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Comparison between pulsed-wave Doppler- and tissue Doppler-derived Tei indices in fetuses with and without congenital heart disease

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KEYWORDS: fetal cardiac function; pulsed-wave Doppler; Tei index; tissue Doppler

ABSTRACT

Objectives *The aim of this study was to compare the right (RV) and left (LV) ventricular Tei indices obtained by pulsed-wave Doppler (PD) and tissue Doppler (TD) methods in fetuses with structurally normal and abnormal hearts.*

Methods *This was a retrospective cross-sectional study of 147 fetuses that had a fetal echocardiogram and Tei index measured during a 2-year period. The RV and LV Tei indices were measured using both PD and TD methods. The difference between the two methods of Tei index measurement was tested using paired sample* t*-test, Pearson correlation coefficient was used to examine their relationship, and the agreement between the methods was tested using Bland–Altman analysis.*

Results *A total of 87 fetuses had normal hearts and 60 had a congenital heart defect. Both PD and TD Tei indices were measured successfully from at least one ventricle in 123 cases and from both ventricles in 110 cases. The mean TD Tei index was significantly higher than the mean PD Tei index for both ventricles (*$P < 0.0001$*). There was a weak but statistically significant correlation between the PD and TD Tei indices of the right ventricle (*$r = 0.20$*,* $P = 0.029$*), whereas the PD and TD Tei indices of the left ventricle did not correlate significantly (*$r = 0.04$*,* $P = 0.684$*). When pairs of Tei indices measured by two different methods (123 pairs for the right ventricle and 111 for the left ventricle) were tested with Bland–Altman analysis, the bias and precision were 0.147 and 0.254, respectively, for the right ventricle, and 0.299 and 0.276, respectively, for the left ventricle.*

Conclusions *Correlation between Tei indices measured by PD and TD methods is weak and the agreement between individual measurements is poor. Therefore, they should not be used interchangeably in the assessment of fetal cardiac function. Copyright © 2008 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

The Tei index[1] has been used widely as a measure of global (combined systolic and diastolic) myocardial function in adults and children. Recently, it has also been shown to be useful in the assessment of fetal cardiac function[2–4]. Traditionally, this index has been calculated from the pulsed-wave Doppler (PD) recordings of ventricular inflow and outflow blood velocity waveforms as a ratio between the sum of isovolumic times and ejection time (ET). This ratio can also be derived from the recordings of myocardial wall motion during a cardiac cycle using tissue Doppler (TD) imaging. The PD-derived Tei index has been shown to correlate well with a cardiovascular profile score[5] that has been used in the assessment of fetal congestive heart failure[6,7]. A previous study in human fetuses with congenital heart failure[8] suggested that the TD-derived Tei index might be useful in the assessment of cardiac dysfunction.

Because of the parallel arrangement of the fetal circulation, it is important to assess the function of the right and left ventricles separately. In the fetus, the left ventricular (LV) Tei index can be calculated from simultaneous recording of inflow and outflow blood velocity waveforms during a single cardiac cycle using

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PD imaging, but this is more difficult to achieve for the right ventricle if one is to avoid changes in the heart rate between time measurements. Using TD imaging it is possible to calculate the Tei index for both ventricles[9] as well as the interventricular septum from a single heart beat without having to obtain sequential Doppler recordings from two different views, thus eliminating the effect of slight variations with time in cardiac cycle length.

Both LV[10] and right ventricular (RV)[11] TD Tei indices have been shown to correlate with PD Tei indices in healthy children. However, whether this is also true for the fetal heart has not been investigated. We tested the null hypothesis that there is no significant correlation between TD and PD Tei indices in the fetus. The aim of our study was to compare the LV and RV Tei indices obtained by two different methods in fetuses with structurally normal and abnormal hearts.

METHODS

This was a retrospective cross-sectional study of 147 patients who attended the non-invasive laboratory at the All Children's Hospital, St Petersburg, USA for a fetal echocardiogram during a 2-year period (2005 and 2006). A total of 1107 echocardiograms were performed on 701 fetuses during the study period. However, only 147 fetuses that were examined by one of two experienced echocardiographers (L.E. or D.N.) and had the Tei index measured to evaluate global myocardial performance were included in this study. The Tei index was routinely measured in all cases when a congenital heart defect was diagnosed. The mean gestational age at examination was 28 weeks and 3 days (range, 18–41 weeks). The study protocol was approved by the local institutional review board.

All examinations were performed using an Acuson Sequoia 512 ultrasound system (Mountain View, CA, USA) equipped with a 2–6-MHz curvilinear transducer and a 4–5-MHz phased-array transducer. The fetal heart was evaluated for any congenital malformations or signs of heart failure. The RV and LV Tei indices were calculated using both PD[12–16] and TD[8] methods as described previously: Tei index = $(a - b)/b$, where a equals the sum of isovolumic contraction time (ICT), isovolumic relaxation time (IRT) and ET, and b equals the ET of a cardiac cycle. Time interval measurements were obtained from three consecutive cardiac cycles and the average value was used for analysis. Tei indices were obtained only from the functional ventricle in cases with a univentricular heart. All Doppler recordings were made during a stable heart rate in the absence of fetal movements or breathing.

Pulsed-wave Doppler-derived Tei index

The atrioventricular and semilunar valve movements (clicks) seen on the Doppler velocity waveform patterns were used as the reference points while measuring the cardiac cycle time intervals (the components of Tei index). To calculate the LV Tei index, PD blood velocity waveforms were obtained simultaneously from the inflow and outflow of the left ventricle, and measurements of a and b components were made from the same cardiac cycle. The component a was measured as the time interval from the closure click to the subsequent opening click of the mitral valve, and the b component was measured from the opening to the closure of the aortic valve (Figure 1). The LV IRT was measured from the closure of the aortic valve to the opening of the mitral valve.

The RV Tei index was calculated by measuring a and b components of the cardiac cycle from the PD blood velocity waveforms of the RV inflow and outflow obtained in series (one after another) from separate cardiac cycles (Figure 2). Care was taken to ensure that the heart rate variation was not more than 10 beats/min (bpm) during the acquisition of inflow and outflow blood velocity waveforms. The component a was measured as the time interval from the closure click to the subsequent opening click of the tricuspid valve, and the b component was measured from the opening to the closure of the pulmonary valve (Figure 2).

Tissue Doppler-derived Tei index

For calculation of the TD Tei index, pulsed-tissue Doppler recordings of longitudinal myocardial wall motion were obtained at the level of mitral and tricuspid valve annuli in an apical four-chamber view. The measurement technique is demonstrated in Figure 3. For both ventricles, the a component was measured as the time interval from the end of the myocardial lengthening velocity waveform during the late ventricular filling (atrial contraction) phase of diastole (A′) to the beginning of the myocardial lengthening velocity waveform during early ventricular filling (E′). The waves of isovolumic myocardial contraction (IVCV) and relaxation (IVRV) velocities were included in this measurement. The b

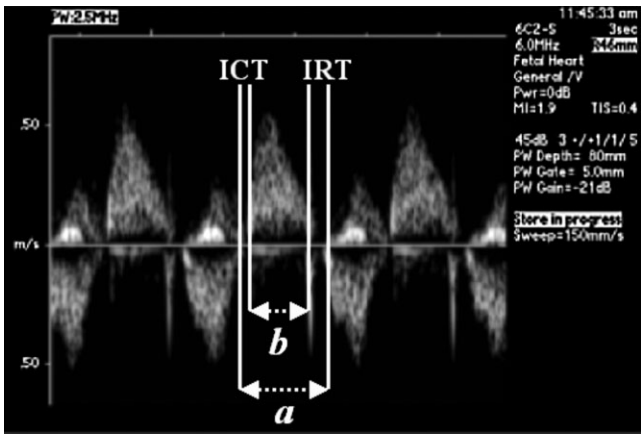

Figure 1 Left ventricular Tei index measurement using pulsed-wave Doppler-derived blood flow velocity waveforms obtained simultaneously from the mitral and aortic valves. *a*, time interval from closure to opening of the mitral valve; *b*, time interval from opening to closure of the aortic valve (ejection time).
ICT, isovolumic contraction time; IRT, isovolumic relaxation time; Tei index = $(a - b)/b$.

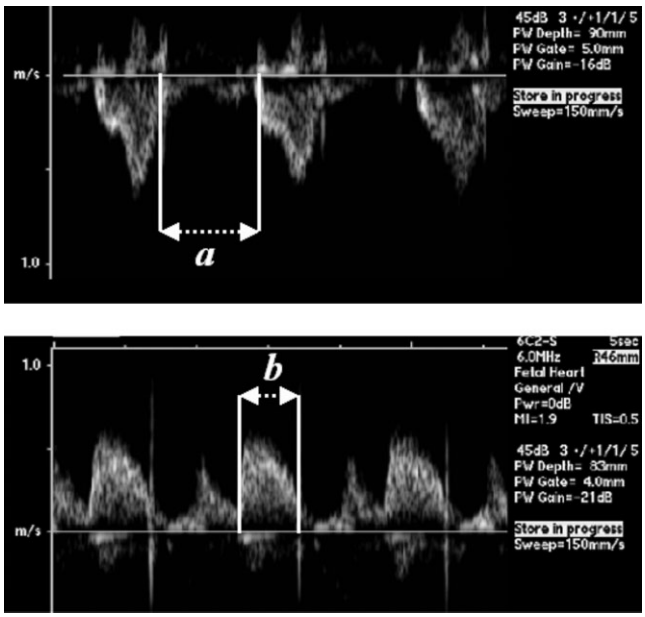

Figure 2 Right ventricular Tei index measurement using pulsed-wave Doppler-derived blood flow velocity waveforms obtained from the pulmonary and tricuspid valves in series. *a*, time interval from closure to opening of the tricuspid valve; *b*, time interval from opening to closure of the pulmonary valve (ejection time); Tei index = $(a - b)/b$.

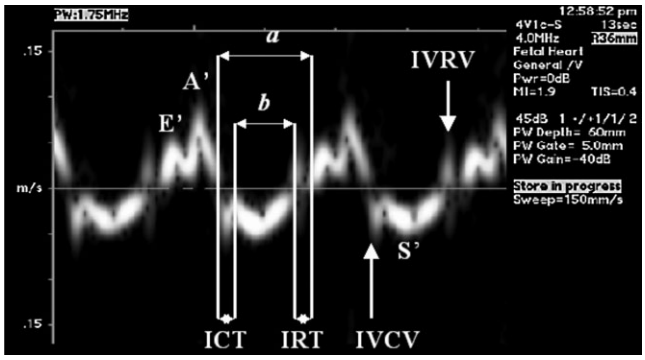

Figure 3 Right ventricular Tei index measurement using tissue Doppler-derived longitudinal myocardial wall motion velocities obtained at the tricuspid annulus. A′, myocardial lengthening velocity during the late ventricular filling (atrial contraction) phase of diastole; *a*, time interval from the end of the A′ wave to the beginning of the E′ wave; *b*, time interval from the beginning to the end of the S′ wave; E′, myocardial lengthening velocity during early ventricular filling; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; IVCV, isovolumic myocardial contraction velocity; IVRV, isovolumic myocardial relaxation velocity; S′, myocardial shortening velocity during ventricular systole; Tei index = $(a - b)/b$.

component was measured as the time interval from the beginning (excluding IVCV) to the end of the myocardial shortening velocity waveform (S′) during the ventricular systole of the same cardiac cycle. The IRT was measured from the end of the S′ wave to the start of the E′ wave.

Reproducibility

The reliability of measurements of PD and TD Tei indices between two observers (L.E. and D.N.), and the intraobserver and interobserver variability, were assessed in 15 fetuses with normal cardiac structure using intraclass correlation and coefficients of variation, respectively.

Statistical analysis

Data were analyzed using SPSS for Windows version 14.0 (SPSS Inc., Chicago, IL, USA). We used paired sample *t*-test for differences between PD and TD Tei indices and their components (time intervals). Agreement between two methods of Tei index measurement was tested using Bland–Altman analysis for bias and precision[17]. Bias was defined as the mean of all Tei index measurement differences and precision as the SD of these differences. Pearson correlation coefficient was used to examine the relationship between parametric variables.

RESULTS

A total of 87 fetuses were normal and 60 had congenital heart disease, which included univentricular hearts ($n = 16$), conotruncal defects ($n = 9$), obstructive lesions of the left or right ventricular outflow ($n = 8$), atrioventricular septal defects ($n = 6$), ventricular septal defects ($n = 5$), Ebstein's anomaly ($n = 1$), anomalous pulmonary venous drainage ($n = 1$), coarctation of the aorta ($n = 4$) and complex cardiac defects ($n = 10$). The RV Tei index was obtained successfully from 134 fetuses using PD imaging and from 132 fetuses using TD imaging. The LV Tei index was obtained from 128 fetuses using PD imaging and from 120 fetuses using TD imaging. Both PD and TD Tei indices were successfully measured from at least one ventricle in 123 cases and from both ventricles in 110 cases.

The mean values for the cardiac cycle time interval, Tei index and its components obtained by PD and TD recordings from the right and left ventricles are presented in Table 1. The fetal heart rates obtained by both techniques were almost identical for both ventricles. The mean TD Tei index was significantly higher than the mean PD Tei index for both ventricles ($P < 0.0001$). For the right ventricle this was mainly due to a longer TD isovolumic time (i.e. sum of ICT and IRT) than that measured by PD imaging, and for the left ventricle it was due to a combination of longer TD isovolumic time and shorter ET.

The results of the reproducibility study are presented in Table 2. The reproducibility of both PD and TD Tei indices was similar, with the coefficients of variation ranging between 7.2% and 11.0% and the intraclass correlation coefficients from 0.76 to 0.94. The reproducibility of measurements was not affected by the heart rate (range, 118–155 bpm).

There was a weak but statistically significant correlation between the RV PD and TD Tei indices ($r = 0.20$, $P = 0.029$), but the LV PD and TD Tei indices did not correlate significantly ($r = 0.04$, $P = 0.684$). The correlation between PD and TD Tei indices was not found

Table 1 Cardiac cycle time (RR) interval, Tei index and its components obtained by pulsed-wave Doppler and tissue Doppler imaging from the left and right ventricles

Parameter	*Pulsed-wave Doppler*	*Tissue Doppler*	P
Left ventricle			
RR interval (ms)	426 ± 25	425 ± 34	0.534
Time *a* (ms)	243 ± 18	274 ± 23	< 0.0001
Time *b* (ms)	176 ± 14	164 ± 23	< 0.0001
Total isovolumic time (ms)	66 ± 17	108 ± 29	< 0.0001
IRT (ms)	44 ± 10	57 ± 19	< 0.0001
Tei index	0.38 ± 0.1	0.70 ± 0.3	< 0.0001
Right ventricle			
RR interval (ms)	427 ± 30	427 ± 31	0.983
Time *a* (ms)	253 ± 26	275 ± 25	< 0.0001
Time *b* (ms)	175 ± 16	173 ± 21	0.367
Total isovolumic time (ms)	77 ± 31	101 ± 28	< 0.0001
IRT (ms)	NA	55 ± 17	NA
Tei index	0.45 ± 0.2	0.61 ± 0.2	< 0.0001

Data are presented as mean ± SD. IRT, isovolumic relaxation time; NA, not applicable.

Table 2 Reproducibility of left (LV) and right (RV) ventricular Tei indices measured by pulsed-wave Doppler (PD) and tissue Doppler (TD) methods

Parameter	*ICC*	*CV (%, 95% CI)*
Intraobserver		
LV PD Tei index	0.94	7.2 (4.5–9.1)
RV PD Tei index	0.88	7.8 (5.5–9.6)
LV TD Tei index	0.90	7.4 (4.7–9.3)
RV TD Tei index	0.90	8.7 (4.1–11.5)
Interobserver		
LV PD Tei index	0.91	8.2 (5.2–10.4)
RV PD Tei index	0.87	10.5 (6.5–13.3)
LV TD Tei index	0.86	8.5 (4.2–11.2)
RV TD Tei index	0.76	11.0 (4.7–14.8)

CV, coefficient of variation; ICC, intraclass correlation coefficient.

to be significant when the data were analyzed separately for fetuses with or without congenital heart disease.

When pairs of Tei index measurements performed by two different methods (123 pairs for the right ventricle and 111 pairs for the left ventricle) were tested with Bland–Altman analysis (Figures 4 and 5), the bias and precision were 0.147 and 0.254, respectively, for the right ventricle, and 0.299 and 0.276, respectively, for the left ventricle. For the left ventricle, the agreement between the PD and TD methods of Tei index measurement was poorer with increasing Tei index values.

DISCUSSION

Both PD and TD Tei indices are known to correlate with invasive measurements of global LV performance in adults[18,19]. In healthy children, the LV TD Tei index has been shown to correlate well with the PD Tei index[10] but not under altered loading conditions[20]. To

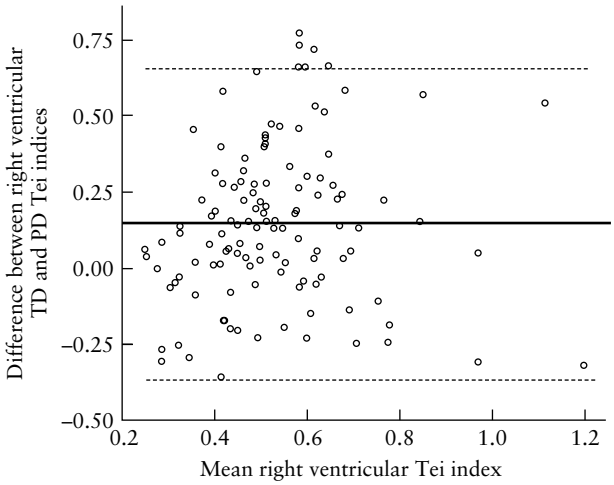

Figure 4 Bland–Altman plot of difference against mean for the right ventricular Tei index measured by tissue Doppler (TD) and pulsed-wave Doppler (PD) methods. The lines represent mean and 95% limits of agreement.

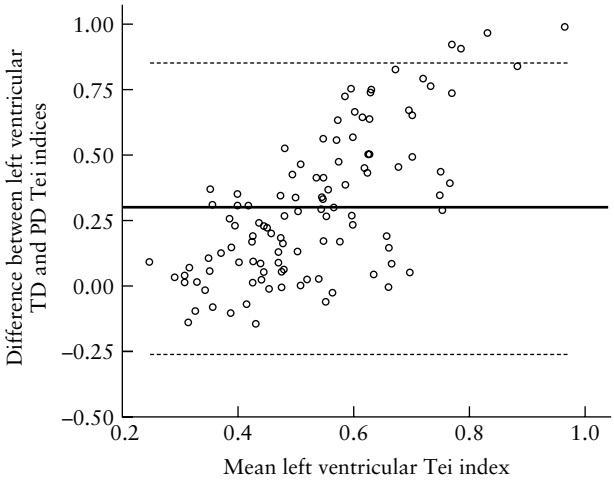

Figure 5 Bland–Altman plot of difference against mean for the left ventricular Tei index measured by tissue Doppler (TD) and pulsed-wave Doppler (PD) methods. The lines represent mean and 95% limits of agreement.

our knowledge, there are no published studies on the correlation between Tei indices measured by these two different techniques in human fetuses. We found the correlation between Tei indices measured by PD and TD techniques to be weak and the precision to be poor, despite similar reproducibility. When the correlation between two measurement methods is weak and the difference between individual measurements is inconsistent, it cannot be adjusted by adding or subtracting the mean difference. Similarly, when the precision is poor (i.e. the measurement differences have a large SD and widely spaced limits of agreement), one measurement cannot be substituted for the other[17].

The Tei index values for both ventricles obtained by the TD technique were significantly higher than values obtained by the PD technique. This is consistent with findings in adults[21] and may be related to methodological differences as the timing of hemodynamic events may

differ from that of myocardial motion events. However, the reason for higher TD than PD Tei index values was slightly different for each ventricle. For the right ventricle this was mainly due to the longer TD isovolumic time (i.e. sum of ICT and IRT) compared with that obtained by PD imaging, and for the left ventricle it was due to a combination of longer TD isovolumic time and shorter ET. As the reproducibility of measurements was similar for both ventricles, this is likely to be related to different loads faced by the ventricles resulting from the parallel arrangement of the fetal circulation. The accuracy of ET measurement by the TD technique has been validated in animal experiments, and the duration of the mitral annular systolic wave (S′) has been shown to correspond well to ET, measured as the interval between the onset of aortic pressure and the dicrotic notch on aortic pressure tracings[22]. A shorter LV ET may be explained by the relatively lower preload of the fetal left ventricle owing to RV dominance.

The PD Tei index is calculated from the cardiac cycle time intervals based on blood flow events, whereas the TD Tei index is based on myocardial motion events. Therefore, what these two indices describe may be essentially different. For example, in patients with valve lesions, the PD Tei index may be influenced by abnormal hemodynamics related to valve dysfunction even before secondary myocardial dysfunction occurs, whereas the TD Tei index may be more sensitive in detecting primary myocardial dysfunction. Experimental studies on fetal animal models using Doppler echocardiography and 'gold standard' invasive measures of cardiac function (e.g. dP/dtmax (rate of maximum isovolumic ventricular pressure rise), ventricular outputs, end-systolic elastance, time constant of isovolumic relaxation (τ), ventricular end-diastolic pressure) may provide some insight into what these non-invasive indices actually describe. The temporal relationship between myocardial depolarization, activation of ventricular contraction and hemodynamic events is influenced by several factors, and varies between different sites of interrogation. In children, it has been shown that TD time *a* begins and ends after the PD time *a*, and the TD time *b* begins and also ends before the PD time *b*[10].

Different conditions and diseases may have a differential effect on cardiac cycle events. The PD Tei index, although initially thought to be independent of heart rate, ventricular geometry and loading conditions, has been shown to be load dependent[23–25] and may not reflect global myocardial function when loading conditions are altered[23,26]. In the fetus, abnormal loading conditions can result from increased peripheral impedance (e.g. placental insufficiency), anemia, tumors, arteriovenous fistulae, twin–twin transfusion syndrome, valve insufficiency, etc. The total isovolumic time of the cardiac cycle can be prolonged by an increased ventricular afterload or intrinsic myocardial dysfunction, whereas the ET can be prolonged by increased preload. The TD Tei index is relatively less affected by changes in loading condition[27], but may be more sensitive to other adverse effects (e.g. acidosis, infection, cardiotoxic drugs) that cause intrinsic myocardial dysfunction.

The PD Tei index has been shown to be a useful index of fetal global myocardial performance[2–4], but whether the TD Tei index is more sensitive than the traditional PD Tei index in the assessment of fetal heart function is not known. A study by Aoki *et al.* showed that the RV TD Tei index was not sensitive enough in identifying fetuses with congestive heart failure[8]. However, this study had a very small number of observations (seven fetuses with heart failure and 36 controls) and wide confidence intervals, reducing the power of discrimination. On the other hand, the TD Tei index has been reported to be a more sensitive parameter of RV function than the PD Tei index in children with pulmonary regurgitation after the repair of tetralogy of Fallot[28]. Although our study included fetuses with a variety of congenital heart defects, the numbers with each defect are too small to make any meaningful comparison when looking for differences in Tei index between lesions.

We found TD Tei indices to be much higher than traditional PD Tei indices in fetuses both with and without congenital heart disease. Regarding the validity of our PD Tei index measurements, the values are consistent with those reported by others[5,14]. Although appropriate reference ranges for the TD Tei index for both ventricles in fetuses are still lacking, our results for the right ventricle compare favorably with those of Aoki *et al.*[8]. Therefore, the TD Tei index cut-off value for the diagnosis of any fetal cardiac dysfunction is likely to be higher than that for the PD Tei index.

Reproducibility for the LV PD Tei index has been shown to be better when inflow and outflow velocities are recorded simultaneously rather than in series, thus eliminating the effect of heart rate variability, and when valve clicks are used to identify opening and closure of the mitral and aortic valves[16]. We applied this technique to obtain the LV PD Tei index in our study and used valve clicks routinely for RV Tei index calculations. One potential advantage of using TD imaging to derive the Tei index is that the inaccuracies resulting from heart rate fluctuations can be avoided and the isovolumic time intervals (ICT and IRT) can also be measured separately for the right ventricle (Figure 3) as it does not require sequential Doppler recordings from two different views.

In conclusion, the correlation between Tei indices measured by PD and TD methods is weak and the agreement between individual measurements is poor. Therefore, they should not be used interchangeably in the assessment of fetal cardiac function.

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