Evaluation of Right Myocardial Performance Index of In Vitro Fertilization Fetuses and Spontaneous Pregnancy Fetuses: A Cross-Sectional Study

Shaoqi Chen
First Affiliated Hospital of Shantou University Medical College
Zemin Zhuang
First Affiliated Hospital of Shantou University Medical College
Qingzi Chen
First Affiliated Hospital of Shantou University Medical College
Xiya Du
First Affiliated Hospital of Shantou University Medical College
Xuerui Tan (doctortxr@126.com)
First Affiliated Hospital of Shantou University Medical College

Research

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Abstract

OBJECTIVE

To establish normal reference range for the fetal right myocardial performance index (RMPI), and compare the reference range between in vitro fertilization (IVF) fetuses and spontaneous pregnancy (SP) fetuses by automatic measurement of the RMPI.

METHODS

From September 2019 to January 2020, 410 participants, who were at 19-40 weeks' gestation, were enrolled into the current study. Among 410 participants, there were 371 spontaneous pregnancies which were matched as control group, and the experimental group involved 39 singleton pregnancies conceived by IVF. RMPI was calculated as (a-b)/b. The three readings were obtained and averaged per examination, with intra-observer repeatability assessed by intraclass correlation coefficient (ICC) and 95% confidence interval (CI). The 'a' and 'b' intervals were measured at 3 different caliper positions in each fetus: beginning of the original valve clicks ('original'), beginning of the reflected tricuspid and pulmonary closure clicks ('reflected'), and peak of valve clicks ('peak').

RESULTS

The RMPI of SP fetuses was 0.43±0.05 (mean ± standard deviation (SD)), and the RMPI of IVF fetuses was 0.42 ±0.05 (mean ± SD). There was no significant difference in normal reference range of right MPI between IVF fetuses and SP fetuses. No strong correlation was also noted between RMPI with gestational age and heart rate.

CONCLUSION

Normal reference ranges of RMPI of IVF fetuses and SP fetuses were established, and no significant difference between IVF fetuses and SP fetuses was found.

Introduction

Assisted reproductive technology (ART) includes medical procedures used primarily to address infertility. This subject involves procedures, such as in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), cryopreservation of gametes or embryos, and/or the use of fertility medication. However, its safety is still controversial, and the birth defects of its offspring have greatly attracted scholars' attention. Yan et al. reported that there was no significant increase in birth defects in the ART offspring [1]. However, a number of scholars pointed out that infants born after ART treatment had a higher risk of birth defects than those who conceived spontaneously, and the risk of congenital heart defect (CHD) in ART fetuses was higher than that in spontaneous pregnancy (SP) fetuses [2-3]. Children conceived by ART manifested the existence of cardiac and vascular remodeling in fetal life and persisted in postnatal life, suggesting opportunities for early detection and potential intervention [4]. However, several pregnant women prefer IVF in ART, thus it is of great importance to compare the safety of IVF with ICSI.

The myocardial performance index (MPI) was first proposed by Tei et al. [5] for the evaluation of heart function in adults with dilated cardiomyopathy. The non-invasive, Doppler-derived MPI has been reported to be useful as a combined index of global myocardial function. The MPI is defined as the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET) [6-8]. However, due to anatomical factors, numerous scholars have concentrated on the left MPI. To our knowledge, the right ventricle indicates physiological dominance and is more sensible to the change in fetuses, thus, the right ventricle may change before the left when neonatal hypoxia-ischemia happens. In other words, the right MPI may be more representative and can sensitively reflect the fetal cardiac function.

Although the MPI is a promising indicator, the measurement of traditional right MPI is more complicated compared with the left MPI. Recently, automatic measurement of fetal right MPI (RMPI) from pulsed wave Doppler spectrum was described by Suresh et al. [9]. This method can simplify the mensuration of RMPI. In the present study, we aimed to propose a new method to measure the RMPI of Spontaneous Pregnancy (SP) fetuses and IVF fetuses, and compare the reference range of IVF and SP fetuses.

Patients And Methods

This was a prospective cohort study approved by the Ethics Committee of the First Affiliated Hospital of Shantou University Medical College (Shantou, China). Written informed consent was obtained from all participants. From September 2019 to January 2020, 410 participants, who were at 19-40 weeks' gestation, were enrolled into the current study. There were 371 spontaneous pregnancies that were matched as control group and 39 singleton pregnancies conceived by IVF. All the participants underwent transabdominal fetal ultrasound to gain fetal biometric parameters. Patients were excluded if they had any maternal diseases, such as high blood pressure and diabetes. Additionally, if there were any fetal malformations, e.g. CHD at the time of undergoing ultrasound or later diagnosis of any fetal malformation, the patients were excluded as well.

An HERA W10 ultrasound system (Samsung, Seoul, Korea) equipped with a 1-7 MHz probe was used to perform MPI. Mechanical and thermal indices were defined < 1.0 and < 2.0, respectively. The angle of insonation was kept below 30°. The measurement of RMPI included two steps. Firstly, the transverse four-chamber view of the fetal thorax with an apical or bottom heart and the outflow tract of right ventricle were obtained to show the tricuspid valve and pulmonary valve clearly, and the Doppler gate was put at the tips of the tricuspid and pulmonary leaflets to capture inflow image and the outflow image, respectively. The images showed opening and closing of the valves (Figs. 1-3). Secondly, the inflow image and the outflow image were captured together (Fig. 4). Then, an automatic measurement system applied a novel “coarse-to-fine” strategy to detect the coarse cardiac cycle (CC) and valve click (VC) range (inflow/outflow peaks) [9]. RMPI was calculated as (a-b)/b. The three readings were obtained and averaged per examination, with intra-observer repeatability assessed by intraclass correlation coefficient (ICC) and 95% confidence interval (CI). The ‘a’ and ‘b’ intervals were measured at 3 different caliper positions in each fetus: beginning of the original valve clicks (‘original’), beginning of the reflected tricuspid and pulmonary closure clicks (‘reflected’), and peak of valve clicks (‘peak’).

Statistical Analysis

SPSS 23.0 software (IBM, Armonk, NY, USA) was used to perform statistical analysis. Kolmogorov-Smirnov test (K-S test) and Shapiro-Wilk test (S-W test) were applied to assess normal distribution of the data. Normally distributed data were expressed as mean ± standard deviation (SD). Student’s t-test was utilized for comparing normally distributed data, including RMPI, total spent time (TST), ICT, IRT, and ET between IVF fetus and SP fetus. The relationships of the RMPI, TST, ICT, IRT, and ET with gestational age (GA) and heart rate (HR) were analyzed by linear regression analysis. $P<0.05$ was considered statistically significant.

Results

There were totally 410 subjects included in this study. The control group was composed of 371 SP pregnancies, and the average age was 29 years old (range of age, 18–45 years old). The experimental group was composed of 39 IVF pregnancies, and the average age was 32 years old (range of age, 20-40 years old).

There was no significant difference between IVF fetuses and SP fetuses in TST ($P>0.05$), ICT ($P>0.05$), IRT ($P>0.05$), ET ($P>0.05$), and MPI ($P>0.05$) (Table 1). There was no strong correlation between RMPI and GA (SP fetuses, $r^2=0.1061$; IVF fetuses, $r^2=0.0004$), and between RMPI and HR (SP fetuses, $r^2=0.1145$;IVF fetuses, $r^2=0.0834$) in SP fetuses and IVF fetuses (Figs. 5-8).

Table 1 Summary of parameters

	SP fetus	IVF fetus	p
TST	248.06±15.64	242.92±13.73	0.053
ICT	30.98±9.99	28.36±10.27	0.120
IRT	44.23±10.02	44.08±10.12	0.926
ET	172.86±11.43	169.97±10.12	0.133
MPI	0.43±0.05	0.42 ±0.05	0.891

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Discussion

There are increasingly IVF pregnancies, thus, it is very beneficial for patients to indicate whether the fetal cardiac function is abnormal or not by non-invasive methods. Therefore, it is highly essential to determine the reference range of fetal cardiac function.

In this study, linear regression analysis was used to show that there was no strong correlation between RMPI and GA, and between RMPI and HR in SP fetuses and IVF fetuses (Figs. 5-8). Ghawi et al. reported that MPI is independent from GA and HR [10]. They pointed out that systolic ventricular function changes from high- to low-level, while diastolic ventricular function is gradually matured from low- to high-level with the increase of GA [10]. MPI is advantageous for comprehensive evaluation of cardiac systolic and diastolic ventricular functions, therefore, this may be the reason why MPI does not change with GA.

The method of automatic measurement of RMPI used in the present study is time-consuming, eliminating the need to measure ICT and IRT time, respectively. This is also essential to measure the spectrum of tricuspid valve and pulmonary valve, put the two pictures together, and then select the appropriate CC, and the system will automatically calculate the values of ICT, IRT, ET, and MPI. The values measured by this method are similar to those reported by Ghawi et al. [10] and Hamela-Olkowska et al. [11].

The present study unveiled that there was no significant difference in normal reference range of right MPI between IVF fetuses and SP fetuses. This may suggest that there was no obvious cardiac abnormality in IVF fetuses during the fetal period, or the change of cardiac function may not occur at the beginning of the IVF fetus. The normal reference range of cardiac RMPI in the SP fetus and the IVF fetus can be shared as well.

Valenzuela-Alcaraz et al. pointed out that the cardiac and vascular remodeling exist in the fetuses received by ART [4]. In theory, compared with IVF fetuses, ICSI fetuses were not fertilized by natural selection. During the operation of ICSI, there is a greater threat to children’s health. Compared with IVF, ICSI bypasses the natural selection barrier of oocytes to sperm and may inject poor quality sperm to pass on certain genetic defects and high genetic risk genes to the next generation [12-13]. This may indicate that ART technology may affect fetal cardiac function, while IVF may be relatively safe. However, we still cannot conclude that IVF has no influence on fetal cardiac function. In the current study, we measured the RMPI of IVF fetuses in the second and third trimesters of pregnancy and the impact of IVF on fetal cardiac function could not be assessed during measurement.

There were a number of limitations in the present study. Firstly, the sample size of IVF fetuses was extremely small. Secondly, we did not collect ICSI fetuses for the study. Collecting ICSI fetuses for making comparison with other parameters may increase the accuracy of our findings. In addition, this was a cross-sectional study and was limited to the second and third trimesters of pregnancy [14]. Last but not the least, our study lacked an invasive gold standard to determine the accuracy of RMPI measurements. Thus, further experiments with large sample size are required to confirm our findings and eliminate the above-mentioned deficiencies.

Conclusions

During fetal period, no significant difference was noted in RMPI between IVF fetuses and SP fetuses. This may suggest that IVF is more secure than ART technology. Therefore, the normal range of RMPI values of SP fetuses and IVF fetuses can be shared during fetal period.

Declarations

Ethical Approval and Consent to participate The Ethics Committee of the First Affiliated Hospital of Shantou University Medical College had approved this study.

Consent for publication Each author has confirmed compliance with the journal's requirements for authorship and all the authors agree to publish.

Availability of data and materials The data that supports the findings of this study are available in the supplementary material of this article.

Competing interests The authors did not report any potential conflicts of interest.

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Authors' contributions Each author has confirmed compliance with the journal's requirements for authorship.

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Abbreviations

1. IVF in vitro fertilization
2. SP spontaneous pregnancy
3. RMPI right myocardial performance index
4. SD standard deviation
5. ICT isovolumetric contraction time
6. IRT isovolumetric relaxation time

7. ET ejection time
8. TST total spent time
9. ART assisted reproductive technology
10. ICSI intracytoplasmic sperm injection
11. CC cardiac cycle
12. VC valve click
13. ICC intraclass correlation coefficient
14. CI confidence interval
15. CHD congenital heart defect
16. HR heart rate
17. GA gestational age

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Figures

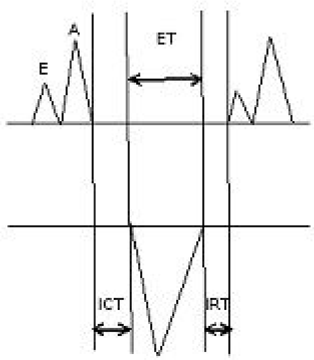

Figure 1

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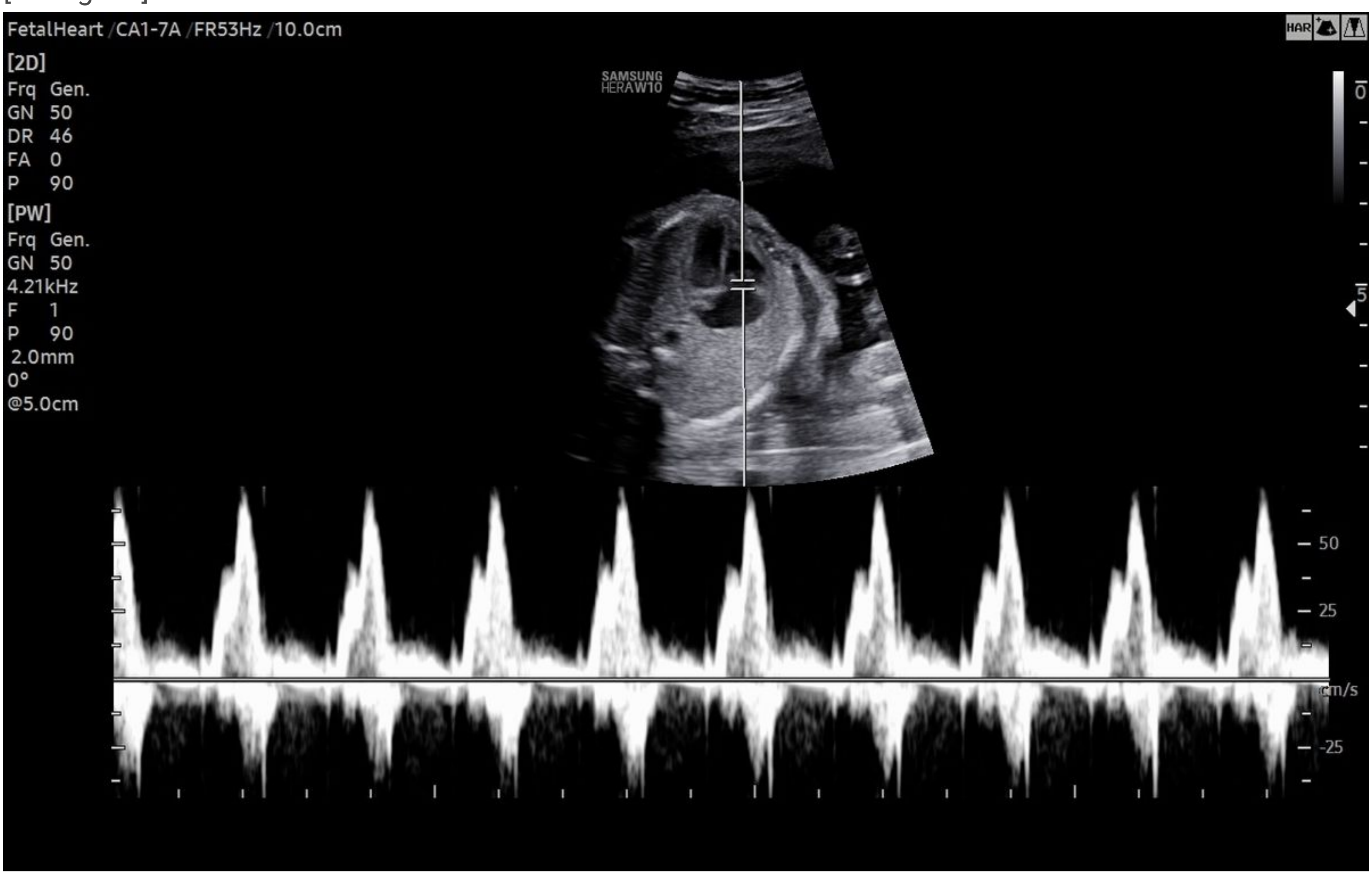

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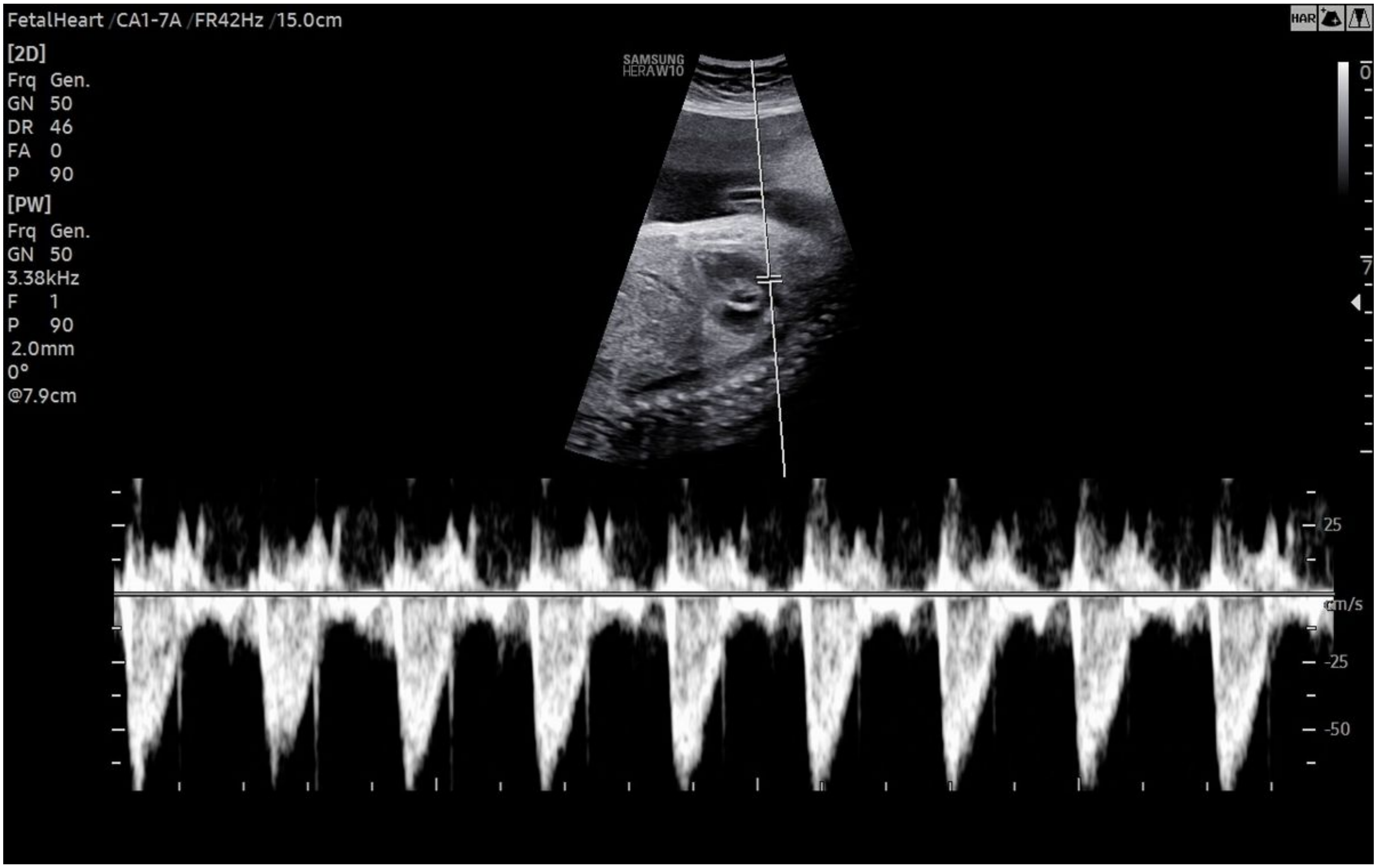

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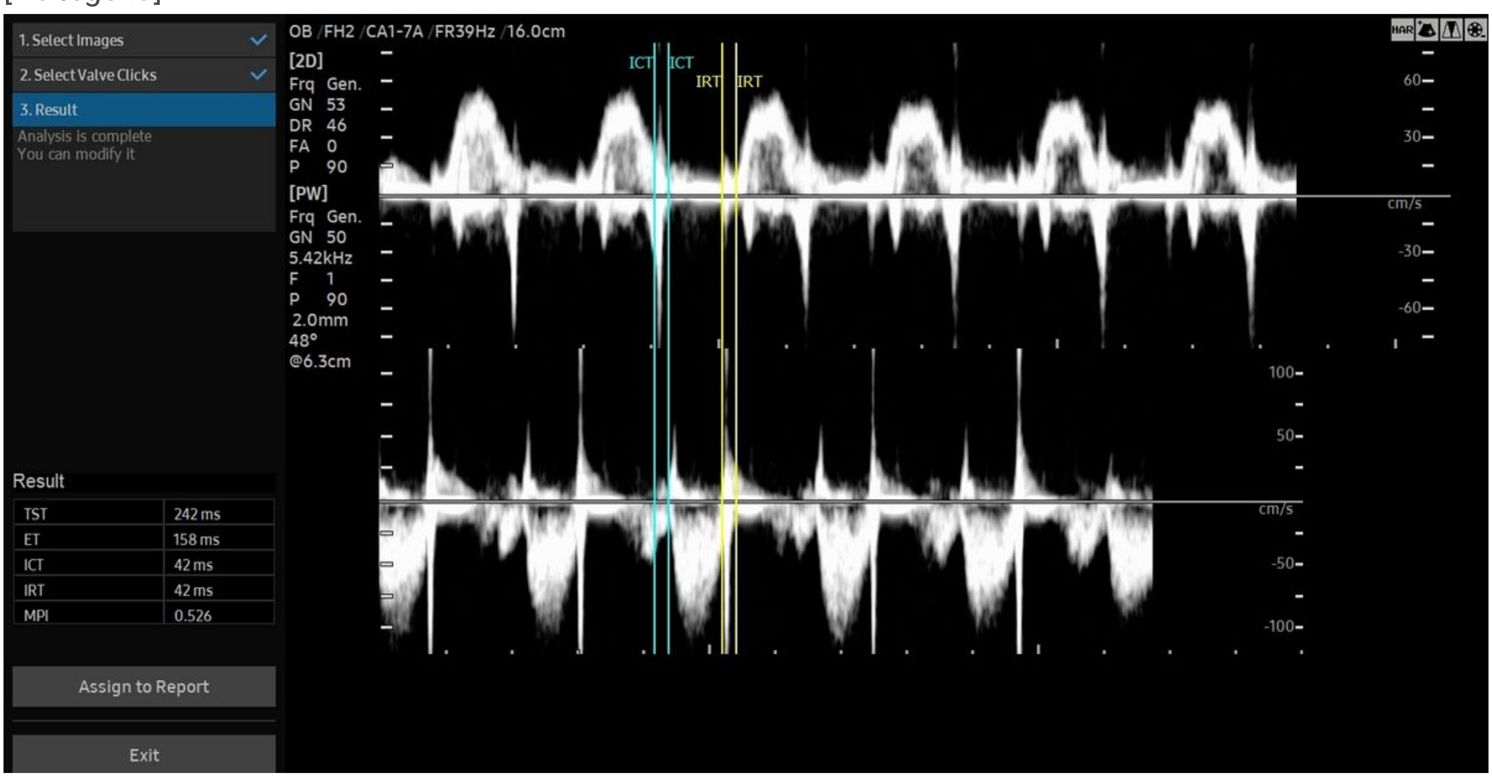

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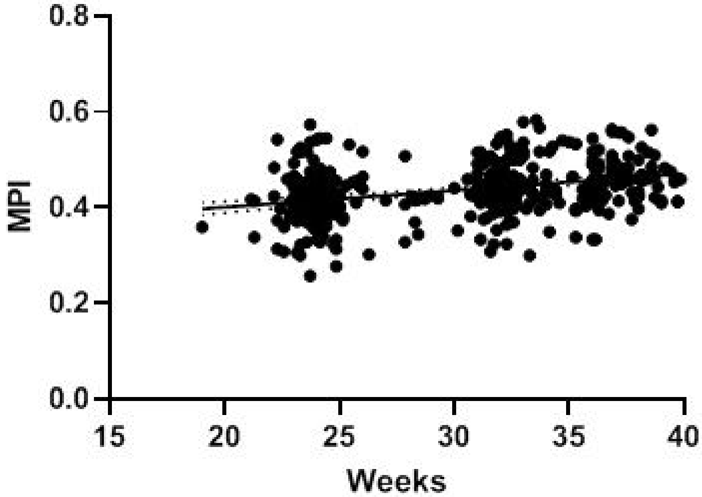

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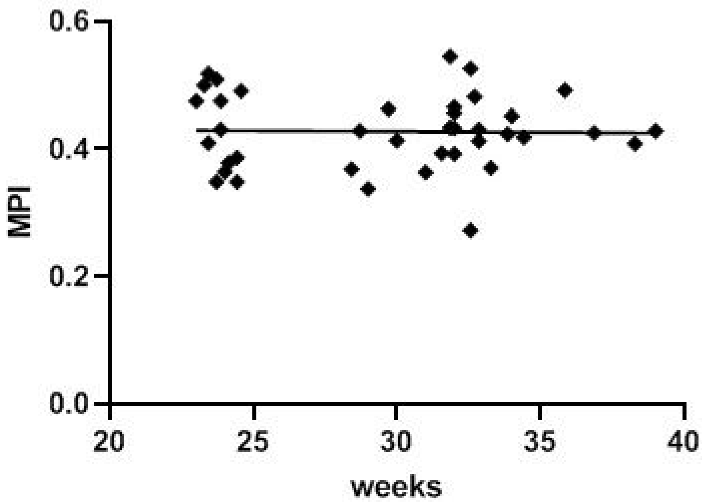

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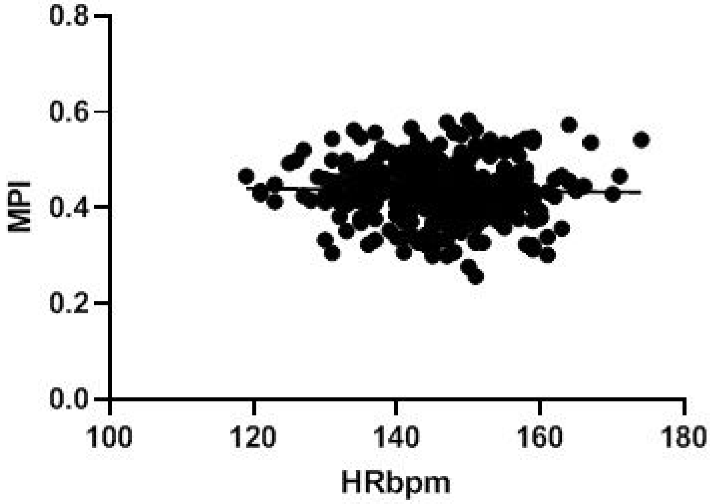

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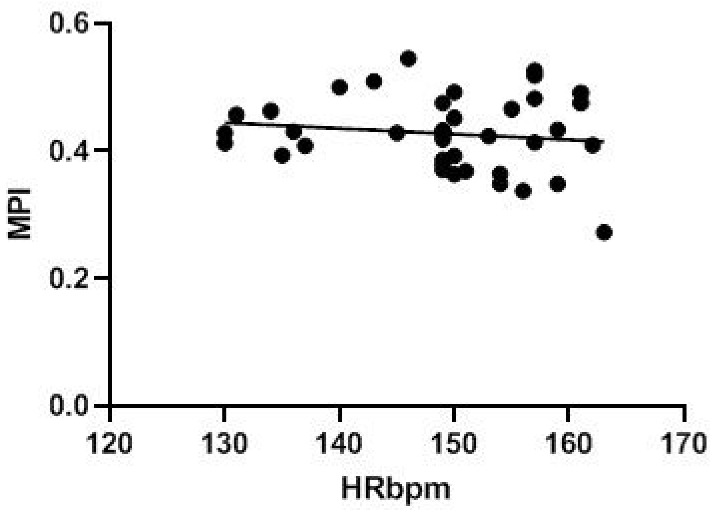

Figure 8

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- SPfetusandIVFfetus.xlsx