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Risk stratification for irregular fetal heart rhythm: practical approach to management

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Irregular fetal heart rhythm

Risk stratification - a practical approach to management

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Auscultation of the fetal heart using Doppler devices is an integral part of routine antenatal care. It is reassuring for mothers and healthcare professionals to hear the fetal heart beating regularly and at a fast pace, compared to postnatal life. In practice, rates between 120 and 160 bpm are considered normal and accepted as gestational-age-independent reference range. However, it is long known that fetal heart rate (FHR) decreases with gestational age[1] and more recently, gestational-age reference centile chart has become available[2]. However, and despite FHR being an important parameter to assess fetal well-being and easily obtained, the actual value (in bpm) may not, and is often not recorded during the 20-week anomaly scan, subsequent growth scans or at the time of routine antenatal visits.

Rhythm irregularity is relatively common, being present in 1.7% of normal pregnancies towards term[3] and mostly due to atrial ectopic beats, also named premature atrial contractions (PACs). Their audial or visual perception by Doppler or scan respectively, is that the fetal heart is 'missing or skipping' a beat, which is frequently worrisome to the pregnant woman and health professionals alike, despite PACs being benign, self-limited and of no clinical significance in the majority of cases. However, in a small proportion (~2-3%), irregular rhythms may be associated with clinically significant arrhythmias[4, 5] or may evolve into tachyarrhythmias (~5%) [6]. In most instances, PACs occur in structurally normal hearts and typically they are not associated with increased risk of congenital heart disease (CHD), although the two can certainly co-exist[4, 6, 7].

These facts lead to an important clinical question: 'How to manage an irregular rhythm when this is an incidental finding during a routine antenatal appointment or routine obstetric scan?'

The systematic review by Bet and colleagues[8]in this issue of the Journal aimed to evaluate two important clinical aspects of rhythm irregularities: the incidence of CHD and the risk of complications. The meta-analysis suggested that the overall risk of CHD in fetuses with PACs is 4 to 5 times that encountered in the general population. It also concluded that the risk of tachyarrhythmias, heart failure and fetal demise was low (<2%). Based on these

results the authors advised performing an advanced ultrasound in all cases of PACs to exclude CHD and better characterise the arrhythmia. Furthermore, they also advise weekly FHR monitoring for early detection of tachyarrhythmias, thus avoiding development of heart failure. However, these recommendations also raise several practical questions. Should they apply to all fetuses with PACs without considering other variables? Are there enough medical and allied health professional resources to implement this strategy of advanced scanning and weekly FHR surveillance to all cases of PACs? Are weekly antenatal visits to monitor FHR necessary or practical for all pregnant women, if most cases of PACs resolve with no further consequences? A closer look at the meta-analysis, which included 19 studies, indicates that only six of these were from low-risk population, that is, pregnancies referred solely because of a rhythm irregularity. In nine, there were additional reasons for referral and the pregnancies were considered high-risk. In the remaining four, the indications for referral were not available and these studies were analysed together with those referred for rhythm abnormalities, i.e. low-risk pregnancies. From the pooled analysis, the overall incidence of CHD in all 19 studies was 2.8% (95%-CI 1.5-4.1), but 1.7%, (95%-CI 0.8-2.7) when two outliers were removed. When considering only the 10 low-risk population studies, the pooled incidence was much lower at 0.9% (95%-CI 0.0-2.0), which was similar to that encountered in the general population, quoted from a historical reference registry (0.6%)[9]. This data suggests that when patients are referred for irregular rhythm and without other known associated risk factors, the probability of associated CHD is similar to the background risk. With regards risk factors for development of tachyarrhythmias, such as their frequency or presence of bigeminal or trigeminal patterns, the meta-analysis did not allow better characterisation of PACs, which is relevant to management.

To return to the question of how to manage rhythm abnormalities, the simple answer is, they should not be ignored, but pregnancies should be risk stratified. An appropriate clinical algorithm should identify those fetuses at greater risk, so their care is escalated appropriately and in a timely fashion and at the same time, pregnancies at lower risk can be similarly reassured without causing unnecessary anxiety. The aim of such a strategy is two-folded: (1) to exclude CHD or to identify the small number of cases in which cardiac malformations may trigger the arrhythmia and (2) to plan further investigations and FHR

surveillance appropriate to individual cases, based mainly on frequency and pattern of ectopic beats.

The accompanying flow chart (Figure 1) addresses these issues in a systematic way, by considering FHR and frequency of ectopic beats as a starting point. It also considers current practice that relies on widespread screening for CHD using five axial planes, in accordance with established guidelines[10, 11], allowing the use of local resources as the first point of care. The initial scan, which can be organised locally, should be targeted to evaluate normality of the five cardiac screening views, including assessment of heart size and to exclude fetal hydrops or abnormal fluid accumulation in various fetal compartments. It is also important to assess amniotic fluid level. Disturbances of the fetal circulation account for 7% of hydramnios[12]. CHD and persistent tachyarrhythmias may cause heart failure, resulting in elevation of venous pressure, extravasation of fluid into the interstitial space, placental oedema and polyhydramnios[12-15]. Thus, not only the presence of cardiomegaly, pleural, pericardial effusion or ascites, but also increased amniotic fluid in a fetus with frequent ectopic beats should raise the possibility of an underlying intermittent tachyarrhythmia and trigger escalation of care.

If FHR is within normal range and ectopics are infrequent, the likelihood is they will resolve spontaneously (Figure 2). Therefore, the initial scan can be organised locally, done by practitioners who are familiar with performing 'well-being' or 'growth' scans, but also confident in assessing the fetal heart. Normality of this scan is important and those fetuses without persistent irregularities can be followed up with routine prenatal care[4]. In these cases, documenting FHR on subsequent routine antenatal visits and or routine scans is good practice. However, if the irregular rhythm persists for more than 1-2 weeks, it is reasonable to perform an echocardiogram, which is also in line with the American Heart Association (AHA) scientific statement for the diagnosis and treatment of fetal cardiac disease[16].

If FHR is within normal range and ectopics are frequent, there is a small but important risk that the fetus may develop tachyarrhythmia and expert assessment of the mechanism of arrhythmia is warranted. It is also possible that there is an underlying cardiac abnormality such as rhabdomyomas, which may trigger the ectopics. Therefore, whilst an initial local

scan is also good practice, referral for a more advanced ultrasound or fetal echocardiography should not be delayed. The AHA advises fetal echocardiography if ectopics occur every 3-5 beats on average[16].

If FHR is at the lower end of normality, by far the most common reason for the irregular rhythm is the presence of frequent atrial ectopics that can occur as blocked trigeminy (Figure 3) or conducted bigeminy. The majority will also resolve spontaneously even though they can at times persist for weeks, without causing haemodynamic disturbance. Much less frequently however, the same arterial signal pattern, may represent 2nd degree atrioventricular block with variable conduction (Figure 3), which has a different outcome. Furthermore, PACs that manifest with a bigeminal or trigeminal pattern are at increased risk of evolving into tachycardia, but there is also a chance that they may evolve into a bradyarrhythmia, typically caused by blocked atrial bigeminy, when FHR is often around 70-80bpm. This ectopic-related bradycardia also has a benign nature but needs to be differentiated from 2nd degree atrioventricular block[17] (Figure 3). Much less frequently, the ectopics may be of ventricular origin. Figure 4 shows examples of isolated ventricular ectopic as well causing to ventricular bigeminy or ventricular trigeminy (Figure 4). Therefore, the presence of an irregular rhythm with FHR < 120bpm should also trigger escalation of care, with referral for fetal echocardiography.

If FHR is < 110bpm or > 180bpm, the irregular rhythm is, by definition, an irregular bradycardia or tachycardia, respectively, which constitutes an indication for fetal echocardiography.

In summary, PACs are by far the most common reason for rhythm irregularities in the fetus and the majority will have no implications whatsoever for the fetus or pregnancy. If observed as an incidental finding in low-risk population, the risk of associated CHD is small and does not differ significantly from the background risk. Despite the risk of tachyarrhythmia being small, it is significant enough to warrant risk stratification to identify those fetuses who are at-risk and to institute a surveillance plan that allows timely identification of the tachycardia, and to prevent further complications.

Figure legends:

Figure 1

Flowchart with a suggested algorithm to help management of irregular rhythms in the fetus, See text for additional explanation.

Figure 2

Composite figure of pulsed wave Doppler signals in pulmonary vessels (a, b) and LV inflow and outflow (c, d) and M-mode echocardiogramms (e, f) from different fetuses, at different gestational ages with normal heart ate, showing normal rhythm (a, c, e), and atrial ectopic beats (b, d, f). In (b) the single * indicates an atrial ectopic that is not conducted to the ventricles, i.e. blocked atrial ectopic. In (b, d and f) the double * indicates atrial ectopics that are conducted to the ventricles as these are followed by ventricular activity (V). A, atrial activity, E, early diastolic phase.

Figure 3

Composite figure of arterial signals (a, b), pulsed wave Doppler in pulmonary vessels (c, d) and M-mode echocardiograms (e, f), obtained from two different fetuses at 25 weeks (a, c, e) and 21 weeks (b, d, f). In both examples, the arterial signals look similar (a, b) but do not allow distinction between two different arrhythmias, with different clinical implications: blocked atrial trigeminy shown in (c, e) and 2nd degree atrioventricular (AV) block shown in (d, f). Note that in trigeminy (c, e), atrial activity is irregular. There are two atrial contractions (A) leading to two ventricular contractions (V), followed by an atrial ectopic beat (*), which is not conducted to the ventricles. Note that in AV block (d, f), atrial activity is regular. The first two atrial signals are followed by two ventricular signals, indicating they are conducted, but with increasing length of the AV interval, shown in (d) as (1) and (2), and the subsequent atrial signal is blocked (Wenckebach phenomenon).

Figure 4

Composite figure of M-mode echocardiograms (a-c, e) and cross-sectional images (d, f), obtained from three different fetuses at 36 weeks (a, b), 35 weeks (c, d) and 31 weeks (e, f). In (a, b) note examples of isolated ventricular (a) and atrial (b) ectopic beats (*), that resolved spontaneously. In (c, d) note images related to ventricular ectopics (*, in b) in a normal heart, occurring every other beat, e.g. ventricular bigeminy, with accompanying mild mitral and tricuspid regurgitation (arrows, in d). The ventricular ectopics resolved spontaneously after birth. Images in (e, f) also show ventricular ectopics (*, in e), occurring every third beat, e.g. ventricular trigeminy, associated with an aneurysm of the left ventricular free wall (arrows, in f), which required anti-arrhythmic treatment. A, atrial contraction, LV, left ventricle, RV, right ventricle, V, ventricular contraction.

References

1. Wheeler T, Murrills A. Patterns of fetal heart rate during normal pregnancy. *Br J Obstet Gynaecol* 1978; **85**: 18-27.

2. Mitchell JL, Cuneo BF, Etheridge SP, Horigome H, Weng HY, Benson DW. Fetal heart rate predictors of long QT syndrome. *Circulation* 2012; **126**: 2688-2695.

3. Southall DP, Richards J, Hardwick RA, Shinebourne EA, Gibbens GL, Thelwall-Jones H, de Swiet M, Johnston PG. Prospective study of fetal heart rate and rhythm patterns. *ArchDisChild* 1980; **55**: 506-511.

4. Copel JA, Liang RI, Demasio K, Ozeren S, Kleinman CS. The clinical significance of the irregular fetal heart rhythm. *AmJObstetGynecol* 2000; **182**: 813-817.

5. Cuneo BF, Strasburger JF, Wakai RT, Ovadia M. Conduction system disease in fetuses evaluated for irregular cardiac rhythm. *Fetal DiagnTher* 2006; **21**: 307-313.

6. Simpson JL, Yates RW, Sharland GK. Irregular heart rate in the fetus: not always benign. *CardiolYoung* 1996; **6**: 28-31.

7. Tulzer G, Huhta JC, Gudmundsson S, Tews G, Arzt W, Schmitt K. Fetal supraventricular extrasystole: indication for fetal echocardiography? *Klin Padiatr* 1994; **206**: 430-432.

8. Bet BB, de Vries JM, Limpens J, van Wely M, van Leeuwen E, Clur SA, Pajkrt E. Implications of fetal premature atrial contractions: systematic review. *Ultrasound Obstet Gynecol* 2022. DOI: 10.1002/uog.26017.

9. Loane M, Dolk H, Kelly A, Teljeur C, Greenlees R, Densem J, Group EW. Paper 4: EUROCAT statistical monitoring: identification and investigation of ten year trends of congenital anomalies in Europe. *Birth Defects Res A Clin Mol Teratol* 2011; **91 Suppl 1**: S31-43.

10. Carvalho JS, Allan LD, Chaoui R, Copel JA, DeVore GR, Hecher K, Lee W, Munoz H, Paladini D, Tutschek B, Yagel S. ISUOG Practice Guidelines (updated): sonographic screening examination of the fetal heart. *Ultrasound Obstet Gynecol* 2013; **41**: 348-359.

11. Yagel S, Cohen SM, Achiron R. Examination of the fetal heart by five short-axis views: a proposed screening method for comprehensive cardiac evaluation. *Ultrasound ObstetGynecol* 2001; **17**: 367-369.

12. Fischer R, Glob. libr. women's med., (ISSN: 1756-2228) 2008; DOI 10.3843/GLOWM.10208. Amniotic fluid: physiology and assessment.

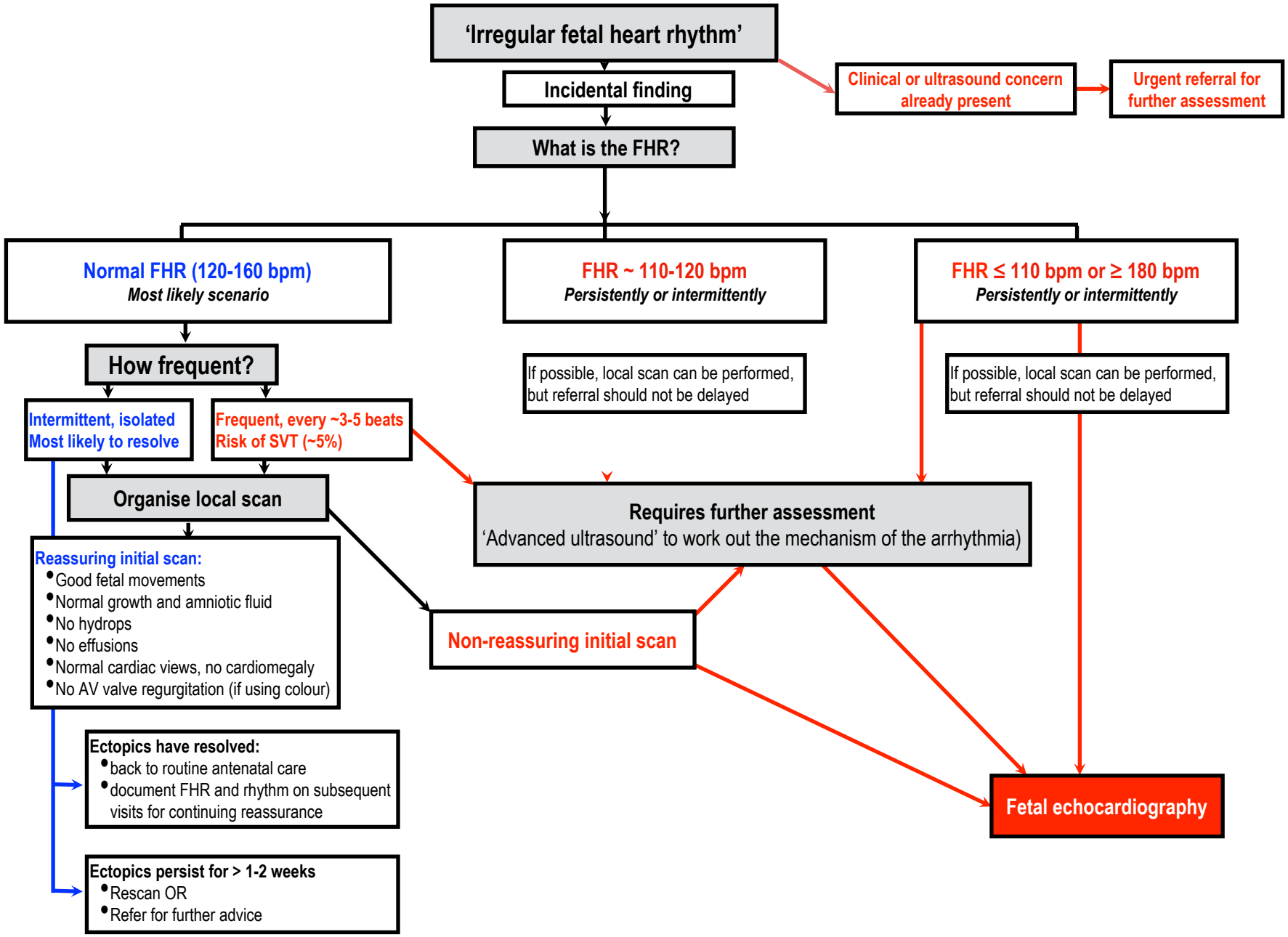
13. Gembruch U, Krapp M, Baumann P. Changes of venous blood flow velocity waveforms in fetuses with supraventricular tachycardia. *Ultrasound ObstetGynecol* 1995; **5**: 394-399.

14. Miyoshi T, Hosoda H, Minamino N. Significance of Atrial and Brain Natriuretic Peptide Measurements in Fetuses With Heart Failure. *Front Physiol* 2021; **12**: 654356.

15. Huhta JC. Fetal congestive heart failure. *Semin Fetal Neonatal Med* 2005; **10**: 542-552.

16. Donofrio MT, Moon-Grady AJ, Hornberger LK, Copel JA, Sklansky MS, Abuhamad A, Cuneo BF, Huhta JC, Jonas RA, Krishnan A, Lacey S, Lee W, Michelfelder EC, Rempel GR, Silverman NH, Spray TL, Strasburger JF, Tworetzky W, Rychik J. Diagnosis and Treatment of Fetal Cardiac Disease: A Scientific Statement From the American Heart Association. *Circulation* 2014; **129**: 2183-2242.

17. Sonesson SE, Acharya G. How to differentiate second-degree atrioventricular block from extrasystoles in fetuses with a bigeminal ventricular rhythm. *Acta Obstet Gynecol Scand* 2020; **99**: 1260-1261.


'Irregular fetal heart rhythm'
Incidental finding
What is the FHR?
Clinical or ultrasound concern already present
Urgent referral for further assessment
Normal FHR (120-160 bpm)
Most likely scenario
FHR ~ 110-120 bpm
Persistently or intermittently
FHR ≤ 110 bpm or ≥ 180 bpm
Persistently or intermittently
How frequent?
If possible, local scan can be performed, but referral should not be delayed
If possible, local scan can be performed, but referral should not be delayed
Intermittent, isolated
Most likely to resolve
Frequent, every ~3-5 beats
Risk of SVT (~5%)
Organise local scan
Requires further assessment
'Advanced ultrasound' to work out the mechanism of the arrhythmia)
Reassuring initial scan:
Good fetal movements
Normal growth and amniotic fluid
No hydrops
No effusions
Normal cardiac views, no cardiomegaly
No AV valve regurgitation (if using colour)
Non-reassuring initial scan
Ectopics have resolved:
back to routine antenatal care
document FHR and rhythm on subsequent visits for continuing reassurance
Fetal echocardiography
Ectopics persist for > 1-2 weeks
Rescan OR
Refer for further advice

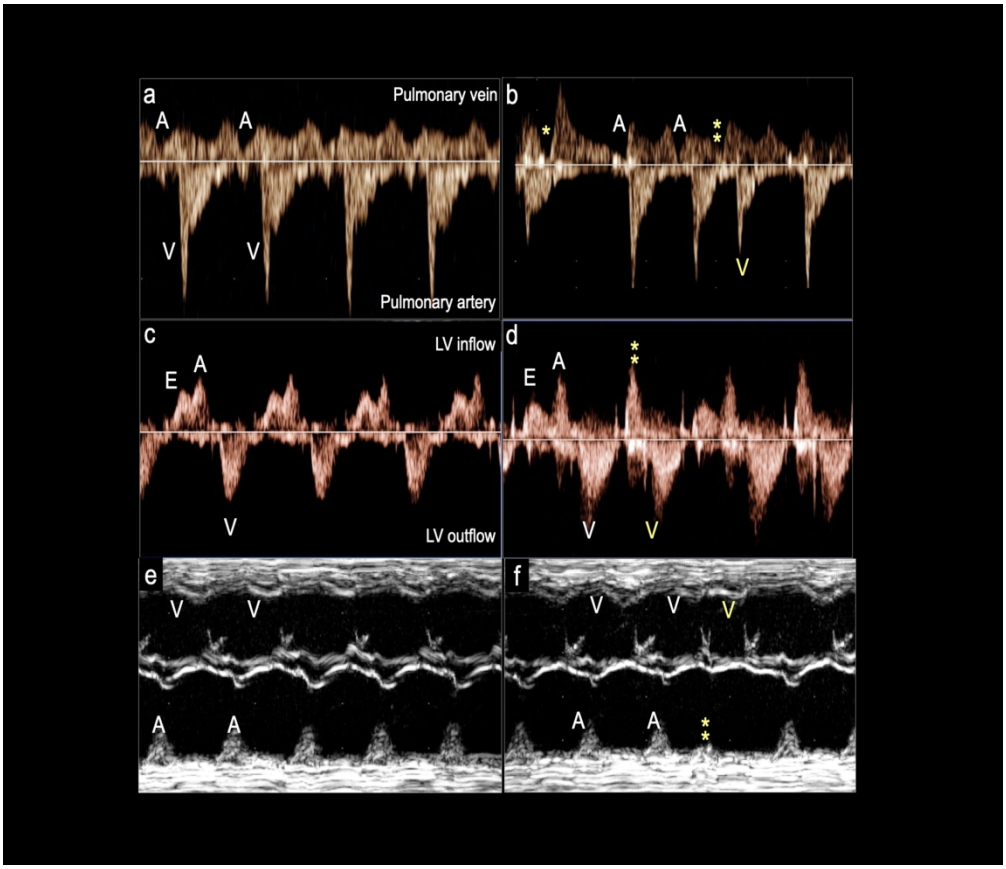


Figure 2

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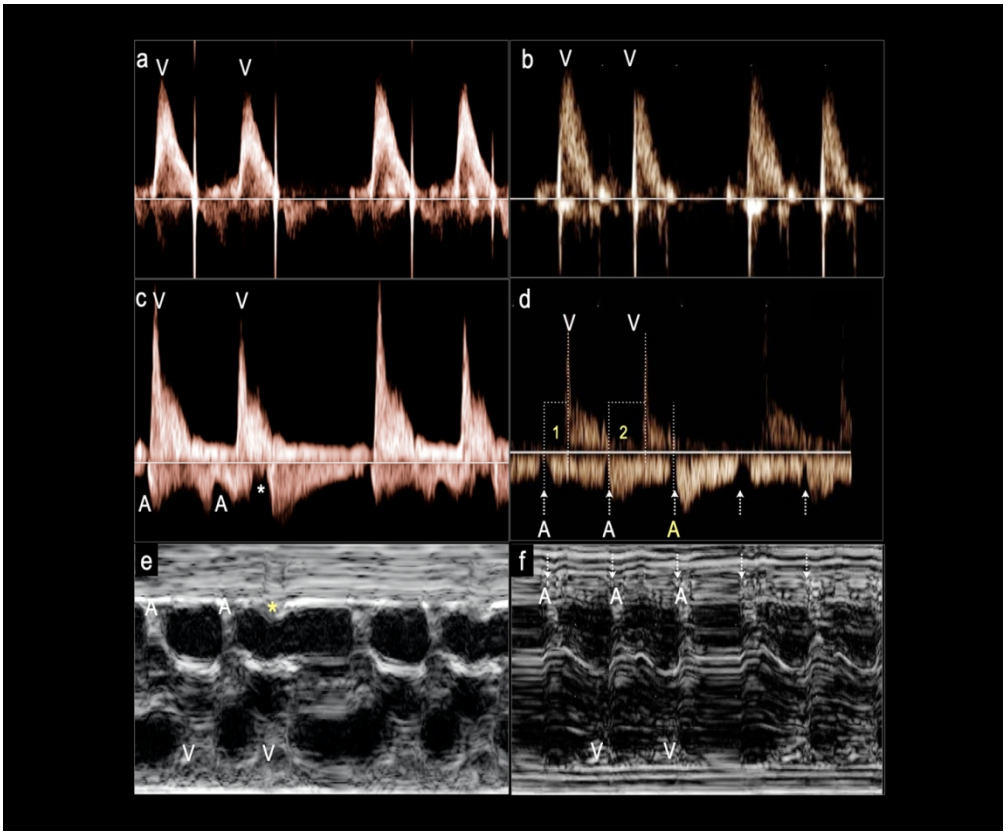

Figure 3

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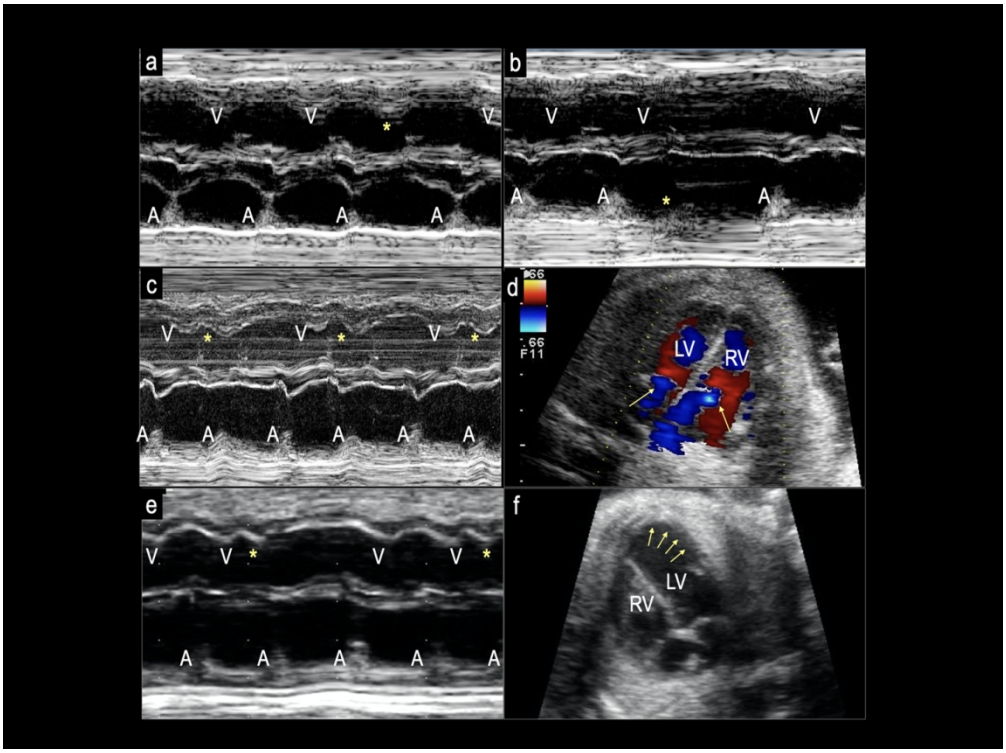

Figure 4

127x94mm (300 x 300 DPI)