

Thickness measurement of fetal epicardial adipose tissue in structurally normal fetuses between 24 and 28 weeks of gestation

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Abstract

Objective: Ultrasonographic measurement of epicardial adipose tissue (EAT) is carried out frequently adults as an indirect indicator of lipogenesis and metabolic syndrome. However, the information on the measurement of this tissue in fetus is limited. Our aim is to determine the measurement values of fetal EAT thickness according to the weeks in non-complicated pregnancies.

Methods: Thirty-nine pregnant women, who admitted to maternity clinic between 24 and 28 weeks of gestation for routine follow-up and who had no problem in their fetal and maternal follow-ups, were included in our study. Fetal EAT thickness was measured in the Perinatology Clinic. The relationship of fetal EAT measurements with the week of gestation was evaluated statistically.

Results: Maternal age ($p=0.33$) and body mass index ($p=0.88$) according to the weeks of gestation were similar. Median [interquartile range] fetal EAT thicknesses at 24+, 25+, 26+ and 27+ weeks of gestation were 1.29 mm [1.267–1.320], 1.295 mm [1.275–1.305], 1.325 mm [1.297–1.355] and 1.34 [1.330–1.355], respectively. There was a significant difference only in the measurements between 25 and 26 weeks of gestation ($p=0.048$).

Conclusion: Fetal EAT thickness increases in direct proportion to the week of gestation. Proportionately, the highest increase is between 25 and 26 weeks of gestation.

Keywords: Epicardial adipose tissue, fetal epicardial adipose tissue, fetal echocardiogram, reference range.

Özet: Yapısal olarak normal fetüslerde 24–28. gebelik haftaları arasında fetal epikardiyal yağ dokusu kalınlık ölçümü

Amaç: Epikardiyal yağ dokusunun (EYD) ultrasonografik ölçümü lipogenez ve metabolik sendromun dolaylı bir göstergesi olarak erişkinlerde sıkça yapılmaktadır. Ancak fetüste bu dokunun ölçümü ile ilgili bilgiler kısıtlıdır. Bizim amacımız komplike olmayan gebeliklerde haftalara göre fetal EYD kalınlığının ölçüm değerlerinin belirlenmesidir.

Yöntem: Çalışmamıza gebe polikliniğine 24–28. gebelik haftaları arasında rutin takip için başvuran, fetal ve maternal takiplerinde herhangi bir sorun olmayan 39 gebe dahil edildi. Perinatoloji kliniğinde fetal EYD kalınlığı ölçüldü. Alınan fetal EYD ölçümlerinin gebelik haftası ile ilişkisi istatistiksel olarak değerlendirildi.

Bulgular: Gebelik haftalarına göre anne yaşı ($p=0.33$) ve vücut kitle indeksi ($p=0.88$) benzerdi. Sırasıyla medyan [çeyrekler açıklığı] fetal EYD kalınlığı; 24+, 25+, 26+ ve 27+ gebelik haftalarında 1.29 mm [1.267–1.320], 1.295 mm [1.275–1.305], 1.325 mm [1.297–1.355] ve 1.34 [1.330–1.355] olarak ölçüldü. Sadece 25 ile 26. gebelik haftalarındaki ölçümler arasında anlamlı fark mevcuttu ($p=0.048$).

Sonuç: Fetal EYD kalınlığı, gebelik haftasıyla doğru orantılı olarak artmaktadır. Oransal olarak en fazla artış 25 ve 26. gebelik haftası arasındadır.

Anahtar sözcükler: Epikardiyal yağ dokusu, fetal epikardiyal yağ dokusu, fetal ekokardiyografi, referans aralığı.

Introduction

The heart is surrounded by parietal and visceral (serous) pericardium. Visceral pericardium is of mesothelial origin and named as epicardium. Epicardial adipose tissue (EAT) is the region between myocardium and visceral

pericardium, and it directly contacts with myocardium.^[1,2] As there is no fascia which separates EAT from myocardium, they share the same micro-circulation.^[3] It is originated from brown adipose tissue during embryogenesis.^[1] Since it originates from brown adipose tissue,

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it is thought that it has a protective effect on heart against hypothermia.^[4] Also, EAT absorbs free fatty acids and protect heart in this environment when it is of high amount during circulation, it also may function as energy source in cases when energy need increases.^[5] EAT contains more proteins than other adipose tissues and it has a faster fatty acid synthesis and degradation.^[6] It is metabolically very active tissue. It secretes many proinflammatory, proatherogenic cytokines and vasoactive peptide associated with obesity, hypertension and coronary heart disease such as interleukin 6, tumor necrotizing factor alpha, angiotensin 2, plasminogen activator, omentin and neuronal growth factor.^[7,8] It also secretes anti-inflammatory and antiatherogenic adipokines such as adiponectin and adrenomedullin.^[9]

EAT measurement was first done by Iacobellis.^[10] The thickest location of EAT is the perpendicular wall of right ventricle. Therefore, the measurement is done on this location.^[11] EAT thickness varies between 1 and 23 mm in adults.^[12] EAT thickness can be decreased by weight loss in obese individuals.^[13]

Since EAT measurement is not affected by the differences in skin and muscle tissue layers, it shows visceral adiposity more precisely than abdominal circumference measurement. In the studies performed, EAT was measured by echocardiogram and a close correlation was found with abdominal adipose tissue measured by MRI and CT.^[10] It was reported that EAT increases in insulin resistance and diabetes mellitus.^[14] There are studies reporting that EAT thickness is correlated with the presence and severity of coronary artery disease.^[15]

EAT is still a popular measurement which is frequently carried out in adults and inspires many researches. However, fetal data on this measurement is very limited. In our study, we aimed to find normal fetal EAT thicknesses by measuring fetal EAT thickness according to the weeks of gestation for the first time in a Turkish population as far as we know.

Methods

A total of 39 pregnant women, who had no anomaly according to fetal anatomy screening and fetal echocardiogram performed in our clinic previously and were between 24 and 28 weeks of gestation according to their last menstrual period, were included in our study. Pregnant women who were taking drugs other than

multivitamins, who did not know their last menstrual date, who had concomitant disease(s) and macrosomic or fetal growth retardation were excluded from the study. Body mass index (BMI) values of all pregnant women were calculated by measuring their heights and weights. Pregnant women whose BMI values and ages were similar were included in the study.

Fetal ultrasonographic measurements were carried out with Voluson E6 (General Electric, Tiefenbach, Austria) ultrasonography device and 2–7 MHz convex abdominal probe by a single perinatologist. Fetal EAT measurement was performed through perpendicular wall of right ventricle at 3rd cardiac cycle at the end of diastole perpendicular to the positions of aortic valves, as described by Iacobellis for adults previously^[10] (**Fig. 1**).

Pregnant women at each week of gestation were separated into different groups and their data were recorded. The data were represented by median and interquartile range. Kruskal-Wallis and Mann-Whitney U tests were used for comparison. Analyses were done on SPSS 22.0 (SPSS Inc., Chicago, IL, USA). In all analyses, $p < 0.05$ was considered statistically significant.

Results

There were 10, 10, 10 and 9 pregnant women on 24+, 25+, 26+ and 27+ weeks of gestation, respectively. There was no statistical difference between weeks of gestation and BMI and maternal age ($p = 0.88$ and 0.33 , respectively). Fetal EAT thicknesses at 24+, 25+, 26+ and 27+ weeks of gestation were 1.29 mm [1.267–1.320], 1.295 mm [1.275–1.305], 1.325 mm [1.297–1.355] and 1.34 mm [1.330–1.355], respectively (**Table 1**). It was seen that EAT thickness increased as week of gestation advanced. While no significant difference was found among median values at 24–25 and 26–27 weeks of gestation ($p = 0.87$ and 0.231 , respectively), there was significant increase between 25 and 26 weeks of gestation ($p = 0.048$) (**Fig. 2**).

Discussion

EAT thickness measurement in adults by transthoracic echocardiogram has become a popular research topic recently. Jeong et al. found mean EAT thickness in Caucasian race as 7 mm in males and 6.3 mm in females.^[16] In our study, we measured mean EAT thickness in structurally normal fetuses as 1.29, 1.295, 1.32

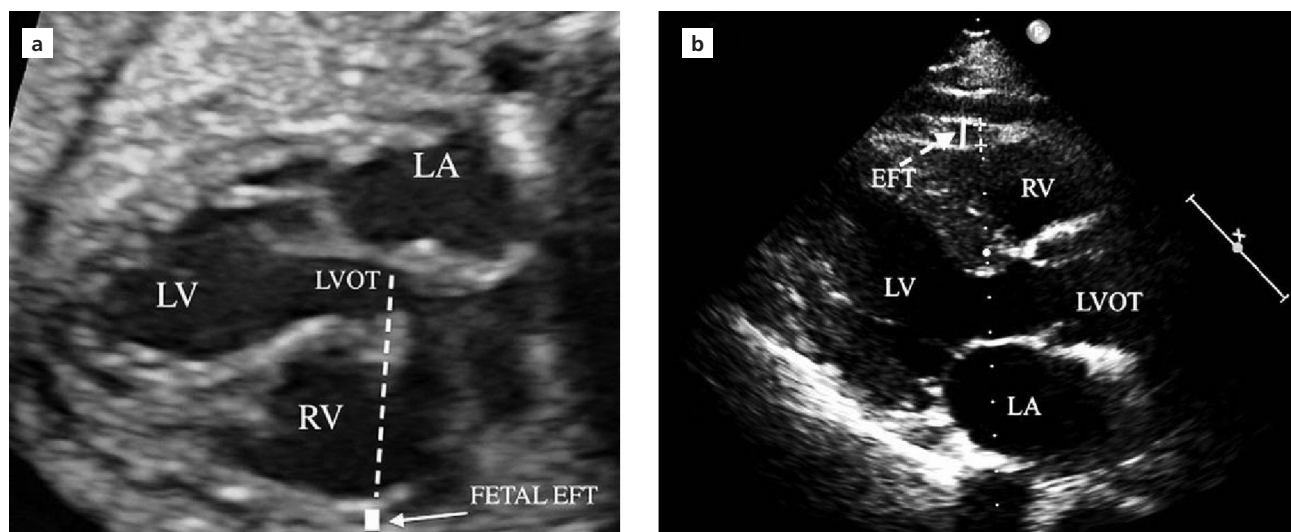


Fig. 1. The measurement of epicardial adipose tissue thickness, which is between epicardium and myocardium on aortic outflow level, in (a) fetus and (b) adult (EFT: Epicardial fat thickness, LA: Left atrium, LV: Left ventricle, LVOT: Left ventricle outflow tract, RV: Right ventricle) (Reprinted with kind permission of © Georg Thieme Verlag KG from Yavuz A, Akkurt MO, Yalcin S, Karakoc G, Varol E, Sezik M. Second trimester fetal and maternal epicardial fat thickness in gestational diabetic pregnancies. *Horm Metab Res* 2016;48:595–600).

and 1.34 mm in 24, 25, 26 and 27 weeks of gestation, respectively. The reason for choosing these weeks is to ensure the most appropriate measurement. Carrying out the measurement at early or late weeks is technically difficult and decreases the precision of the measurement.

A correlation was found between epicardial adipose and hypertension in adults, and increased EAT thickness was reported in hypertensive individuals.^[17,18] In the measurements done in pregnant women in recent years, similar relationship was found between gestational hypertensive diseases and maternal EAT. Can et al. measured maternal EAT thickness, total cholesterol level, left ventricular end systole and diastole volumes in 40 preeclamptic and 38 normal pregnant women. In the study, EAT value was found thicker in preeclamptic pregnant women (7.2 mm) than normal pregnant women (5.6 mm).^[19] Total cholesterol and left ventricular end systole and diastole volumes were found similar. In the same study, preeclampsia group were divided into two sub-groups (severe and mild). EAT thickness value was found significantly thicker in severe preeclamptic group (7 mm) than the mild preeclamptic group (6.6 mm).^[19] In a similar study, Oylumlu et al. found that EAT thickness was higher, which was statistically significant, in preeclamptic pregnant women (6.9 mm) than normal pregnant women (5.6 mm).^[20]

In many studies, EAT increase was associated with metabolic syndrome and coronary heart diseases.^[14,15, 21] A connection was found between EAT and fasting blood glucose and diabetes mellitus (DM) in previous studies.^[22] Çalışkan et al. found EAT thickness significantly increased in women with previous history of gestational diabetes mellitus (GDM) compared to the control group.^[23] According to a study conducted on pregnant women, mean EAT value was measured 7.2 mm in pregnant women with GDM, it was 5.6 mm in the control group ($p < 0.001$). In the same study, a correlation was found between EAT and postprandial glucose level.^[24] In our study, we found that fetal EAT thickness measurements increased in proportion to the

Table 1. The distribution of BMI, maternal age and fetal EAT measurement according to the weeks of gestation.*

Weeks of gestation	24th week (n=10)	25th week (n=10)	26th week (n=10)	26th week (n=9)
BMI	27.7±3.6	26.8±3.6	27.9±1.4	27.5±1.2
Maternal age	25.2±7.3	29.3±7	27.8±5	28.1±5.3
Fetal EAT	1.292±0.031	1.296±0.036	1.326±0.032	1.340±0.017
25th percentile	1.267	1.275	1.297	1.330
50th percentile	1.290	1.295	1.325	1.340
75th percentile	1.320	1.305	1.355	1.355

*The data have been given as median±standard deviation.

week of gestation. We detected that the only statistically significant increase was between 25 and 26 weeks of gestation. This increase may arise from the increase of diabetogenic hormones at second trimester of pregnancy or secondary to the thickening in the parallel tissue upon the growth of fetus.

Jackson et al. performed fetal EAT measurement for the first time during the pregnancies of diabetic women.^[25] In this study, EAT thicknesses of fetuses of 28 diabetic and 28 non-diabetic pregnant women between 20 and 28 weeks of gestation were measured retrospectively. While EAT thickness was 1.43 mm in the diabetic group, it was 1.11 mm in the non-diabetic group and it was found statistically different ($p=0.02$). There was no significant difference between two groups in terms of age, BMI, hemoglobin A1C, week of gestation, estimated fetal weight, fetal abdominal circumference and subcutaneous adipose thickness. Although the first fetal EAT measurement was carried out by Jackson et al., it is not possible to take the mean values by measuring through 3rd cardiac cycle at diastole end as described by Iacobellis since it was a retrospective study. In a study we performed previously, we performed fetal EAT thickness measurement prospectively for the first time. In this study, we made maternal and fetal EAT measurements in pregnant women with GDM and normal pregnant women. While maternal EAT thickness was 6.9 mm in the GDM group, it was 5.3 mm in the control group ($p<0.001$). We found statistically significant increase in the fetal EAT thickness in GDM group (1.34 mm) compared to normal pregnant women (1.31 mm) ($p=0.004$). While there was no difference in EAT thickness in terms of fetal sex, maternal and fetal EAT thicknesses had a correlation.^[26] In our study, consistent with the data of these two studies, fetal EAT thickness was between 1,267 and 1,355 mm in non-complicated pregnancies at 24–27 weeks of gestation.

Conclusion

As far as we know, this is the first study on fetal EAT thickness in non-complicated pregnancies in our society. However, low number of cases is the limitation of our study. Fetal EAT measurement is a very new parameter which is non-invasive and painless, does not need any preparation in advance and does not take time. On the other hand, it is a test which needs high-resolution ultra-

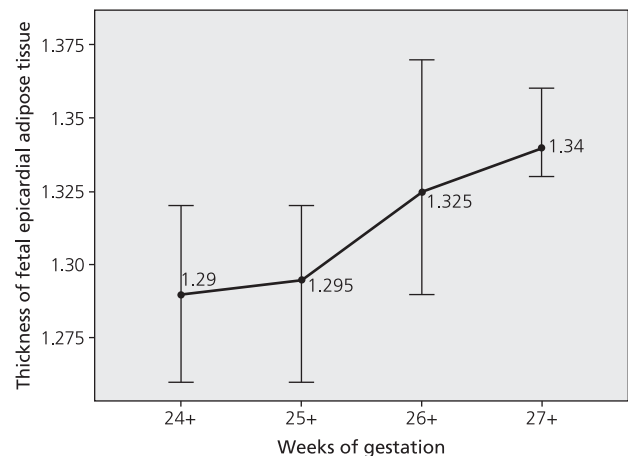


Fig. 2. The change of fetal EAT thickness according to the weeks of gestation.

sound device and personnel specialized on fetal echocardiogram and quite difficult to measure when heart is posterior position and patient is on early weeks of gestation. Therefore, measurement is not considered in routine pregnancy follow-ups. However, these measurements can be performed in perinatology centers on selected patient groups. Further wide prospective studies are needed to create a nomogram according to the weeks of gestation and to identify if pregnancy is complicated in abnormal measurements and to understand the importance of this measurement by following up newborns after their births.

Conflicts of Interest: No conflicts declared.

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