Kocatepe Tıp Dergisi
Kocatepe Medical Journal
24:83-88 / Ocak 2023 Sayısı

ARAŞTIRMA YAZISI / RESEARCH ARTICLE

TELARŞLI PUBERTE PREKOKS HASTALARINDA VASKÜLARİTENİN DOPPLER ULTRASONOGRAFI YÖNTEMLERİ İLE DEĞERLENDİRİLMESİ

ASSESSMENT OF VASCULARITY WITH DOPPLER ULTRASONOGRAPHY METHODS IN PATIENTS OF PUBERTY PRECOCIOUS WITH THELARCHE

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ÖZET

AMAÇ: Bu çalışmanın amacı; telarş değerlendirilmesinde meme vaskülarite düzeyi ile Tanner evrelemesi arasındaki korelasyonun araştırılması ve vaskülaritenin gösterilmesinde doppler yöntemlerinin karşılaştırılmasıdır.

GEREÇ VE YÖNTEM: Ekim - Aralık 2017 tarihleri arasında puberte prekoks ön tanısı ile başvuran ve memede şişlik şikâyeti olan, radyoloji kliniğine refere edilen 6-10 yaş arası kız çocukları çalışmaya dahil edildi. Katılımcıların hepsine meme ultrasonografi (US) ve renkli doppler ultrasonografi (CDUS) tetkiki yapıldı. Tüm katılımcıların takvim yaşı, Folikül Stimülan Hormon (FSH), Luteinizan Hormon (LH), Estradiol (E2), telarş evresi, her iki meme volümü değerlendirildi. Her iki meme için renkli doppler (CD), Power doppler (PD) ve superb mikrovasküler görüntüleme (SMI) yöntemleri kullanılarak vasküler skorlar ölçüldü.

BULGULAR: Çalışmaya 116 kız çocuğu, 213 telarşlı meme dahil edildi. Her bir meme için ölçülen derinlik transvers, longitudinal çap ölçümleri ve meme volümü ile sonografik Tanner sınıflaması arasında anlamlı korelasyon bulundu (sırasıyla: rs=0,762, rs=0,830, rs=0,774 rs=0,824, p<0,001). Doppler yöntemleri arasında en yüksek korelasyon PD'de saptanmakla birlikte (PD rs =0,68, CD rs =: 0,61, SMI rs =:0,61, p<0,001) yöntemlerin birbirlerine üstünlükleri yoktu (p>0,05). PD ile damarlanma gösterilemeyen 65 memeden 30'unda SMI ile damarlanma gösterildi. Bu 30 olgunun %90'ı (n:27) Tanner evre I ve II'ydi.

SONUÇ: Sonuç olarak; SMI tekniği telarş vaskülaritesinin değerlendirilmesinde konvansiyonel doppler yöntemleri kadar başarılı olmakla birlikte bazı olgularda daha fazla veri sağlayabilir.

ANAHTAR KELİMELER: Puberte prekoks, Ultrasonografi, Doppler, Meme

ABSTRACT

OBJECTIVE: The aim of this study is to investigate the correlation between breast vascularity level and Tanner staging in the evaluation of thelarche, and to compare Doppler methods for demonstrating vascularity.

MATERIAL AND METHODS: Girls aged 6–10 who were referred to the radiology clinic with a complaint of breast swelling and prediagnosed with precocious puberty between October and December 2017 were included in the study. Breast ultrasonography (US) and color doppler ultrasonography (CDUS) examinations were performed on all participants. Age, Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), thelarche stage, both breast volumes were recorded for all participants. Vascular scores were measured for both breasts using imaging modalities such as color doppler (CD), Power US (PD), and superb microvascular imaging (SMI).

RESULTS: We included 116 girls and 213 thelarche breasts in the study. A significant correlation was found between the depth and transverse and longitudinal diameter for each breast and breast volume and Tanner stages (rs = 0.762, rs = 0.830, rs = 0.774 rs = 0.824, respectively; p < 0.001). Although the highest correlation between Doppler methods was found in PD (PD rs =0.68, CD rs =: 0.61, SMI rs =:0.61, p<0.001), the methods did not have any superiority over each other (p>0.05). Vascularization with SMI was demonstrated in 30 of 65 breasts for which vascularization could not be demonstrated with power Doppler. Among these 30 cases, 90% (n = 27) were Tanner stage I and II.

CONCLUSIONS: In conclusion, although SMI is as successful as conventional Doppler methods in the evaluation of thelarche vascularity, it can provide more data in some cases.

KEYWORDS: Puberty precocious, Ultrasonography, Doppler, Breast

Geliş Tarihi / Received: 12.08.2021
Kabul Tarihi / Accepted: 11.05.2022
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Etik Kurul / Ethical Committee: Keçiören Eğitim ve Araştırma Hastanesi Etik Kurulu (2017-15/1526).

INTRODUCTION

Precocious puberty is the development of secondary sex characters before the age of 8 in girls and 9 in boys (1). The development of breasts (thelarche) is the first to occur during puberty in girls. The 5-stage Tanner scale is used to monitor thelarche (1). With clinical examination, a subjective evaluation can be made about the glandular breast tissue volume. However, breast ultrasonography (US) can show the presence of glandular tissue, volume, and ductus development and aid in a more objective classification. (2). The US is the first choice for imaging in pediatrics with its radiation-free diagnostic accuracy and noninvasive feature (3). As a result, the US has been used for many years in the evaluation of thelarche in addition to the Tanner scale. In the US, the glandular tissue has a mixed or heterogeneous echogenicity, the adipose tissue is usually hypoechoic, and the fibrous tissue appears hyperechoic (2). There are studies on the correlation of breast vascularization with the Tanner stages or its effect on the stages of gynecomastia in males. (4 - 6). However, there is limited information about the contribution of vascularity assessment or the effectiveness of Doppler methods in the evaluation of thelarche in girls with precocious puberty.

In conventional US methods such as color Doppler (CD) and power Doppler (PD), which are used to investigate the vascularization of tissues, the screening of low-velocity blood flow is prevented by motion artifacts and various wall filters that prevent scattering and provide high-resolution images (7). With the development of technology, Doppler methods that are more successful in showing vascularization in tissues with less vascularity, such as the breast tissue, have been developed. Among these, superb microvascular imaging (SMI), is an up-to-date technology that can view microvascular structures with low-velocity blood flow by overlapping flow signals without filtering tissue movements, unlike conventional Doppler methods (7, 8). Therefore, we think that this may contribute to conventional Doppler methods in the evaluation of vascularity in patients with thelarche. This study aimed to investigate firstly the correlation between the Tanner stages of breast vascularity level, secondly the comparison of conventional Doppler methods and superb microvascular imaging (SMI) findings in demonstrating vascularity.

MATERIALS AND METHODS

This prospective study was initiated after receiving the ethics committee approval from our hospital. Between October and December 2017, girls who consulted the Pediatric Endocrinology clinic with a prediagnosis of precocious puberty and had a complaint of breast swelling were aged 72–126 months and referred to the radiology clinic were included in the study after receiving informed consent from the parents. Breast US and color doppler ultrasonography (CDUS) examinations were performed on all participants. Cases with benign or malignant lesions in the breast and cases with retroareolar adipose tissue hypertrophy were excluded.

US-CDUS (Canon Medical Systems, Otawara, Japan) examinations were performed, by one radiologist (10 years experience), in the supine position under average room temperature. A high-frequency linear ultrasound probe (5–14 MHz) was used for the breast US. Vascular scores were measured using the chronological age of all participants; follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) levels; the thelarche stage, the volume of both breasts; and CDUS, PD, and SMI methods for both breasts.

The depth, transverse, and longitudinal dimensions of both breasts as well as the glandular tissue volume was measured for evaluating thelarche (1, 6). The sonographic Tanner staging (I–V) was done as follows (3): Tanner Stage I; ill-defined hyperechoic retroareolar tissue, Tanner Stage II; retroareolar hyperechoic tissue with a central, star-shaped hypoechoic area, Tanner Stage III; wider retroareolar hyperechoic area and central spider-shaped hypoechoic appearance, Tanner stage IV; fibroglandular tissue, mostly periareolar, is accompanied by a prominent central hypoechoic area and sometimes adipose tissue, Tanner stage V; hyperechoic glandular tissue with increased subcutaneous fat tissue and without hypoechoic central nodule. Vascular scoring was done using CD, PD, and SMI. Examinations were carried out on the

low current setting-scale: 5 cm/s for CD and PD, scale: 1.5–2 cm/s for SMI, wall filter: 50–100 Hz and the gain was increased until an acceptable noise was reached. In vascular scoring, the breast was divided into five regions: the upper outer quadrant, upper inner quadrant, lower outer quadrant, lower inner quadrant, and retroareolar region. The methods described in previous studies were modified, by counting the vascular structures observed in each region, a score of 1 was assigned to each vascular structure to obtain the total vascular score for one breast, with the lowest vascular score being 0 and the highest vascular score being 10 (5, 6). For both breasts, the correlation between the Tanner stage and vascular scores was analyzed.

Ethical Committe

The study protocol complied with the ethical principles of the Declaration of Helsinki and received full approval from the institutional review boards of Keçiören Training and Research Hospital Ethics Committee (No.2017-15/1526).

Statistical Analysis

Analyses were completed in the IBM, SPSS, and V 23 programs. Descriptively, for numerical variables; mean, standard deviation, median, minimum, and maximum were given; and for categorical variables, frequency and percentage were given. Whether continuous numerical variables showed normal distribution was examined with the help of the Kolmogorov–Smirnov normality test and graphs (histogram, Q-Q-plot, and box-plot). Relationships between numerical variables were analyzed with Spearman's rank correlation coefficient.

RESULTS

We included 116 girls (mean age: 107.2 months ± 11.1) and 213 thelarche breasts found in these girls in the study **(Table 1)**.

Table 1: Characteristics of the cases

	Mean (±SD)	Minimum–Maximum (median)
Age (month)	107.27 ± 11.19	63–126 (109)
Breast volume (mm^3)	6096 ± 8130	19–48048 (4193)
Breast transverse diameter (mm)	25.98 ± 13.69	3–73 (28)
Breast depth (mm)	10.27 ± 4.85	3–27 (10)
Breast longitudinal diameter (mm)	23.20 ± 12.95	4–70 (24)
LH	1.01 ± 1.56	0.01–8.90 (0.35)
FSH	4.46 ± 2.55	0.60–16.50 (4.07)
Estradiol (E2)	28.56 ± 17.33	10–97.10 (25.00)

In a total of 19 (8.2%) breasts (7 on the right and 12 on the left), the breast tissue was not detected. The distribution of the Tanner stages in both breasts is shown in **Table 2**.

Table 2: Tanner stage distributions

	The number of cases (n)	Percentage (%)
Tanner stage 1	64	30.0
Tanner stage 2	60	28.2
Tanner stage 3	52	24.4
Tanner stage 4	22	10.3
Tanner stage 5	15	7.0
Total	213	100.0

A significant correlation was found between the depth and diameter measurements obtained for each breast and the Tanner stages (depth: $r_s = 0.762$, transverse diameter: $r_s = 0.830$, longitudinal diameter: $r_s = 0.774$ $p < 0.001$). A high level of correlation was found between the breast volume and the Tanner stages ($r_s = 0.824$, $p < 0.001$).

In the total of 213 breasts with thelarche, vascularization was detected using at least one Doppler method in 175 (82%) breasts. For each Doppler US, breast vascularization was detected in 148 (69%) breasts using PD, 143 (67%) breasts using CD, and 175 (82%) breasts using SMI **(Figure 1 - 5)**.

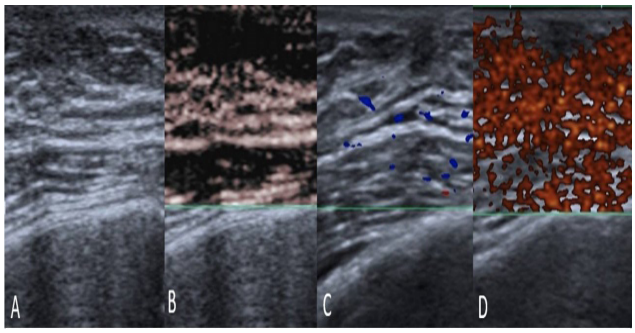

Figure 1: 7-year-old girl, Tanner stage I (A), no vascularization on SMI (B), CD (C), PD (D)

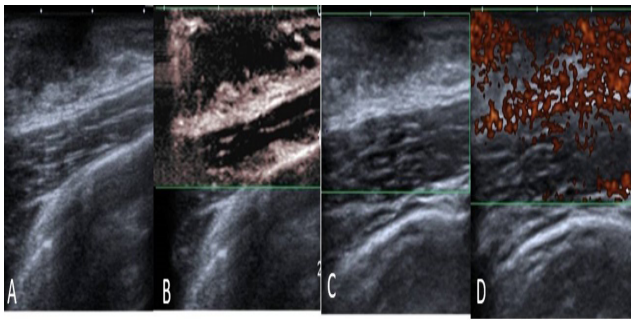

Figure 2: 9-year-old girl, Tanner stage II (A), no vascularization on SMI (B), CD (C), PD (D)

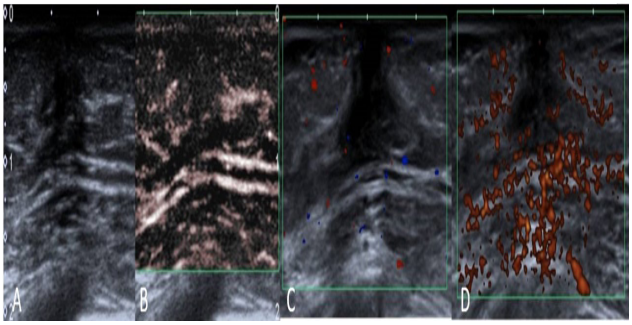

Figure 3: 9-year-old girl, Tanner stage III (A), no vascularization on SMI (B), CD (C), PD (D)

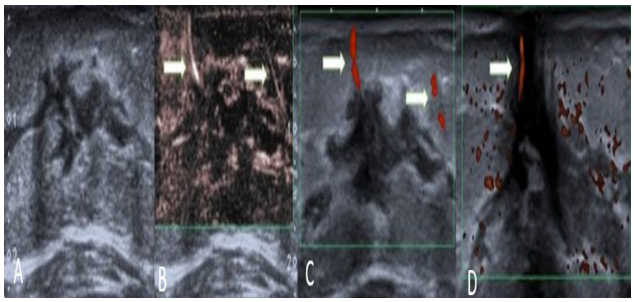

Figure 4: 10-year-old girl, Tanner stage IV (A), 2 vessels on SMI (B), CD (C), PD (D) (white arrows)

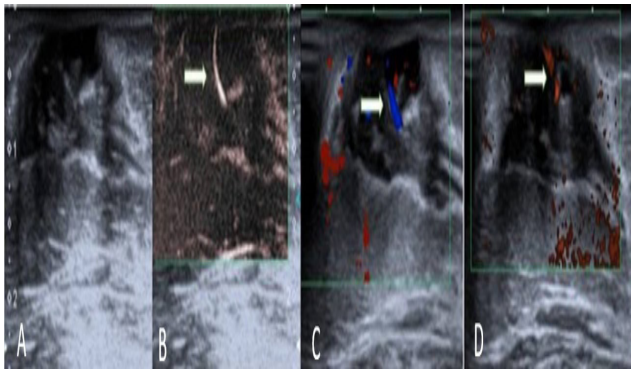

Figure 5: 9-year-old girl, Tanner stage V (A), SMI (B), CD (C), PD (D) images show vascularization (white arrows)

Vascularization could also be demonstrated with PD and SMI for each breast whose vascularization was shown with CD. Vascularization with SMI was demonstrated in 30 of 65 breasts for which vascularization could not be demonstrated with PD. 90% of these 30 cases were of the Tanner stage I (n:17) and II (n:10). When each Doppler method was compared with the Tanner stages, it was observed that they all showed moderate correlation. Although the highest correlation among them was detected in PD r_s = 0.68, CD r_s = 0.61, SMI r_s = 0.61, $p<0.001$), the methods were not superior to each other in terms of the Tanner stages in the thelarche breast ($p>0.05$). The distribution of Doppler scores according to the Tanner stages is shown in **Figure 6**. When the highest Tanner stage and LH, E2, FSH values of each case were compared, moderately significant relationships were found with LH and E2 (r_s = 0.544 and r_s = 0.443, respectively) and low level significant relationships with FSH (r_s = 0.265) ($p<0.05$).

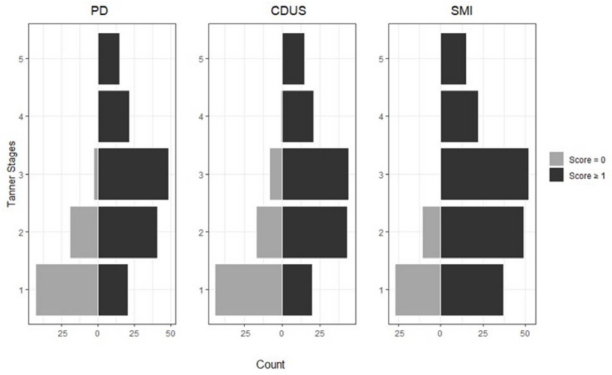

Figure 6: Distribution of doppler scores according to the Tanner stage

DISCUSSION

Puberty is a dynamic complex process, which is a transition from childhood to adulthood, wherein secondary sex characters develop accompanied by growth and rapid progress in bone age (9). Precocious puberty is generally defined as the onset of puberty before the age of 8 in girls and 9 in boys (9). It is approximately 2–23 times more common in girls than in boys (10). Early diagnosis and treatment are important due to the emotional consequences of precocious puberty (early adolescence problems, early fertility, etc.) and its effects on health (rapid progression in bone age and early outcome of growth, etc.) (10). US imaging of the breast and pelvic organs is often used in children with suspected precocious puberty. In our study, the correlation between breast US findings and different Doppler US methods (CD, PD, and SMI) was investigated in the evaluation of thelarche in girls with precocious puberty. In all Doppler US methods, especially in PD, which was moderately correlated with the increase in the sonographic Tanner stage, an increase in vascularization was found. However, vascularization with SMI, a newly developed technology, was demonstrated in 30 breasts (Tanner stage I, II, III; 17, 10, 3, respectively) where vascularization could not be demonstrated with PD.

Tanner stage distribution of cases, it was observed that 15 (7%) cases presented with Tanner stage V. This rate may be high but, in the literature, Tanner stage V cases are given at rates

varying between 1-20% (1, 5, 6). We think that this may be due to the difference in the population and age group included in the study. Clinical Tanner staging has been widely used for many years in the evaluation of the development of secondary sex characters in precocious puberty cases. The Tanner scale, which is based on physical examination findings in the evaluation of thelarche, may be insufficient for differentiating glandular tissue from retroareolar adipose tissue deposition. Therefore, in some cases, the reliability of the Tanner staging in the evaluation of thelarche is controversial. In contrast, breast US is a radiation-free, easily accessible, simple, and noninvasive imaging method that can be used to differentiate between the fibroglandular and adipose tissues. Garcia et al. (3) described the sonographic features of each Tanner stage during normal breast development. A study reported the sonographic breast volume to be an independent factor that can be used in the distinction between two types of precocious puberty, one with a rapidly progressive course and one with a slow course (11). In a study by Bruserud et al. (2), it was observed that in breast development staging between I-V, the visual image in the sonograph is a reliable method for staging the thelarche in healthy girls, but glandular depth and diameter measurements do not have sufficient sensitivity to determine breast development. In our study, there was a stronger correlation between the Tanner stages and the transverse diameter and breast volume measurements. This may be because volume measurements give more information about the amount of breast tissue in contrast to diameter measurements in the evaluation of thelarche staging and precocious puberty.

PD and CD have been used as conventional Doppler methods for many years in the evaluation of the vascularization of the lesion or normal tissues. However, it is known that CD and PD have limitations in showing low-velocity blood flow in small vascular structures due to the filters used to prevent motion artifacts and their poor signal-to-noise ratio (12, 13). Conversely, SMI is an up-to-date technology that can show microvascular blood flow, distinguish motion artifacts from vascular flow, and thus allow a more detailed evaluation of low-velocity blood flow in thin vascular structures (14). In a study comparing CD, PD, and SMI methods to show normal pediatric testicular blood supply (15), while there was a significant difference in the assessment of vascularity between SMI and CD, no significant difference was found between PD and SMI. Furthermore, studies comparing SMI with CD and PD in the differentiation of benign and malignant breast lesions (16, 17) report that SMI gives more information than CD and PD for evaluating the blood supply and vascular pattern of the lesion. In our study, although there was no statistically significant difference between the three Doppler methods, SMI was the method that mostly detects vascularization in the breast. Considering its correlation with the Tanner stages, all three Doppler methods showed higher vascularity scores as the stage increased with PD being the most prominent.

Our study had some limitations. The cases were evaluated by the same radiologist in a single session; therefore, inter and the intraobserver agreement could not be examined between the Doppler methods. Since the cases were not classified as rapid or slow progression, the amount of information this vascularization level could provide about the course of the thelarche could not be evaluated.

Although there is no statistically significant difference between the three Doppler methods in our study, the SMI technique is as successful as conventional Doppler methods in the evaluation of the thelarche vascularity, while in some cases it can provide more data.

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