Normal Offset of the Tricuspid Septal Leaflet in Thai Fetuses

Thitinan Tansathit MD*,
Boonchai Uerpairojkit MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital*

Objective: *To quantify the correlation between gestational age and the normal distance between the insertion of the medial leaflets of the mitral valve and tricuspid valve in Thai fetuses.*
Material and Method: *A prospective study was constructed using an apical 4-chamber view at end diastole to measure the mitral valve-tricuspid valve distance (MTD) in 169 confirmed-dated singleton normal fetuses between 18 and 40 weeks of gestation at King Chulalongkorn Memorial Hospital from August 2005 to July 2006. The recorded distances were plotted against gestational ages. The 5th, 50th, and 95th centile of MTD were calculated and the relationship between MTD and gestational age was determined with regression model. One hundred and forty-seven measurements were validated for analyses.*
Results: *Regression analysis demonstrated a linear correlation of MTD with gestational age with each increase of 1 week in gestational age, there was an increase of 0.12 mm of MTD ($p < .001$). The linear regression curve that correlated MTD with gestational age showed a gradual slope ($r = 0.84$; $p < 0.001$). The MTD range from 1.3 to 5.1 mm (mean $\pm$ SD = 2.6$\pm$ 0.9). A significant difference in MTD was noted on comparing to the data in Western study. Intra-observer reliability was 0.92.*
Conclusion: *The present findings support the positive correlation between MTD and advancing gestational age. However, clinically significant differences of MTD between the presented population and Caucasian fetuses underline the need for employing a locally derived data on assigning the fetal cardiac abnormality.*

Keywords: *Ebstein's anomaly, Echocardiography, Endocardial cushion defects, Tricuspid valve insufficiency, Congenital heart defect*

J Med Assoc Thai 2007; 90 (9): 1738-43
Full text. e-Journal: *http://www.medassocthai.org/journal*

Fetal echocardiography has been widely accepted as a standard investigation in detection of fetal structural cardiac anomalies for several decades. A four-chamber view is the simplest plane employed in detection of several fetal cardiac anomalies including hypoplastic left heart, hypoplastic right heart, atrioventricular septal defect as well as Ebstein's anomaly.

The diagnosis of Ebstein's anomaly has relied mainly on a documentation of a downward displacement of medial leaflet of tricuspid valve, which is usually relatively subjective. In certain situations, the displacement of the tricuspid valve or the mitral valve-tricuspid valve distance (MTD) may not be definitive. This can render a difficulty in assigning an abnormality if there is no standard normal range of this distance available to compare with. To date, there has been a standard reference range of normal offset of medial leaflet of tricuspid valves in autopsy specimen. The only prenatal ultrasonographic reference range of MTD was published recently in a Western population by Vettraino et al[1]. The question arises whether or not the previous reported MTD reference range can be applied in the present population. The authors conducted the present study to investigate the relationship between MTD and gestational age in the presented population and comparing it to the published reference range in a Western population.

Correspondence to: Uerpairojkit B, Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Praram four Rd, Pratumwan, Bangkok 10330, Thailand. Phone: 0-2256-4824, Fax: 0-2256-4825, E-mail: boonchaiu@hotmail.com

Material and Method

The present study was approved by the Ethical Committee of Faculty of Medicine, Chulalongkorn University. From August 2005 to July 2006, the authors enrolled the pregnant women between 18 and 40 weeks' gestation who came for ultrasonographic screening at King Chulalongkorn Memorial Hospital with various obstetric indications such as advanced maternal age, previous child with abnormalities, placenta previa, etc. All patients had one last menstrual period with sonographic-confirmed gestational age at the beginning or early in the second trimester. Fetal structural survey was performed to ensure a normalcy of the fetuses. Fetuses with abnormal anatomical findings in prenatal screening or abnormal karyotypes were excluded. Birth information and discharge summaries were reviewed. Fetal normalcy was again confirmed at 4 months by telephone calls. The sonographic equipment employed was ALOKA Prosound SSD-5000 SV (ALOKA Co., Ltd. Tokyo, Japan) equipped with 3.5 and 5.0 MHz abdominal transducer.

The MTD was obtained in a four-chamber view of the fetal heart at end diastole. The apex was positioned at the top in all studies. Calipers were placed parallel to the ventricular septum, with 1 caliper on the superior portion of the medial insertion of the tricuspid valve and a second caliper on the inferior portion of the medial insertion of the mitral valve as described previously[1,2] (Fig. 1). The MTD was measured three times for each fetus and mean MTD was calculated. If the optimal position of the fetal heart was initially not possible, the authors made another appointment for a more proper measurement. All images were obtained by TT and reviewed by UB. Any images where both investigators did not agree would be excluded. The mean MTDs were plotted against gestational age.

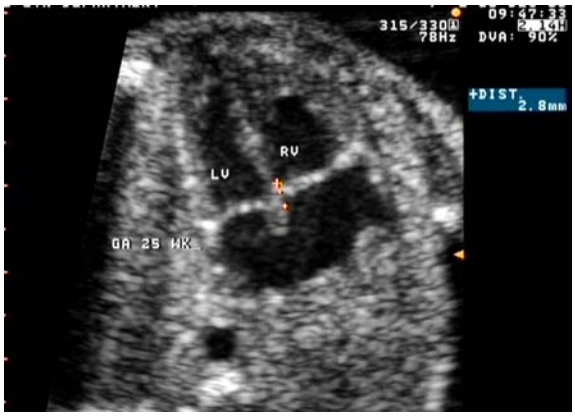

Fig. 1 Normal 4-chamber view of the second-trimester heart with calipers placed for MTD; LV, left ventricle; and RV, right ventricle

The correlation between MTD and gestational age was constructed on the basis of the method described by Cohen[3]. A power analysis revealed that a sample size of at least 112 fetuses would be sufficient to have 90% confidence in detecting a relationship of at least 0.30 at $p \leq .05$ between valve displacements at various gestational ages. Descriptive results of baseline and outcome characteristics were used range, mean, standard deviation (SD) and 10^{th}-90^{th} percentile. Linear regression and Pearson's correlation were used to examine the relationship between estimated gestational age and the MTD. All data were analyzed using the Statistical Package for the Social Sciences 13.0 (SPSS Inc, Chicago, IL).

Results

The MTDs were measured in 169 fetuses in that period. Twenty-two cases were excluded from the present study. The reasons for exclusion were the following: patients loss to follow-up in six cases, subsequently found to have unilateral multicystic kidney disease at birth in one case, fetal death *in utero* after amniocentesis for 2 weeks in one case, maternal gestational diabetes in 10 cases; and the images were not in agreement by both investigators in six cases. This left 147 fetuses included for the analyses. Fetal karyotypes were performed in 81 fetuses (55.1%) mostly due to advanced maternal age and all revealed normal chromosomes. Demographic characteristics of the study population are presented in Table 1. There was no newborn of Apgar score at 5 minutes below 7. Discharge summaries and telephone calls revealed no newborn with any clinical evidences of cardiac abnormalities.

Correlation analysis showed a positive relationship between MTD and gestational age (the Pearson's correlation coefficient [r] = 0.84; $p < 0.001$). The regression model for MTD was best fit by allowing a polynomial for gestational age of the following equation: $MTD = -0.45 + 0.12(GA)$, (the coefficient of determination [r^2] = 0.70, $p < 0.001$). While GA represents gestational age between 18 to 36 weeks of gestation, the linear regression curve showed a gradual slope indicating that with each increase of 1 week in gestational age, there was an increase of 0.12 mm of MTD ($p < 0.001$).

With the use of this regression equation, the predicted MTD for the 10^{th} and 90^{th} centiles were calculated for each gestational age. The MTDs for 147

Table 1. Baseline and outcome characteristics of the study population (n = 147)

Characteristics	Range	Mean ± SD
Maternal age (years)	16-42	32.60 ± 6.24
Gestational age at examination (weeks)	18-36	25.60 ± 6.16
Gestational age at delivery (weeks)	30-42	38.00 ± 1.757
Birthweight at delivery (g)	1700-4000	3099.00 ± 421.583
Apgar score at 1 minute	5-9	8.82 ± 0.673
Apgar score at 5 minutes	9-10	9.00 ± 0.199

Table 2. The results of the linear regression analysis between gestational age and MTD (n = 147)

Gestational age (weeks)	Mean MTD (mm)	MTD of 10th centile (mm)	MTD of 90th centile (mm)
18	1.70	0.91	2.49
19	1.82	1.03	2.61
20	1.94	1.15	2.73
21	2.06	1.27	2.85
22	2.18	1.39	2.97
23	2.30	1.51	3.09
24	2.42	1.62	3.21
25	2.54	1.75	3.32
26	2.65	1.86	3.44
27	2.77	1.98	3.56
28	2.89	2.10	3.68
29	3.01	2.22	3.80
30	3.13	2.34	3.92
31	3.25	2.46	4.04
32	3.37	2.58	4.16
33	3.49	2.70	4.28
34	3.61	2.82	4.41
35	3.73	2.93	4.53
36	3.85	3.05	4.65
37	3.97	3.17	4.77
38	4.09	3.29	4.89
39	4.21	3.41	5.01
40	4.33	3.52	5.13

fetuses at various gestational ages are presented in Table 2. Intra-observer reliability calculated by intra-class correlation coefficient was 0.92 (95% CI, 0.89-0.94).

Discussion

Ebstein's anomaly encompasses a spectrum of structural cardiac abnormalities with an apical displacement of malformed tricuspid valve tissue in the right ventricle. In the past, diagnosis of this specific anomaly had been established by using several M-mode echocardiographic criteria. These included an increased excursion of anterior tricuspid leaflet, delayed tricuspid valve closure, slowing of EF slope, abnormal septal motion, and variable enlargement of right atrium and ventricle. The most specific finding amongst these is the delayed closure of tricuspid valve of more than 65 ms as compared with that of mitral valve[4]. One limitation of employing M-mode technique is that it does not provide information regarding the severity of the disease[5]. More recently, two-dimensional real-time imaging have proved beneficial in diagnosis of this problem with an ability to assess the severity of the defect by defining the degree of displacement of the tricuspid valve and the size of the atrialized right ventricle[5]. The ratio of mitral-to-apex and tricuspid-to-apex reported by Ports et al[5] and Roudaut et al[6] has been

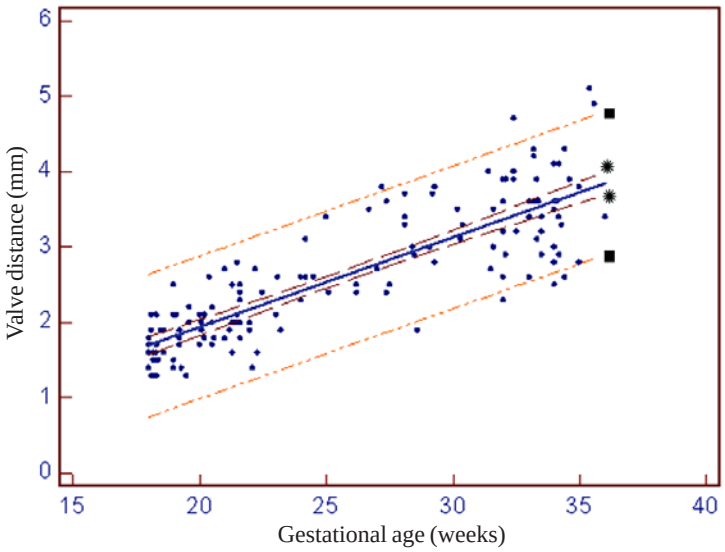

Fig. 2 Relationship between valve distance for fetuses without abnormalities and gestational age: scatter plot and regression analysis
Stars indicate 95% and 5% confidence limits of the point estimates; and squares indicate 95% and 5% confidence limits of the average of the point estimates

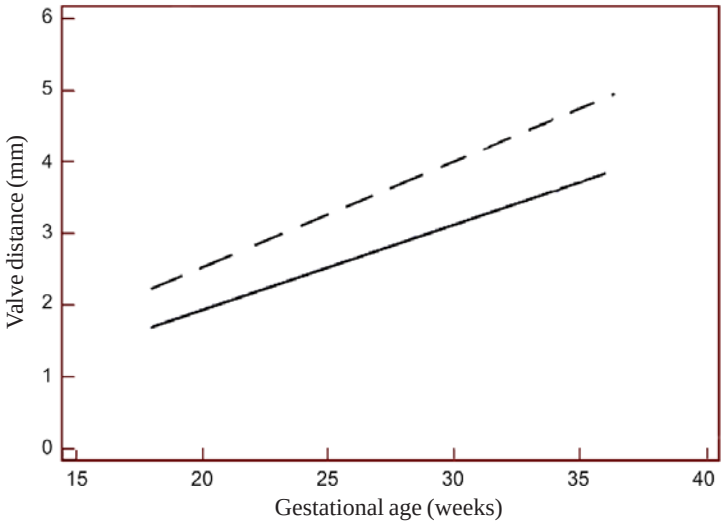

Fig. 3 The difference between mean valve distance of Caucasian and of Thai fetuses; the dash line represent mean valve distance of Caucasian fetuses in the previous study[1]; the continuous line represent mean valve distance of Thai fetuses

proposed for diagnosis of the problem. Nevertheless, there are important confounders to this measurement, especially when there is a hypertrophy or dilatation in right or left ventricle. The mitral-to-apex or the tricuspid-to-apex distance can be inevitably altered.

Direct assessment of valve displacement by measuring the MTD has been studied to use for diagnosis in the newborn and adults. Recently, the MTDs in fetuses have also been reported to increase linearly across gestational age with an increment of 0.15 mm

per week ($b = 0.15 \pm 0.011$; $p < 0.001$)[1]. The present findings demonstrated a consistent result of a positive correlation of MTD with gestational age with smaller increment of the distance per week. A slight but crucial difference between a previous study [1] and the present study is that the mean MTDs in any given gestation in the present study were lower (Fig. 3). The reasons for these could be attributed to the differences in ethnics or fetal habitus. Unfortunately, no information on fetal weights from previous studies is available for a comparison.

In contrast with the exaggerated MTD in Ebstein's anomaly, a narrowing of the tricuspid valve offset recently proved suggestive of endocardial cushion defects that occur when a single multi-leaflet atrioventricular valve replaces separate mitral and tricuspid valves. Bolnick et al derived a second trimester MTD and employed a cut-off of MTD less than 5th centile for the diagnosis of endocardial cushion defects; they revealed a 69% sensitivity and 100% specificity on using a threshold of 5th centile in the diagnosis of endocardial cushion defects[7]. More recent implication of abnormal MTD has also been reported by Fredouille et al on screening of Down syndrome, they studied fetal cardiac specimens and demonstrated that in the absence of atrioventricular septal defect, an absence of a normal downward displacement of tricuspid valve; so called a linear insertion of atrioventricular valve in an otherwise normal fetal heart is an echographic marker for a Down syndrome[8]. Furthermore, in their subsequent study in 2005 [9], they found that 23 of 34 cases with linear insertion of the atrioventricular valves without defect had abnormal karyotype. Ninety-one percent of the trisomy 21 fetuses were diagnosed. All this evidence underlines an importance of focusing on MTD during a fetal echocardiographic examination.

In conclusion, the authors believe that a local derived reference range for MTD is beneficial in establishing the correct diagnosis of Ebstein's anomaly as well as atrioventricular defect. Careful echographic evaluation is crucial in fetuses with MTD values remote from this regression model. More recent ultrasound technology such as Doppler with color-coded systems will have an adjunct role in a more difficult case.

Acknowledgements

The authors wish to thank Professor Sompop Limpongsanurak, Chairman of the Department of Obstetrics and Gynecology, Associate Professor Dhiraphongs Chareonvidhya , Head of the Division of Maternal Fetal Medicine, Faculty of Medicine, Chulalongkorn University for his permission to conduct and report this study and Dr Surasit Chaithongwongwathana, Department of Obstetrics and Gynecology, King Chulalongkorn University, for his assistance in research methodology and statistical analysis.

References

1. Vettraino IM, Huang R, Comstock CH. The normal offset of the tricuspid septal leaflet in the fetus. J Ultrasound Med 2002; 21: 1099-104.
2. Gussenhoven EJ, Stewart PA, Becker AE, Essed CE, Ligtvoet KM, De Villeneuve VH. "Offsetting" of the septal tricuspid leaflet in normal hearts and in hearts with Ebstein's anomaly. Anatomic and echographic correlation. Am J Cardiol 1984; 54: 172-6.
3. Cohen J. Statistical power analysis for the behavioural sciences. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
4. Gussenhoven WJ, Spitaels SE, Bom N, Becker AE. Echocardiographic criteria for Ebstein's anomaly of tricuspid valve. Br Heart J 1980; 43: 31-7.
5. Ports TA, Silverman NH, Schiller NB. Two-dimensional echocardiographic assessment of Ebstein's anomaly. Circulation 1978; 58: 336-43.
6. Roudaut R, Dudeffant P, Billes MA, Choussat A, Dallocchio M. Two-dimensional echocardiographic study of Ebstein's disease. Apropos of 16 cases. Arch Mal Coeur Vaiss 1981; 74: 1177-84.
7. Bolnick AD, Zelop CM, Milewski B, Gianferrari EA, Borgida AF, Egan JF. Use of the mitral valve-tricuspid valve distance as a marker of fetal endocardial cushion defects. Am J Obstet Gynecol 2004; 191: 1483-5.
8. Fredouille C, Piercecchi-Marti MD, Liprandi A, Duyme M, Gonzales M, Bigi N, et al. Linear insertion of atrioventricular valves without septal defect: a new anatomical landmark for Down's syndrome? Fetal Diagn Ther 2002; 17: 188-92.
9. Fredouille C, Develay-Morice JE, Gonzales M, Duyme M. A new echographic marker for 2nd-3rd trimester prenatal diagnosis of trisomy 21: the linear insertion of the atrioventricular valves without defect about 40740 pregnancies. Ultrasound Obstet Gynecol 2005; 26: 326.

ระยะห่างระหว่างลิ้นหัวใจไมทรัลและลิ้นหัวใจไตรคัสปิดในครรภ์ที่ปกติของทารกไทย

ธิตินันท์ ตัณสถิตย์, บุญชัย เอื้อไพโรจน์กิจ

วัตถุประสงค์: *เพื่อศึกษาหาความสัมพันธ์ระหว่างอายุครรภ์และระยะห่างระหว่างลิ้นหัวใจไมทรัลและลิ้นหัวใจไตรคัสปิดในทารกในครรภ์ที่ปกติ*

วัสดุและวิธีการ: *ทำการตรวจคลื่นเสียงความถี่สูงวัดระยะห่างระหว่างลิ้นหัวใจไมทรัลและลิ้นหัวใจไตรคัสปิด โดยใช้ระนาบที่เห็นหัวใจทั้งสี่ห้องของทารกในครรภ์ที่ปกติของสตรีตั้งครรภ์เดี่ยวที่มีอายุครรภ์ระหว่าง 18-40 สัปดาห์ จำนวน 147 คน แล้วนำค่าที่ได้มาคำนวณสมการถดถอยเพื่อหาความสัมพันธ์ของอายุครรภ์และระยะห่างระหว่างลิ้นหัวใจทั้งสอง ในช่วงเดือนสิงหาคม พ.ศ. 2548 - กรกฎาคม พ.ศ. 2549*

ผลการศึกษา: *พบความสัมพันธ์ระหว่างระยะห่างระหว่างลิ้นหัวใจทั้งสองและอายุครรภ์เป็นแบบเส้นตรง ($r = 0.84$; $p < 0.001$) โดยจะมีระยะห่างเพิ่มขึ้น 0.12 มม. เมื่ออายุครรภ์เพิ่มขึ้นแต่ละสัปดาห์ ระยะห่างระหว่างลิ้นหัวใจไมทรัลและลิ้นหัวใจไตรคัสปิดโดยเฉลี่ย 1.3-5.1 มม. (mean $\pm$ SD = 2.6 $\pm$ 0.9)*

สรุป: *ระยะห่างระหว่างลิ้นหัวใจไมทรัลและลิ้นหัวใจไตรคัสปิดมีความสัมพันธ์เชิงบวกกับอายุครรภ์และพบมีความแตกต่างจากทารกในครรภ์ของชาวตะวันตกที่ได้ศึกษาก่อนหน้านี้*