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## **ABSTRACT**

**OBJECTIVES:** We propose an image scoring method to improve the quality and the reproducibility of measurement of the AV interval before establishing reference tables of the measurements and studies on the prevention and treatment of first-degree AV block especially if the first child has been diagnosed AV block.

**METHOD :** Prospective study from May 2015 to June 2016. Sonographers were asked to measure AV interval with pulsed Doppler in a five-chamber view in standard second-trimester screening before and after having received our image scoring method. Images were scored by 2 blinded reviewers.

**RESULTS:** The intra-class correlation coefficient (ICC) between the two reviewers for the overall score was 0.91. On average, the measurement quality increased by 2.5 points/10 (95% CI 1.0-4.0). In the second set of images, after the scoring method was given, the score started at 6.50 for the first image, with a significant improvement of 0.18 ( $p=0.016$ ) per subsequent image comparing to a non significant improvement for the first set of image. There was a significant improvement in intra-observer reliability, ICC: 0.680 [95% CI 0.606-0.854] versus 0.458 [95% CI 0.140-0.651]

**CONCLUSION:** The use of this scoring method is simple, reproducible and improves image quality and reproducibility of AV interval measurement in a five-chamber view.



## Introduction

Congenital heart block occurs in 1 in 15000 live births<sup>1</sup> and is usually diagnosed between 20 and 24 weeks of gestation<sup>2,3</sup>. Complete atrioventricular block (AVB) occurs in 2% of fetuses with anti-SSA/SSB-positive mothers<sup>4</sup> and results in 16 to 20% mortality<sup>2-6</sup>.

Transplacental passage of maternal autoantibodies can result in damage to the heart conduction system or fibrosis of fetal cardiomyocytes<sup>7</sup>. The natural history of AVB remains unclear. Some authors report progression from AVB 1 and 2 to complete AVB, even after birth<sup>2</sup>, whereas some authors do not<sup>8</sup>. Although there is a debate about treatment of AVB such as steroids<sup>7-16</sup> or hydroxychloroquine<sup>17,18</sup>, screening for AVB 1 and 2 during pregnancy might be of interest in high-risk pregnancies to follow progression of AVB, warn mothers and pediatricians before birth and would help an effective therapy to be found to avoid incomplete AVB becoming complete. Although M mode ultrasound can be used to screen for complete heart block, the Doppler method is generally used to detect first-degree AVB (AVB 1) and has been shown to be superior<sup>19,20</sup>. The recommendation for now, even if there is no official guidelines for prevention or treatment of AVB is to perform fetal echocardiography every two weeks between 16 and 26 weeks of gestation and every week if there is a previous child affected<sup>21, website</sup>

reference 1

The AV interval is a reflection of the electrical PR interval. Measurement by pulsed Doppler techniques of the electrical PR interval by the mechanical AV interval is an interesting but challenging method. Of the different methods for measuring the AV interval one, in a five-chamber view, consists in placing the pulsed Doppler gate in the left ventricle, at the junction of the anterior leaflet mitral valve and left ventricular

outflow tract. This records velocities in both the mitral valve and the aortic outflow tract. The AV interval is measured between the beginning of the A wave (atrial contraction) and the beginning of ventricular ejection.

We propose an image scoring method based on a grid for measurement of the AV interval in a five-chamber view with pulsed Doppler as a routine tool to facilitate initial learning and ongoing audit. The aim of this study was to evaluate our scoring method. We compared image quality and intra observer variability (accuracy and reproducibility of the measurement) for AV interval measurement, by comparing images before and after using the scoring grid. We also evaluated the reviewers agreement by comparing scores from grids filled by two independent reviewers.

## **Methods**

Our image scoring method for AV interval measurement was developed by two sonographers based on quality criteria concerning anatomic and general Doppler settings. The scoring grid was composed by five criteria related to anatomic conditions and five to Doppler settings (Table 1). Ultrasound images from anti-SSA/SSB-positive mothers were used to highlight technical difficulties and help initial learning and internal audits.

To evaluate this scoring, we performed a prospective study from May 2015 to June 2016 with ultrasonographers trained in antenatal diagnosis.

Flow chart is presented in figure 1.

First, to estimate the impact of the grid on image quality, 4 sonographers trained in antenatal diagnosis were asked by email to measure the AV interval in standard

screening ultrasound between 22 and 24 weeks of gestation. They were told to record pulsed Doppler in a five-chamber view (Figure 2) on ten consecutive fetuses and then to email the images. After the first ten fetuses, we sent them the image scoring method plus all information needed to understand each quality criterion. They then did new measurements using our scoring method on ten other fetuses and emailed us the new images. We collected data concerning fetus presentation, placental position and fetal back position, and maternal body mass index (BMI). At the end of this part, all images were scored anonymously and shuffled by two blinded reviewers (one junior and one senior in antenatal diagnosis) to test the reviewers agreement. The following principles were evaluated in the score: anatomical identification was valid if the five-chamber view was correctly done (with the vertical interventricular septum, the mitral valve and the left ventricular outflow tract visible with aortic valve); the heart had to occupy  $\frac{3}{4}$  of the image; pulsed Doppler had to be gated on the left ventricle, on the junction of the anterior leaflet mitral valve and left ventricular outflow tract for a five-chamber view (overlapping the mitral valve); the angle between blood flow and baseline had to be  $<25^\circ$ ; the pulsed Doppler gate had to be less than or equal to 3 mm. The onset of atrial and ventricular contraction had to be correctly identified on spectral analysis; the velocity scale had to be between four and six cycles per image; the pulse repetition frequency had to be set 10 cm/s above systolic wave velocity; Filter eliminate artefacts from pulsating vessel walls and has to be set for each measurement, it had to be properly configured so as not to lose or highlight information around the baseline. Each item was worth one point for a total of ten points. The image was considered valid if the score was greater than or equal to seven.

Secondly, we analyzed intra-observer variability before and after using the scoring grid with four new sonographers. Intra observer variability is the variability between two repeated measurements done by the same sonographer on the same fetus. The variability tests the accuracy and reproducibility of the measurements. Sonographers were asked to do the same designed study except that they had to perform two PR interval measurements per fetus (with a few minutes interval).

Reviewers agreement was assessed using an intra-class correlation coefficient for overall score and Cohen's kappa for each criterion. The mean of the two reviewers' scores was used to compare the scores before and after using the image scoring method. A t test was used to compare the overall scores before and after the score using a p value < 0.05 as significant. The best statistical model was selected by applying the Akaike information criterion and included the sonographer's initial level and individual learning curve. The impact on scoring of BMI, fetal presentation, placental position and fetal back position were evaluated by means of Anova with a p value < 0.05 taken as significant.

The intra observer variability was assessed using an intra-class correlation with bootstrap confidence intervals (1000 replicates). Means of atrio ventricular measurement were compared with mixed model including the sonographers, fetus and measures as random effect and time (before and after) and five chamber view as fixed effect with a p value <0,05. Patients gave agreement to have this AV interval measurement, and data were collected anonymously.

## **Results**

### **Reviewers agreement on scoring and impact of the scoring method on image quality**

In the first part of the study, four sonographers participated. Eighty images were included in the study. All were recorded by means of scores given by the two reviewers. Mean gestational age was 23.9 weeks of gestation before scoring (SD 3.6) and 23,9 after (SD 2,9).

Internal consistency (reviewer agreement on scoring) for each image-scoring criterion was evaluated according to Landis and Koch<sup>22</sup> and is reported in Table 2. The intra-class correlation coefficient for the overall score was 0.91. The intra-class correlation coefficient excluding filter criteria was 0.89.

Each sonographer improved his overall score. The scores were (mean±SD) 4.1 ± 2.28; 6.95 ± 1.19; 3.65 ± 1.70; 5.35 ± 1.58 before using the image scoring method and respectively 8.65 ± 1.40; 7.8 ± 0.88; 5.75 ± 1.40; 7.8 ± 1.73 after (p=0.0018). On average, there was an increase of 2.5 points (CI95 1-4) for every image.

A statistically significant increase was noted for anatomical structure identification, pulsed Doppler gate position, pulsed Doppler gate size, angle correction, identification of onset of atrial contraction, identification of onset of ventricular contraction, and velocity scale (Table 3).

On the first image, before the scoring method was provided, the mean score for all sonographers was 4.69 points with a non significant improvement of 0.06 points for every subsequent image (p=0.53). On the first image, after the scoring method was given, the score for all sonographers was 6.50 with a significant improvement of 0.18 (p=0.016) for every subsequent image. Thus, there was no significant improvement on the first ten images (without the scoring method). The difference between the first image before scoring and the first image after scoring was 1.81 (p=0.0269).

None of the following parameters had a significant impact on the score: fetal presentation, back position, placental position, maternal BMI.

### **Impact of the scoring method on intra observer variability**

In the second part of the study, four new sonographers trained in antenatal diagnosis participated. 34 fetuses were screened before scoring, 38 after. 152 images were collected (72 before scoring, 80 after). Mean gestational age was 23.9 weeks of gestation before scoring (SD 3.84) and 24.8 after (SD 4.54). The mean AV interval was 116.5 ms (SD 16.1) before scoring and 114 ms after (SD 13.4). There was no significant difference ( $p=0.414$ ) for the AV measurement using the scoring method or not. Two fetuses had a measurement above 150 ms.

The intra-observer variability (agreement between two repeated measures by same sonographer on same fetus) in AV measurement was improved with the scoring method: the intra-class correlation coefficient (ICC) was 0.458 [95% CI 0.140; 0.651] in the first series of images and 0.680 [95% CI 0.606; 0.854] in the second series after the scoring method.

The AV measurement depended on cardiac frequency and gestational age. The ICC adjusted for those parameters was 0.500 [95% CI 0.228; 0.727] before the scoring method and 0.623 [95% CI 0.503; 0.827] after.

## **Discussion**

This prospective study shows that our image scoring method is simple to use, it significantly improved the image quality and the intra-observer accuracy and reproducibility of AV interval measurement in a five-chamber view.

### **Reviewer agreement and impact on image quality**

Images were scored by two blinded reviewers (one junior and one senior) to assess their agreement. Intra-class correlation for overall score and internal consistency for each criterion except filter criteria were consistent, showing that our image scoring method is simple and reproducible, independently of the skills of the reviewer in antenatal diagnosis.

The sonographers' scores increased significantly for seven criteria and non-significantly for three.

Although the sonographers were contacted by email with an attached article explaining how to measure the AV interval<sup>23</sup>, all had a mean overall score under 7. The use of the new scoring method enhanced image quality in terms of anatomical structure identification and Doppler settings. Criteria concerning anatomical structure identification, such as a vertical interventricular septum, which provides a higher quality Doppler spectrum, were respected more in the second series of images. Pulsed Doppler gate size and velocity scale were improved using the image scoring method. These parameters are predefined by the manufacturers and must be modified to improve the

Doppler spectrum. For example, too large a Doppler gate size has a huge impact on spectral Doppler, because it leads to artifactual noises from the heart walls or valves, or from turbulent flow. The identification of the onset of atrial and ventricular contraction was also enhanced by using the scoring method, while the zoom and pulse repetition frequency (PRF) were not. The score for PRF goes from 0,58 to 0,7 so there is an improvement but not statistically; the first score 0,58 means that PRF was already optimized by sonographers before using the new image scoring method, so they may be used to adjust it already and thus the improvement seen here isn't statistically significant. In contrast, the zoom was insufficiently adjusted in the second part of the study, even though it is important for the quality of measurement of pulsed Doppler signals. The criteria to have a point was to have a zoom enough for the Doppler waveform to take part of  $\frac{3}{4}$  of the image, which is maybe a little bit strict.

There was fair agreement for filter criteria. Filtering is a key Doppler setting in cutting out noise and was one of the items in the initial image scoring. It was difficult to evaluate from the Doppler waveform if the filter was correctly set and complementary training might be needed. The overall intra-class correlation was analyzed again without this criterion but was not enhanced. As it didn't changed the overall score and although it seems to be difficult to evaluate, we thought that it was an important criterion to remind to improve the image quality and to keep it in the final score.

The Doppler method is usually used to detect first-degree AV block and has proven superior<sup>19,20</sup> to TM mode Doppler, but is more difficult to learn. Some ultrasound equipment now has two pulsed Doppler gates at the same time, which helps sonographers perform this measurement.

All sonographers included found AV interval measurement difficult. One sonographer had a mean score below seven after using the image scoring method, which shows that the measurement is difficult and presupposes both theoretical and practical learning.

A score of 7 out of ten was used to accept the measurement. This threshold may appear high compared with the Herman scoring method<sup>24,25</sup>, but this method has minor and major criteria and a distribution of scores in four groups to avoid a too large dispersion of scores. There is no such thing in our scoring and several individual points may be validated without an acceptable image quality.

Fetal presentation, back position, placental position, and maternal BMI had no impact on the score, which emphasizes the skills of the sonographers who agreed to participate, all of whom work in prenatal diagnosis centers and are used to dealing with the technical constraints of ultrasound measurements.

#### **Impact on intra observer accuracy and reproducibility**

Intra-observer variability (variability between two repeated measures by same sonographer on same fetus, which represents the accuracy and reproducibility of the measure) was analyzed using the intra-class correlation coefficient. ICC was improved using the image scoring method in a five-chamber view. These results were difficult to compare to those already published in the scientific literature. Indeed, we found one study<sup>20</sup> in which the intra-observer ICC was 0.90 [95% CI 0.81-0.95] for the five-chamber view. This result is much higher than our own, but it is important to notice that this study was conducted in by cardiologists specialized in pediatrics participated, and that there were only two of them. Their greater experience in the Doppler use may explain this difference.

The means of AV intervals in our study are similar to those found in the literature<sup>26,27</sup>. Wojakowski *et al*<sup>26</sup> found a variability depending on gestational age and cardiac frequency: in 336 fetuses, AV interval increased with gestational age and inversely decreased with cardiac frequency. In our study we found a similar significant result for cardiac frequency, but results for gestational age were not significant. Glickenstein *et al*<sup>27</sup> found no variation in any of those two parameters, but their study sample was smaller (56 fetuses).

### **Interest of an image scoring method**

First, Crowse *et al*<sup>28</sup> show that diagnosis of AVB is still a field of interest as there was the 9th International Conference of Reproduction, Pregnancy and Rheumatic Diseases where AVB in fetuses exposed to anti SSA/SSB antibodies was one of the topics. We have limited evidence to support approaches to prevent, predict or treat AVB, so we have to still document this disease by following up fetuses exposed to anti SSA/SSB antibodies.

For now, AIUM Practice Guidelines<sup>21</sup> revised in 2013 recommend fetal echocardiography to be performed in case of maternal anti SSA antibodies. In France it is recommended to perform this echocardiography every two weeks between 16 and 26 weeks of gestation and every week if there is a previous child affected website reference 1.

The scoring method we propose helps to make AV measurement, to detect PR prolongation, which is the definition of AVB 1, not AVB 2 or 3. Eventually you might use it to detect AVB 2 Mobitz 1 if you repeat the measure on several consecutive waveforms. Is this measurement useful? Buyon *et al*<sup>2</sup> described nine AVB 1 on 187 fetuses exposed to

anti SSA and SSB, among them 4 shows progression after birth. Krishnan *et al*<sup>14</sup> on 140 fetuses exposed to anti SSA/SSB antibodies didn't detect any AVB 2 or 3, and detected only five AVB 1, which didn't progress. But there was a second cohort in this study (fetuses referred for AVB with subsequent known of exposition to antibodies) where an AVB 2 reverted to AVB 1 without treatment. Levesque *et al*<sup>13</sup>, treat about AVB 2 and 3, AVB 1 are excluded from the study but described regression to AVB 1 in cases of untreated fetuses. Doti *et al*<sup>16</sup> presented 18 fetuses with AVB, among them only one did have AVB 1 and didn't progress, and another one had AVB 2 regressing to AVB 1 with dexamethasone. Eliasson *et al*<sup>15</sup> didn't support therapeutic strategy with steroids for regression of third degree BAV but concluded that there might be an interest in second degree AVB.

Thus the pathophysiological background to AV block remains unclear : some intermediate AVB progress to complete AVB, some regress and the treatment to avoid this progression is still debated. We think there is an interest to know how to detect AVB 1 in mother with anti SSA antibodies during the pregnancy to warn mothers and pediatricians and follow properly those children after birth, even if there is no treatment recommended for now during pregnancy .

A first thing to do is to define a threshold to describe an AVB 1. The threshold varies from one study to another<sup>3,10,27</sup>. This lack of consensus highlights the difficulty of interpreting the literature about the natural history of AV block and of possible therapeutics, including treatment to avoid progression to AVB 2 or 3. The first step before performing studies about prevention and treatment of first-degree AV block is to have correct quality images and to enhance the intra-observer reproducibility of measurement. It may also help in

future studies to establish new reference tables for AVB measurements in fetuses of patients with and without anti-SSA/SSB antibodies.

For all those arguments we think that the scoring method we propose is useful. It is still important to help sonographers to do this measurement properly, to define clearly the threshold of AVB 1, to have more information on progression of the disease, and eventually make new studies to find another treatment.

Our image scoring method can enhance initial learning and internal audit or external audit, as does the scoring method proposed by Herman *et al*<sup>24,25</sup> for nuchal translucency, except that it concerns a specific population.

### **Conclusion:**

We propose an image scoring method for AV interval measurement with pulsed Doppler in a five-chamber view to improve initial learning and ongoing audit. Our findings show that this scoring method significantly improves the quality of the measurement and intra-observer accuracy and reproducibility on the atrioventricular interval. It may help sonographers to detect fetal AV block in anti-SSA/SSB-positive mothers.

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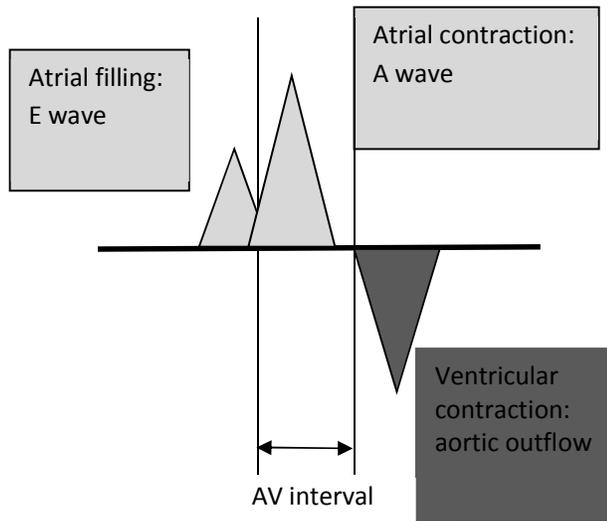
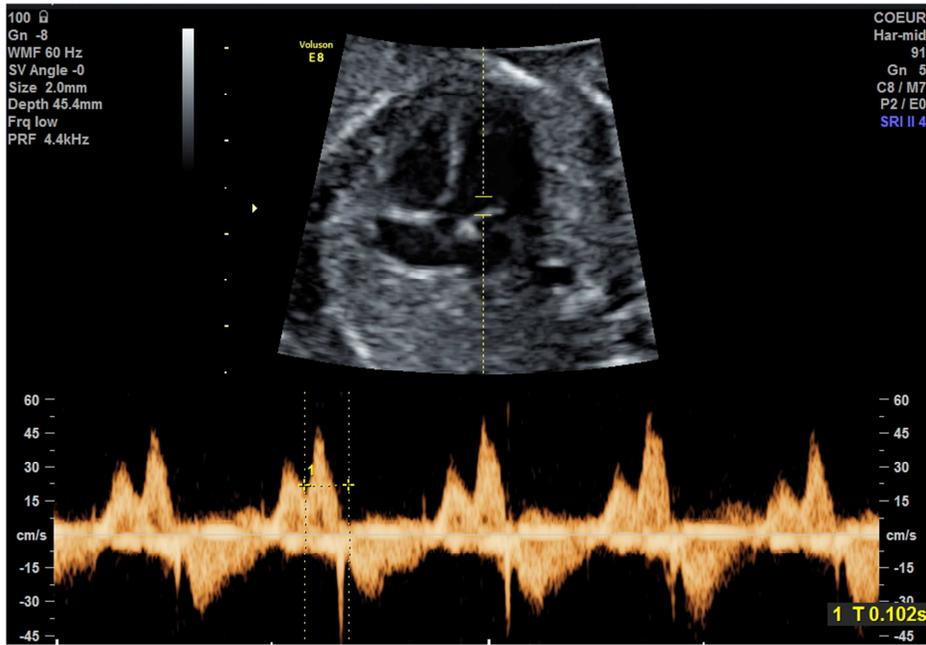
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Janvier 2010

Figure 1: Pulsed Doppler for atrioventricular interval measurement in five chamber view



Atrioventricular interval in the five-chamber view is measured from the intersection between E wave and A wave to the onset of ventricular contraction



Table 1: Image scoring for atrioventricular interval measurement

Image analysis		Spectral analysis	
<p>Anatomical structure identification:</p> <p>Five-chamber view with vertical interventricular septum, mitral valve, left ventricular outflow tract visible with aortic valve</p> <p>superior vena cava/ascending aorta : ascending aorta adjacent to superior vena cava draining in the right atrium</p>	1 pt	Identification of onset of atrial contraction	1pt
Zoom: 3/4 of image	1pt	Identification of onset of ventricular contraction	1pt
<p>Pulsed Doppler gate position:</p> <p>Five-chamber view: gate on left ventricle, junction of anterior leaflet mitral valve and left ventricular outflow tract</p> <p>superior vena cava/ascending aorta: gate at junction of the two vessels</p>	1pt	Velocity scale (4-6 cycles/image)	1pt
Pulsed Doppler gate size ( $\leq 3$ mm)	1pt	Pulse repetition frequency (10 cm/s above systolic wave)	1pt
Angle between blood flow and baseline (<25°)	1pt	Filter	1pt
Total	5 pt		5pt

Table 2: Internal consistency between the two reviewers for each criterion

Kappa Cohen Test		
Anatomical structure identification	0.62	Substantial agreement
Zoom	0.72	Substantial agreement
Pulsed Doppler gate position	0.59	Moderate agreement
Pulsed Doppler gate size	0.92	Almost perfect agreement
Angle correction	0.68	Substantial agreement
Identification of onset of atrial contraction	0.85	Almost perfect agreement
Identification of onset of ventricular contraction	0.82	Almost perfect agreement
Velocity scale	0.80	Substantial agreement
Pulse repetition frequency	0.62	Substantial agreement
Filter	0.32	Fair agreement

Table 3: Score (/1point) for each criterion before and after using the image scoring

T -Test	Before	After	p value
Anatomical structure identification	0.55	0.81	0.005
Zoom	0.39	0.53	0.188
Pulsed Doppler gate position	0.73	0.9	0.025
Pulsed Doppler gate size	0.31	0.93	<0.001
Angle correction	0.33	0.64	0.002
Onset of atrial contraction identification	0.63	0.95	<0.001
Onset of ventricular contraction identification	0.7	0.95	0.002
Velocity scale	0.31	0.54	0.03
Pulse repetition frequency	0.58	0.7	0.2
Filter	0.5	0.56	0.49

Table 4: Impact of ultrasound constraints on score

ANOVA	P value
Fetal position	0.7
Back position	0.22
Placental position	0.35
BMI	0.3