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Pregnancy and Cardiovascular Disease (N Scott, Section Editor)

The Use of Echocardiography and Advanced Cardiac Ultrasonography During Pregnancy

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Abstract

Purpose of review Pregnancy is a time of significant cardiovascular change. Echocardiography is the primary imaging modality used to assess cardiovascular anatomy and physiology during pregnancy. Both two-dimensional (2D) echocardiography and advanced cardiac ultrasound modalities play pivotal roles in identifying and monitoring these changes, especially in women with preexisting or new cardiac disease. This paper reviews the role of echocardiography and advanced cardiac ultrasound during normal pregnancy and pregnancy complicated by hypertensive disorders, valvular disorders, and cardiomyopathy. It also examines the role of echocardiography in guiding decisions about delivery.
Recent findings The data establishing normal echo parameters during pregnancy are inconsistent. In addition, there is limited research exploring the role of advanced cardiac ultrasound modalities, such as tissue Doppler imaging or speckle tracking echocardiography, in assessing cardiac function during pregnancy. What data there are suggest that these advanced modalities can be used to identify subclinical changes before traditional echocardiography can, and thus have clear utility in identifying early abnormal cardiac responses to pregnancy.

Summary Echocardiography is the modality of choice for imaging the heart in pregnant women. Advanced ultrasound modalities increasingly play a role in identifying abnormal adaptations to pregnancy and detecting subclinical changes. This, in turn, can help promote a healthy pregnancy for both mother and fetus.

Introduction

Pregnancy is associated with significant cardiovascular changes. These require the heart to adapt to increased plasma volume [1–3], increased cardiac output (up to 50%) [1, 4, 5••, 6], and decreased peripheral vascular resistance [1, 4, 5••]. The heart must further adapt to an acute increase in workload during labor and delivery, and then subsequently readjust in the weeks after pregnancy as these changes resolve [7]. Given these significant hemodynamic changes, pregnancy is a high-risk period for women with pre-existing cardiac conditions. In addition, pregnancy-induced cardiovascular changes can stress maternal physiology sufficiently to reveal previously undiagnosed cardiac conditions or vulnerabilities [8–11]. Finally, pregnancy itself can lead to adverse cardiovascular sequelae, especially in women who develop preeclampsia or other hypertensive disorders of pregnancy (HDP) [12–16].

Because of these numerous physiologic changes, there is great interest in better characterizing the risk of cardiovascular complications during pregnancy and delivery [17, 18, 19•]. Echocardiography (Echo) plays a key role in risk stratification because it is ubiquitous, safe for both mother and fetus, and comprehensive in assessing cardiac structure and physiology. Traditional 2D and Doppler echo techniques are often used to detect valvular diseases, structural abnormalities, and systolic dysfunction, while advanced cardiac ultrasound modalities, including tissue doppler imaging and speckle tracking echocardiography, can detect diastolic dysfunction and sub-clinical systolic dysfunction. Because of its versatility, there are numerous indications for echo evaluation during pregnancy. Any woman with known pre-existing cardiac disease should undergo echocardiography as part of a standard pre-pregnancy screening, and any pregnant woman who develops a concerning murmur (i.e. diastolic, continuous, or systolic murmur ≥ III/VI in intensity), significant dyspnea, or heart failure symptoms should also be imaged [5••]. In addition, echo data is increasingly used to predict maternal cardiovascular risk, including in validated pregnancy risk stratification tools such as CARPREG (Cardiac Disease in Pregnancy), ZAHARA (Zwangerschap bij vrouwen met een Aangeboren HARtAfwijking-II), and World Health Organization (WHO) risk calculators [17, 18, 20–22].

In this article, we focus on the role of echocardiography and advanced echo techniques in assessing the heart during pregnancy. We briefly describe expected echocardiographic findings in normal pregnancy, and then focus on the role of echo in evaluating key gestational and postpartum cardiac conditions including hypertensive disorders of pregnancy, valvular lesions, and cardiomyopathies.

Brief introduction to echo and advanced echo modalities

Most of the approaches for acquiring echo images in pregnant women are similar to those in the non-pregnant patient. The subcostal view can be limited by the gravid uterus during pregnancy; however, most other views are achievable. In each view, conventional 2D imaging is performed, which is useful in assessing basic cardiac parameters such as valvular structures, chamber size, ventricular function, and congenital variants (Fig. 1a). In addition to 2D imaging, Doppler echocardiography is used to detect shunts and assess for valvular disease. Doppler can also measure peak early (E) and late (A) diastolic blood flow velocities across the mitral valve, which are two commonly reported values for assessing diastolic function [23](Fig. 1b). Pregnant women may also be imaged with the advanced echo techniques discussed below, which can identify subtle changes in cardiac function such as sub-clinical systolic and diastolic abnormalities.

Tissue Doppler imaging

Tissue Doppler imaging assesses changes in the myocardium itself [24, 25]. Most commonly, it is used to sample longitudinal myocardial tissue velocity near the mitral valve, thus providing insight into the behavior of the left ventricle throughout the cardiac cycle. Clinically, it is most

Examples of Echo Imaging Modalities

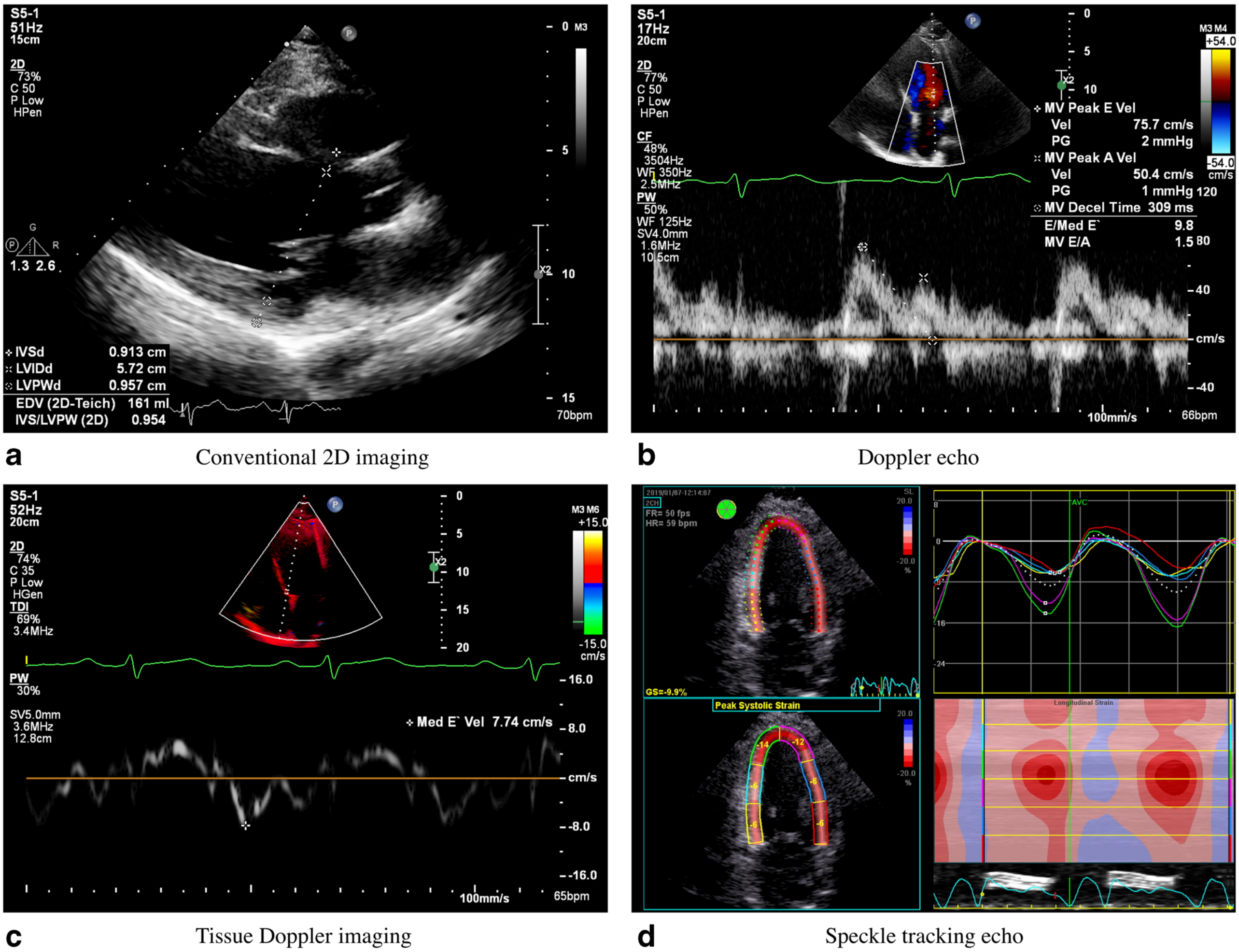

Fig. 1. Examples of echo imaging modalities. **a** Conventional 2D imaging. **b** Doppler echo. **c** Tissue Doppler imaging. **d** Speckle tracking echo.

often used to assess diastolic function, usually by measuring the peak early velocity of the mitral annulus (e′) [23](Fig. 1c). In patients with diastolic dysfunction, e′ values are lower, since myocardial relaxation is impaired.

Speckle tracking echocardiography and strain

Speckle tracking monitors the movement of individual myocardial speckles. Speckles are optical phenomena created by the scattering of the ultrasound beam due to movement of the myocardium [26, 27]. Software using this modality can track all speckles in a given 2D view, allowing for highly accurate assessment of myocardial movement, including the motion of speckles in relation to each other [28]. While it is useful in assessing both systolic and diastolic function, it is most often used to determine myocardial systolic strain [27]. Strain is a measure of tissue deformation and assesses lengthening and shortening of the myocardium in comparison to its original length [25, 27, 29, 30]. In so doing, it provides information regarding the behavior of individual functional units of the myocardium [30, 31] (Fig. 1d). Systolic strain percentages are calculated for all segments of the myocardium, with differences between various segments attributed to regional wall motion abnormalities. In addition, overall myocardial systolic strain rates are calculated by averaging strain data for a broad area of the myocardium. For both overall and segmental systolic strain measurements, rates are reported as a negative percentage, with absolute percentages greater than − 19.5%

considered normal. When compared to 2D echo, systolic strain measurements are more sensitive and specific for detecting systolic dysfunction, especially in patients with normal left ventricular ejection fractions [32, 33].

Normal echo findings during pregnancy

Most uncomplicated pregnancies never require echocardiography, and thus the data reporting echo characteristics in healthy pregnant women is fairly limited. A few cohort studies have proposed normal echo values, though the reported data are variable because values were obtained at different stages of pregnancy. In addition, measurements can be affected by differences in patient positioning, since both cardiac preload and afterload change with positional shifts of the gravid uterus [34]. Thus, it is important to incorporate information regarding gestational age and patient position (i.e., supine versus left lateral decubitus) when interpreting echo findings in pregnant women [35]. With these caveats, the following three sections summarize the best available data, which is also shown in Table 1.

Chamber size

All four cardiac chambers dilate during normal pregnancy [4, 34, 35]. The speed and amount of dilation are variable, and there are no consensus guidelines proposing pregnancy-specific definitions of normal chamber size [35–38]. Regardless of the precise dimensions, chamber dilation is thought to be a response to the increased blood volume that develops during the second and third trimester of pregnancy. Mean left atrial (LA) and right atrial (RA) area likely reach 14.15–18 cm^2 and 13.3–14.6 cm^2, respectively [36–39] . Mean left ventricle (LV) diameter is an average of 4.2–5.0 cm in diastole and 2.38–3.0 cm in systole [39, 40]. Right ventricle (RV) size changes are less well-reported, but available data suggests that mean RV area during diastole is 17.9–18.3 cm^2 and in systole 9.2–9.6 cm^2 [41]. Of note, these slightly larger chamber sizes in pregnancy remain within the upper range of normal for non-pregnant patients. There are additional changes in cardiac structure during this time, including eccentric increases in LV wall thickness and mass, which peak in the third trimester [4, 35, 42–44]. Within weeks after delivery, these parameters revert back to the pre-partum state [7, 42, 45].

Valves

Physiologic increases in blood flow and heart enlargement alter the way blood flows through the valves during pregnancy. Although pregnancy does not change the extent of pre-existing valvular stenosis, transvalvular velocities increase due to the increased blood flow that occurs during pregnancy. Velocity-derived pressure gradients, therefore, correlate less well with stenosis severity during pregnancy [35, 46]. Measuring transvalvular flow by Doppler echo remains useful because it can be used to calculate valve area and stenosis severity even in the presence of increased blood flow [46, 47]. Although pregnancy does not inherently increase the degree of stenosis, it does lead to mild increases in valvular regurgitation. This is because of exaggerated separation of the valve leaflets that result from physiologic cardiac dilation and increases in mitral, tricuspid, and pulmonary annular dimensions [4, 45, 46, 48, 49]. Notably, regurgitation across the aortic valve develops less commonly despite a small increase in aortic root size [46]. Like many of the adaptations seen during pregnancy, valvular regurgitation tends to resolve soon after pregnancy.

Systolic and diastolic function

Given the evolving loading conditions on the heart during pregnancy, as well as the relative impact of patient position on echo parameters, the information on normal systolic and diastolic function during pregnancy is variable. Nevertheless, recent studies have utilized more advanced echo techniques that are less load-dependent and thus provide more consistent data [50].

There is some debate about whether the LV ejection fraction (LVEF) increases or remains unchanged during pregnancy, and there are additional data to suggest that EF fluctuates throughout pregnancy [4, 35, 37, 42, 51, 52]. The majority of studies, however, show no notable changes in LVEF [5••, 7, 34, 53, 54]. Similar to LVEF, data regarding myocardial contractility in pregnancy are also conflicting, with most studies suggesting it either decreases or remains largely unchanged [52, 53, 55]. Although end-diastolic dimensions tend to increase throughout pregnancy, overall end-systolic dimensions show minimal increases compared to the pre-pregnant state [34, 39, 45, 47, 49, 52, 56]. Most but not all studies demonstrate that diastolic function is not inherently impaired in pregnancy, especially in studies utilizing tissue Doppler imaging and strain assessment [34, 37, 44, 50, 52, 57, 58]. Of note, the increased volume state associated with pregnancy affects interpretation of the E/A ratio, which is a supplemental echo measurement used to assess diastolic function. This ratio decreases during pregnancy, especially in the third

Table 1. Changes in echo cardiovascular measures during normal pregnancy

Systemic hemodynamics	Change in pregnancy
Systemic vascular resistance	↓
Heart rate	↑
Stroke volume	↑
Cardiac output	↑
Plasma volume	↑
Cardiac anatomic changes	
Left atrial dimension	↑
Right atrial dimension	↑
Left ventricular dimension	↑
Right ventricular dimension	↑
LV mass	↑
Mitral annulus dimension	↑
Tricuspid annulus dimension	↑
Pulmonary annulus dimension	↑
Aortic annulus dimension	↑
Blood flow	↑
Systolic and diastolic function	
Ejection fraction	↔
Myocardial contractility	↓ or ↔
End-diastolic dimensions	↑
End-systolic dimensions	↔
E/A ratio	↓
e′	↔

trimester, but does not suggest intrinsic diastolic dysfunction in the context of pregnancy [4, 35, 44–45]. Pregnancy does not affect the E/e′ ratio, however, which is a largely load-independent measure of diastolic function [41, 45, 59].

In summary, the normal heart during pregnancy has four-chamber dilation, eccentric LV hypertrophy, and mild valvular regurgitation due to anatomic remodeling and increased transvalvular flow. Systolic, diastolic, and contractile function are most likely unchanged, although all may be influenced by altered loading conditions. To address these variations and uncertainties, more studies are needed to establish consensus for gestational age-specific parameters for normal cardiac findings during pregnancy.

Echocardiography and hypertensive disorders of pregnancy

Hypertension is the most common medical problem encountered during pregnancy and is the second leading cause of maternal mortality [60, 61]. Hypertensive disorders of pregnancy (HDP) include chronic hypertension (hypertension which either predates pregnancy or is diagnosed < 20 weeks gestation), gestational hypertension (hypertension that develops > 20 weeks gestation and is not associated with proteinuria), pre-eclampsia (hypertension that develops > 20 weeks gestation or early in the postpartum period with concurrent proteinuria and/or evidence of end organ dysfunction (new neurologic changes, acute kidney injury, liver dysfunction, hemolysis or thrombocytopenia, or fetal growth restriction)), and preeclampsia superimposed on chronic hypertension [13, 60, 62].

Echocardiography, especially when strain imaging is performed, plays an important role in the assessment of HDP-related cardiac remodeling, because it can potentially detect subtle changes in cardiovascular function before there is worsening hypertension or other clinical complications [14, 26, 36, 44, 51, 63, 64•]. Echo can detect HDP-associated increased LV mass and concentric hypertrophy, which is especially common in women with preeclampsia, and can distinguish between this type of abnormal hypertrophy and the expected eccentric LV hypertrophy associated with normal pregnancy [65–67]. In addition, echo can identify HDP-associated chamber enlargement, which is most notable in the left atrium [36, 68].

Echo data for systolic function in patients are different across the spectrum of HDP disorders. In gestational hypertension, for instance, there is no change in systolic function [64•, 65, 69]. Preeclampsia, however, is more consistently associated with systolic dysfunction, with more severe or early onset preeclampsia associated with greater dysfunction [36, 55, 64•, 69–71]. For all types of HDP, most data suggest an association with diastolic dysfunction, particularly in patients with pre-eclampsia [14, 15, 36, 44, 70].

Although current practice does not include routine monitoring, the echo abnormalities associated with HDP underscore the importance of imaging in women with, or who are at risk for, HDP. In these women, we suggest performing at least one echocardiogram early in pregnancy because subtle cardiac findings may be identified prior to clinical deterioration [36]. Patients with pre-eclampsia with severe features and other high-risk subgroups are at an especially high risk for pulmonary edema and other cardiovascular complications, and probably benefit from serial echocardiography (Table 2). These studies should include advanced cardiac echo techniques because these techniques are especially valuable in monitoring subclinical heart dysfunction in pregnancy and can potentially allow for intensified monitoring and intervention prior to clinical deterioration [26, 36].

Echocardiography and valvular disorders of pregnancy

More women of childbearing age with pre-existing valvular lesions are becoming pregnant. As pregnancy progresses and the hemodynamic changes intensity, valvular lesions initially well tolerated during early pregnancy can become poorly tolerated. In general, regurgitant lesions—whether pre-existing or new—tend to have fewer complications than stenotic ones. Regardless of the specific valvular disorder, all women with valvular lesions should undergo echocardiography early in pregnancy [48, 72, 77, 78] (Table 2). Echo can characterize valvular lesions and determine disease severity, and thus provide key information regarding maternal risk-stratification [5••, 77]. It is reasonable to perform serial echocardiography at least once a trimester, but imaging can be more frequent if the mother develops new or worsening cardiac symptoms, or if the patient has a severe valvular lesion [5••, 79].

Although any severe valvular lesion can lead to complications, left-sided stenotic lesions are associated with the highest morbidity and mortality [72]. In particular, rheumatic mitral stenosis (MS), the most frequently encountered stenotic valvular lesion in pregnancy, should be serially imaged both before and during pregnancy [48, 80]. The pressure gradient across the mitral valve, which is measured by Doppler, has significant prognostic value, with mean gradients > 17 mmHg and peak diastolic gradients > 25 mmHg strongly associated with subsequent pulmonary edema [81]. In addition, echocardiographic evidence of moderate or severe mitral stenosis (severe MS has a calculated valve surface area < 1.5 cm^2), MS mean gradient > 10 mmHg, or severe pulmonary hypertension (pulmonary artery systolic pressure > 50 mmHg) greatly increase the risk in pregnancy [77, 82, 83]. These women should be counseled against pregnancy until the mitral valve has been repaired or replaced [81, 82, 84, 85].

When compared to MS, aortic stenosis (AS) is much less frequently encountered in women of childbearing

Table 2. Suggested frequency of echo monitoring during pregnancy

Cardiovascular disease	Monitoring frequency
Hypertensive disorders of pregnancy	• At least once during pregnancy if cardiac symptoms or signs develop [64•] • Monitoring frequency should increase if cardiac symptoms worsen
Valvular disorders	• Prior to or early in pregnancy, and repeat every trimester [72] • Monitoring frequency should increase if disease severity increases [73]
Aortic stenosis (AS)	• *Severe AS:* every 1–2 months depending on symptoms [5••]
Mitral stenosis (MS)	• *Mild MS:* each trimester and prior to delivery [5••] • *Moderate to severe MS:* every 1–2 months depending on symptoms and disease severity [5••]
Cardiomyopathies	
Dilated cardiomyopathy	• Each trimester • Monitoring frequency should increase if symptoms develop
Hypertrophic cardiomyopathy	• *Low risk disease (WHO Class II):* each trimester [5••, 74] • *High risk of complications (WHO Class III):* every 1–2 months [5••, 75]
Peripartum cardiomyopathy	• *After initial diagnosis:* 6 months post-partum • *Subsequent pregnancies:* End of 1st and 2nd trimesters, and 1 month both prior to and after delivery [76] • Monitoring frequency should increase if cardiac symptoms worsen

age. If present, the most likely cause is a congenital bicuspid aortic valve [82]. Regardless of the etiology, mild AS is well tolerated in pregnancy [82]. However, both moderate and severe AS increase the risk of cardiovascular events and overall morbidity during pregnancy [86]. Severe aortic stenosis, which is defined by a reduced valve area (< 1.0 cm^2), increased peak aortic velocity (≥ 4 m/s), or mean pressure gradient (≥ 40 mmHg), is especially associated with pregnancy complications, even in the absence of symptoms [87–88]. For pregnant patients with AS and cardiac symptoms, morbidity and mortality is prohibitively high due to a higher risk of new-onset heart failure, arrhythmias, and aortic dilation [72, 88]. For this reason, pregnancy is contraindicated in women with uncorrected severe, symptomatic AS [5••, 72, 83, 88].

Echocardiography and cardiomyopathy and heart failure in pregnancy

Women with normal pregnancies can develop dyspnea, leg edema, and fatigue, all of which are also symptoms of heart failure. Echocardiography plays an important role in determining if these symptoms are due to normal changes of pregnancy, or if they are due to a new underlying cardiomyopathy such as peri-partum cardiomyopathy. Echo is also helpful in assessing change in cardiac function in women with pre-existing cardiomyopathies, including dilated and hypertrophic cardiomyopathies. Though data is limited, the frequency of monitoring throughout pregnancy should vary with disease severity, ranging from every 4–8 weeks to every trimester [75, 84] (Table 2). Although there is little data, tissue Doppler and strain imaging may also be helpful because they can detect diastolic dysfunction and subtle systolic dysfunction that can be harbingers of adverse events.

Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) can occur before and during pregnancy. The most common cause is idiopathic, though possible triggers include genetic abnormalities, infections, and toxins [89]. Echo can help diagnose DCM if the LV end diastolic dimension is greater than 112% of the upper limit of normal and the LVEF is less than 45% [89, 90]. Although the impact of DCM on pregnancy is not well characterized, the general consensus is that pregnancy should be avoided in those with DCM and LVEF < 30% [7, 20, 22, 91]. In those with LVEF > 30% who become pregnant, the risk of cardiac events (especially heart failure) is significantly higher with lower systolic function, poorer pre-pregnancy functional status (New York Heart Association Class III or IV), or in the presence of pre-existing cardiac comorbidities [74, 91].

Echo plays a critical role in initial risk stratification and throughout pregnancy. Since LVEF can change during pregnancy, we suggest routine serial echocardiography for asymptomatic patients and urgent echocardiography if new symptoms develop.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is an autosomal dominant condition characterized by ventricular wall hypertrophy, often most pronounced in the septum, and LV outflow tract (LVOT) obstruction [92, 93]. Although the overall literature on HCM in pregnancy is limited, most patients tolerate pregnancy well [74, 75, 90, 93–95]. In some women with HCM, pregnancy is associated with diastolic heart failure or arrhythmias, especially atrial fibrillation [96]. The risk of complications is especially high in women with significant septal hypertrophy and LV outflow obstruction (especially if the pressure gradient > 50 mmHg), pre-pregnancy arrhythmias, or limited pre-pregnancy functional status [18, 74, 75, 93]. Given the role of echo in both identifying and monitoring many of the anatomic changes associated with HCM, all women with HCM should have a pre-pregnancy echo to risk-stratify them [75, 84].

Peri-partum cardiomyopathy

Peri-partum cardiomyopathy (PPCM) is unique to pregnancy. Though its underlying etiology is not known, it is defined as the onset of systolic dysfunction (LVEF < 45%) and heart failure symptoms within the last month of pregnancy or the first five postpartum months [73, 92, 97]. Echocardiography can help predict prognosis in patients with PPCM [72, 98, 99]. For instance, higher LVEF at time of diagnosis is associated with better outcomes [76, 98]. In particular, women with LVEF ≥ 30% have a higher likelihood of recovery, while women with LVEF < 25% have higher rates of persistent cardiac dysfunction and need for subsequent cardiac transplant [76, 98, 100]. LV chamber size at time of diagnosis also has prognostic significance, as patients with LV end-diastolic dimension ≤6 cm at the time of diagnosis have better outcomes [101]. RV fractional area change, a measure of RV systolic function, can also predict recovery, with lower values associated with increased cardiovascular morbidity and mortality [102]. Advanced echo modalities including tissue Doppler and strain have a plausible role in the earlier identification of women with PPCM; however, their role in diagnosis and prognosis remain unclear [103–105].

The role of echocardiography during delivery

Multiple rapid hemodynamic changes occur immediately before and during delivery. Regardless of cardiovascular disease status, delivery is therefore a high-risk period and can lead to rapid decompensation. In women with cardiovascular disease, echo has an important role in predicting who will poorly tolerate these changes and thus merit management at a tertiary care center [106]. Echo data can also help guide decisions regarding method of delivery. Though vaginal delivery is generally preferred even in the presence of cardiovascular disease, echocardiographic evidence of severe aortic dilation (> 45 mm), acute heart failure, severely symptomatic valvular stenosis (aortic or mitral), or severe pulmonary hypertension (systolic pulmonary artery pressures > 50 mmHg), compel consideration for cesarean delivery [5••, 72, 82, 107]. In summary, echo can help prior to delivery by providing additional information regarding how, and where, safe delivery should occur [7].

Conclusion

Echocardiography can help diagnose and guide the management of pregnant women with pre-existing heart disease or in those who develop cardiac complications during pregnancy. Echocardiography can detect cardiac changes even before evidence of clinical disease develops, and advanced echo techniques can allow for even earlier detection of subtle cardiac changes. We believe echo, especially advanced echo modalities, has tremendous value in evaluating women who are pregnant, and call for further studies to definitively determine the value of imaging in pregnant women who develop, and are at risk for, specific cardiovascular diseases. For women with either pre-existing or de novo cardiovascular disease during pregnancy, we also suggest frequent use of this modality, because echo can identify maladaptive or dangerous responses to hemodynamic fluctuations of pregnancy before clinical complications develop. This, in turn, may lead to significant changes in management and help ensure safe pregnancies and deliveries for both mother and fetus.

Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Halpern DG, Weinberg CR, Pinnelas R, Mehta-Lee S, Economy KE, Valente AM. Use of medication for cardiovascular disease during pregnancy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2019;73(4):457–76.
2. Easterling TR, Benedetti TJ, Schmucker BCR, Carlson KR, Millard SP. Maternal hemodynamics and aortic diameter in Normal and hypertensive pregnancies. Obstet Gynecol. 1991;78(6):1073–7.
3. Chapman AB, Abraham WT, Zamudio S, Coffin C, Merouani A, Young D, et al. Temporal relationships between hormonal and hemodynamic changes in early human pregnancy. Kidney Int. 1998;54(6):2056–63.
4. Liu S, Elkayam U, Naqvi TZ. Echocardiography in Pregnancy: Part 1. Curr Cardiol Rep. 2016;18(9) [cited 2019 Jan 30]. Available from: http://link.springer.com/10.1007/s11886-016-0760-7.
5.•• Regitz - Zagrosek V, Roos - Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165–241.
This is a well written consensus statement from the European Society of Cardiology outlining the diagnosis and management of cardiovascular disease during pregnancy.
6. Desai DK, Moodley J, Naidoo DP. Echocardiographic assessment of cardiovascular hemodynamics in Normal Pregnancy. Obstet Gynecol. 2004;104(1):20–9.
7. Siu S, Colman J. Heart disease and pregnancy. Heart. 2001;85(6):710–5.
8. Clevenger N, Hutchison JD, Hertz AD. Unmasking Valvular heart disease in Pregnancy [31B]. Obstet Gynecol. 2017;129:28S.
9. Hauspurg A, Ying W, Hubel CA, Michos ED, Ouyang P. Adverse pregnancy outcomes and future maternal cardiovascular disease. Clin Cardiol. 2018;41(2):239–46.
10. Peters SAE, Regitz-Zagrosek V. Pregnancy and risk of cardiovascular disease: is the relationship due to childbearing or childrearing? Eur Heart J. 2017;38(19):1448–50.
11. Pieper PG. Expected and unexpected cardiac problems during pregnancy. Neth Heart J. 2008;16(12):403–5.
12. Behrens I, Basit S, Lykke JA, Ranthe MF, Wohlfahrt J, Bundgaard H, et al. Hypertensive disorders of pregnancy and peripartum cardiomyopathy: a nationwide cohort study. PLoS One. 2019;14(2):e0211857.
13. Brown MA, Magee LA, Kenny LC, Ananth KS, McCarthy FP, Shigeru S, et al. Hypertensive disorders of Pregnancy. Hypertension. 2018;72(1):24–43.
14. Melchiorre K, Sutherland GR, Liberati M, Thilaganathan B. Preeclampsia is associated with persistent postpartum cardiovascular impairment. Hypertension. 2011;58(4):709–15.
15. Melchiorre K, Sutherland G, Sharma R, Nanni M, Thilaganathan B. Mid-gestational maternal cardiovascular profile in preterm and term pre-eclampsia: a prospective study. BJOG Int J Obstet Gynaecol. 2013;120(4):496–504.
16. Melchiorre K, Sharma R, Thilaganathan B. Cardiovascular implications in preeclampsia: an overview. Circulation. 2014;130(8):703–14.
17. Elkayam U, Goland S, Pieper PG, Silversides CK. High-risk cardiac disease in Pregnancy: Part I. J Am Coll Cardiol. 2016;68(4):396–410.
18. Drenthen W, Boersma E, Balci A, Moons P, Roos-Hesselink JW, Mulder BJM, et al. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J. 2010;31(17):2124–32.
19.• Silversides CK, Grewal J, Mason J, Sermer M, Kiess M, Rychel V, et al. Pregnancy outcomes in women with heart disease: the CARPREG II Study. J Am Coll Cardiol. 2018;71(21):2419–30.
This is a follow-up of a landmark study and highlights the persistent morbidity of cardiovascular disease during pregnancy.
20. Billebeau G, Etienne M, Cheikh-Khelifa R, Vauthier-Brouzes D, Gandjbakhch E, Isnard R, et al. Pregnancy in women with a cardiomyopathy: outcomes and predictors from a retrospective cohort. Arch Cardiovasc Dis. 2018;111(3):199–209.
21. Khairy P, Ouyang DW, Fernandes SM, Lee-Parritz A, Economy KE, Landzberg MJ. Pregnancy outcomes in women with congenital heart disease. Circulation. 2006;113(4):517–24.
22. Thorne S, Nelson-Piercy C, Rosenthal E, Macgregor A, Gibbs S, Crowhurst J, et al. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plan Reprod Health Care. 2006;32(2):75–81.
23. Porter TR, Shillcutt SK, Adams MS, Desjardins G, Glas KE, Olson JJ, et al. Guidelines for the use of Echocardiography as a monitor for therapeutic intervention in adults: a report from the American Society of Echocardiography. J Am Soc Echocardiogr. 2015;28(1):40–56.
24. Ho Carolyn Y, Solomon Scott D. A Clinician's guide to tissue Doppler imaging. Circulation. 2006;113(10):e396–8.
25. Steeds RP. Echocardiography: frontier imaging in cardiology. Br J Radiol. 2011;84(Spec Iss 3):S237–44.
26. Sajid S, Julie R, Hacker Michele R, Gaurav G, Mitchell JD, Phil H, et al. Subclinical left ventricular dysfunction in Preeclamptic women with preserved left ventricular

ejection fraction. Circ Cardiovasc Imaging. 2012;5(6):734–9.

27. Blessberger H, Binder T. Two dimensional speckle tracking echocardiography: basic principles. Heart. 2010;96(9):716–22.
28. Bansal M, Kasliwal RR. How do I do it? Speckle-tracking echocardiography. Indian Heart J. 2013;65(1):117–23.
29. Abraham TP, Dimaano VL, Liang H-Y. Role of tissue Doppler and strain Echocardiography in current clinical practice. Circulation. 2007;116(22):2597–609.
30. Dandel M, Lehmkuhl H, Knosalla C, Suramelashvili N, Hetzer R. Strain and strain rate imaging by Echocardiography – basic concepts and clinical applicability. Curr Cardiol Rev. 2009;5(2):133–48.
31. Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: how useful is it in clinical decision making? Eur Heart J. 2016;37(15):1196–207.
32. Marwick TH, Shah SJ, Thomas JD. Myocardial strain in the assessment of patients with heart failure: a review. JAMA Cardiol. 2019;4(3):287–94.
33. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. Heart. 2014;100(21):1673–80.
34. Valente AM. Pregnancy and heart disease. In: Lai WW, Mertens LL, Cohen MS, Geva T, editors. Echocardiography in pediatric and congenital heart disease. Oxford: Wiley; 2016. p. 815–33. [cited 2019 Feb 4]. Available from: http://doi.wiley.com/10.1002/9781118742440.ch43.
35. Silversides CK, Siu SC. Heart Disease in Pregnancy. In: Practice of clinical echocardiography. 5th ed. Philadelphia: Elsevier; 2017. p. 861–78. [cited 2019 Jan 30]. Available from: http://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323401258000433.
36. Vaught AJ, Kovell LC, Szymanski LM, Mayer SA, Seifert SM, Vaidya D, et al. Acute cardiac effects of severe pre-eclampsia. J Am Coll Cardiol. 2018;72(1):1–11.
37. Tso G, Lee J, Lui G, Trivedi H, Cohen M, Bernstein P, et al. Range of echocardiographic parameters during Normal Pregnancy. J Am Coll Cardiol. 2018;59(13 Supplement):E1301.
38. Yosefy C, Shenhav S, Feldman V, Sagi Y, Katz A, Anteby E. Left atrial function during Pregnancy: a three-dimensional echocardiographic study. Echocardiography. 2012;29(9):1096–101.
39. Savu O, Jurcuţ R, Giuşcă S, van Mieghem T, Gussi I, Popescu BA, et al. Morphological and functional adaptation of the maternal heart during pregnancy. Circ Cardiovasc Imaging. 2012;5(3):289–97.
40. Adeyeye VO, Balogun MO, Adebayo RA, Makinde ON, Akinwusi PO, Ajayi EA, et al. Echocardiographic assessment of cardiac changes during Normal Pregnancy among Nigerians. Clin Med Insights Cardiol. 2016;10:157–62.
41. Tso GJ, Lee JM, Shaban NM, Lui GK, Trivedi HA, Cohen MN, et al. Normal echocardiographic measurements in uncomplicated Pregnancy, a single center experience. J Cardiovasc Dis Res. 2014;5(2):3–8.
42. Schannwell CM, Zimmermann T, Schneppenheim M, Plehn G, Marx R, Strauer BE. Left ventricular hypertrophy and diastolic dysfunction in healthy pregnant women. Cardiology. 2002;97(2):73–8.
43. Cornette J, Ruys TPE, Roos-Hesselink JW. Assessment of the right ventricle in pregnant women with and without structural heart disease. Int J Cardiol. 2013;168(3):3087.
44. Melchiorre K, Sharma R, Thilaganathan B. Cardiac structure and function in normal pregnancy. Curr Opin Obstet Gynecol. 2012;24(6):413–21.
45. Tsiaras S, Poppas A. Cardiac disease in Pregnancy: value of Echocardiography. Curr Cardiol Rep. 2010;12(3):250–6.
46. Campos O. Doppler Echocardiography during Pregnancy.: physiological and abnormal findings. Echocardiography. 1996;13(2):135–46.
47. Silversides CK, Warnes CA. Pregnancy and heart disease. In: Braunwald's heart disease: a textbook of cardiovascular medicine. 11th ed. Philadelphia: Elsevier; 2019. p. 1780–98. [cited 2019 Jan 30]. Available from: http://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323463423000906.
48. Roeder HA, Kuller JA, Barker PCA, James AH. Maternal Valvular heart disease in Pregnancy. Obstet Gynecol Surv. 2011;66(9):561–71.
49. Kamiya C, Nakatani S, Hashimoto S, Masuda Y, Neki R, Ikeda T. Role of Echocardiography in assessing pregnant women with and without heart disease. J Echocardiogr. 2008;6(2):29–38.
50. Vogt M, Müller J, Kühn A, Elmenhorst J, Mühlbauer F, Oberhoffer R. Cardiac adaptation of the maternal heart during Pregnancy: a color-coded tissue Doppler imaging study – feasibility, reproducibility and course during Pregnancy. Ultraschall Med - Eur J Ultrasound. 2015;36(03):270–5.
51. Cong J, Yang X, Zhang N, Shen J, Fan T, Zhang Z. Quantitative analysis of left atrial volume and function during normotensive and preeclamptic pregnancy: a real-time three-dimensional echocardiography study. Int J Cardiovasc Imaging. 2015;31(4):805–12.
52. Estensen ME, Beitnes JO, Grindheim G, Aaberge L, Smiseth OA, Henriksen T, et al. Altered maternal left ventricular contractility and function during normal pregnancy. Ultrasound Obstet Gynecol. 2013;41(6):659–66.
53. Bamfo JEAK, Kametas NA, Nicolaides KH, Chambers JB. Maternal left ventricular diastolic and systolic long-axis function during normal pregnancy. Eur J Echocardiogr. 2007;8(5):360–8.
54. Poppas A, Shroff SG, Korcarz CED, Hibbard JU, Berger DS, Lindheimer MD, et al. Serial assessment of the cardiovascular system in Normal Pregnancy: role of arterial compliance and pulsatile arterial load. Circulation. 1997;95(10):2407–15.
55. Melchiorre K, Sharma R, Khalil A, Thilaganathan B. Maternal cardiovascular function in Normal

Pregnancy: evidence of maladaptation to chronic volume overload. Hypertension. 2016;67(4):754–62.
56. Rubler S, Damani PM, Pinto ER. Cardiac size and performance during pregnancy estimated with echocardiography. Am J Cardiol. 1977;40(4):534–40.
57. Moran AM, Colan SD, Mauer MB, Geva T. Adaptive mechanisms of left ventricular diastolic function to the physiologic load of pregnancy. Clin Cardiol. 2002;25(3):124–31.
58. Fok WY, Chan LY, Wong JT, Yu CM, Lau TK. Left ventricular diastolic function during normal pregnancy: assessment by spectral tissue Doppler imaging. Ultrasound Obstet Gynecol. 2006;28(6):789–93.
59. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by Echocardiography. J Am Soc Echocardiogr. 2009;22(2):107–33.
60. Mammaro A, Carrara S, Cavaliere A, Ermito S, Dinatale A, Pappalardo EM, et al. Hypertensive disorders of Pregnancy. J Prenat Med. 2009;3:1):1–5.
61. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2(6):e323–33.
62. American College of Obstetricians and Gynecologists, American College of Obstetricians and Gynecologists, editor. Hypertension in pregnancy. Washington, DC: American College of Obstetricians and Gynecologists; 2013. 89 p.
63. Shahul S, Ramadan H, Nizamuddin J, Mueller A, Patel V, Dreixler J, et al. Activin a and late postpartum cardiac dysfunction among women with hypertensive disorders of Pregnancy. Hypertension. 2018;72(1):188–93.
64.•• Castleman S, Ganapathy YH, Taki P, Lip P, Steeds P, Kotecha P. Echocardiographic structure and function in hypertensive disorders of pregnancy: a systematic review. Circ Cardiovasc Imaging. 2016;9(9):e004888–8
This examines the role of echocardiography in evaluating the hypertensive disorders of pregnancy, and highlights the potential for echocardiography to help risk stratify and guide management prior to clinical deterioration.
65. Vlahović-Stipac A, Stankić V, Popović ZB, Putniković B, Nešković AN. Left ventricular function in gestational hypertension: serial echocardiographic study. Am J Hypertens. 2010;23(1):85–91.
66. Borghi C, Esposti DD, Immordino V, Cassani A, Boschi S, Bovicelli L, et al. Relationship of systemic hemodynamics, left ventricular structure and function, and plasma natriuretic peptide concentrations during pregnancy complicated by preeclampsia. Am J Obstet Gynecol. 2000;183(1):140–7.
67. Simmons LA, Gillin AG, Jeremy RW. Structural and functional changes in left ventricle during normotensive and preeclamptic pregnancy. Am J Physiol-Heart Circ Physiol. 2002;283(4):H1627–33.
68. Mattioli AV, Pennella S, Demaria F, Farinetti A. Atrial remodeling in pregnant hypertensive women: comparison between chronic and gestational hypertension. Open Cardiovasc Med J. 2012;6:9–14.
69. Trasca LF, Patrascu N, Mihalcea D, Lungeanu L, Mihaila S, Bruja R, et al. Gestational hypertension and preeclampsia are associated with subclinical left ventricular systolic and diastolic dysfunction. J Am Coll Cardiol. 2019;69(11 Supplement):818.
70. Valensise H, Vasapollo B, Gagliardi G, Novelli GP. Early and late preeclampsia: two different maternal hemodynamic states in the latent phase of the disease. Hypertension. 2008;52(5):873–80.
71. Novelli GP, Valensise H, Vasapollo B, Larciprete G, Di Pierro G, Altomare F, et al. Are gestational and essential hypertension similar? Left ventricular geometry and diastolic function. Hypertens Pregnancy. 2003;22(3):225–37.
72. Safi LM, Tsiaras SV. Update on Valvular heart disease in Pregnancy. Curr Treat Options Cardiovasc Med. 2017;19(9):70.
73. Elkayam U, Bitar F. Valvular heart disease and Pregnancy: part I: native valves. J Am Coll Cardiol. 2005;46(2):223–30.
74. Van Tintelen JP, Pieper PG, Van Spaendonck-Zwarts KY, Van Den Berg MP. Pregnancy, cardiomyopathies, and genetics. Cardiovasc Res. 2014;101(4):571–8.
75. Pieper PG, Walker F. Pregnancy in women with hypertrophic cardiomyopathy. Neth Heart J. 2013;21(1):14–8.
76. Elkayam U. Risk of subsequent pregnancy in women with a history of peripartum cardiomyopathy. J Am Coll Cardiol. 2014;64(15):1629–36.
77. Reimold SC, Rutherford JD. Valvular heart disease in Pregnancy. N Engl J Med. 2003;349(1):52–9.
78. Sliwa K, Johnson MR, Zilla P, Roos-Hesselink JW. Management of valvular disease in pregnancy: a global perspective. Eur Heart J. 2015;36(18):1078–89.
79. Lao TT, Sermer M, Magee L, Farine D, Golman JM. Congenital aortic stenosis and pregnancy—a reappraisal. Am J Obstet Gynecol. 1993;169(3):540–5.
80. Pessel C, Bonanno C. Valve disease in pregnancy. Semin Perinatol. 2014;38(5):273–84.
81. Leśniak-Sobelga A, Tracz W, KostKiewicz M, Podolec P, Pasowicz M. Clinical and echocardiographic assessment of pregnant women with valvular heart diseases—maternal and fetal outcome. Int J Cardiol. 2004;94(1):15–23.
82. Westhoff-Bleck M, Podewski E, Hilfiker A, Hilfiker-Kleiner D. Cardiovascular disorders in Pregnancy: diagnosis and management. Best Pract Res Clin Obstet Gynaecol. 2013;27(6):821–34.
83. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. J Am Soc Echocardiogr. 2009;22(1):1–23.
84. Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, Cifkova R, Ferreira R, Foidart J-M, et al. ESC guidelines on the management of cardiovascular diseases during pregnancyThe task force on the Management of

Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J. 2011;32(24):3147–97.
85. Bonow RO, Carabello BA, Chatterjee K, de Leon AC, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the Management of Patients with Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (writing committee to revise the 1998 guidelines for the Management of Patients with Valvular Heart Disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists Endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2006;48(3):e1–148.
86. Arias F, Pineda J. Aortic stenosis and pregnancy. J Reprod Med. 1978;20(4):229–32.
87. Otto CM, Nishimura RA. New ACC/AHA valve guidelines: aligning definitions of aortic stenosis severity with treatment recommendations. Heart. 2014;100(12):902–4.
88. Orwat S, Diller G-P, van HIM, Schmidt R, Tobler D, Greutmann M, et al. Risk of Pregnancy in moderate and severe aortic stenosis: From the Multinational ROPAC Registry. J Am Coll Cardiol. 2016;68(16):1727–37.
89. Elliott P. Cardiomyopathy. Diagnosis and management of dilated cardiomyopathy. Heart. 2000;84:106–12.
90. Herrey AS. Pregnancy in inherited and acquired cardiomyopathies. Best Pract Res Clin Obstet Gynaecol. 2014;28(4):563–77.
91. Grewal J, Siu SC, Ross HJ, Mason J, Balint OH, Sermer M, et al. Pregnancy outcomes in women with dilated cardiomyopathy. J Am Coll Cardiol. 2009;55(1):45–52.
92. Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F, Charron P, et al. Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases. Eur Heart J. 2008;29(2):270–6.
93. Autore C, Conte MR, Piccininno M, Bernabò P, Bonfiglio G, Bruzzi P, et al. Risk associated with pregnancy in hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002;40(10):1864–9.
94. Avila WS, Rossi EG, Ramires JAF, Grinberg M, Bortolotto MRL, Zugaib M, et al. Pregnancy in patients with heart disease: experience with 1,000 cases. Clin Cardiol. 2003;26(3):135–42.
95. Avila WS, Amaral FMC, Ramires JAF, Rossi EG, Grinberg M, Bortolotto MRL, et al. Influência da gestação na evolução clínica materno-fetal de portadoras de cardiomiopatia hipertrófica. Arq Bras Cardiol. 2007;88(4):480–5.
96. Goland S, van Hagen IM, Elbaz-Greener G, Elkayam U, Shotan A, Merz WM, et al. Pregnancy in women with hypertrophic cardiomyopathy: data from the European Society of Cardiology initiated registry of Pregnancy and cardiac disease (ROPAC). Eur Heart J. 2017;38(35):2683–90.
97. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the heart failure Association of the European Society of cardiology working group on peripartum cardiomyopathy. Eur J Heart Fail. 2010;12(8):767–78.
98. Goland S, Bitar F, Modi K, Safirstein J, Ro A, Mirocha J, et al. Evaluation of the clinical relevance of baseline left ventricular ejection fraction as a predictor of recovery or persistence of severe dysfunction in women in the United States with Peripartum cardiomyopathy. J Card Fail. 2011;17(5):426–30.
99. Sugahara M, Mcnamara D, Rajagopalan N, Briller J, Damp J, Wells G, et al. Global longitudinal strain at PRESENTATION is prognostic of subsequent left ventricular recovery in patients with PERIPARTUM cardiomyopathy. J Am Coll Cardiol. 2016;67(13):1288.
100. Habli M, O'Brien T, Nowack E, Khoury S, Barton JR, Sibai B. Peripartum cardiomyopathy: prognostic factors for long-term maternal outcome. Am J Obstet Gynecol. 2008;199(4):415.e1–5.
101. Chapa J, Heiberger H, Lang RM, Hibbard J. Prognostic value of echocardiography at diagnosis of peripartum cardiomyopathy. Am J Obstet Gynecol. 2004;191(6, Supplement):S87.
102. Blauwet Lori A, Antonia D-M, Keiko R, Marek Josef J, Rami A, Mather Paul J, et al. Right ventricular function in Peripartum cardiomyopathy at Presentation is associated with subsequent left ventricular recovery and clinical outcomes. Circ Heart Fail. 2016;9(5):e002756.
103. Karaye KM, Henein MY. Peripartum cardiomyopathy: a review article. Int J Cardiol. 2013;164(1):33–8.
104. Briasoulis A, Mocanu M, Marinescu K, Qaqi O, Palla M, Telila T, et al. Longitudinal systolic strain profiles and outcomes in peripartum cardiomyopathy. Echocardiography. 2016;33(9):1354–60.
105. Attalla W, Gaber R, Bayomy S. Detection of early left ventricular dysfunction in patients with maternal placental syndrome using tissue Doppler and strain rate imaging. Hypertens Pregnancy. 2015;34(1):80–9.
106. Jastrow N, Meyer P, Khairy P, Mercier L-A, Dore A, Marcotte F, et al. Prediction of complications in pregnant women with cardiac diseases referred to a tertiary center. Int J Cardiol. 2011;151(2):209–13.
107. Skyler JS, Bergenstal R, Bonow RO, Buse J, Deedwania P, Gale EAM, et al. Intensive glycemic control and the prevention of cardiovascular events: implications of the ACCORD, ADVANCE, and VA diabetes trials: a position statement of the American Diabetes Association and a scientific statement of the American College of Cardiology Foundation and the American Heart Association. Diabetes Care Alex. 2009;32(1):187–92.

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