a transient contraindication or interruption in ICD care such as infection	IIa	C
Use of WCDs is reasonable as a bridge to more definitive therapy such as cardiac transplantation	IIa	C
Use of WCDs may be reasonable when there is concern about a heightened risk of SCD that may resolve over time or with treatment of left ventricular dysfunction; for example, in ischemic heart disease with recent revascularization, newly diagnosed nonischemic dilated cardiomyopathy in patients starting guideline-directed medical therapy, or secondary cardiomyopathy (tachycardia mediated, thyroid mediated, etc.) in which the underlying cause is potentially treatable	IIb	C
WCDs may be appropriate as bridging therapy in situations associated with increased risk of death in which ICDs have been shown to reduce SCD but not overall survival such as within 40 days of M	IIb	C
WCDs should not be used when nonarrhythmic risk is expected to significantly exceed arrhythmic risk, particularly in patients who are not expected to survive >6 mo	III: No benefit	C

and without successful revascularization; shock success was 95% in revascularized versus 84% in non-revascularized patients [11]. The WEARIT-II Registry enrolled 2000 patients of which 40% were ischemic and 46% nonischemic cardiomyopathy [12]. Of note, median daily use was reported as 22.5 hours. A total of 120 sustained ventricular tachyarrhythmias in 41 patients were reported with 54% receiving appropriate shock. Only 10 patients (0.5%) received inappropriate WCD therapy. In other work, Ellenbogen and colleagues found that WCD use was potentially beneficial in patients with explanted ICDs [13]. However, such studies were observational in nature; randomized trial data were needed to demonstrate the effectiveness of WCDs in at-risk patients.

The VEST Trial

In 2018, the randomized, multi-center VEST trial [14] results were published, showing that among patients with a recent myocardial infarction and an ejection fraction of 35% or less, the wearable cardioverter–defibrillator did not lead to a significantly lower rate of the primary outcome of arrhythmic death than control (Fig. 2).

An important insight from the VEST trial is that the mean number of hours worn per day was 14.0 ± 9.3. This is significantly below recommended use, and suggests that one potential contributing factor to the negative outcome of the trial was suboptimal compliance. Thus, future iterations of the WCD with improved wearability and comfort may provide higher levels of compliance, increasing the probability of successful WCD therapy.

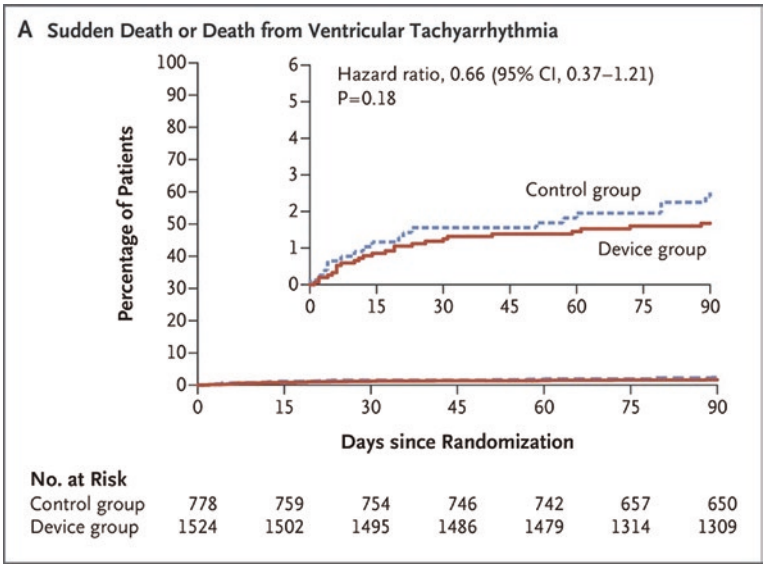

Fig. 2 Sudden death from ventricular arrhythmias from the VEST trial [14]. Reprinted with permission

Controversies in WCD Use

At present, use of the WCD for routine patients diagnosed with new-onset cardiomyopathy with EF < 35% is uncertain. Based on the results of the VEST trial, routine use may not improve outcomes. However, there may be high-risk subgroups of this population for whom WCD use may be beneficial. Despite the perceived need for such technology, observational WCD studies for the prevention of sudden cardiac death (SCD) have demonstrated conflicting data leading to significant practice variation in prescribing WCD [15].

Limitations to WCD

Several limitations exist to the current iteration of the WCD. As previously suggested, WCD efficacy in detecting and treating VT and VF may be inherently linked by its wearer's compliance. In the WEARIT/BIROAD study, 68 of 289 quit due "comfort issues or adverse reactions," with skin rash or itching also being reported by others in the study [16]. In addition, the device cannot offer protection around times of bathing or active water sports. Lastly, as the device is worn externally, no post-shock pacing or bradycardia pacing capability is available.

Current Recommendations

Optimal WCD use remains controversial. However, the authors recommend WCD therapy for patients felt to be at significantly increased risk of SCD including patients awaiting cardiac transplantation and those meeting ICD indication but have delay or interruption of implant due to vascular access or ongoing management of systemic infection. Utilization in other patients felt to be at particularly high risk of SCD may be considered on a case-by-case basis.

Future Directions

New technologies are being developed to address the limitations of currently available wearable cardioverter defibrillators. Although not yet cleared by the US Food and Drug Administration nor available on the market, a patch version of the WCD is being developed by Element Science that consists of 2 small patches that can be worn under clothes. These and other such technologies that are designed to be more comfortable and waterproof may improve user compliance.

Case Conclusion

Because of his low (<25%) left ventricular function and frequent nonsustained ventricular tachycardia, the patient introduced earlier in this chapter was believed to be as enhanced risk for sudden death, and was prescribed a WCD. On day 17 of WCD therapy, he experienced sustained ventricular tachycardia and syncope. His WCD appropriately detected the arrhythmia and delivered a lifesaving shock (Fig. 3 A–F). The patient subsequently received permanent ICD therapy 3 months after admission, and continues to follow-up with the Electrophysiology service.

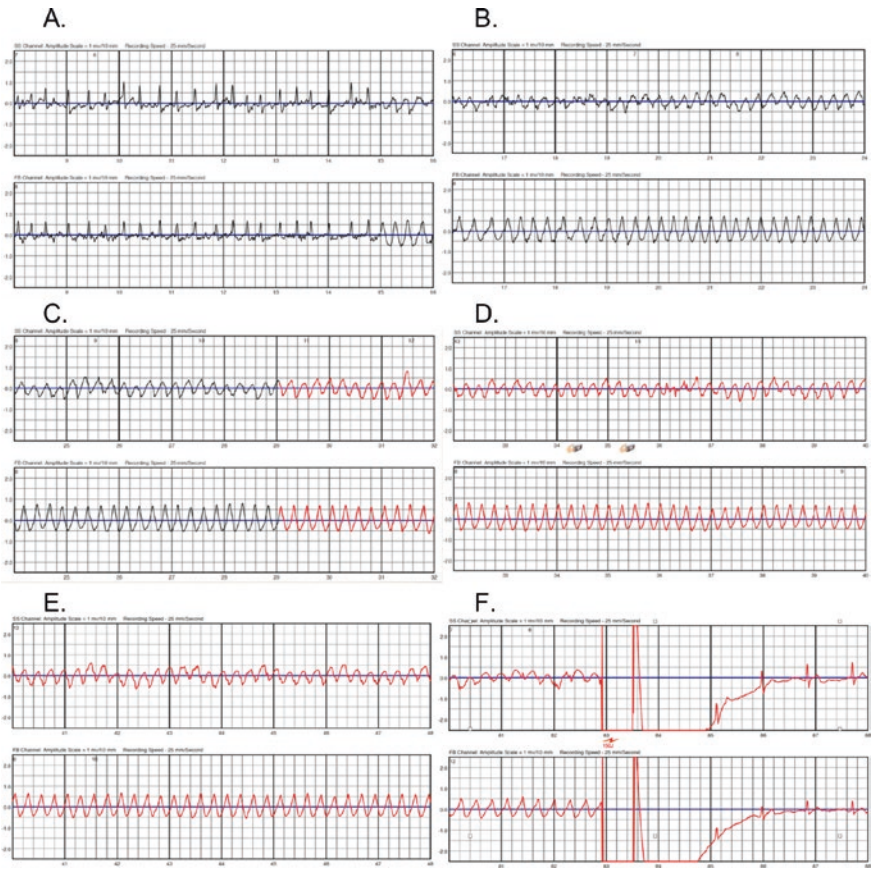

Fig. 3 (Panel A) WCD episode report with typical format of two consecutive electrocardiogram channels (SS and FB). This particular report begins with rapid atrial fibrillation which appears to degenerate into sustained ventricular tachycardia (VT). (Panels B and C) WCD-detected VT. (Panel D) WCD alerts wearer of impending shock and awaits response from wearer (Panel E). (Panel F) A successful shock is delivered, restoring sinus rhythm

Key Points

- WCD use remains controversial due to the negative result of the VEST trial
- Expert opinion that reasonable indications include:
  - Patients with interrupted ICD therapy (device extraction)
  - Patients awaiting cardiac transplantation
  - Patients believed to be at enhanced risk for SCD on case-by-case basis.

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Cardiac Device Management in Palliative Care

Patrick Azcarate and Stephanie Yoakum

Case Vignette 1

GJ is a 94-year-old man with a history of persistent atrial fibrillation, sick sinus syndrome s/p dual chamber pacemaker, ischemic cardiomyopathy with EF 20–30% s/p upgrade to Bi-Ventricular implantable cardioverter-defibrillator (ICD). GJ ventricular paces 97% of the time with an underlying heart rate in the 40–50 bpm. He has 9 months left on the battery of his ICD. He presented to clinic stating that he has had 4 falls in the past few months and that as his quality of life continues to decline he will be ready to die. He is worried that if wife were to die first he would not have anyone to take care of him. He would like his wife to be able to visit her family in Japan and live her life. GJ is requesting that ICD therapies be turned off but is unsure if he would want a generator change.

Introduction

It is estimated that one million people receive cardiac implanted electronic devices (CIEDs) such as pacemakers (PMs) and implantable cardioverter-defibrillators (ICDs) every year. While these advances have increased quality of life and decreased mortality, all patients will eventually reach the end of their lives due to progression of their cardiac disease or other health problems such as cancer, neurologic or respiratory diseases. In the last weeks of their life, twenty percent of

P. Azcarate (✉) · S. Yoakum
Division of Cardiology, Department of Internal Medicine, University of California, 9452 Medical Center Dr #7411, La Jolla, San Diego, CA 92037, USA
e-mail: pazcarate@health.ucsd.edu

U. Birgersdotter-Green and E. Adler (eds.), *Case-Based Device Therapy for Heart Failure*, https://doi.org/10.1007/978-3-030-70038-6_17

patients with ICDs will receive shocks that are known to cause pain and decrease quality of life [1–3]. The desire not to prolong life or experience pain and suffering may lead patients and their families to request that an ICD or pacemaker be deactivated or therapies modified.

Navigating Discussions

Deactivation of CIEDs can lead to emotional distress and bring up ethical, religious and in some cases legal issues. Some may question if withdrawing CIED therapy is akin to assisted suicide or euthanasia. The HRS Expert Consensus Statement on the Management of CIEDs in patients nearing end of life or requesting withdrawal of therapy [4] refutes this assertion. In this circumstance, the clinician's intent is to discontinue a therapy that is no longer wanted and to allow the patient to die naturally of the underlying disease and not to terminate the patient's life [5, 6] Patient autonomy is of utmost importance. The Patient Self Determination Act affords patients or their surrogate the protection to decide what is best for them after discussion with the clinical team. If conflicts exist between patients, families or surrogate decision makers an ethics consult should be considered.

Studies have shown that patients, families and some clinicians view deactivating CIEDs differently than discontinuing other therapies such as mechanical ventilation, dialysis or feeding tubes. It is the clinician's responsibility to discuss and educate patients, families and colleagues that there is no ethical or legal distinction between treatment that is within the body versus outside the body. Also, patients at end of life should be made aware that deactivating their CIED is an option just like withdrawal or discontinuation of other care (Fig. 1).

It is imperative that clinicians utilize shared decision making prior to CIED implantation and have proactive conversations with patients and their families to minimize suffering at the end of life. Patients with CIEDs should strongly be encouraged to have an advanced directive to avoid ethical dilemmas for surrogate decision makers.

When having these discussions with patients and family members, it is important to clairfy the difference between ICDs and pacemakers. An ICD delivers tachy-therapy or treatment of arrhythmias such as ventricular tachycardia or ventricular fibrillation. Pacemakers are used to prevent bradycardia or treat AV nodal blockade. It is possible to turn off ICD and maintain pacemaker function or simply turn off both. If this is done, patients and families need to be aware that if they are pacemaker-dependent, death may occur quickly. The distinction between deactivating tachy-therapies (ICD) and brady therapies (pacemakers) needs to be clear to all parties involved. Clinicians have the right to decline to turn off pacemakers on any grounds. In this situation, another physician can and should assume care of the patient.

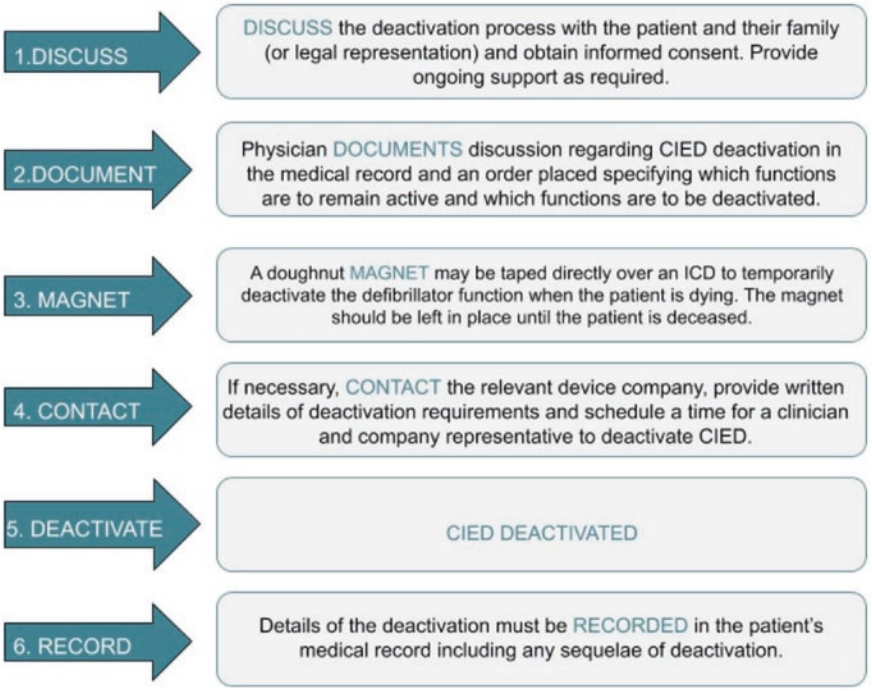

Fig. 1 CIED deactivation process

How to Deactivate Pacemakers and Defibrillators

All physicians or facilities that implant and follow CIEDS should have a clearly defined process or standardized procedure for withdrawal of pacemaker and ICD therapies. Members of the multidisciplinary team, including consulting teams, social work, palliative care e.g. should participate in the deactivation process if appropriate. Ideally discussions relating to CIED deactivation should be initiated early, rather than at the terminal stage.

As part of the discussion with patients and families the following points should be discussed:

- Deactivating CIEDs is not painful
- If the patient's circumstances change following the deactivation, the patient can request re-activation of the CIED
- Deactivating the defibrillator function of the ICD does not deactivate the pacemaker function
- In patients who are pacemaker dependent, death may occur quickly.

Logistics of CIED Deactivation

- CIED deactivation can take place in the acute care setting, outpatient setting, skilled nursing facility or patient's home
- After discussion with patient, if cognitively competent, and their families or designated surrogate decision makers when the patient is not capable of participating in the process, informed consent should be obtained.
- Thorough documentation of the discussion including consequences of deactivation and plan to deactivate the device should be documented in the medical record
- An order from the responsible physician to deactivate the device should be placed in the medical record including specific therapies that are to be deactivated, as well as, therapies that are NOT to be deactivated (if any)
- An experienced clinician or industry employed allied professional (IEAP) may deactivate device or turn off specific therapies under the direction and supervision of medical personnel
- Deactivation may result in patient symptoms and thus appropriate medications should be ordered prior to deactivation and readily available for administration.

ICD Deactivation

- A doughnut magnet can be placed over an ICD to disable anti-tachycardia therapies if there will be a logistical delay in turning off therapies; bradycardia pacing will not be affected
- Anti-tachycardia therapies should be turned off by re-programming in all zones according to physician orders
- It is important to clarify if both shocking therapies and anti-tachycardia pacing therapies should be turned off as some patients may not want to be shocked but would want pacing therapies which are not painful
- All remote monitoring and audible alerts reporting deactivation of anti-tachycardia therapies should be turned off.

Pacemaker Deactivation

- Pacing therapy may be withdrawn by programming to specific modes such as OOO, ODO or OSO
- If these modes are not available the rate can be lowered and the outputs adjusted to subthreshold
- All remote monitoring and audible alerts reporting deactivation of pacing should be turned off

- Again, Patients and families should be made aware that death may occur quickly if the patient is pacemaker dependent
- If patient is on telemetry, consider turning off monitor as alarms may be distressing.

Case Conclusion

After discussion with GJ and his wife, he elected to have his ICD therapies turned off. GJ ultimately decided to undergo a generator change but waited until device had reached end of life to make a final decision. GJ elected to keep anti-tachycardia therapies off at time of generator change. His health has continued to declined and he and his wife have moved to another city to be closer to family for support.

Clinical Case #2

Mr. MP is a 78-year old man with a history of heart failure due to left ventricular systolic dysfunction from ischemia. His most recent ejection fraction by echocardiography is 15%. In the last 6 months he has been admitted twice to the local hospital. He is now waking up two times a night with shortness of breath and has shortness of breath just walking to the bathroom. His legs are swollen all the time. His caregiver is concerned since he cannot travel with her anymore. Patient subsequently underwent HM2 LVAD placement with a post-operative course complicated by a pneumonia. Eventually he was discharged home and at a follow-up visit a few weeks later was found to be recovering well. Six months later he was admitted for fatigue and was found to be in VT which required cardioversion. He reported he had been feeling fatigued, worsening pain and had a depressed mood. Palliative care and psychiatry were consulted. They recommend better pain control and he was placed on an SSRI. Six months later, he was still having uncontrolled pain. After a goals of care conversation between the patient, his caregiver, and his cardiologist, the patient clarified that should his pain continue to worsen of functional status decline, he would prefer comfort focused treatment. His caregiver asked what comfort care would look like with an LVAD.

LVAD Considerations in Palliative care

Between 2013 and 2016 there were 6.2 million heart failure patients in the U.S. In parallel to the rising incidence of heart failure, the number of patients receiving left ventricular assist devices (LVADs) is also increasing, from 98 in 2006 to 2,423 in 2014 [8]. An LVAD is a mechanical circulatory support device that may be offered to patients with stage D heart failure as a bridge to recovery, a bridge to transplant, a bridge to decision, or as destination therapy (DT). While

initially LVADs were mainly used as a bridge to other therapies, now the proportion of LVADs as DT has increased from 14.7% in 2006 to 45.7% in 2014 [8]. This increase in use of LVADs for DT is likely because they have been shown to improve symptoms and survival in patients with advanced heart failure compared to medical therapy alone [9] and advancements continue to improve survival [10]. In addition to these potential benefits, however, there remains morbidity and mortality with the most common complications being infection, bleeding, and stroke. Prior to undergoing LVAD implantation, patients must understand the benefits and risks of this device in addition to one other important consideration: when to withdraw therapy of the device. End of life care discussions are encouraged for all patients with advanced heart failure but is even more important in those with an LVAD given the unique ethical discussions it creates [11].

Navigating Discussions

Understanding what patients and caregivers would want at the end of life prior to LVAD implantation is important for several reasons. Firstly, most patients who get an LVAD will die with one. This may be because it was implanted as destination therapy, or it was initially meant to be a bridge but they no longer are offered a transplant. Second, it is difficult to picture the end of life with an LVAD and patients and caregivers often express confusion about the process Having an honest conversation on the process and certain indications that would prompt device withdrawal are imperative. Finally, it is important to have these conversations prior to implantation since the patient may decompensate quickly and may then no longer be able to participate in the goals of care conversations. In general, discussions about discontinuation of an LVAD must include reasons why it is turned off and it must include what the process will look like including the setting, management of symptoms, and prognosis once device is turned off. For these situations it may be helpful to consult palliative care providers who can provide an additional layer of support for these discussions.

There are three types of clinical scenarios where LVAD deactivation may be requested. These include an abrupt pump failure or LVAD complication (sepsis or stroke), a poor quality of life, or the development of serious comorbidities such as cancer or dementia (Fig. 2) [11, 12]. If these occur, either the patient or caregiver will request device deactivation or the healthcare provider may recommend it. Withdrawal of this device does create a unique ethical discussion since some patients and caregivers may see withdrawal of LVAD support as physician assisted suicide or euthanasia and still others may see it as contradictory to their religious beliefs [13]. According to the Patient Self Determination Act, however, a patient has the right to withdraw or refuse medial therapy to allow a natural death [13]. This act protects a patient's right to withdraw an LVAD, which is a life-supporting device, and allow end-stage heart failure to progress naturally towards death [4]. In contrast, as noted above, euthanasia or physician assisted suicide causes death by a lethal

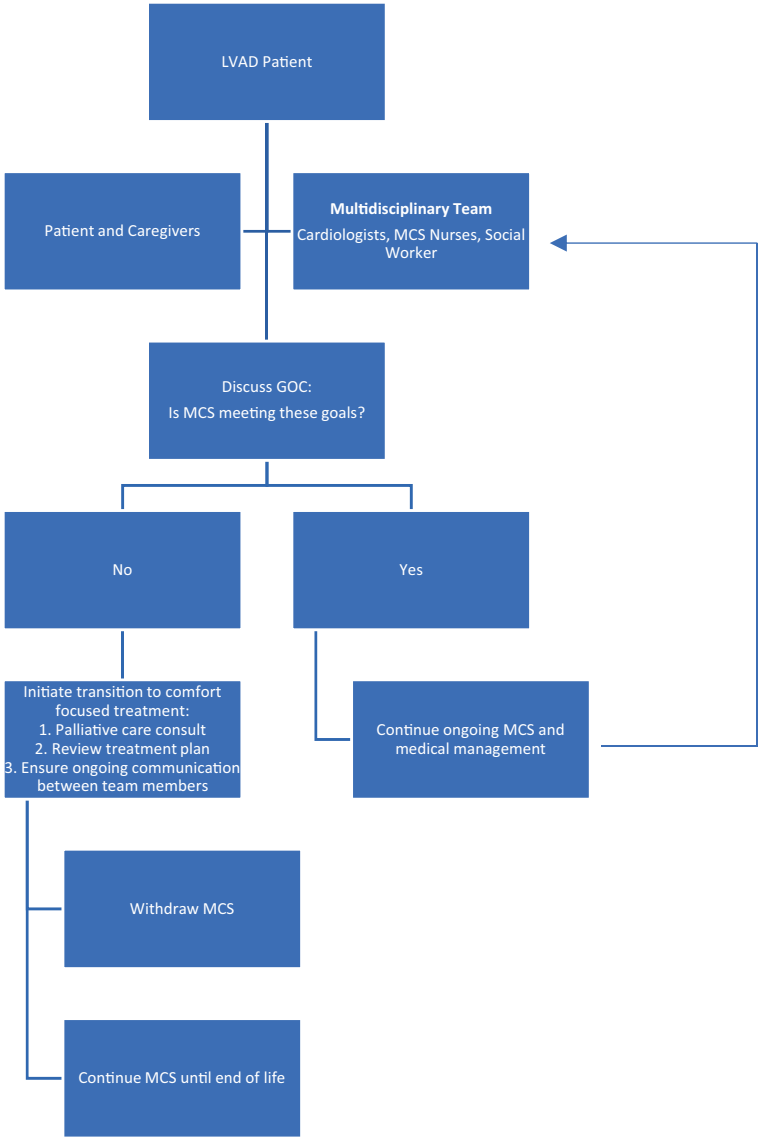

Fig. 2 Flow chart for approach to LVAD and palliative care *LVAD*: *Left ventricular assist device. GOC: Goals of care. MCS: Mechanical circulatory support*

action on behalf of the patient or the provider. Explaining this difference to patients and their caregivers is helpful to guide conversations about device deactivation.

Other important considerations include what other forms of treatment are to be continued or discontinued. Specifically, providers should consider discontinuing antibiotics, vasopressors, tube feeds, ICDs, and mechanical ventilation at the

time of LVAD deactivation. This may be overwhelming to patients and their caregivers therefore it may be helpful to provide more specific recommendations and reassure them that whatever discomfort may arise from discontinuation of a specific treatment will be treated [13, 14]. Finally, the team should discontinue any monitoring that is not directed at symptom relief. This includes non-invasive blood pressure monitoring and pulse oximeters.

LVAD Deactivation

If device deactivation is requested, it is important to review the deactivation process, medications that will be started and/or discontinued, and the expected prognosis without the LVAD. In terms of the setting, LVAD discontinuation usually occurs in the hospital but there have been some cases where this was performed at home [15]. In this situation, a multi-disciplinary team of cardiology, palliative care, case managers and social workers is required to carry this out. First, the process is described to the family. Next the patient and caregivers may decide when and where this will happen. They should be aware that once the pump is off their prognosis is likely a few hours though some patients have been known to survive a few days off their LVAD. Once a time and place has been decided, then the rest of the team can meet the patient and their caregivers.

Prior to LVAD deactivation, it is important to remember than once the pump is turned off, the cardiac output will decrease significantly therefore limiting circulation of these medications. As such it is important to properly medicate patients prior to device deactivation [16]. General goals for premedication include decreasing the respiratory rate to a goal of 16–20 breaths per minute with SQ opioid and SQ anxiolytic to help treat dyspnea and anxiety which will occur after device deactivation [17]. Additional medications may include sublingual opioids or anxiolytics, anticholinergics for increased secretions, or haloperidol for agitation. Symptom onset may be rapid, therefore, providers should be vigilant and be readily able to administer medications quickly to maximize patient's comfort.

Once adequate premedication has been achieved, then they may proceed to LVAD deactivation. To turn off the device, one must turn off the alarms in parallel to turning off the pump in order to avoid setting of an alarm that would be very distressing the patient and their caregivers. This LVAD deactivation can be done by a provider of the MCS team who knows the device. While there are different types of LVADs, the basic deactivation sequence is similar and can be done by a provider or a device representative (Box 1). Alternatively with the Heartmate II or 3 one may reduce the speed below 8,000 rpm or 4,000 rpm respectively to activate the extended silence alarm option (deactivates all alarms for 4 h). Once the pump is off, a patient may experience shortness of breath and anxiety which can be treated with sublingual medications. Patients can decompensate quickly therefore it is important to have a provider nearby who can administer medications efficiently.

Providers should also discuss the plan for after the patient dies since the LVAD may need to be removed before cremation. In this case it may be helpful for providers to communicate with the funeral home to clarify what they would prefer to be done with the machine. If the patient passes at home then they also need to be aware what devices can be kept or which should be returned (e.g. batteries, cables, etc.).

Case Conclusion

Several weeks passed and Mr. MP's functional status continued to decline. Eventually he presented to the hospital with worsening shortness of breath and was found to have recurrent VT which would require cardioversion again. After discussing and clarifying his goals of care with the cardiology, palliative care, and psychiatry teams, the decision was made to proceed to LVAD deactivation and comfort-focused treatment. The patient and his caregiver were made aware of his prognosis of less than a day and after his family and friends gathered the primary cardiology and LVAD teams proceeded with device deactivation. Anxiolytics and pain medications were given to prevent dyspnea and treat his pain. The device was turned off and patient passed away comfortably after 8 h. Condolences were expressed to his caregiver.

Box 1: How to Deactivate an LVAD

Basic Deactivation Sequence Checklist for HeartMate II or 3 LVAD*
1. Remove the battery in the system controller to disable back-up alarms. 2. Press alarm silence button on the controller. 3. Remove power from the controller by removing the black and white cables coming from the main power base unit (simultaneous removal of both cables will limit alarms). 4. Detach the LVAD driveline exiting patient from the controller

*Deactivation sequence for a Heartware LVAD is similar, however, Step 1 may be skipped. (*Adapted from Gafford* et al. *[17])*

Key Points:

- CIED's and LVADs can legally be deactivated at the request of the patient or their appointed surrogate decision maker
- Facilities that take care of patients with CIED's and LVADs should have a protocol in place for CIED deactivation
- Prior to CIED or LVAD deactivation, clinicians should have a discussion with the patient and/or their surrogate decision maker regarding the deactivation process and what the potential outcomes may be. This discussion should be documented in the medical record.
- Deactivation of a CIED requires an order from the responsible physician specifying what therapies should be turned off and what therapies should remain on

- Deactivation of a CIED or LVAD should be done by a knowledgeable and competent clinician or industry employed allied professional according to the order A clinician may opt to not participate in deactivation of a CIED however, they should find a qualified clinician to take their place.

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Section V
Cardiac Resynchronization Therapy (CRT)

Section Editor: Gordon Ho

Indications for Cardiac Resynchronization Therapy

Douglas Darden and Jonathan C. Hsu

Clinical Vignette

A 70-year-old man with chronic ischemic cardiomyopathy (New York Heart Association III, left ventricular ejection fraction (LVEF) 20%), percutaneous coronary intervention to left anterior descending artery and right coronary artery one year prior, and hyperlipidemia presents to clinic to discuss cardiac resynchronization therapy (CRT) candidacy. He is currently tolerating maximal doses of carvedilol, lisinopril, and spironolactone. Electrocardiogram shows normal sinus rhythm, left axis deviation, and nonspecific intraventricular conduction delay with QRS duration 140 ms. Repeat echocardiogram shows a severely dilated left atrium and mildly dilated left ventricle with LVEF 20% and global hypokinesis, unchanged in the past year. Is CRT recommended for this patient?

Introduction

Impaired electromechanical coupling is frequently seen in the progression of heart failure (HF), manifesting as prolonged interventricular conduction on the electrocardiogram or a prolonged QRS duration >120 ms (ms). Approximately one-third of patients with heart failure with reduced ejection fraction (HFrEF) have prolongation of the QRS duration. Furthermore, those with a wide QRS with left bundle branch block (LBBB) morphology have increased mortality compared to those with right bundle branch block (RBBB) [1]. Such dyssynchrony can result in further reductions in cardiac output, worsening functional mitral regurgitation,

D. Darden · J. C. Hsu (✉)
Division of Cardiology, Department of Internal Medicine, University of California, 9452 Medical Center Dr, MC7411, La Jolla, San Diego, CA 92037, USA
e-mail: Jonathan.Hsu@ucsd.edu

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adverse left ventricular (LV) remodeling, and ultimately, worse prognosis [2–7]. Cardiac resynchronization therapy (CRT), by allowing simultaneous pacing of the ventricles, has emerged as a therapeutic strategy to promote reverse remodeling and improvement in mitral regurgitation, systolic function, and cardiac chamber dimensions [8, 9]. Robust data from several large randomized control trials (RCTs) have firmly established the clinical benefit of CRT in alleviating symptoms, preventing hospitalizations, and improving mortality in appropriately selected patients [10, 11].

In this chapter, an overview of the current indications for CRT will be discussed with an emphasis on the 2012 American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) Focused Update on Guidelines for Device-Based Therapy and highlighting the landmark trials.

Indications for CRT

Over the last two decades, the use of CRT has rapidly evolved from a last resort in select patients with severe LV systolic dysfunction and LBBB to a standard therapy in heart failure as tested and validated in large randomized controlled trials, as shown in Table 1. Prior to understanding the specifics of the indications, it is important to first understand when to consider a potential candidate for CRT. The appropriate patient has HFrEF as defined as LVEF $\leq$ 35%, on maximally tolerated doses of guideline-directed medical therapy (GDMT) for HF for at least three months, at least 40 days after a myocardial infarction without revascularization or three months after revascularization, and have treated any reversible cause of LV dysfunction [12]. It is also important to avoid implantation in those with significant comorbidities and/or frailty that limits expected survival to less than a year.

1. **Recommendations for Patients in Sinus Rhythm**

The 2012 ACC/AHA/HRS Focused Update on 2008 Guidelines for Device-Based Therapy proposed several key changes in the recommendations for CRT, as seen in Table 2 [12]. First, a Class I indication was limited to patients with NYHA II, III, or ambulatory IV symptoms despite optimal GDMT and QRS duration $\geq$150. Multiple trials and analyses have showed that the benefit of CRT appears dependent on QRS duration, particularly with more favorable outcomes in those with QRS $\geq$150 ms as compared to those with QRS <150 ms [13–16]. A Class II recommendation is given to patients with QRS $\geq$120 to 150 ms who otherwise qualify for CRT. Those with a QRS <120 ms fail to benefit from CRT even with evidence of mechanical dyssynchrony on echocardiogram, thus CRT is a contraindication in these patients in the absence of a need for frequent ventricular pacing [17, 18].

Secondly, the current guidelines also limit the Class I indication to patients with LBBB. In a meta-analysis of four trials including 5,356 patients, CRT significantly

Table 1 Landmark trials in cardiac resynchronization therapy

Trial, year of publication	N	Patient population	Trial design (follow-up duration)	Endpoints	Findings
Normal Sinus Rhythm and Advanced Heart Failure					
MIRACLE, 2002 [15]	453	• NYHA III-IV • LVEF ≤ 35% • QRS ≥ 130 ms	CRT-P versus OMT (6 mo)	Primary: NYHA class, QOL Secondary: Peak VO_2, LVEDD, clinical composite response	CRT-P ↑ 6MWD (+39 m versus +10 m), ↑ QOL, ↓ NYHA class, ↑ peak VO_2, ↑ LVEF (4.6 vs -0.2%)
COMPANION, 2004 [10]	1520	• NYHA III-IV • LVEF ≤ 35% • QRS ≥ 120 ms	CRT-P/CRT-D versus OMT (15 mo)	Primary: all-cause mortality and hospitalization Secondary: all-cause mortality	↓ primary endpoint for CRT-P and CRT-D (34% and 40%, respectively) versus OMT; ↓ all-cause mortality (CRT-P ↓ 24% [p = 0.06], CRT-D ↓ 36%)
CARE-HF, 2005 [37]	813	• NYHA III-IV • LVEF ≤ 35% • QRS ≥ 120 ms • LVEDD > 30 mm	CRT-P versus OMT (29.4 mo)	Primary: all-cause mortality or CV hospitalization Secondary: all-cause mortality, NYHA, QOL	CRT-P ↓ all-cause mortality or hospitalization; ↓ all-cause mortality; ↑ LV measures and QOL
Normal Sinus Rhythm and Mild Heart Failure					
REVERSE, 2008 [47]	610	• NYHA I-II • LVEF ≤ 40% • QRS ≥ 120 ms • LVEDD > 5.5 cm	CRT-on versus CRT-off (12 mo)	Primary: HF clinical composite score Secondary: LVESV index, HF hospitalizations and all-cause mortality	No improvement in primary endpoint in CRT-on versus CRT-off (16% vs 21%, p = 0.10). CRT-on did have ↓ LVESV, ↑ LVEF, and delay in time-to-first hospitalization (HR: 0.47, p = .03)
MADIT-CRT, 2009 [48]	1820	• NYHA I-II • LVEF ≤ 30% • QRS ≥ 130 ms	CRT-D versus ICD (2.4 years)	Primary: all-cause mortality or HF hospitalizations Secondary: All-cause mortality or LVESV	↓ primary endpoint with CRT-D (17% vs 25% with HR 0.66, p = 0.001) driven by 41% reduction in HF events. ↓ LVSEV. No reduction in all-cause mortality
RAFT, 2010 [11]	1798	• NYHA II-III • LVEF ≤ 30% • QRS ≥ 120 ms	CRT-D versus ICD (40 mo)	Primary: all-cause mortality or HF hospitalizations Secondary: all-cause mortality or cardiovascular death	CRT-D ↓ primary endpoint (33% vs 40%). ↓ mortality (29% vs 35%).

(continued)

Table 1 (continued)

Trial, year of publication	N	Patient population	Trial design (follow-up duration)	Endpoints	Findings
Chronic RV Pacing and Permanent Atrial Fibrillation					
BLOCK-HF, 2013 [32]	918	• NYHA I-III • LVEF ≤ 50% • Indication for pacing with AV block	CRT versus RV pacing (37 mo)	Primary: all-cause mortality, acute HF, increase in LVESV > 15% Secondary: composite of all-cause mortality, acute HF, and hospitalization	CRT ↓ composite outcome (HR 0.74; 95% CI, 0.60–0.90); CRT ↓ secondary outcomes except death
APAF-CRT, 2018 [49]	102	• Permanent atrial fibrillation • Narrow QRS (≤110 ms) • One HF hospitalization in previous year	AV junction ablation and CRT versus OMT (16 mo)	Primary: Death due to HF, HF hospitalization, worsening HF Secondary: All-cause mortality, HF hospitalization, worsening HF.	Ablation + CRT ↓ primary endpoint (20% vs 38%) and ↓ secondary endpoint in ablation + CRT
Narrow QRS					
RethinQ, 2007 [17]	172	• NYHA III • LVEF ≤ 35% • QRS < 130 ms	CRT-D versus ICD (6 mo)	Primary: Peak VO_2	No change in peak VO_2
ECHO-CRT, 2013	1680	• NYHA I-IV • LVEF ≤ 35% • QRS <130 ms • Evidence of echo dyssynchrony	CRT-on versus CRT-off (19 mo)	Primary: all-cause mortality or HF hospitalization Secondary: HF events	Study stopped with significant ↑ in mortality with LVEF ≤ 35% and narrow QRS

Abbreviations: NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; OMT, optimal medical therapy; CRT-P, cardiac resynchronization therapy pacing; CRT-D, cardiac resynchronization therapy defibrillator; QOL, quality of life; LVEDD, left ventricular end diastolic dimension; HR; hazard ratio; CV, cardiovascular; LVESV, left ventricular end systolic volume; ICD, implantable cardiac defibrillator; AV, atrioventricular

reduced the composite adverse clinical events by 36% in those with a LBBB [19]. No benefit was observed in those with right bundle branch block (RBBB) or nonspecific intraventricular conduction delay (NICD). Nonetheless, other studies still suggest a wide QRS duration in patients with advanced HF and non-LBBB morphologies is associated with enhanced reverse remodeling and improved long-term outcomes following CRT [11, 20].

Lastly, perhaps the most significant changes of the updated guidelines include the expansion of Class I recommendation to NYHA class II patients (with QRS $\geq$ 150 ms and LBBB) and the addition of a Class IIb recommendation to patients with NYHA class I patients (with LVEF $\leq$ 30%, ischemic etiology of HF, and LBBB $\geq$ 150 ms). These changes are largely due to the publication of three major trials: REVERSE (Resynchronization Reverses Remodeling in Systolic LV Dysfunction), MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial with CRT), and RAFT (Resynchronization-Defibrillation for Ambulatory HF Trial) as described in Table 1.

2. **Recommendations for Patients in Permanent Atrial Fibrillation**

Another update based on the most recent guidelines from 2012 involves a class II recommendation for CRT in patients with permanent AF and LVEF < 35% with important caveats: if the patient requires ventricular pacing or otherwise eligible for device therapy, and atrioventricular (AV) nodal ablation or pharmacological rate control will allow near 100% ventricular pacing [12]. As clinical trials of CRT have included patients mainly in sinus rhythm, concerns exist in whether patients with permanent atrial fibrillation (AF) derive similar benefit. The presence of AF may compete with CRT pacing due to sensed events, preventing effective biventricular pacing. RAFT remains the largest randomized trial to date to include a substantial portion of patients with AF receiving a CRT device (n = 229 or 12.7%) [11]. A post hoc analysis of RAFT failed to show a benefit in patients with permanent AF who were randomized to CRT-D as compared to ICD alone [21]. However, several studies have suggested that benefit from CRT is most evident in patients when it is coupled with atrioventricular nodal ablation, thereby avoiding potentially deleterious effects of chronic RV pacing [22–26]. Although AV nodal ablation combined with CRT may be considered in those with permanent AF with persistently high ventricular rates, it is not without risk and concerns exist that AV nodal ablation renders patients pacemaker-dependent. Other strategies, particularly the use of ablation with pulmonary vein isolation in patients with HF and paroxysmal or persistent AF, should be considered first [27].

3. **Recommendations for Anticipated Significant Ventricular Pacing**

Chronic right ventricle (RV) pacing can mimic the dyssynchronous effects of LBBB, leading to progressive LV dysfunction, particularly in patients with pre-existing LV dysfunction [28]. The deleterious effects of chronic RV pacing were evaluated in the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial. The trial showed that patients with LVEF $\leq$ 40% with an implantable cardiac defibrillator (ICD) programmed to dual-chamber pacing had increased HF admissions

and mortality rate compared to sinus rhythm [29]. A post hoc analysis found that patients with RV pacing cut-off of >40% was associated with worse outcomes [30]. A similar finding was observed in the MADIT II trial where those with >50% RV pacing had worse outcomes [31]. Based on the available literature at the time, the current guidelines provide a Class IIa recommendation for CRT in patients with LVEF ≤ 35% and are undergoing new or replacement device with anticipated requirement for significant (>40%) RV pacing.

Since the publication of the 2012 updated guidelines, the results of the BLOCK-HF (Biventricular Pacing for Atrioventricular Block and Systolic Dysfunction) demonstrated the benefit of CRT in a select group of patients not currently represented by the guidelines. Published in 2013, the trial demonstrated superior outcomes in patients implanted with CRT as compared to RV-only pacing in those with NYHA class I-III, LVEF ≤ 50% and atrioventricular block, in which ventricular pacing is obligatory [32]. The results of the BLOCK-HF study have already changed clinical practice and will likely liberalize the LVEF cut-off in those with high anticipated RV pacing in future guidelines.

4. **Recommendations for Upgrade to CRT**

Based on extrapolation from the 2012 updated guidelines, in patients with HFrEF who have a single or dual chamber pacemaker or ICD that subsequently develop worsening HF with high burden of RV pacing or a wide QRS that then meet criteria for CRT, an upgrade to CRT may be considered. Despite lack of evidence-based data, upgrade procedures are becoming increasingly common, particularly with heightened awareness of detrimental high RV pacing burden [33]. Importantly, upgrade procedures may be associated with worse outcomes than de novo implantations [34–36]. Thus, the benefits of CRT upgrade should be weighed against the procedural risk and complexity of adding the additional lead.

5. **Recommendations for CRT-D versus CRT-P**

The guidelines do not make specific recommendations regarding the choice between CRT-D and CRT-P. The COMPANION trial failed to show a difference in outcomes between CRT-P and CRT-D, although it lacked powered [10]. The CARE-HF trial was the first to provide evidence that CRT-P alone reduces mortality compared to medical therapy, but CRT-D was not compared [37]. It remains unclear if CRT reduces the need for an ICD by reverse remodeling and reduction in arrhythmia burden. Although a post hoc analysis from the REVERSE trial demonstrated that reverse remodeling with CRT was associated with a reduction of ventricular tachycardia (VT) [38], causal inferences cannot be made. Understandably, if a patient is scheduled for ICD implantation based on the current recommendations and is also eligible for CRT with life expectancy >1 year, then CRT-D should be considered. However, there may be a role for CRT-P in

Table 2 Indications for CRT implantation based on the 2012 ACCF/AHA/HRS focused update guidelines for device-based therapy

Patients in sinus rhythm with moderate to severe heart failure (NYHA III-IV)	
Class I, Level of Evidence A	• LVEF ≤ 35% despite OMT • LBBB • QRS ≥ 150 ms
Class IIa, Level of Evidence A	• LVEF ≤ 35% despite OMT • Non-LBBB • QRS ≥ 150 ms
Class IIa, Level of Evidence B	• LVEF ≤ 35% despite OMT • LBBB • QRS 120–149 ms
Class IIb, Level of Evidence B	• LVEF ≤ 35% despite OMT • Non-LBBB • QRS 120–150 ms
Class III: No Benefit	Comorbidities and/or frailty limit survival with good functional capacity < 1 year
Patients in sinus rhythm with mild heart failure (NYHA II)	
Class I, Level of Evidence B	• LVEF ≤ 35% despite OMT • LBBB • QRS ≥ 150 ms
Class IIa, Level of Evidence B	• LVEF ≤ 35% despite OMT • LBBB • QRS 120–149 ms
Class IIb, Level of Evidence B	• LVEF ≤ 35% despite OMT • Non-LBBB • QRS ≥ 150 ms
Class III: No Benefit	• LVEF ≤ 35% • Non-LBBB • QRS ≤ 150 ms
Patients in sinus rhythm and mild heart failure (NYHA I)	
Class IIb, Level of Evidence C	• LVEF ≤ 35% despite OMT • LBBB • QRS ≥ 150 ms • Ischemic cardiomyopathy
Class III: No Benefit	• QRS ≤ 150 ms • Non-LBBB
Special CRT indications	
Class IIa, Level of Evidence B	Anticipated to require frequent ventricular pacing (>40%) with LVEF ≤ 35%
Class IIa, Level of Evidence B	Atrial fibrillation, if ventricular pacing is required and rate control will result in near 100% biventricular pacing

Abbreviations: NYHA; New York Heart Association; LVEF, left ventricular ejection fraction; OMT; optimal medical therapy; LBBB, left bundle branch block

select patients for relief of symptoms without defibrillation back-up, such as elderly and frail patients with significant co-morbidities, such as severe renal insufficiency or dialysis, advanced heart failure [12, 39, 40], or controversially, those with non-ischemic cardiomyopathy [41, 42]. Until randomized data provides insight into this clinical dilemma, the choice of the device will largely be decided by the implanting physician.

6. Pre-Implantation Considerations for Predicting Response in CRT Recipients

At least one-third of patients fail to achieve benefit from CRT [43]. Although there currently does not exist a standard definition to define response, several studies have used various clinical, functional, and structural measures with various predictors of response (Table 3). In a subanalysis of the MADIT-CRT, Hsu et al. identified six baseline factors that predicted LVEF super-response in CRT-D patients, defined as the top quartile of LVEF change (mean increase $17.5 \pm 2.7\%$) [44]. The predictors included female sex, no prior myocardial infarction, left bundle branch block, QRS duration $\geq$150 ms, body mass index <30 kg/m^2, and smaller baseline left atrial volume index. As evidenced by the trials and guidelines, those with LBBB and QRS duration >150 ms have the highest likelihood of response, thus earning the highest recommendation [12]. However, women have consistently been under-represented in large-scale clinical trials of CRT and guidelines fail to differentiate gender. Gender has been shown to have differing impacts on CRT response in relation to QRS duration, as women tend to respond favorably to CRT at a markedly higher rate than men at QRS < 150 ms [45]. Furthermore, the benefits of CRT in those with RBBB, regardless of QRS duration, may have little benefit from CRT [46]. Understanding the clinical predictors that can affect the likelihood of CRT response will help with optimizing patient selection and maximizing response.

Table 3 Pre-implantation predictors of CRT response

High likelihood of response	Less likely to respond	Likely no benefit
Female	QRS duration 120–150 ms	RBBB
LBBB	High LV scar burden	End stage renal disease
QRS duration $\geq$150 ms	Atrial fibrillation	QRS $\leq$ 120 ms without pacing requirement
Nonischemic cardiomyopathy	Advanced co-morbidities	Life expectancy < 1 year
Body mass index <30 kg/m^2	Medical therapy not optimized	
Small left atrial volume index[a]	NICD	
	Right ventricular dysfunction	

[a]Per 1-U standard deviation below mean

Case Conclusion

To review, the patient is a 70-year-old man with ischemic cardiomyopathy (LVEF 20%) despite OMT, NYHA class III, normal sinus rhythm with a QRS duration of 140 ms with a non-LBBB morphology. He is expected to live >1 year. CRT recommendation for this patient is currently a Class IIb, level of evidence B. Importantly, the patient has unfavorable characteristics that suggest he is less likely to respond to CRT, such as ischemic etiology, non-LBBB, QRS <150 ms, and male gender. After a shared decision-making discussion regarding continued symptoms, potential benefits, and risks of the procedure, the patient elected to proceed with CRT implantation. Given his life expectancy and personal choice, he elected for CRT-D.

Future Directions

Improved algorithms are being developed and tested to optimize patient selection and optimization for CRT and LV lead targeting using electrocardiographic and imaging techniques to identify sites of dyssynchrony.

Key Points:

- The highest recommendation for CRT is in those with patients in sinus rhythm, LVEF <35%, QRS >150 ms with a LBBB morphology.
- As QRS duration shortens or in those with non-LBBB morphology, the guideline recommendations become weaker for CRT.
- Patients in permanent atrial fibrillation derive less benefit from CRT than patients in sinus rhythm and may benefit from AVN ablation with CRT.
- Patients with HF and anticipated or high RV pacing (>40%) benefit from CRT as opposed to dual chamber pacemaker.
- Data is limited on the CRT-D versus CRT-P and is often left to physician discretion.

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Implant Considerations for the CRT Device

Douglas Darden and Jonathan C. Hsu

Clinical Vignette

A 65-year-old woman with history of ischemic cardiomyopathy (New York Heart Association class (NYHA) III, left ventricular ejection fraction (LVEF) 30% with left bundle branch block and QRS duration 150 ms, coronary artery bypass surgery, hypertension, and hyperlipidemia presents to clinic six months post cardiac resynchronization therapy (CRT) implantation. She is currently tolerating maximal doses of carvedilol, sacubitril/valsartan, and spironolactone. Follow-up echocardiogram remains unchanged with LVEF 30% and she reports no change in symptoms. What important implant consideration should be reviewed?

Introduction

The CRT device includes three leads (right atrial, right ventricle (RV), and left ventricle (LV)) with a three-lead pulse generator. The RV pacing lead or defibrillation lead is secured into the RV apex, apical septum, mid septum, or outflow tract. It is often placed first to provide back-up in case of complete heart block. The right atrial lead allows sensing and tracking of sinus rhythm to synchronize ventricular activation, although occasionally the right atrial lead may be omitted in patients with permanent AF. It is typically placed last in order to avoid lead dislodgement during LV lead placement. While inserting the right atrial and right ventricular leads are typically straightforward, the LV lead implantation may be more complex. There are several factors that affect final LV lead location,

D. Darden · J. C. Hsu (✉)
Division of Cardiology, Department of Internal Medicine, University of California, 9452 Medical Center Dr, MC7411, La Jolla, San Diego, CA 92037, USA
e-mail: Jonathan.Hsu@ucsd.edu

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including varied venous anatomies, delivery and stability of the LV implantation tools, presence of phrenic nerve stimulation, and high LV pacing thresholds. Implanters need to be prepared to address all potential challenges in order to provide long-term effective therapy.

1. **Location and Cannulation of Coronary Sinus**

The coronary sinus (CS) ostium is located in the posterior and inferior portion of the right atrium, medial to the inferior vena cava opening and superior to the tricuspid valve septal leaflet (Fig. 1A). Locating the CS ostium has improved with the telescopic sheath-in-sheath system connected to a contrast injection system, which allows for direct CS visualization and cannulation with the use of a small guide wire [1]. By first placing the guide catheter at the tricuspid annulus or into right ventricle, counterclockwise torque is then applied to direct the guide posteriorly and upward toward the CS ostium. Puffs of contrast may be used to help locate the CS ostium. Once identified, the guidewire is then advanced. If cannulation is difficult, a new catheter can be chosen, or alternatively, an electrophysiology CS catheter (to record intracardiac electrocardiogram) or interventional guide catheter can be used [2].

Failure to cannulate the coronary sinus (CS) is a common reason for failed LV lead implantation [3]. Various shapes of catheters are available to aid in cannulation, and the chosen method depends on the implanter's techniques and patient-specific variations of right atrium anatomy.

2. **Coronary Sinus Venography and Selection of Target Vein**

Although it is possible to place the LV lead without venography, it may be advisable to visualize the branches to ensure optimal placement. Once the CS is successfully entered, non-occlusive venography may be sufficient to identify the optimal target vein, a lateral, posterolateral, or anterolateral branch of the CS (Fig. 1B). If unsuccessful, occlusive venography with a balloon-tip catheter can be performed. Multiple views should be used to identify all possible target branches and allow adequate cine time to visualize late filling vessels (Fig. 2).

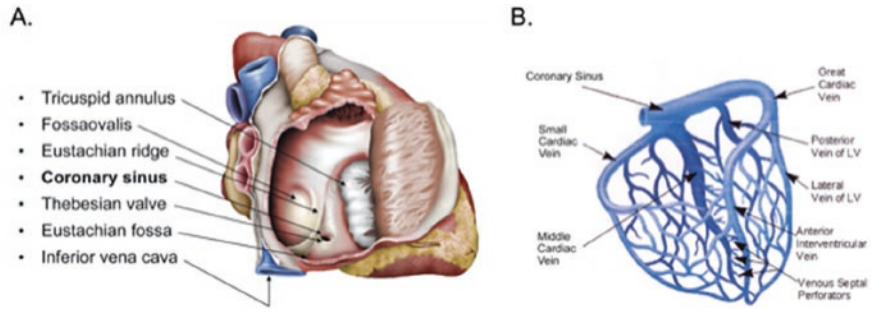

Fig. 1 (**A**) Anatomy demonstrating the location of the coronary sinus ostium. (**B**) Cardiac venous anatomy

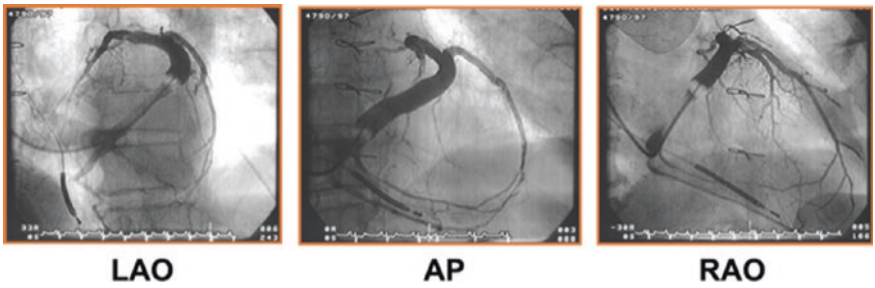

Fig. 2 Left anterior oblique (LA), anteroposterior (AP), and right anterior oblique (RAO) fluoroscopic venography images

3. **LV Lead Placement**

Depending on the anatomy, this step can be either straightforward or tedious. To advance the LV lead into the CS vasculature, a guide wire and the LV lead are passed through the guide catheter. An inner guide may be used for stability and to aid in advancement. The guide wire is then advanced as far as possible into the target vein and the lead can then be tracked along the guide wire to the desired location.

The optimal target vein for the LV lead is a location that will preferably avoid scar and will pace at the site of the greatest electrical and mechanical delay. As the lateral wall is the last segment to contract in the setting of a LBBB, targeting the anterolateral, lateral, posterior, or posterolateral branches of CS are preferred locations, as shown in Fig. 3 [4]. LV apical pacing should be avoided as post hoc analysis from the MADIT-CRT trial showed LV apical pacing was associated with higher risk of heart failure hospitalization and death [5]. Furthermore, achieving maximal and electrical separation between the right and left ventricular leads has shown to result in improved synchrony and hemodynamics [6].

At the target vein site, threshold testing is performed to confirm adequate pacing thresholds, as areas of scar may be difficult to capture [7]. Additionally, high output pacing is performed to assess for phrenic nerve stimulation, given its close anatomical proximity to the lateral pacing sites [8]. The selection of the optimal pacing vector is often chosen by the greatest narrowing of the QRS complex or lowest threshold. In addition, electrical delay can be assessed during implantation by calculating the delay between the surface QRS and the initial sensed LV lead electrogram (Q-LV). LV lead placement at the site of increasing Q-LV has been shown to be associated with greater rates of reverse remodeling and symptom improvement [9].

The use of the quadripolar pacing leads (three spaced electrodes and a tip electrode) allows more pacing options to avoid high pacing thresholds and phrenic nerve stimulation and ensure optimal LV lead placement during and post-implantation [10–12]. The quadripolar LV leads have been associated with a reduction in LV lead deactivation, replacement, and mortality [13]. Of importance, if a hemodynamically suboptimal LV lead is unavoidable transvenously, it may be reasonable to implant an epicardial lead instead.

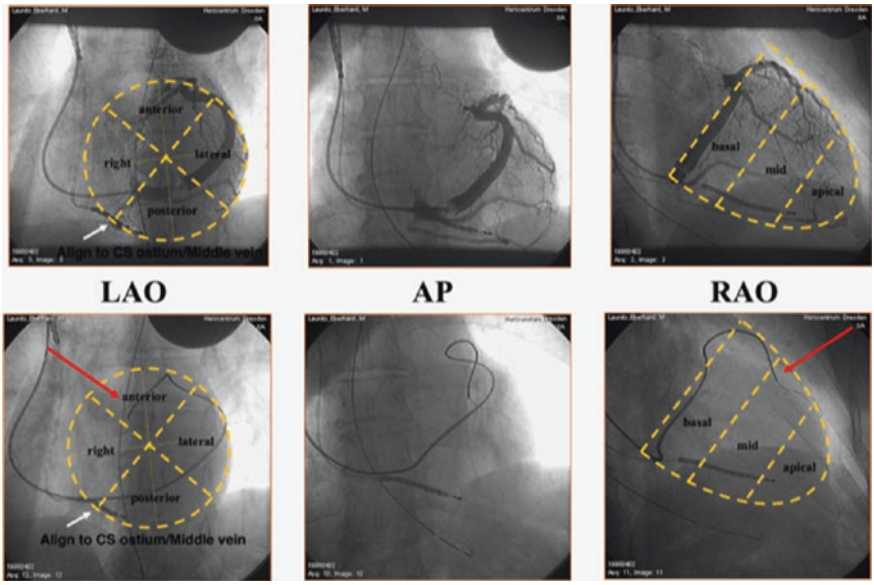

Fig. 3 Fluoroscopic projections demonstrating appropriate left ventricular lead placement in the anterolateral cardiac vein as depicted by red arrow

Once an acceptable position is obtained, the guidewire and guide catheter are withdrawn. LV lead redundancy is best observed in the right anterior oblique (RAO) view and should be excessive as this can contribute to lead dislodgment.

4. His Bundle Pacing

His bundle pacing may be a potential alternative to CRT. His bundle pacing (HBP) is theoretically an ideal site for synchronized ventricular pacing as it retains the intrinsic conduction system and narrow QRS [14]. However, the first pilot trial, His-SYNC (His Bundle Pacing versus Coronary Sinus pacing for CRT), randomized 41 patients to His-CRT or biventricular-CRT with a 12-month follow-up [15]. The trial showed no difference in respect to improvements in QRS or LVEF or time to cardiovascular hospitalization or death. Given the small sample size and high crossover rates, larger prospective trials will be needed.

5. Troubleshooting

Success in CRT implantation is over 90%, however issues may arise that implanting physicians need to be able to overcome [16]. Table 1 lists common problems and potential solutions.

Access Problems

Especially in CRT upgrades, the ipsilateral subclavian vein may appear occluded. Venography should be performed initially. If an occlusion is confirmed, a few

Table 1 Troubleshooting CRT implantation

Problem	Solution
Difficult venous access	• Perform LV venography on ipsilateral arm • Percutaneous venoplasty • Tunneling the LV lead from contralateral side • Abandonment of original device and then implantation on contralateral side • Epicardial LV lead placement
Difficulties in coronary sinus cannulation and advancement	• Use telescopic sheath-in-sheath system with contrast *The besian valve or tortuous proximal segment* • Advance inner 5F inner guide catheter over guide-wire to create a "rail" to advance CS sheath • Balloon dilatation and guide-wire advancement *Vieussens valve* • Carefully use 0.035-inch guidewire or steerable EP catheter
Difficulties in LV lead implantation	• Use stiffer wire • Snaring technique with goose neck snare • Venoplasty of target vein • Consider surgical LV lead placement

options exist. First, crossing the occlusion with a wire to perform venoplasty may be attempted. Secondly, obtaining access and placing the lead on the contralateral side followed by tunneling the lead anteriorly to the sternum and then to the original device pocket can be used in CRT upgrades. Similarly, implanting on the contralateral while abandoning the original leads may be considered. Lastly, epicardial lead placement can be utilized.

Coronary Sinus Cannulation and Advancement Issues

If coronary sinus localization is unsuccessful with contrast injection and catheter manipulation, then coronary sinus atresia may be considered [17]. Also, occasionally a prominent Thebesian valve, a fold at the origin of the CS, or proximal tortuous segment may prevent the outer catheter from advancing. A few options may be considered. Entering from the inferior and ventricular portion where the valve is less prominent may suffice. Otherwise, the use of a steerable EP catheter may be advanced to provide support for the guiding catheter. Another technique includes advancing a guidewire and then advancing a 5F catheter straight, hydrophilic inner catheter over the wire to create a "rail" to pass the CS sheath. If there is still resistance to the CS sheath, then can use a stiff 0.035-inch wire to provide additional support. Another approach uses an occlusive balloon is dilated to straighten tortuous segments to allow CS sheath advancement [1]. The valve of Vieussens may be found at the junction of the great cardiac vein and CS that may also cause resistance. Typically, gently passing 0.035-inch wire will allow adequate support to advance the lead.

Difficulties in Placing LV Lead
In situations where the guidewire is delivered to the target vein, but the LV lead fails to advance, a stiffer wire will provide additional support and may allow advancement. If still unsuccessful, snaring of the distal end of the guidewire may provide the needed additional support. The snare technique first involves advancing the guidewire retrograde to the CS through the target branch and back into the main body of the CS via collateral vessels. If a 9F catheter CS guide is a used, a 4F catheter Gooseneck snare and lead are advanced into the lumen through the guide. Smaller CS sheaths require separate venous access for snaring and another CS cannulation. The use of the snare technique avoids the use of venoplasty, which may be another option [18]. If there is still failure to deliver LV lead, the surgical LV lead placement should be considered as opposed to unsuitable target vein location.

Conclusion

Optimal placement of the LV lead of the CRT device is a requirement for favorable CRT response. In order to ensure success and optimization of the CRT device, knowledge of implantation strategies and techniques to overcome challenges are essential.

Case Conclusion

To review, the patient is a 65-year-old woman with ischemic cardiomyopathy (LVEF 35%, NYHA III) post six months CRT implantation with no improvement in LVEF or symptoms. She was appropriately selected by guideline recommendations (Class IA). In clinic, an electrocardiogram was performed that showed a negative QRS in lead V1 and chest X-ray revealed the LV lead was likely placed in the anterior interventricular vein. The patient returned to the electrophysiology lab to successfully reposition LV lead into a posterolateral venous branch. At three-month follow-up, the patient had improvement in LVEF to 45% and improvement in symptoms, now NYHA class II.

Key Points:

- The telescopic sheath-in-sheath system results in higher success in CS cannulation and LV lead insertion.
- The lateral or posterolateral branches of CS are preferred locations for LV lead delivery. Testing to avoid locations of scar should be performed.
- The quadripolar LV leads have been associated with a reduction in LV lead deactivation, replacement, and mortality.

- Successful CRT implantation requires knowledge of the tools and techniques to overcome challenges, such as difficulties in access, CS cannulation and advancement, and LV lead implantation.

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Cardiac Resynchronization Therapy Programming and Troubleshooting

Kunal Shah and Farshad Raissi

Case Scenario

A 55 year old female with nonischemic cardiomyopathy, ejection fraction of 25%, chronic left bundle branch block presents to clinic with ongoing dyspnea. She experiences shortness of breath while climbing stairs or walking more than one block with her dog. She has been on guideline directed medical therapy with carvedilol, valsartan, spironolactone and furosemide for the last 4 months. Her electrocardiogram(EKG) is shown below (Fig. 1).

Given her clinical scenario, the patient qualifies for cardiac resynchronization therapy-defibrillator (CRT-D) implantation based on American College of Cardiology (ACC) guidelines as a IIA recommendation [1]. While her QRS is not greater than 150 ms, she can still potentially receive benefit from CRT given her persistent NYHA II symptoms.

CRT Pacing

In contrast to implantable cardioverter-defibrillators (ICDs), the goal of CRT is 100% biventricular (BiV) pacing to overcome conduction delays and improve cardiac function. Appropriate CRT can reduce mortality, hospitalizations and improve symptoms [2, 3].

Improving CRT response begins with patient selection. Classically, a high likelihood of positive clinical response is seen in female, non-ischemic patients with left bundle branch block of more than 150 ms [3]. There are nuances to this and

K. Shah · F. Raissi (✉)
University of California San Diego, 9452 Medical Center Dr, 3rd Floor Rm 3E-507, La Jolla, San Diego, CA 92037, USA
e-mail: fraissi@health.ucsd.edu

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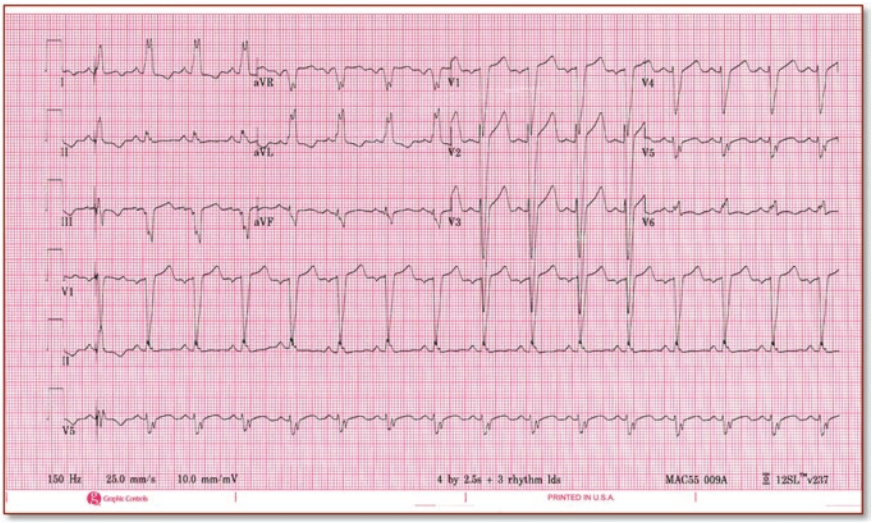


Fig. 1 Electrocardiogram obtained from the clinic visit in the case vignette, showing sinus rhythm with a left bundle branch block with QRS duration 140 ms

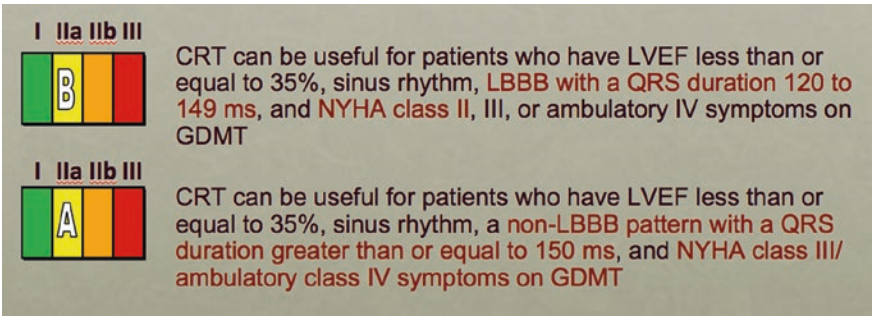


Fig. 2 Other clinical scenarios to consider cardiac resynchronization therapy, listed as Class IIA indications taken from the 2012 ACC/AHA guidelines [Tracy et al, Circulation, 2012]

the ACC/HRS guidelines shown below depict other possible scenarios where CRT might be beneficial [1] (Fig. 2).

During left ventricular (LV) lead implantation, electrophysiologists localize ideal lateral and basal lead positions to provide adequate separation from the right ventricular (RV) lead. Contemporary LV leads have 4 poles which provide numerous pacing vector options [4]. The available options for choice of vectors varies among manufacturers (Fig. 3).

Pacing from a site with more delayed electrical activation leads to improved clinical outcomes [4, 5]. This electrical delay is measured as the QLV. It is defined

Vector	Cathode to Anode
Vector 1	Distal 1 to Mid 2
Vector 2	Distal 1 to Proximal 4
Vector 3	Distal 1 to RV Coil
Vector 4	Mid 2 to Proximal 4
Vector 5	Mid 2 to RV Coil
Vector 6	Mid 3 to Mid 2
Vector 7	Mid 3 to Proximal 4
Vector 8	Mid 3 to RV Coil
Vector 9	Proximal 4 to Mid 2
Vector 10	Proximal 4 to RV Coil

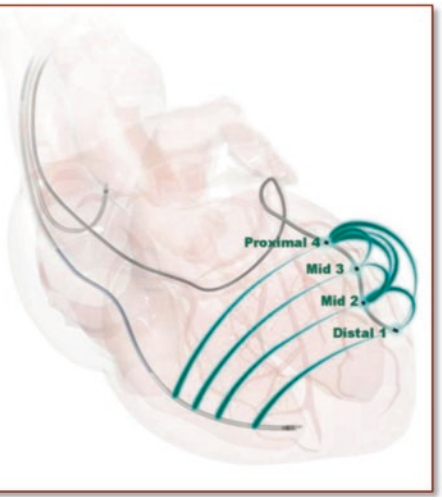


Fig. 3 Contemporary quadripolar provide more pacing options to optimize cardiac resynchronization therapy, such as avoiding phrenic capture

as the interval from earliest onset QRS on surface EKG to the center of largest peak on unipolar LV lead electrogram(EGM) [see examples below]. The ratio of QLV over QRS duration (QRSd) can serve as a marker of optimal position. A QLV to QRSd ratio of >0.7 has been show to correlate with reduced mortality and HF hospitalizations [5, 6] (Fig. 4).

Another marker of desirable late activation is a longer activation between RV and LV lead EGMs. An RV to LV difference of greater than 67 ms has been shown to correlate with better clinical outcomes including heart failure free survival [7] (Fig. 5).

Features such as LV capture management (Medtronic) can help with automatic adjustment of LV pacing output to ensure LV capture and hence true biventricular (BiV) pacing. Many of these features are now automated and can scan all possible vectors for threshold outputs, optimal timing intervals and expected effect on battery life. The Medtronic Vector Express is shown below as an example of this automation (Fig. 6).

Pacing Modes

In general, DDD (or DDDR) mode is the preferred mode for maximized CRT in patients in sinus rhythm. In this mode, sensing and pacing is performed both in atrial and ventricles. In patients with atrial fibrillation or atrial arrhythmias VVI (and times VDIR mode) is preferred.

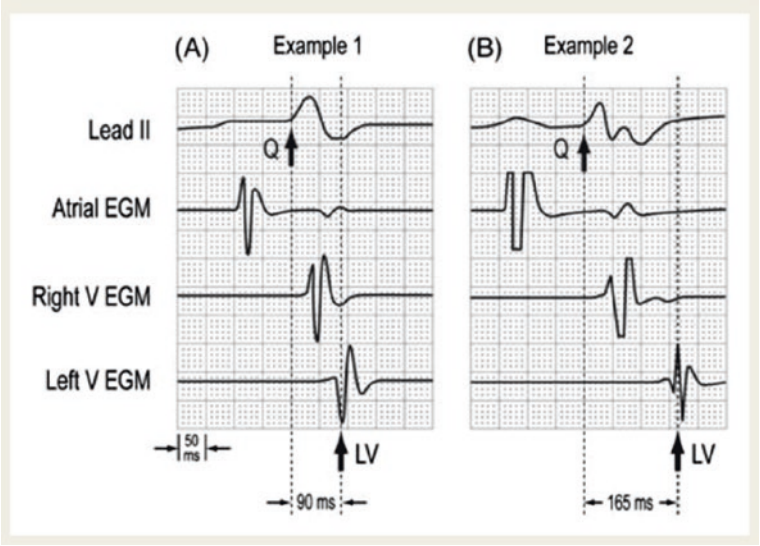


Fig. 4 Measurement of latest activation (QLV) of the LV lead electrode, as measured from the onset of QRS to sharpest peak of LV electrogram. [QLV: intrinsic left ventricular delay, LV: left ventricular] Reprinted with permission from Gold et al, Heart Rhythm, 2017

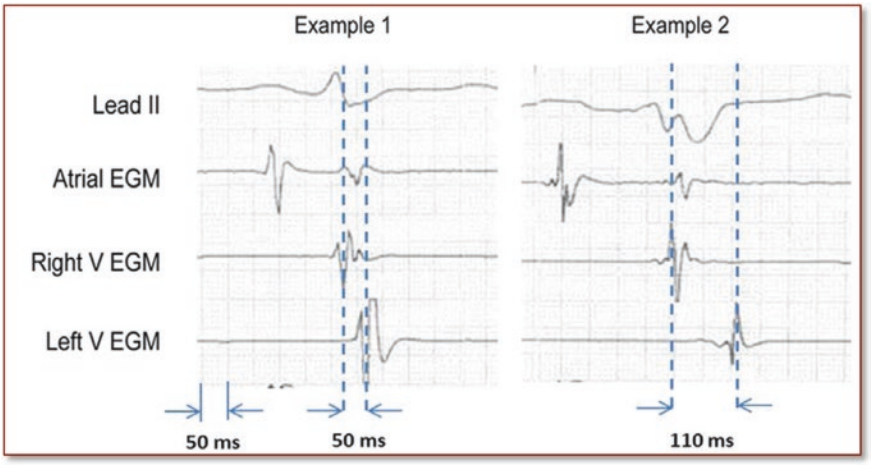


Fig. 5 LV capture management feature from Medtronic to ensure true left ventricular capture. Reproduced with permission from Medtronic Inc

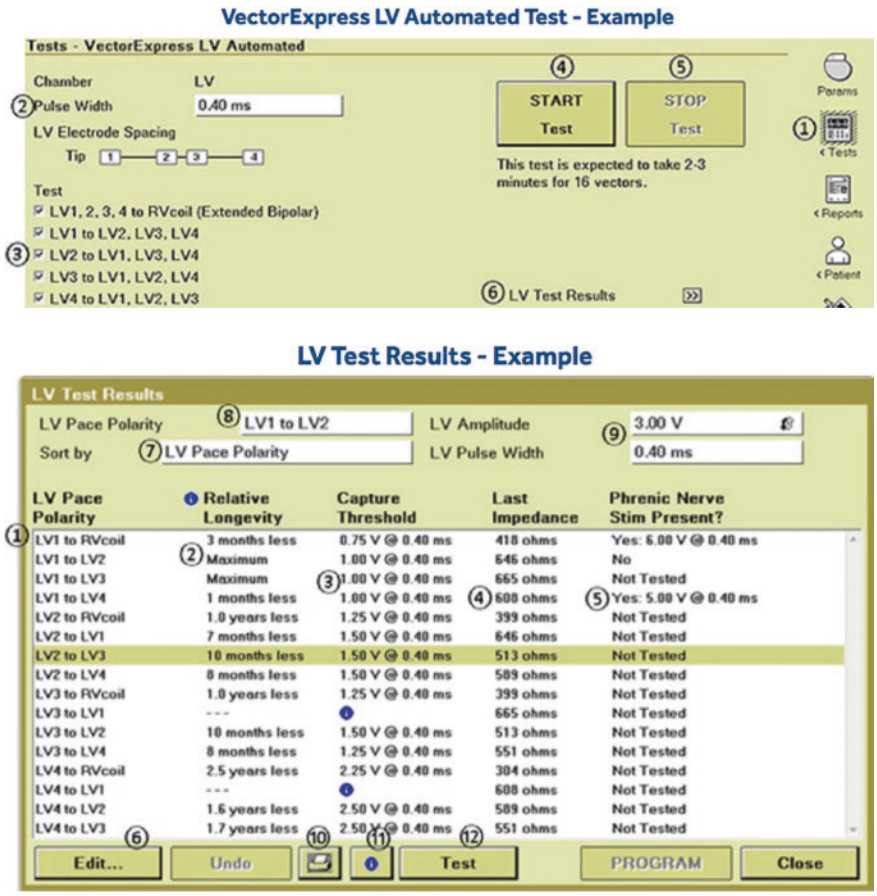


Fig. 6 (2 panels). Example of the VectorExpress optimization toolkit from Medtronic to optimize A-V and V-V timing and thresholds. Reproduced with permission from Medtronic Inc

CRT Programming

Over the last two decades, there has been much effort in optimizing electrical and mechanical synchrony and many modalities attempted to provide the best response from CRT. For example, early methods involved adjust timing based on real time echocardiographic findings in attempt to maximize LV filling. A summary of the various modalities and their advantages and shortcoming is displayed below

Table 1 Advantages and disadvantages of methods to optimize cardiac resynchronization therapy

CRT optimization method	Advantages	Disadvantages
Echocardiogram	> Noninvasive > Portable > Widely available > Multiple variables assessed in one exam	> Cost $$ > Time > Limited repeatability > Operator dependent
MRI	> High spatial resolution > Accurate chamber size quantification > Reproducible	> Cost $$$ > Time > Complex post processing techniques > Limited availability
Invasive hemodynamics/ Pressure volume loop	> Real time information on contractility and true cardiac output	> Cost $$$$ > Invasive > Time > Limited repeatability
EKG and EGM based	> Automated options on select CRT platforms > Ease of use, can be done repeatedly in clinic setting	> Variable accuracy > Inconsistency with clinical outcome

(Table 1). The rigorous 2008 PROSPECT study analyzed 12 different echocardiographic parameters to discern if any could predict CRT response; however, no echocardiographic parameter of dyssynchrony improved patient selection for CRT nor consistently provided accurate prediction of outcome.

Unfortunately, no one method has proven to be superior in producing enhanced clinical outcomes.

There has been a more recent trend to use electrocardiographic and device-based approach to CRT optimization in clinical day-to-day practice. Each device company has unique optimization algorithms to make CRT as effective as possible.

Atrioventricular (AV) Timing

The first programming consideration is to identify the optimal AV delay. A suboptimal AV delay can lead to suboptimal CRT, decreased cardiac output and worse outcomes [8]. In the past, echocardiographic-guided AV delay settings were attempted; however, subsequent trials have disproven a consistent benefit and this labor-intensive method has fallen out of favor [8–10].

One method of optimization utilizes a dynamic and shortened AV delay to create fusion between intrinsic conduction and pacing and can result in more electrical synchrony [11].

As an example, Abbott utilizes an algorithm called SyncAV which attempts to optimize AV timing. Every 256 beats, it extends the paced and sensed AV delay in order to measure the intrinsic AV conduction. An programmable offset (nominal 50 ms) is then subtracted from the intrinsic conduction and applied to the AV delay for the next 255 beats. The creates a dynamic AV delay which adjusted for physiologic changes throughout the day (Table 2).

Table 2 Various CRT optimization algorithms from different manufacturers [CRT: cardiac resynchronization therapy]

	Abbott	Biotronik	Boston scientific	Medtronic
Quadripolar lead (Available pacing vectors)	Yes (14)	Yes(20)	Yes(17)	Yes(16)
Multisite pacing available	14 vectors with MultiPoint Pacing (MPP)	15 vectors with MultiPole Pacing	17 vectors with MultiSite Pacing (MSP)	5 vectors with VectorExpress
Optimization algorithm name	SyncAV, QuickOpt	AutoAdapt	SmartCRT, SmartDelay	Adaptiv CRT
Algorithm basics	Dynamically adjusts AV delay every 256 cycles AV delay: Intrinsic AV delay - 50 ms(SyncAV CRT Delta) BiV or LV only pacing programmable Multi point pacing available	Necessary criteria: Atrial rate <100 bpm and AV conduction <250 ms Measures A to RV and A to LV delays 1. A-RV > A-LV: LV only pacing with Adaptive AV 2. A-RV = A-LV: BiV with Adaptive AV 3. A-RV > A-LV: BiV with programmed AV delay Adaptive AV delay(shorter of two): 70% of AV delay or AV delay—40 ms	Measures A to RV and A to LV delays, suggests AV delay to achieve maximum fusion If RV sense and LV sense <20 ms apart: BiV pace If RV sense and LV sense >20 ms apart and intrinsic conduction <270 ms: LV pace	Continuously assesses: Rhythm, Conduction, HR If *regular* rhythm, intact conduction *AND* HR < 100 bpm: LV only pacing, AV = shorter of 70% of intrinsic AV or intrinsic AV—40 ms If *irregular* rhythm, prolonged conduction *OR* increased HR: BiV pacing, AV = shorter of P wave + 30 ms or intrinsic AV - 50 ms
Associated clinical trial	Varma, JAHA, Feb 2018 FREEDOM	N/A	SMART-AV	ADAPTIV-CRT

Ventriculoventricular (VV) Timing

The next programming consideration should be the timing difference between the RV and LV electrical activation. All CRT systems offer an option of LV or RV first offset. Nominally, this is set to zero ms, meaning that LV and RV pacing occur simultaneously. Because of differences between the RV and LV electrical activation, this nominal setting may not always results in the most effective method of pacing.

Although optimizing VV timing might be beneficial in select subgroup of patients, no such benefit is demonstrated in trials such as RHYTHM II ICD or FREEDOM.

The dynamic nature of the conduction cycle, which is influenced by autonomic input and loading conditions, may require a dynamic VV timing.

Other Optimizations

Various manufactures have incorporated various device-based algorithm to maximize CRT efficacy. As an example, Medtronic uses an algorithm called AdaptivCRT to minimize RV pacing and maximize LV pacing instead. If AV conduction is intact, it delivers LV only pacing timed slightly before intrinsic RV activation. If AV conduction is delayed more than 200 ms or heart rate more than 100 bpm, it delivers BIV pacing slightly faster than native AV conduction and selects the shortest VV interval that allows LV preactivation (Table 2). This method of continually adjusting pacing intervals has been shown to improve clinical outcomes and is easily programmable [12]. Importantly, these algorithms should be turned off if there is complete heart block or patient has undergone AV nodal ablation.

Additionally, pacing from multiple poles of the LV lead (multi-point pacing) can capture a larger area of myocardium and can potentially improve efficiency and clinical outcomes [13].

Rate Response in CRT Patients

In patients with chronotropic incompetence or after AV nodal ablation, the rate response feature may improve exercise tolerance and possibly hard outcomes such as survival [14, 15]. The rate response feature allow patients' baseline heart rate to increase with exercise usually based on accelerometer or minute ventilation. The need for rate response should be considered for all CRT patients.

Phrenic Nerve Stimulation

Due to the anatomical course of the phrenic nerve along the left lateral heart border, it can occasionally be stimulated by LV lead pacing. This stimulation leads to diaphragmatic contraction and can be very bothersome for the patient. Phrenic nerve capture is assessed during every LV lead implant in an effort to avoid this clinical scenario. However, diaphragm stimulation can occur after implant due to positional changes or movement of the LV lead.

When this occurs, the flow of troubleshooting should be:

1. Attempt to program a *different LV pacing vector* that will capture myocardium but not the phrenic nerve
2. Attempt to *lower LV pacing output* such that LV pacing still occurs without stimulating the phrenic nerve
3. Assess *LV lead position* on two view CXR and make a referral to EP if diaphragm stimulation still occurring despite first two steps.

Post Implant Optimization

While the device interrogation may report a high percentage of BiV pacing, it is critical to follow stepwise approach to ensure every patient is actually getting the most benefit.

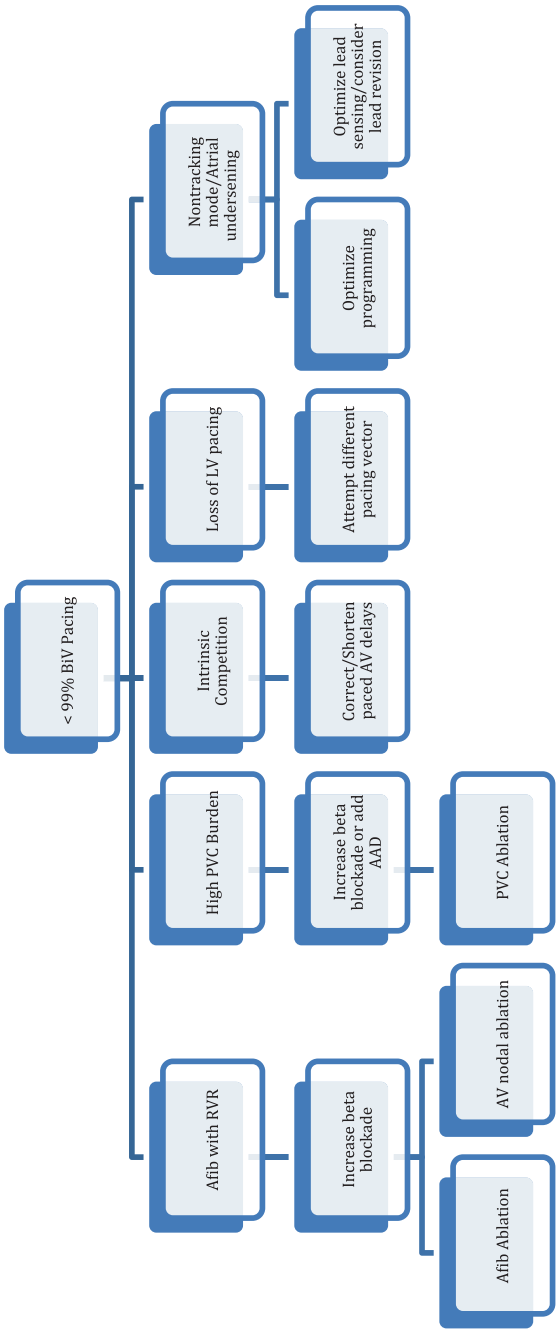
3 key components to obtain for every CRT patient:

1. Device reported % of BiV pacing (Graph 1)
2. 12 lead EKG
3. 2 view chest radiograph (CXR) (Graph 2)

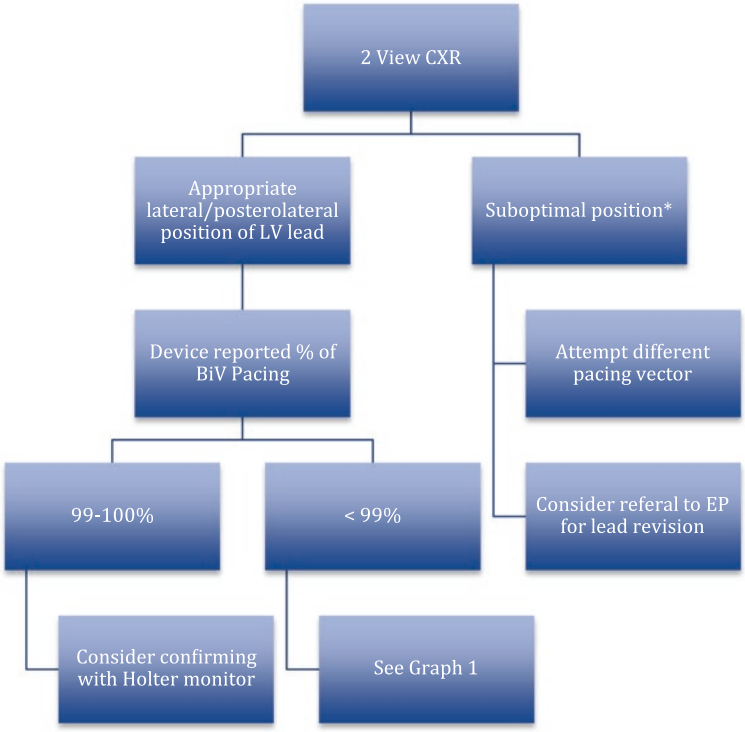
CRT Nonresponders

Despite optimal device implant and programming, roughly 20–40% of CRT patients will be deemed as "nonresponders" and would not experience symptomatic improvement or have imaging finding of positive LV remodeling [17]. The most common associated factors with nonresponders are [17]:

- Male gender
- Ischemic etiology
- Large scar burden



Graph 1 Causes of low biventricular pacing burden

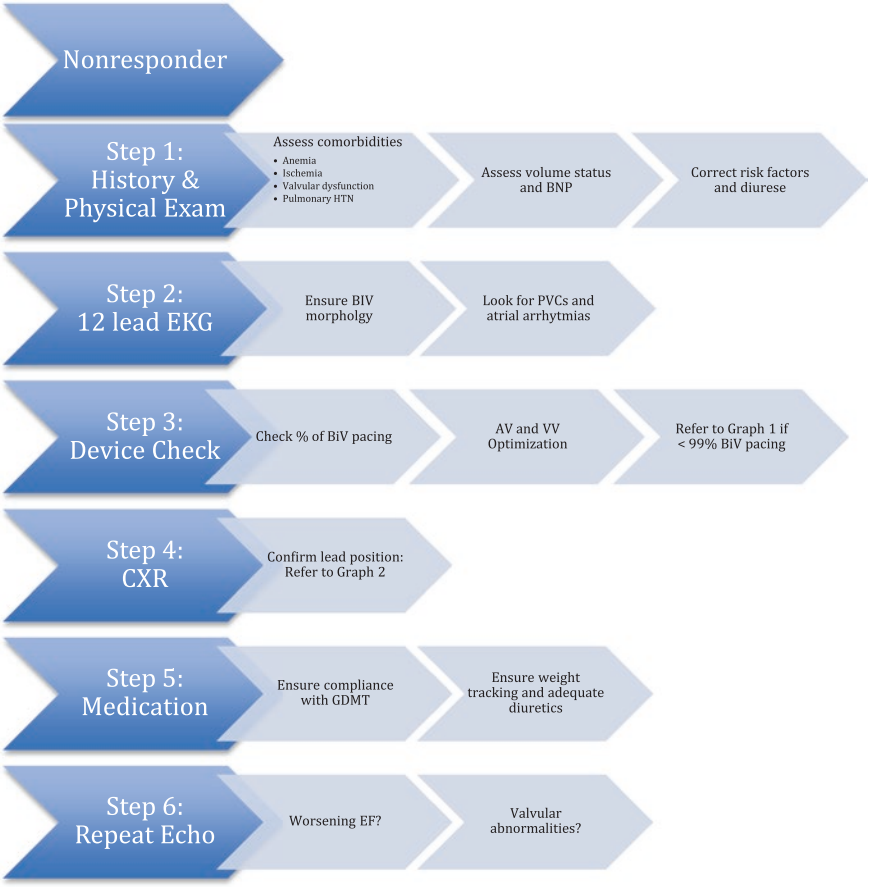


Graph 2 Evaluation of CRT non-response using the chest X-ray [CRT: cardiac resynchronization therapy]. *Occasionally a Chest CT is needed to confirm precise LV lead position as localization by CXR may be deceiving, inaccurate and not reproducible [16].

- NYHA Class IV
- Severe mitral regurgitation
- Severe left atrial dilation

It is important to have well-defined clinical end-points for response. These indices include improved LV ejection fraction, decreased LV end-systolic diameter/volume or improved functional mitral regurgitation in follow up imaging studies.

When a potential "nonresponder" presents for clinical evaluation, it is important to follow a stepwise approach in evaluating the patient. Graph 3 summarizes the steps for "non-responder" workup. This workup shall include investigating for non-CRT related etiologies such as suboptimal HF medical therapy, comorbidities and accompanying arrhythmias.



Graph 3 Suggested workup for potential causes of poor response to cardiac resynchronization therapy

Case Wrap Up

During implant, our patient had a QLV of 100 ms and QLV/QRSd of 0.8 with BiV paced 12-lead EKG shown below. Within 2 months of implant, her symptoms greatly improved and she is now able to walk for 30 min at a time without significant shortness of breath. Post implant EKG is show below with a narrow QRS 110 ms (was 140 ms prior to implant) (Fig. 7).

Key Points

- CRT is an effective therapy for HF patients, especially those with LBBB >150 ms and symptomatic heart failure with NYHA II or greater

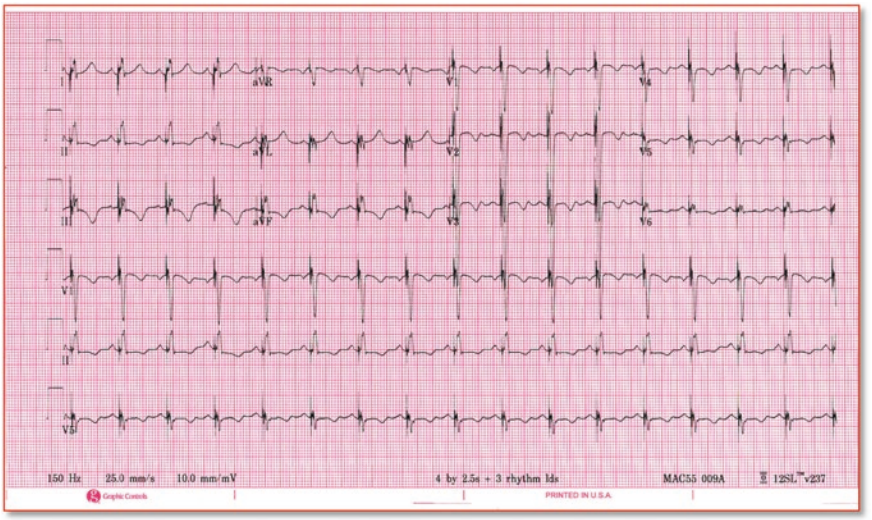


Fig. 7 ECG obtained from the patient from the case vignette after CRT implantation showing a narrow QRS of 110 ms. [[CRT: cardiac resynchronization therapy]

- The goal of CRT is successful and effective pacing >99% of the time
- LV lead position is one of the most critical components of successful CRT
- Device-based programming can help optimize CRT by adjusting delays and pacing vectors
- When <99% BiV pacing occurs or patient is deemed a "nonresponder", follow a step-wise approach to troubleshooting.

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His Bundle and Physiologic Pacing for Cardiac Resynchronization Therapy

Amir A. Schricker and Jonathan Salcedo

Clinical Vignette

A 69-year-old man with a chronic non-ischemic cardiomyopathy (New York Heart Association class III, left ventricular ejection fraction 25%) on optimal guideline-directed medical therapy is referred for cardiac resynchronization therapy and implantable cardioverter-defibrillator (CRT-D). His electrocardiogram reveals sinus rhythm with a left bundle branch block with QRS duration 161 ms. He agrees to CRT-D implantation, but during the procedure difficulty is encountered during coronary sinus (CS) lead implantation, with a contrast venogram demonstrating an atretic CS with no viable branches except for an anterior interventricular vein (AIV.) As a result, further attempts at a coronary sinus lead are aborted, and the patient receives only a single-chamber implantable cardioverter-defibrillator. He presents one month later for follow-up to discuss his options. What options for resynchronization are available for this patient?

Introduction

Cardiac resynchronization therapy (CRT) has emerged as a well-proven treatment for cardiomyopathy and advanced heart failure associated with dyssynchrony (i.e. electromechanical delay). Vast data from multiple clinical trials have demonstrated that CRT improves quality of life, left ventricular (LV) systolic function, number of hospitalizations, and mortality [1–6]. However, traditional CRT—typically performed via biventricular pacing using a coronary sinus (CS) lead to achieve LV

A. A. Schricker (✉) · J. Salcedo
Division of Cardiology, Mills-Peninsula Medical Center, Palo Alto Medical Foundation, 1501 Trousdale Drive, 2nd Floor Cardiology, Burlingame, CA 94010, USA
e-mail: amirschricker@gmail.com

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pacing—suffers from a 30% to 40% rate of non-response, typically distinguished as the lack of derived benefits including improvement in clinical symptoms, left ventricular ejection fraction (LV EF), or LV dimensions [2, 7, 8]. The etiology of non-response is likely multifactorial, and multiple strategies exist to attempt to optimize CRT response [9]. Furthermore, LV lead implantation itself carries an overall failure rate of 3.6% but can be as high as 17.9%, typically due to inability to access the coronary sinus or absence of a suitable venous branch [10].

Bearing this in mind, His bundle pacing has recently emerged as a viable alternative to biventricular pacing to achieve CRT. In this chapter, an overview of His bundle pacing (HBP) and another technique of physiologic pacing, left bundle branch pacing (LBBP), to achieve CRT will be discussed. Although HBP has not yet entered current guidelines from the major North American and European professional societies, the multiple published studies demonstrating the feasibility and benefit of HBP for resynchronization will be reviewed. The most common methods of performing HBP and LBBP are described along with a brief troubleshooting discussion.

His Bundle Pacing: Rationale and Evidence

His bundle pacing (HBP) was first described in humans by Deshmukh et al. in 2000, who established that in patients with dilated cardiomyopathy and atrial fibrillation (AF) undergoing atrioventricular (AV) nodal ablation, direct HBP with a fixed screw-in lead was feasible [11]. In their study, 12 of 18 patients with atrial fibrillation, dilated cardiomyopathy, and narrow QRS demonstrated a His bundle that could be reliably stimulated with a permanent pacemaker lead. Compared to baseline, they exhibited improvements in LV systolic function and dimensions.

In the years that followed, multiple published reports explored the feasibility of permanent HBP and identified its potential acute clinical benefits over right ventricular (RV) pacing [12–16]. Comparisons of HBP with LV or biventricular (BiV) pacing have provided insight as to whether HBP represents an option for CRT eligible populations, as direct HBP and BiV pacing have been shown to improve acute hemodynamics to a similar degree in patients with non-LBBB [17] and LBBB [18].

While fewer studies exist demonstrating its chronic benefits, HBP appears to improve clinical outcomes in the medium to long term. In an unselected population requiring pacemaker implantation, permanent HBP was performed at one hospital, was successful in 80%, and RV pacing was performed at a second hospital. After 2 years of follow-up, and in those with significant (>40%) ventricular pacing, HBP resulted in a significantly reduced rate of heart failure hospitalization compared to RV pacing with a trend toward improved mortality [19]. After 5 years of follow-up, this same HBP subgroup continued to demonstrate a lower rate of death or heart failure hospitalization compared to the RV pacing group. Furthermore, HBP resulted in an unchanged LV EF and lower incidence of

pacing-induced cardiomyopathy [20]. These same authors more recently showed in a large series of patients assigned to HBP or RV pacing that, after a mean follow-up of 725 ± 423 days, HBP was associated with a significantly reduction of the combined endpoint of death, heart failure hospitalization, or upgrade to BiV pacing. This difference was driven primarily by patients with ventricular pacing burden >20% [21].

His Bundle Pacing for Cardiac Resynchronization

Although biventricular pacing via a CS lead has become the cornerstone for CRT, His bundle pacing (HBP) is increasingly being considered as an alternative to CRT eligible patients. Whether used as a primary strategy or as rescue—due to implant failure, CS lead dislodgement, or CRT non-response—resynchronization by HBP offers the theoretic advantage of recruiting the native conducting system to restore electromechanical synchrony. This is thought to be due to the ability of HBP to recruit native fibers past the site of advanced His-Purkinje conduction block or bundle branch block based on the concept of longitudinal dissociation [22], potentially correcting the bundle branch block (Fig. 2). After its initial description in 2005 where selective His pacing was used to achieve resynchronization in patients with infra-Hisian block [23], multiple studies have demonstrated the feasibility of HBP to overcome bundle branch block, improve functional status, reduce dyssynchrony, or improve LV ejection fraction [24–26].

More recent data have expanded the potential role of HBP to heart failure patients with His-Purkinje disease other than LBBB. In patients with LV dysfunction and RBBB (QRS duration >120 ms), Sharma et al. successfully performed HBP in 95% of 39 patients and narrowed the QRS in 78%, with improvement in LV function after mean 15 months follow-up [27].

Recently, a technique for directly pacing the left bundle branch has been shown feasible and may represent yet another strategy when LBBB cannot be corrected by HBP [28], and in 325 CRT-eligible patients, LBB pacing improved clinical and echocardiographic outcomes [29]. Finally, in a head-to-head comparison of HBP and traditional biventricular CRT in 23 patients, HBP was more effective at ventricular resynchronization and with greater acute hemodynamic response [30].

Definitions

A lack of standardization of terminology regarding permanent His bundle pacing has added to the confusion regarding the types of His bundle capture observed. Recently, a multicenter collaboration established a uniform set of definitions encompassing the different types of permanent HBP [31].

Generally, when the region at or near the bundle of His is electrically stimulated, there are two forms of capture: *selective* capture (in which only the His bundle is captured) or *nonselective* capture (in which there is fusion capture of the His bundle and adjacent ventricular tissue) (Fig. 1). Further criteria have been subsequently modified in the presence or absence of His-Purkinje conduction disease:

1. Relationship of the His-QRS and stimulus-QRS intervals
2. Presence or absence of direct capture of the local ventricular electrogram on the pacing lead
3. QRS duration and morphology
4. Capture thresholds

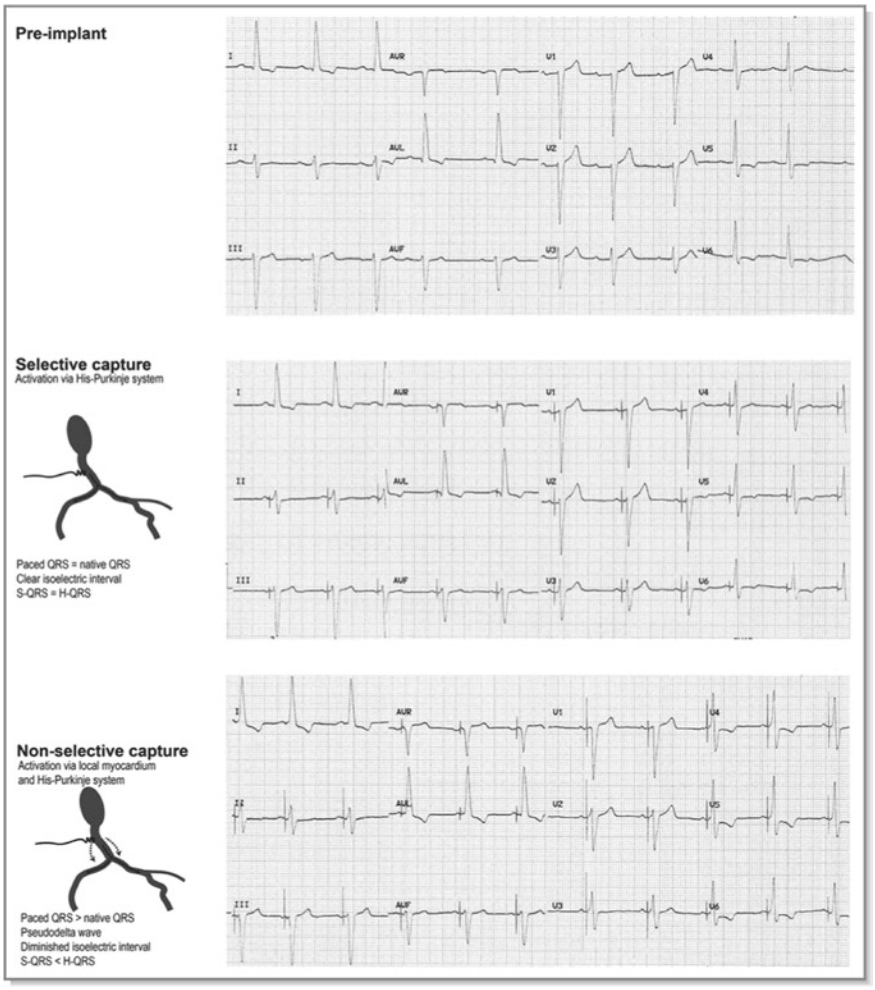

Fig. 1 ECGs from the same patient demonstrating selective and nonselective His bundle capture. (Adapted from [38])

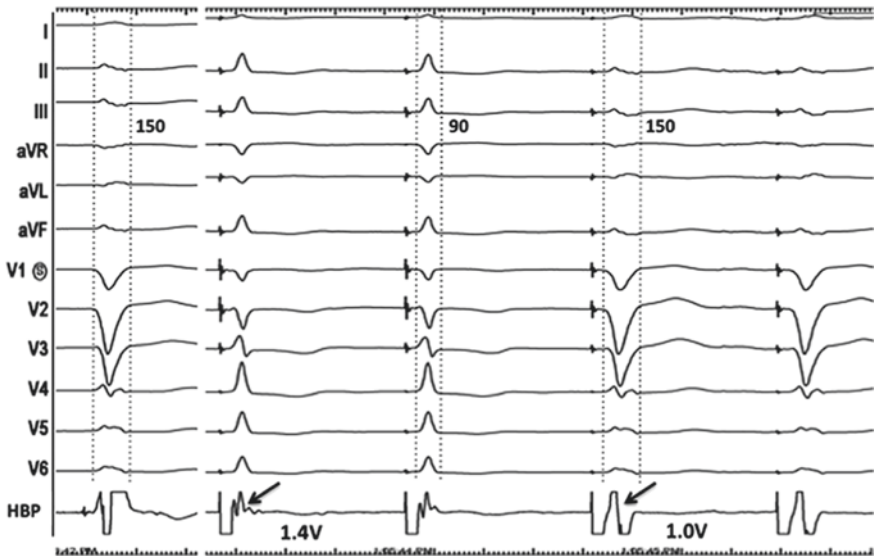

Fig. 2 Selective his bundle pacing in LBBB. (Adapted from [39])

Table 1 summarizes the criteria for selective and nonselective HBP with and without His-Purkinje conduction disease. The extent to which selective HBP is more effective than nonselective HBP remains unclear and is under current investigation.

Implantation Technique—His Bundle Pacing

Initially described by Vijayaraman et al., the current most common method employed for implanting His bundle pacing leads utilizes Medtronic (Minneapolis, MN) products [19]. This entails the 3830 69-cm His lead with a 1.8-mm exposed helix and 4.2F outer diameter with the Medtronic C315 non-deflectable His (C315-His) sheath that involves a broad primary curve proximally that points the lead anteriorly to the superior tricuspid annulus followed by a sharper secondary curve distally that points the lead into the septum. Other methods have been described using stylet-driven leads, which require either shaping the stylet similar to the shape of the C315 His sheath or using traditional coronary sinus (CS) delivery sheaths with a stylet [32]. The following instructions focus on using the Medtronic 3830 lead and C315-His sheath.

1. Patient Preparation and Access

A full 12-lead continuous electrocardiogram (ECG) should be applied to the patient, and the sensing cables for the pacemaker lead should ideally be split between the Medtronic analyzer and EP recording systems with standard filter

Table 1 Criteria for his bundle pacing (Adapted from [31])

	Normal QRS	His-Purkinje conduction disease
Selective HBP	• S-QRS = H-QRS with isoelectric interval • Discrete local ventricular electrogram in HBP lead with S-V = H-V • Paced QRS 1⁄4 native QRS • Single capture threshold (His bundle)	• The S-QRS interval can be shorter than the H-QRS intervals, as in patients with BBB or HV block due to capture of latent fascicular tissue • The paced QRS duration may be narrower than the native QRS with BBB or the escape rhythm • 2 distinct His capture thresholds—with and without correction of underlying BBB—may be seen
Nonselective HBP	• S-QRS<H-QRS (S-QRS = 0, S-QRSend = H-QRSend) with or without isoelectric interval (pseudodelta wave ±) • Direct capture of local ventricular electrogram in HBP lead by stimulus artifact (local myocardial capture) • Paced QRS > native QRS with normalization of precordial and limb lead axes with respect to rapid dV/dt components of the QRS • 2 distinct capture thresholds (His bundle capture, RV capture)	• The paced QRS duration may be narrower than the native QRS due to correction of underlying BBB • 3 distinct capture thresholds may be observed in varying combination (RV capture, His capture with correction of BBB, and His capture without correction of BBB)

settings (30–500 Hz) to enable the operator to accurately identify the His signal. Right or left sided venous access can be used, but the left side is easier due to the sheath being designed to be used from that side. Once venous access is obtained, insert a 7 French peel-away introducer sheath and place a Weitlaner or another self-retaining surgical tool to keep the pocket open. Through this sheath, insert the C315 His sheath over an exchange length wire (at least 60 cm) into the right atrium (RA). Then insert a 69 cm 3830 lead until the helix is just inside the end of the sheath on fluoroscopy. Connect the lead in a unipolar configuration, with the anode cable end clipped to lead tip and cathode clipped to the Weitlaner or skin.

2. Locating the His Signal

Maneuver the C315 sheath to the septum, typically with a clockwise turn, sheath advancement, and then a counterclockwise turn, where atrial and ventricular electrogram (EGM) signals are of equal amplitude. Use very subtle adjustments with the sheath to locate the His region by electrogram analysis. Pacing in unipolar configuration may further help confirm an adequate His position.

3. Implantation

After confirmation of an appropriate His position, implant the lead by slightly advancing the lead within the sheath to allow the helix to engage the endocardial surface (Fig. 3) and then perform 5–7 clockwise whole lead body turns. An injury

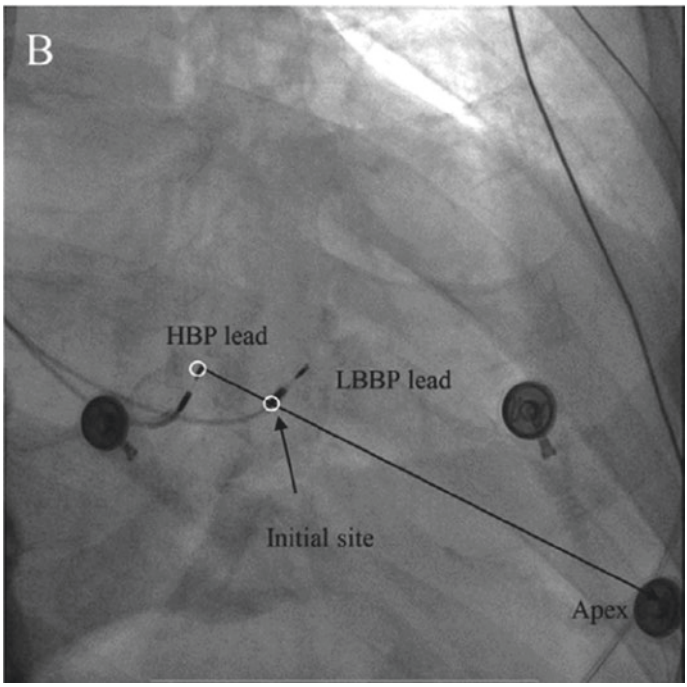

Fig. 3 Right anterior oblique fluoroscopy demonstrating sites of stimulation for His bundle pacing and left bundle pacing. (Adapted from [36])

current on the His signal may be observed, which occurs approximately 37% of the time [33].

4. Testing

Perform pacing at high and low outputs while observing the 12-lead ECG to differentiate left bundle branch narrowing, non-selective His capture, selective His capture, and RV septal capture [31, 34]. Confirmation of stable sensing, impedance, and threshold values should be performed initially with the unipolar configuration. These tests are performed again in a bipolar configuration after pulling back the sheath while advancing the lead, to expose the proximal electrode, and connecting both cathode and anode clips to the lead.

5. Sheath removal, confirmation, and tie-down

Once satisfied with the stability and location of the lead, slit the C315 His sheath with a standard sheath slitter tool while watching the lead on fluoroscopy to ensure lead stability. Advance or retract the lead to ensure appropriate slack. After another round of testing to confirm stable lead values, peel away the 7-French sheath and secure the lead to the pectoral muscle fascia by tying a suture down to the muscle first and then using the ends to tie around the silastic suture sleeve.

The rest of the implant can be performed as usual at this point including implantation of additional leads (right atrial, CS LV, or ICD), generator attachment, and closure of the pocket.

Implantation Technique—Left Bundle Branch Pacing

Implantation of left bundle branch (LBB) pacing leads through deep puncture of the RV septum, first described in 2017 by Huang et al. [28], involves the same Medtronic C315 His sheath and 3830 lead used for HBP but instead is aimed at a target deeper along the RV septum. This is the only method described for direct LBB pacing (i.e. through the interventricular septum) as of this writing [35].

1. Preparation
Prepare the patient the same way as described in the prior section on HBP with a 12-lead ECG monitoring, intracardiac electrogram monitoring, a 7 French peel-away introducer sheath, C315 His sheath, and a 69 cm 3830 lead.

2. Locate Adjacent RV Septum
After locating the His signal, rotate the fluoroscopy camera to right anterior oblique (RAO) 30°. Advance the assembly 1–1.5 cm forward along an imaginary line drawn from the catheter tip to the right ventricular apex on fluoroscopy (Fig. 3). Perform unipolar pace mapping and make slight adjustments to the sheath position to identify a notched S wave in lead V1, also referred to as the "W" pattern [36].

3. Implantation
Once the "W" pattern location is found, rotate the lead 1–2 turns to attach the lead to the septum. Then advance the sheath snugly into the septum and rotate it further counterclockwise an additional 90–18° to ensure that the sheath is perpendicular to the RV septum. Rotate the fluoroscopy camera to left anterior oblique (LAO) 30–45° to confirm this position. Next, start pacing to assess changes in QRS morphology, especially in lead V1, as you perform 4–5 quick lead body turns at a time (release in between sets of turns) with both hands. It is best to have an assistant hold the sheath steady and to try to keep the cable clipped to the end of the lead to be able to watch the pacing morphology as you deeply embed the lead into the interventricular septum. The notch in the S-wave in V1 should start to rise to the baseline and then turn into a qR complex or a right bundle paced complex [35, 36], as you notice an abrupt shortening of pacing stimulus to LV activation time (Stim-LV AT) to <100 ms in leads V4–V6. Concomitantly, you will also see a rise in pacing impedance of 200–300 Ohms. As the helix nears the LV septum, the impedance then starts to drop by ~100 Ohms, which is when you should stop rotations as the lead may perforate into the LV cavity. Inject 1 mL x-ray contrast into the sheath to demonstrate the distance of the RV septal wall to the tip of the helix and thus the depth of implantation. If perforation does occur (impedance drop with

loss of capture), the lead must be positioned in a different location as simple withdrawal into the septum is not sufficient.

Once adequate pacing morphology and capture thresholds are obtained, the rest of the implant can proceed as usual after slitting of the C315 sheath.

Troubleshooting

Occasionally the anatomy of the right atrium and right ventricular septum do not allow the C315 His sheath to adequately reach either the His bundle region or proximal RV septum for deep septal left bundle implantation. The following are options for optimizing the reach to these regions.

- Reshape the C315 His sheath by hand with its dilator inserted for either more anterior or septal reach [37].
- Try another fixed curve sheath such as the Medtronic C315 Model S10, which provides a longer and more anterior reach; this too may require reshaping by hand with its dilator inserted.
- Use the sheath-in-sheath technique with a standard coronary sinus (CS) multipurpose right (MPR) sheath used for conventional LV venous branch delivery. This involves upsizing the 7F peel-away sheath to a 9F sheath and cutting the proximal 10–15 cm of the MPR sheath (the end with the handle), pre-slitting it, and attaching a hemostat to the proximal edge for control [37].
- If available, the Medtronic C304 His steerable sheath has an articulating handle to adjust the primary curve while the secondary septal curve has a fixed shape similar to the end of the C315 His sheath.

Future Directions

The future of HBP and LBB pacing for CRT depend on additional studies and equipment. In the His-SYNC trial, the first prospective randomized clinical trial comparing HBP with traditional biventricular pacing for CRT, there was no significant difference in LV function improvement at 6 months and no difference in cardiovascular hospitalization or death between groups at 12 months. However, this study was limited by a high crossover rate in both directions [34]. As of this writing, the ongoing LBBP-RESYNC study (ClinicalTrials.gov identifier NCT04110431) is randomizing patients to LBB pacing to biventricular pacing in CRT-eligible patients, and will evaluate echocardiographic LV parameters, paced QRS duration, and clinical and biomarker heart failure metrics.

Also needed is the development of additional tools, including a collection of different fixed shaped sheaths for the various anatomies analogous to the CS delivery systems. Another area of development would be for improved electrogram

sensing technologies integrated either at the lead or sheath tip. In addition, for deep septal left bundle branch implantation, an automatic rotational or drilling tool for the 3830 lead versus a longer helix could ease the mechanics of implantation. Longer extendable active (i.e. pacing) helices for standard screw-in pacemaker leads could also make deep septal left bundle implants potentially feasible.

Clinical Vignette: Conclusion

To review, this patient with non-ischemic cardiomyopathy and left bundle branch block (LBBB) had a failed attempt at standard CS biventricular pacing. His bundle pacing was recommended as an alternative, to which the patient agreed. During implantation non-selective His bundle capture was obtained, and the QRS duration narrowed to 118 ms with a residual intraventricular conduction delay. The capture threshold for narrowing the LBBB was 2.0 V. The His bundle lead was connected to the LV port of the pulse generator, and an RA lead was also implanted. Follow-up echocardiogram one year later revealed the LV EF had improved to 43%.

Key Points:

- Cardiac resynchronization therapy (CRT) is a well-proven treatment for heart failure with dyssynchrony.
- His bundle pacing (HBP) can help prevent ventricular dyssynchrony by maintaining normal electrical activation of the ventricles.
- HBP has emerged as an alternative to biventricular pacing to achieve CRT.
- HBP can be performed in routine clinical practice using a lumen-less lead with a non-deflectable sheath.
- Direct left bundle branch pacing is another feasible strategy to achieve physiologic pacing.

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Cardiac Resynchronization Therapy in Patients with Left Ventricular Assist Devices

Andrew Lin and Gordon Ho

Clinical Vignette

65-year-old male with history of ischemic cardiomyopathy and heart failure with reduced ejection fraction status CRT-D upgrade 2 years ago is admitted to the heart failure service for cardiogenic shock. A transthoracic echocardiogram demonstrates an ejection fraction of 14%. Given his rapid decline despite maximal inotropic support, decision was made to proceed with left ventricular assist device (LVAD) placement. The patient's clinical course improves and is ready for discharge in the coming days. His CRT device interrogation reveals three years of battery life remaining. The electrophysiology service is consulted on the optimal management of CRT programming in a post-LVAD patient.

Introduction

Cardiac resynchronization therapy (CRT) is known to improve heart failure mortality, functional status, and quality of life. This benefit is thought to derive from the correction of electrical discordance within the conduction system, allowing the left and right ventricles to contract in a synchronized fashion. However, the mechanical unloading following LVAD placement alters intracardiac hemodynamics, and the benefit of CRT in this population remains unclear. There is currently no guideline on management of CRT after LVAD placement given the lack of data in literature. The purpose of this chapter is to discuss the potential benefits

A. Lin · G. Ho (✉)
University of California San Diego Cardiovascular Institute and VA San Diego Healthcare System, 3350 La Jolla Village Drive, Cardiology Section 111A, San Diego, CA 92161, USA
e-mail: goho@ucsd.edu

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of continuing CRT in patients with LVADs, reasons to turn off the left ventricular (LV) lead, and the optimal programming of CRT in pacemaker-dependent patients (Fig. 1).

Benefits of CRT in Patients with LVADs

Data on CRT in patients with LVADs are limited and findings have been inconsistent [1]. The best quality data to date comes from a small, randomized, controlled study of 83 patients with LV turned on or off after LVAD implant [2]. This study did not show any significant difference in clinical outcomes between the two groups, but the lack of significance is likely due to underpowered small sample size. Notably, there was a nonsignificant trend towards reduction in ICD shocks

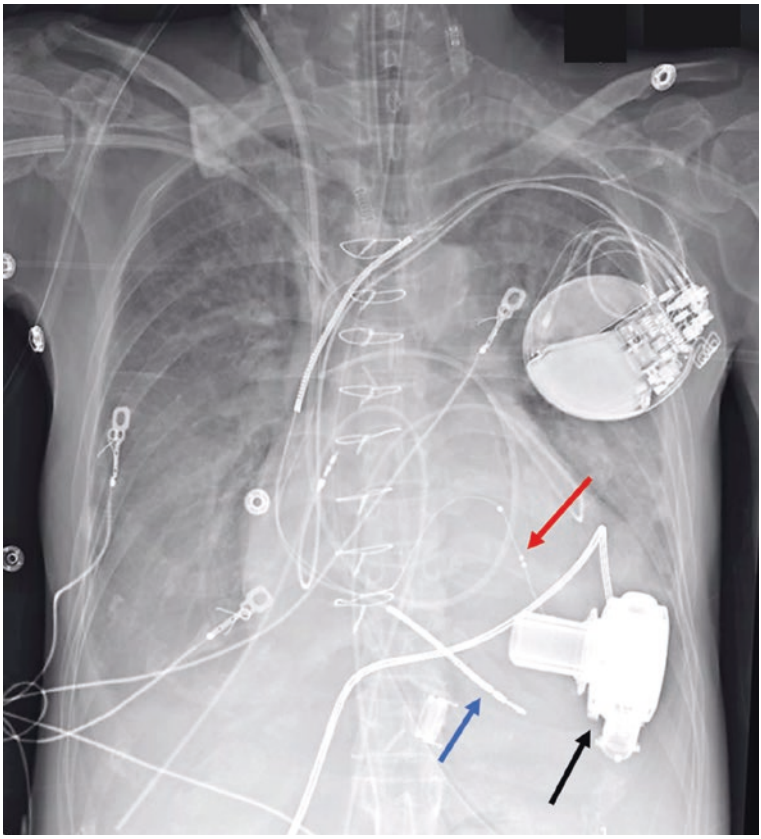

Fig. 1 Chest x-ray (postero-anterior projection) of a patient with a biventricular implantable cardioverter-defibrillator (ICD) and left ventricular assist device (LVAD). Red = LV lead; blue RV ICD lead; black = LVAD

with continued CRT, but there was no difference in mortality. This finding may be supported by a smaller, prospective, non-randomized study consisting of 65 patients that showed implanted cardioverter-defibrillator (ICD) shocks and ventricular arrhythmia burden were significantly reduced in patients with continued CRT after LVAD placement compared to those whose LV lead was turned off [3]. However, the opposite was found in one retrospective study [4] and no difference was observed in three other LVAD cohorts [5–7].

Although CRT with LVAD has not been directly shown to improve cardiac function, it is worth noting that case reports have demonstrated successful explantation of LVAD with CRT support [8–10]. While further studies are certainly needed, continuing CRT may be considered for patients with LVADs as bridge to recovery.

Reasons to Discontinue CRT After LVAD Placement

Recent studies have suggested there may not be significant difference in right heart catheterization hemodynamics [11] and echocardiographic [12] characteristics with CRT versus ICD following LVAD placement. On long term follow up, there was no difference in patients with continued CRT versus ICD in terms of decrease in mortality, right ventricular failure, or heart failure and all-cause hospitalizations [2, 5, 6]. In light of these findings, it is reasonable to discontinue biventricular pacing to preserve battery life and limit the need for generator exchange, which may carry inherent high risks of hematomas and infections in LVAD patients who are more prone to bleeding.

Additionally, although the limited studies in LVAD patients mentioned above showed a trend towards less ventricular arrhythmias in patients with active CRT, there have been several case series and reports in non-LVAD patients reporting ventricular arrhythmias triggered by LV pacing which improved with turning off the LV lead [13–15]. Thus, a patient-specific approach considering all these factors is needed to determine optimal CRT management in LVAD patients (Table 1).

Table 1 Reasons to continue and discontinue CRT in a post-LVAD patient

Reasons to continue CRT	• Possibly decrease ventricular arrhythmia burden • Possibly decrease the number of ICD shocks • Possibly improve left ventricular function and reverse remodeling to allow eventual explantation of LVAD
Reasons to discontinue CRT	• Continuing CRT has not been shown to decrease mortality, right ventricular failure, and number of hospitalizations • Increase battery longevity and limit the need for generator exchange with associated risk for infections and hematomas • Patients with ventricular arrhythmias thought to be triggered by LV pacing

Optimal Programming in Pacemaker-Dependent Patients

While CRT has not been shown to be superior to right ventricular pacing in patients with LVADs, biventricular pacing is often continued in pacemaker-dependent patients following LVAD placement. Increasing pacing rate in patients with complete heart block or junctional escape rhythms have been shown to improve hemodynamics and LVAD flow [16, 17]. However, higher heart rates have also been shown to decrease right ventricular function [11]. In some cases, simultaneous invasive hemodynamic monitoring and echocardiogram optimization can be obtained to determine optimal pacing programming. An individualized approach with interval reassessment should be considered given the paucity of data and lack of guidelines.

Case Conclusion

The electrophysiology service was consulted regarding CRT management prior to our patient's discharge. After thoughtful consideration, decision was made to turn off the left ventricular lead to preserve battery life. The patient was closely followed in clinic and did not experience any significant ventricular arrhythmias. He subsequently underwent successful heart transplant.

Key Points

- Studies comparing the effect of CRT in patients with LVADs are limited due to small sample sizes with contradictory findings.
- The best quality study so far was a small randomized controlled study that showed CRT-on was associated with a nonsignificant trend towards less ICD shocks.
- A personalized approach is advised: consider continuing CRT for patients with history of ventricular arrhythmias and bridge to explantation, while consider discontinuing CRT in patients with limited remaining CRT battery life or ventricular arrhythmias thought to be triggered by the LV lead.

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