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EDITED BY

Oswin Grollmuss,
Université Paris-Sud, France

REVIEWED BY

Federico Gutierrez-Larraya,
University Hospital La Paz, Spain

Liqun Sun,
University of Toronto, Canada

Ashish Garg,
Washington State University Tri-Cities,
United States

*CORRESPONDENCE

Jun-Min Xie
xiejunminxjm@163.com

[†]These authors have contributed
equally to this work

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Evaluation of biventricular longitudinal myocardial function in normal fetuses at different gestational ages using ultrasonic velocity vector imaging

Min Hou^{1†}, Liu Liu^{2†}, Jun-Min Xie^{3*}, Xiao-Jing Duan¹,
Xiao-Lan Lv¹, Xiao-Qing Li⁴ and Qin Zhang⁵

¹Department of Ultrasonography, Affiliated Hospital of Hebei University, Baoding, China,

²Department of Ultrasonography, Baoding Maternal and Child Health Hospital, Baoding, China,

³Department of Cardiology, Affiliated Hospital of Hebei University, Baoding, China, ⁴Department of Ultrasonography, Baoding No.1 Central Hospital, Baoding, China, ⁵Department of Ultrasonography, Gaoyang County Hospital, Baoding, China

Objective: This study aimed to evaluate biventricular myocardial function and biventricular longitudinal global myocardial function of fetuses at different gestational weeks using ultrasonic velocity vector imaging.

Methods: A total of 127 pregnant women were enrolled and divided into five groups according to the gestational age of their fetuses. The velocity, strain, and strain rate of the left and right ventricles were measured, and these biventricular parameters were compared between the groups. The global parameters of the biventricular myocardium were also compared.

Results: A pairwise comparison revealed that the differences in biventricular velocity and strain rate between groups in adjacent gestational weeks were not statistically significant ($P > 0.05$), but velocity increased with gestational age. A comparison of fetal longitudinal global myocardial parameters revealed that the global velocity, strain, and strain rate of the right ventricle were higher than those of the left ventricle, and the differences were statistically significant ($P < 0.05$) in all groups.

Conclusion: The peak velocities of the fetal left and right ventricles increased with gestational age, but the global strain and strain rate did not, suggesting that fetal myocardial function is mature and constant in the middle and late stages of pregnancy and can more reliably reflect myocardial deformation. The peak systolic velocity, global strain, and peak strain rate of the right ventricle were higher than those of the left ventricle, suggesting that the right ventricle dominates longitudinal systolic movement from the second trimester of pregnancy.

KEYWORDS

strain, strain rate, ultrasonic velocity vector imaging, fetus, biventricular longitudinal myocardial function

Introduction

Fetal heart examination, including the evaluation of cardiac structure and function, is a key part of pregnancy screening, and the development of ultrasound technology has allowed the diagnosis of fetal cardiac structural abnormalities to mature. M-mode ultrasound, two-dimensional ultrasound, color Doppler ultrasound, and spectral Doppler ultrasound, among other methods, are traditionally used to analyze and evaluate the global function of the fetal heart according to various parameters, such as ejection and shortening fractions, which are calculated according to the end systolic and end diastolic volume of the left ventricle (1–3). However, because of the influence of various factors, such as the differing technical experience of operators, patient age, bradycardia or tachycardia, and left ventricular load change, the repeatability of the examination results is poor.

Velocity vector imaging (VVI), an echocardiographic technique based on two-dimensional gray scale, was first applied to fetal echocardiography in 2007 (4). VVI has a low dependence on angle and a good signal-to-noise ratio (5, 6). It can also automatically determine the center of motion with high repeatability (7) and can quantitatively provide the peak velocity, strain, and strain rate of the ventricular wall in the long axis, short axis, and axial direction of the segmental myocardium (8). Tissue velocity is expressed in the form of a vector, which displays the movement direction, velocity magnitude, movement distance, velocity gradient change value, and other information related to tissue structure, with the velocity magnitude of tissue movement represented by the length of the vector (the length of the arrow) and the velocity direction of tissue movement represented by the direction of the vector (the direction indicated by the arrow). VVI is less affected by the angle of sound beams and can overcome the impacts of respiration, global cardiac motion, cardiac rotation, and adjacent myocardial segment mortality or restriction.

Common parameters used to describe myocardial function include strain and strain rate. Strain refers to the deformation ability of local myocardial tissue after stress. The strain rate is the rate of deformation, referring to the degree of deformation in unit time. It is less affected by the displacement caused by heart rotation and swing and the traction effect of adjacent tissues and can better reflect the function of the local myocardium (9).

This study aimed to evaluate the biventricular myocardial function and biventricular longitudinal global myocardial

function of fetuses at different gestational weeks using ultrasonic VVI.

Materials and methods

Study participants

A total of 127 pregnant women undergoing examination between January 2016 and April 2018 were enrolled in this study, and their fetuses were divided into five groups according to gestational age. Written informed consent was obtained from all the participants' parents.

Inclusion criteria: (1) the patient had no family history of congenital heart disease; (2) the patient had no infectious diseases; (3) the patient had no systemic diseases, such as hypertension or diabetes; (4) the patient was receiving no medication; (5) the patient had no radiation history; (6) the patient had an accurate menstrual history or the gestational age of the fetus was consistent with the gestational week confirmed by an early pregnancy ultrasound. All the enrolled fetuses were a singleton pregnancy with no cardiac structural malformation or arrhythmia.

Research instruments

The Voluson E8/E10 color Doppler ultrasound diagnostic apparatus (GE Healthcare, China) was used in this study, with a probe frequency of 2–5 MHz. Two-dimensional strain VVI analysis software (TomTec, Germany) was used offline for the post-processing analysis.

Research methods and detection indicators

The data of the fetal apical four-chamber view were stored in the computer to ensure that the endocardial image was clear and legible. The fetal left and right ventricular walls were divided into 12 segments, namely the basal segment, middle segment, and the apical segment of the left and right ventricles and their corresponding ventricular septal side. The ultrasound apparatus was then moved offline, and the image was imported into the VVI analysis software. The static single-frame image in which the endocardial interface was most clearly displayed was selected. The ventricular boundary was then manually traced along the endocardial interface, and the start and end points were located at the root of the tricuspid valve and mitral valve ring, respectively. Subsequently, the velocity, strain, and strain rates of the whole and segmental myocardium were automatically obtained (Figure 1). The average value was calculated from three cardiac cycles.

Abbreviations: VVI, Velocity vector imaging; Vs, Peak systolic velocity; Vd, Peak diastolic velocity; S, Strain; SRs, Systolic strain rate; SRd, Diastolic strain rate; ICC, Intraclass correlation coefficient.

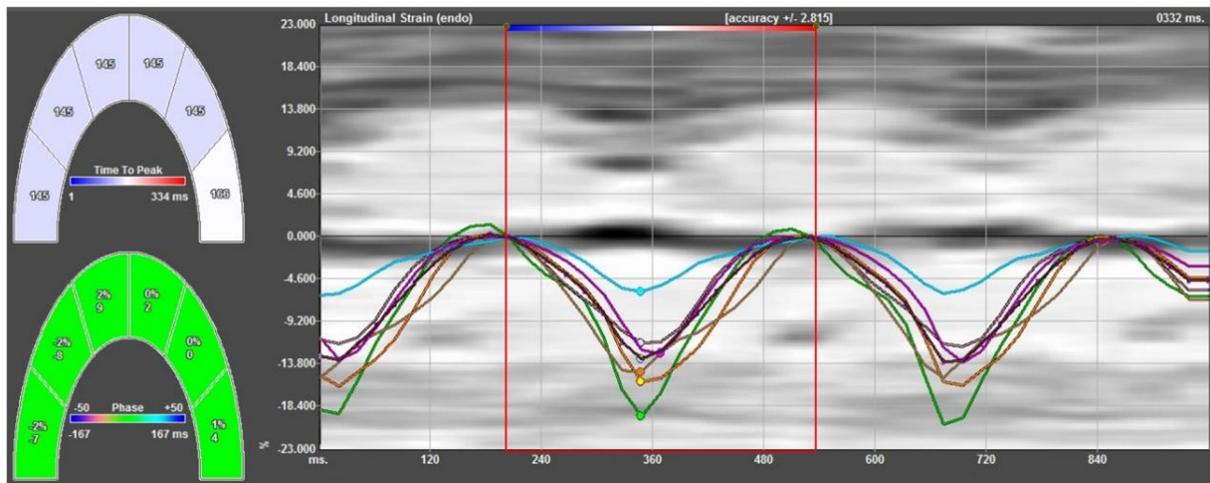


FIGURE 1
 Strain curves of all segments of the left ventricular lateral wall and left ventricular side of the ventricular septum. The strain curve has a negative single peak in the whole cardiac cycle; in the systolic phase, the myocardium shortens longitudinally, developing from zero to negative, and reaches its maximum strain at the end of the systolic phase, gradually returning to zero in the diastolic phase.

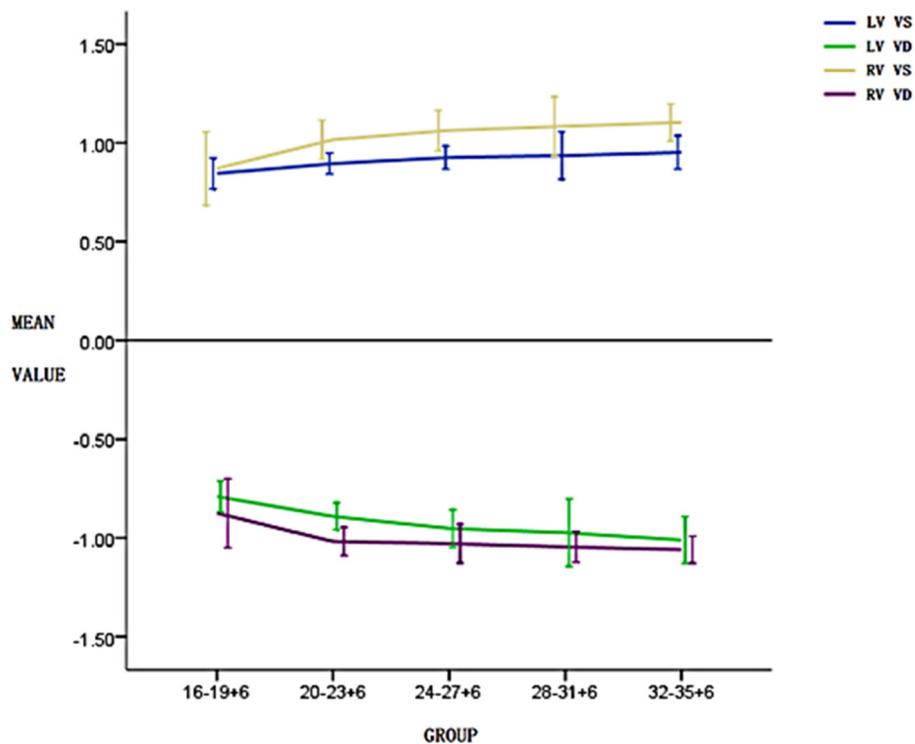


FIGURE 2
 Changes in the left and right ventricular systolic and diastolic global peak velocities in five pregnancy groups. The global peak velocity gradually increases with the increase in gestational weeks and the global peak velocity of the right ventricle in both systolic and diastolic phases is higher than that of the left ventricle.

Statistical methods

Data were analyzed using SPSS 22.0 statistical software. Measurement data first underwent a test of normality. Normally distributed measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm SD$). A comparison between fetuses in the same gestational age group was conducted using a *t*-test. A comparison of parameter values between segments was conducted using a paired *t*-test, and a comparison of parameter values between the left and right ventricles was conducted using an independent *t*-test. The correlation between parameters and gestational age was analyzed, and the linear equation was fitted. A reliability analysis of inter-observer and intra-observer measurements was conducted. $P < 0.05$ was considered statistically significant.

Results

An offline analysis involving 127 fetal examination images was conducted, and 120 cases were successfully analyzed, with a success rate of 94.5%. All the fetuses were divided into five groups according to gestational age: 16–19⁺⁶ weeks (group 1, $n = 14$), 20–23⁺⁶ weeks (group 2, $n = 36$), 24–27⁺⁶ weeks (group 3, $n = 37$), 28–31⁺⁶ weeks (group 4, $n = 20$), and 32–35⁺⁶ weeks (group 5, $n = 13$).

Comparison of parameters of the fetal ventricular longitudinal global myocardium between different gestational ages

Velocity

A pairwise comparison between adjacent gestational age groups revealed no significant differences in systolic and diastolic longitudinal global peak velocities ($P > 0.05$). However, the general trend in global peak velocity was a gradual increase with gestational age (Figure 2), and the global peak VVI parameter values of the right ventricle were larger than those of the left ventricle in both systolic and diastolic phases (Figure 2, Tables 1, 2).

Strain

A pairwise comparison between adjacent gestational age groups revealed no significant differences in the longitudinal peak strain of the fetal left ventricle or right ventricle ($P > 0.05$; Tables 1, 2).

TABLE 1 Global peak velocity, strain and strain rate of fetal left ventricular myocardium in 5 gestational weeks groups in normal pregnancy.

Group (weeks)	Vs	Vd	S	SRs	SRd
16–19 ⁺⁶	0.85 \pm 0.13	–0.79 \pm 0.13	–16.62 \pm 6.40	–1.68 \pm 0.77	1.70 \pm 0.65
20–23 ⁺⁶	0.90 \pm 0.16	–0.89 \pm 0.20	–17.50 \pm 3.72	–1.66 \pm 0.67	1.58 \pm 0.42
24–27 ⁺⁶	0.93 \pm 0.18	–0.95 \pm 0.29	–15.37 \pm 7.44	–1.45 \pm 1.00	1.62 \pm 0.72
28–31 ⁺⁶	0.94 \pm 0.26	–0.97 \pm 0.37	–15.38 \pm 6.16	–1.34 \pm 0.68	1.39 \pm 0.64
32–35 ⁺⁶	0.95 \pm 0.14	–1.01 \pm 0.20	–14.34 \pm 6.81	–1.39 \pm 0.82	1.44 \pm 0.57

Vs, peak systolic velocity (cm/s).

Vd, peak diastolic velocity (cm/s).

S, strain (%).

SRs, systolic strain rate (S^{–1}).

SRd, diastolic strain rate (S^{–1}).

TABLE 2 Global peak velocity, strain and strain rate of fetal right ventricular myocardium in 5 gestational weeks groups in normal pregnancy.

Group (weeks)	Vs	Vd	S	SRs	SRd
16–19 ⁺⁶	0.87 \pm 0.32	–0.87 \pm 0.30	–19.90 \pm 10.21	–1.89 \pm 0.98	2.06 \pm 0.94
20–23 ⁺⁶	1.02 \pm 0.29	–1.02 \pm 0.21	–20.33 \pm 10.52	–2.27 \pm 1.23	2.16 \pm 0.88
24–27 ⁺⁶	1.06 \pm 0.31	–1.03 \pm 0.30	–19.52 \pm 11.12	–1.98 \pm 1.00	2.15 \pm 0.87
28–31 ⁺⁶	1.08 \pm 0.32	–1.05 \pm 0.17	–19.84 \pm 9.73	–1.72 \pm 0.90	1.73 \pm 0.80
32–35 ⁺⁶	1.10 \pm 0.15	–1.06 \pm 0.11	–16.36 \pm 11.37	–2.28 \pm 1.13	1.83 \pm 1.19

Vs, peak systolic velocity (cm/s).

Vd, peak diastolic velocity (cm/s).

S, strain (%).

SRs, systolic strain rate (S^{–1}).

SRd, diastolic strain rate (S^{–1}).

Strain rate

A pairwise comparison between adjacent gestational age groups revealed no significant differences in the longitudinal global peak strain rate of the fetal left ventricle and right ventricle in both systolic and diastolic phases ($P > 0.05$; Tables 1, 2).

Comparison of longitudinal global myocardial velocity vector imaging parameters between fetal left and right ventricles

Velocity

In all groups, in both systolic and diastolic phases, the global peak velocity of the right ventricle was significantly higher than that of the left ventricle ($P < 0.05$; see Table 3).

TABLE 3 Six segments and global velocity, strain and strain rate of left and right ventricular myocardium of normal fetal heart in both systolic and diastolic phases.

	Basal segment		Middle segment		Cardiac apical segment		Global value
	Side wall (free wall)	Ventricular septal side	Side wall (free wall)	Ventricular septal side	Side wall (free wall)	Ventricular septal side	
Left ventricle							
Vs	1.43 ± 0.54*	1.32 ± 0.68*	0.95 ± 0.57*	0.90 ± 0.51*	0.55 ± 0.26	0.44 ± 0.30	
Vd	-1.57 ± 0.49*	-1.29 ± 0.71*	-0.96 ± 0.49*	-0.88 ± 0.61*	-0.57 ± 0.27	-0.45 ± 0.33	
S	-18.00 ± 12.55	-14.77 ± 9.79	-17.34 ± 9.37	-13.59 ± 9.79	-17.95 ± 12.50	-14.73 ± 9.99	
SRs	-1.84 ± 1.25	-1.54 ± 0.90	-1.63 ± 1.28	-1.49 ± 0.89	-1.85 ± 1.25	-1.59 ± 1.06	
SRd	1.75 ± 1.06	1.59 ± 0.81	1.58 ± 0.95	1.48 ± 1.01	1.68 ± 0.85	1.56 ± 0.88	
Right ventricle							
Vs	1.57 ± 0.66*	1.45 ± 0.64*	1.10 ± 0.48*	0.97 ± 0.60*	0.53 ± 0.30	0.43 ± 0.21	
Vd	-1.73 ± 0.79*	-1.67 ± 0.71*	-1.19 ± 0.65*	-0.98 ± 0.52*	-0.57 ± 0.45	-0.49 ± 0.27	
S	-19.59 ± 13.29	-19.42 ± 12.79	-17.07 ± 11.99	-18.73 ± 13.81	-18.16 ± 11.02	-17.39 ± 11.07	
SRs	-1.87 ± 1.19	-2.00 ± 1.73	-1.66 ± 1.36	-1.83 ± 1.46	-1.76 ± 1.15	-1.78 ± 1.21	
SRd	2.08 ± 1.19	2.13 ± 1.73	2.03 ± 1.20	1.97 ± 1.46	1.91 ± 1.13	1.87 ± 1.13	

* Represents left ventricle and right ventricle.

Vs, peak systolic velocity (cm/s).

Vd, peak diastolic velocity (cm/s).

S, strain (%).

SRs, systolic strain rate (S^{-1}).

SRd, diastolic strain rate (S^{-1}).

Strain

The peak systolic strain of the right ventricle was significantly stronger than that of the left ventricle ($P < 0.05$; see Table 3).

Strain rate

In both systolic and diastolic phases, the global peak strain rate of the right ventricle was significantly higher than that of the left ventricle ($P < 0.05$; see Table 3).

Velocity vector imaging parameter repeatability test

Twenty participants were randomly selected for a repeatability test.

Intra-observer consistency test

The VVI parameters in the participants' images were measured repeatedly by the same echocardiographer at an interval of more than 15 days. The intraclass correlation coefficients (ICCs) for segmental peak velocity, strain, and strain rate were 0.89, 0.87, and 0.83, respectively, and the ICCs for global peak velocity, strain, and strain rate were 0.88, 0.86, and 0.89, respectively.

Inter-observer consistency test

The above parameters were measured again by another doctor with equivalent experience. The ICCs for segmental peak velocity, strain, and strain rate were 0.89, 0.90, and 0.87, respectively, and the ICCs for global peak velocity, strain, and strain rate were 0.85, 0.86, and 0.88, respectively.

Discussion

The accurate assessment of fetal cardiac function is helpful for confirming and improving our understanding of the development of fetal diseases and their impact on the fetal heart. Echocardiographic myocardial strain measurements have been demonstrated to be useful in assessing mild myocardial dysfunction and segmental ventricular wall motion abnormalities (10–14).

In VVI, velocity (displacement) is represented as a vector; in addition to velocity, it also indicates direction. Therefore, different spatial components can be verified along the x , y , and z axes, and the longitudinal, circumferential, and axial spatial components can be measured along the anatomical coordinates of the cardiac cavity; all of these parameters are closely related to the mechanical properties of the myocardium. The key advantage of using strain and strain rate relative to displacement is that they are independent of translational motion and reflect segmental function. Generally, strain describes the amplitude

and direction of local myocardial shortening or prolongation; global strain, or more accurately, global longitudinal strain or global circumferential strain, usually refers to the average longitudinal or circumferential strain of the whole myocardium, which can approximate the average strain of the myocardium of each ventricular wall segment.

With the growth and development of the fetus, the heart volume increases, leading to an increase in longitudinal myocardial displacement. When the cardiac cycle becomes relatively constant [the development of cardiac function tends to mature in the second trimester of pregnancy (15)], the instantaneous displacement of the cardiac ventricle increases in both systolic and diastolic phases, resulting in the acceleration of peak velocity with the increase in gestational age. The findings of the present study are therefore consistent with those of previous studies.

In the present study, the changes identified in global strain, strain rate, and gestational age are consistent with the findings of previous studies (16, 17) in that they did not change with the increase in gestational age. Strain is not related to time; thus, it can more reliably reflect the deformation of the myocardium, suggesting that fetal cardiac function is mature and constant in the middle and late stages of pregnancy. Previous studies have also revealed that the global longitudinal strain of the fetal left and right ventricles decreases in the last 4 weeks of pregnancy (18), with only the right ventricular strain changing (19). These differences may be caused by the application of different ultrasound systems, myocardial deformation analysis software packages, and speckle tracking methods to calculate parameters.

The strain and strain rate of the left and right ventricles in the present study did not change with the increase in gestational age, and the comparison between the five gestational age groups revealed no statistically significant differences in these parameters. According to the following strain rate formula,

$$SR = \frac{S}{\Delta t} = \frac{\frac{\Delta L}{L_0}}{\Delta t} = \frac{\Delta L}{L_0 \Delta t} = \frac{\Delta v}{L_0} = \frac{v_1 - v_2}{L_0}$$

(S, strain; SR, strain rate; Δt , time change; Δv , velocity change; L_0 , initial length), strain is stable and unchanged in the middle and late stages of pregnancy; if the fetal heart rate fluctuates within the normal range, then the strain rate does not change with the increase in gestational age.

The present study also revealed that in all the groups, the peak systolic global velocity of the right ventricle was higher than that of the left ventricle, and the longitudinal global strain and peak strain rates of the right ventricle were higher than those of the left ventricle. The study also demonstrated that, during the fetal period, the contraction of the right ventricle mainly occurs in the longitudinal direction. The direction of myocardial fibers

determines the pump function of the myocardium (20, 21). Myocardial fibers can be divided into three layers: the inner longitudinal bunch, medium ring, and outer oblique layer. Although the inner and outer layers of the left and right ventricles have longitudinal and/or oblique fibers, the middle layer's annular fibers only exist in the left ventricle. Therefore, the right ventricle is dominated by longitudinal and/or oblique fibers, whereas the left ventricle has both longitudinal and/or oblique fibers and annular fibers. Compared with the left ventricle, the fiber distribution makes the longitudinal shortening of the right ventricle more obvious during cardiac contraction. Therefore, from the second trimester of pregnancy, the right ventricle dominates longitudinal systolic movement.

This study has some limitations. An evaluation of the ventricular circumferential myocardial function was not performed because the success rate of obtaining the appropriate short-axis image is very low, and the intra-observer and inter-observer consistency tests were poor. Moreover, this process is time-consuming and therefore the clinical application of general fetal evaluation may be limited.

Conclusion

This study revealed that, in normal fetuses, the longitudinal global myocardial peak systolic velocity and peak diastolic velocity of the left and right ventricles increased with gestational age, whereas strain, systolic strain rate, and diastolic strain rate did not change with the change in gestational age, suggesting that they remain stable in the middle and late stages of pregnancy. Furthermore, the global myocardial VVI parameters of the fetal right ventricle were higher than those of the left ventricle, confirming that, from the second trimester of pregnancy, the right ventricle dominates longitudinal systolic movement.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Affiliated Hospital of Hebei University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

MH, LL, and J-MX: conception and design of the research. MH: acquisition of data. MH, LL, J-MX, X-JD, X-LL, X-QL, and QZ: analysis and interpretation of the data. MH, J-MX, X-LL, and X-QL: statistical analysis. MH, LL, J-MX, and X-JD: writing of the manuscript. J-MX: critical revision of the manuscript for intellectual content. All authors read and approved the final draft.

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Conflict of interest

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