

## Original Article

# Diagnostic potential of Shear wave elastography for central precocious puberty with breast development

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**Abstract:** Purpose: The aim of this study was to assess the accuracy and diagnostic use of shear wave elastography (SWE) in differentiating central precocious puberty (CPP) with breast development and to analyze the correlations between sex hormone levels and SWE parameters. Methods: A total of 227 participants were included in this retrospective case-control study, including 113 girls with genuine precocious puberty breast development (the CPP group) and 114 with non-genuine precocious puberty breast development (the non-CPP group). The participants underwent clinical assessment, hormonal assays, and SWE using advanced ultrasound equipment. Statistical analyses, including t-tests, correlation analysis, logistic regression, and receiver operating characteristic (ROC) analysis, were performed to evaluate the diagnostic value of SWE and sex hormone levels in differentiating CPP with breast development. Results: There were no significant differences in clinical characteristics between the two groups. The sex hormone levels of estradiol, testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin in the CPP group were significantly higher than those in the non-CPP group. Shear wave velocity (SWV) Maximum (Max), SWV Minimum (Min), SWV Mean, SWV standard deviation (SD), and SWV coefficient of variation in the CPP group were significantly higher than in the non-CPP group. Correlation analysis demonstrated significant positive correlations between LH, FSH, estradiol, and testosterone levels with various SWE parameters, indicating their clinical relevance. Logistic regression analysis identified substantial predictive potential of sex hormone levels and SWE parameters for genuine precocious puberty breast development. Additionally, the ROC analysis highlighted a high predictive value of the combined model of SWE parameters, with an area under the curve (AUC) of 0.903. Conclusion: The study underscores the correlations between sex hormone levels and SWE parameters. The superior predictive performance of the combined model of SWE parameters emphasizes the value of integrated SWE assessments for improving the accuracy of diagnosing genuine precocious puberty breast development.

**Keywords:** Accuracy, shear wave elastography, central precocious puberty, breast development, sex hormone levels

## Introduction

The onset of puberty, characterized by the development of secondary sexual characteristics, represents a crucial transitional phase in the growth and maturation of children [1-3]. However, instances of precocious puberty, marked by the premature activation of the hypothalamic-pituitary-gonadal axis, pose significant clinical challenges [4]. Central precocious puberty (CPP) is characterized by the early activation of the hypothalamic-pituitary-gonadal axis, leading to the development of secondary sexual characteristics before the age of 8 in girls [5-7]. This aberrant advance-

ment in pubertal development can have profound implications for the affected individuals, including psychological and social consequences, compromised final adult height, and the risk of metabolic and cardiovascular disorders [8, 9]. Hence, accurate differentiation of genuine precocious puberty breast development from other causes of early breast development is pivotal for timely intervention and appropriate management.

The diagnosis of CPP typically involves a comprehensive evaluation encompassing clinical assessment, radiologic imaging, and hormonal assays [10]. Precise and reliable imaging

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modalities play a pivotal role in this diagnostic algorithm, aiding in the differentiation of CPP from other benign precocious conditions. Conventional methods such as clinical breast examination and conventional ultrasound have inherent limitations in accurately assessing breast development [11]. Therefore, there is a growing need for advanced imaging techniques that can offer enhanced discriminatory power in differentiating CPP with breast development.

In recent years, shear wave elastography (SWE), a novel ultrasound-based imaging modality, has emerged as a promising non-invasive tool for assessing tissue stiffness and elastic properties [12]. SWE offers advantages of quantifying tissue stiffness and providing valuable insights into the biomechanical properties of tissues [13]. By measuring the velocity of shear waves propagating through tissues, SWE enables the assessment of tissue elasticity, which has shown utility in differentiating benign from malignant breast lesions in the field of oncology [14]. The potential of SWE in the evaluation of breast tissue extends to the assessment of pubertal breast development, where the differentiation of genuine precocious puberty breast development from non-genuine causes is paramount.

Accurate differentiation of genuine precocious puberty breast development from non-genuine precocious breast development is inherently challenging, emphasizing the necessity for advanced diagnostic modalities that can offer enhanced discriminatory power. SWE holds promise in this context, able to quantify breast tissue elasticity and provide valuable insight into the biomechanical changes associated with early breast development [15]. The ability of SWE to non-invasively assess tissue stiffness and elasticity may offer a valuable adjunct to the existing diagnostic methods for CPP with breast development [16].

In addition to the utility of SWE, the correlation between sex hormone levels and breast development in the context of precocious puberty underscores the multifactorial nature of pubertal maturation. Sex hormones, including estradiol, testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin, play pivotal roles in the regulation of pubertal development, exerting profound effects on

breast tissue maturation and the development of secondary sexual characteristics [17]. Therefore, the integration of sex hormone levels with advanced imaging modalities may contribute to a more comprehensive and accurate diagnostic evaluation of precocious puberty. Understanding the correlations between sex hormone levels and SWE parameters may offer valuable insight into the pathophysiology of pubertal breast development and can contribute to the refinement of diagnostic algorithms.

This study aims to elucidate the accuracy and diagnostic potential of SWE in differentiating CPP with breast development and the correlations between sex hormone levels and SWE parameters. By integrating comprehensive clinical assessment, hormonal assays, and advanced imaging techniques, this investigation seeks to provide valuable insights into the diagnostic accuracy of SWE in the context of precocious puberty. Additionally, the correlations between sex hormone levels and SWE parameters may offer insight into the pathophysiology of pubertal breast development and contribute to the refinement of diagnostic algorithms.

### Materials and methods

#### *Ethical review*

This study adhered to the relevant statements of the Helsinki Declaration and received approval from the ethics committee of Hunan Children's Hospital (Approval No: KYSQ2022-103). All patients provided informed consent before enrollment.

#### *Study design*

This was a retrospective case-control study. In this study, girls undergoing growth and development assessment in pediatric health clinics were randomly selected for inclusion. G\*Power 3.1.9.7 was used to perform a power analysis based on t-tests, with the "Means: Difference between two independent means (two groups)" option and Post hoc analysis. A two-tailed mode, effect size  $d=0.5$ , and  $\alpha$  level of 0.05 were set. Subsequently, the sample sizes for the two groups were input to calculate the statistical power ( $1-\beta$ ). The calculation determined that 210 girls needed to be included in this study. With an additional 10% accounted for likely loss to follow-up. The study ultimately

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included 227 girls, with 114 girls in the genuine precocious puberty breast development group and 113 girls in the non-genuine precocious puberty breast development group.

### *Inclusion and exclusion criteria*

**Inclusion criteria:** Children suspected of having pediatric breast development disorders; Unilateral or bilateral breast enlargement and tenderness; Female gender; Age  $\leq 9$  years; Faster growth rate than normal children; Bone age exceeding the actual age by more than 1 year; Normal mental and cognitive functions; Complete medical records.

**Exclusion criteria:** Concurrent malignant tumors; Non-mass breast lesions; Children with breast inflammation or breast abscess; Severe damage to vital organs; Concurrent other types of endocrine diseases; Immunodeficiency or coagulation disorders; Auditory or language communication disorders that hinder effective communication with the physician

### *Detection methods*

The main indicators in this study were SWE parameters, and the secondary indicators were the levels of sex hormones.

Upon admission, the children's ages were recorded, and their height and weight were measured by pediatric endocrinologists. Height was measured using a stadiometer, with the subjects standing barefoot in an upright position. The body weight was measured using a body composition analyzer (TBF-300GS, TANITA, Japan) with the subjects being barefoot and wearing light clothing, and their BMI value was calculated. BMI was defined as the weight (kg) divided by the square of the height ( $m^2$ ). Subsequently, an X-ray scan of the left-hand wrist of the children was performed in a natural sitting position, with the wrist placed flat, fingers naturally spread, thumb and palm at a 30° angle, and the palm facing down against the examination bed. The X-ray tube center was aligned with the third metacarpal bone, and the X-ray film and tube were maintained at a 90 cm distance to measure bone age.

Ovarian examinations were conducted using an ultrasound diagnostic instrument (Aplio500, TOSHIBA, Japan), with the children lying in a supine position and the bladder moderately

filled. The measurements of ovarian length, width, and anteroposterior diameter were obtained, and the ovarian volume was calculated using the formula: ovarian volume ( $cm^3$ ) = length (cm)  $\times$  width (cm)  $\times$  anteroposterior diameter (cm)  $\times$  0.523.

On the second day of admission, 4 mL of fasting venous blood was collected from all the children, centrifuged to collect serum, and the serum estradiol (E2), testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin (PRL) levels were measured using a fully automated electrochemiluminescence analyzer (COBAS E601, Roche, Switzerland).

Subsequently, the breast development was examined using the SWE ultrasound diagnostic instrument (S3000, SIEMENS, Germany) equipped with SWE multi-imaging software and a 10-14 MHz L4-15 linear array probe. The conventional breast ultrasound examination was first performed to record the sonographic characteristics of breast lesions. The children were instructed to hold their breath in a calm state, after which the SWE mode was activated. The elasticity image was frozen after stabilizing for 3-5 seconds, and the quantitative analysis system (Q-BOX) was used to measure the elastic modulus value of the region of interest. Three repeat measurements were taken in the same area, and the values were recorded. The maximum, minimum, mean, standard deviation of the elastic modulus value, and the shear wave velocity (SWV) coefficient of variation were calculated. The examination images were stored in the instrument and workstation. Breast development stages were categorized into 5 phases: stage I was prepubertal breasts, characterized by slight nipple protrusion; stage II was the budding stage, marked by increased areolar pigmentation, slight elevation of the areola and nipple, with the diameter of the mammary bud not exceeding that of the areola; stage III indicated further enlargement of the breast and areola, with the breast size surpassing the areola, and their fusion forming a prominent elevation; stage IV was represented by the nipple and areola projected above the breast, forming a secondary elevation; and stage V signified the mature stage, with the nipple protruding, the areola receding, and both forming a continuous hemispherical prominent elevation (in cases of asymmetric breast development,

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**Table 1.** Clinical characteristics of study participants

Measure	Non-CPP (n=114)	CPP (n=113)	t/X <sup>2</sup>	P
Age (years)	7.52 ± 0.58	7.48 ± 0.62	0.509	0.612
Height (cm)	125.73 ± 5.51	125.42 ± 5.24	0.442	0.659
Weight (kg)	30.05 ± 3.52	29.61 ± 3.16	0.996	0.321
BMI (kg/m <sup>2</sup> )	19.02 ± 1.84	18.83 ± 1.67	0.806	0.421
Bone age (years)	8.92 ± 1.33	9.13 ± 1.29	1.248	0.213
Left ovarian volume (cm <sup>3</sup> )	2.21 ± 0.35	2.16 ± 0.38	0.961	0.337
Right ovarian volume (cm <sup>3</sup> )	2.19 ± 0.32	2.25 ± 0.33	1.400	0.163
Tanner Stage (breast)			0.353	0.552
TII	68 (59.65%)	62 (54.87%)		
TIII	46 (40.35%)	51 (45.13%)		

Note: CPP, central precocious puberty.

assessment was based on the more developed side).

### Statistical methods

Data analysis was performed using SPSS 29.0 statistical software (SPSS Inc., Chicago, IL, USA). Categorical data were presented as [n (%)] and analyzed using the chi-square test or Fisher's exact probability method. The normality of continuous variables was assessed using the Shapiro-Wilk test. For normally distributed continuous variables, results were expressed as (X±s), and the t-test with corrected variance was utilized. Non-normally distributed data were presented as the median (25th percentile, 75th percentile) and analyzed using the Wilcoxon rank-sum test. A two-sided P < 0.05 was considered significant. Pearson correlation analysis was employed for continuous variables. Variables with significant differences in both difference and correlation analyses were included as covariates in logistic regression analysis. The diagnostic performance of SWE parameters and sex hormone levels, either alone or in combination, for the diagnosis of genuine precocious puberty breast development, was assessed using the area under the receiver operating characteristic (ROC) curve (AUC). In the field of machine learning, the Multivariate Adaptive Regression Splines (MARS) model is one of the widely used regression models. It predicts the response variable by nonlinearly fitting the data. This study used the sklearn-contrib-py-earth package in Python to construct the MARS model. The sklearn-contrib-py-earth package, a machine learning library based on Python, is used for construct-

ing efficient and interpretable nonlinear regression and classification models. The MARS algorithm at the core of this package can handle both discrete and continuous independent variables and can identify interactions within the input data.

### Results

#### Clinical characteristics

A total of 227 participants were included in this study, comprising 114 with non-central precocious puberty (non-CPP) and 113 with CPP (**Table 1**). The clinical characteristics of the study participants, including age, height, weight, BMI, bone age, left and right ovarian volumes, and the distribution of Tanner Stage for breast development, were analyzed. There were no significant differences between the two groups in terms of age, height, weight, BMI, bone age, left ovarian volume, right ovarian volume and Tanner Stage (all P > 0.05). The above studies showed no statistical difference between the two groups and were comparable.

#### Sex hormone levels

In the comparison of sex hormone levels between the NCPP and CPP groups, statistical differences were observed in several hormonal parameters (**Table 2**). Specifically, the levels of estradiol, testosterone, LH, FSH and prolactin were significantly higher in the CPP group than in the non-CPP group. These findings suggest a correlation between sex hormone levels and the differentiation of CPP with breast development, highlighting the utility of SWE in this context.

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**Table 2.** Sex hormone levels compared between CPP and non-CPP groups

Hormone	Non-CPP (n=114)	CPP (n=113)	t	P
Estradiol (pg/mL)	8.76 ± 2.55	9.65 ± 3.22	2.312	0.022
Testosterone (ng/dL)	0.48 ± 0.18	0.54 ± 0.21	2.558	0.011
LH (IU/L)	3.87 ± 0.98	4.92 ± 1.25	7.063	< 0.001
FSH (IU/L)	4.69 ± 1.21	6.11 ± 1.54	7.739	< 0.001
Prolactin (ng/mL)	7.21 ± 1.98	7.83 ± 2.45	2.094	0.037

Note: CPP, central precocious puberty; LH, luteinizing hormone; FSH, follicle-stimulating hormone.

**Table 3.** Comparison of shear wave elastography parameters between the two groups

Parameter	Non-CPP (n=114)	CPP (n=113)	t	P
SWV Max (m/s)	2.65 ± 0.25	2.89 ± 0.25	7.263	< 0.001
SWV Min (m/s)	2.13 ± 0.15	2.26 ± 0.18	6.018	< 0.001
SWV Mean (m/s)	2.35 ± 0.18	2.57 ± 0.23	8.226	< 0.001
SWV SD (m/s)	0.19 ± 0.07	0.21 ± 0.07	2.295	0.023
SWV Coefficient of Variation (%)	6.63 ± 1.03	6.95 ± 1.26	2.110	0.036

Note: CPP, central precocious puberty; SWV, Shear wave velocity; SD, standard deviation.

**Table 4.** Correlation analysis of shear wave elastography parameters and sex hormone levels in relation to breast development in CPP

Parameter	r	R <sup>2</sup>	P
Estradiol (pg/mL)	0.152	0.023	0.022
Testosterone (ng/dL)	0.168	0.028	0.011
LH (IU/L)	0.426	0.182	P < 0.001
FSH (IU/L)	0.459	0.211	P < 0.001
Prolactin (ng/mL)	0.138	0.019	0.037
SWV Max (m/s)	0.436	0.19	P < 0.001
SWV Min (m/s)	0.373	0.139	P < 0.001
SWV Mean (m/s)	0.481	0.232	P < 0.001
SWV SD (m/s)	0.151	0.023	0.023
SWV Coefficient of Variation (%)	0.139	0.019	0.036

Note: CPP, central precocious puberty; LH, luteinizing hormone; FSH, follicle-stimulating hormone; SWV, Shear wave velocity; SD, standard deviation.

relation to breast development in CPP, several significant correlations were identified (**Table 4**). Estradiol levels exhibited a weak positive correlation with SWV Max ( $r=0.152$ ,  $R^2=0.023$ ,  $P=0.022$ ), while testosterone levels also showed a weak positive correlation with SWV Max ( $r=0.168$ ,  $R^2=0.028$ ,  $P=0.011$ ). Additionally, strong positive correlations were observed between LH and FSH levels with SWV Max, SWV Min, SWV Mean, and SWV SD parameters ( $r$  ranging from 0.426 to 0.481,  $R^2$  ranging from 0.139 to 0.232, all  $P < 0.001$ ). Prolactin levels showed a weak positive correlation with SWV Max ( $r=0.138$ ,  $R^2=0.019$ ,  $P=0.037$ ), while SWV SD and SWV Coefficient of Variation

exhibited weak positive correlations with estradiol levels ( $r=0.151$ ,  $R^2=0.023$ ,  $P=0.023$  and  $r=0.139$ ,  $R^2=0.019$ ,  $P=0.036$ , respectively). These findings underscore the clinical relevance of SWE parameters in association with sex hormone levels in the context of breast development in CPP.

### Logistic regression analysis

In predicting the risk of genuine precocious puberty breast development based on SWE parameters and sex hormone levels, the analysis revealed significant predictive associations (**Table 5**). Estradiol levels demonstrated a mod-

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SWV Maximum (Max), SWV Minimum (Min), SWV Mean, SWV Standard deviation (SD), and SWV Coefficient of Variation were significantly higher in the CPP group than in the non-CPP group (**Table 3**). These results indicate a promising potential for SWE in differentiating CPP with breast development and its use in clinical practice.

### Correlation analysis

In the correlation analysis of shear wave elastography parameters and sex hormone levels in



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**Table 5.** Prediction of the risk of genuine precocious puberty breast development based on shear wave ultrasound elastography parameters and sex hormone levels

Measure	Odds ratio	Lower CI	Upper CI	B	beta	P
Estradiol (pg/mL)	1.113	1.016	1.223	2.269	0.107	0.023
Testosterone (ng/dL)	5.86	1.5	24.203	2.501	1.768	0.012
LH (IU/L)	2.289	1.76	3.057	5.898	0.828	< 0.001
FSH (IU/L)	2.159	1.713	2.796	6.178	0.769	< 0.001
Prolactin (ng/mL)	1.134	1.008	1.281	2.067	0.126	0.039
SWV Max (m/s)	43.384	13.444	156.645	6.04	3.77	< 0.001
SWV Min (m/s)	146.037	24.399	1039.455	5.223	4.984	< 0.001
SWV Mean (m/s)	233.188	48.99	1326.64	6.498	5.452	< 0.001
SWV SD (m/s)	95.416	1.922	5519.895	2.253	4.558	0.024
SWV Coefficient of Variation (%)	1.279	1.018	1.62	2.08	0.246	0.038

Note: CPP, central precocious puberty; LH, luteinizing hormone; FSH, follicle-stimulating hormone; SWV, Shear wave velocity; SD, standard deviation.

**Table 6.** Predictive value of shear wave ultrasound elastography parameters and sex hormone levels for genuine precocious puberty breast development

Measurement	Sensitivity	Specificity	AUC	Youden index
Estradiol (pg/mL)	0.283	0.868	0.578	0.151
Testosterone (ng/dL)	0.319	0.851	0.583	0.17
LH (IU/L)	0.611	0.763	0.741	0.374
FSH (IU/L)	0.646	0.763	0.762	0.409
Prolactin (ng/mL)	0.602	0.632	0.595	0.234
SWV Max (m/s)	0.743	0.667	0.751	0.41
SWV Min (m/s)	0.549	0.789	0.708	0.338
SWV Mean (m/s)	0.628	0.842	0.783	0.47
SWV SD (m/s)	0.239	0.904	0.577	0.143
SWV Coefficient of Variation (%)	0.54	0.64	0.576	0.18

Note: LH, luteinizing hormone; FSH, follicle-stimulating hormone; SWV, Shear wave velocity; SD, standard deviation.

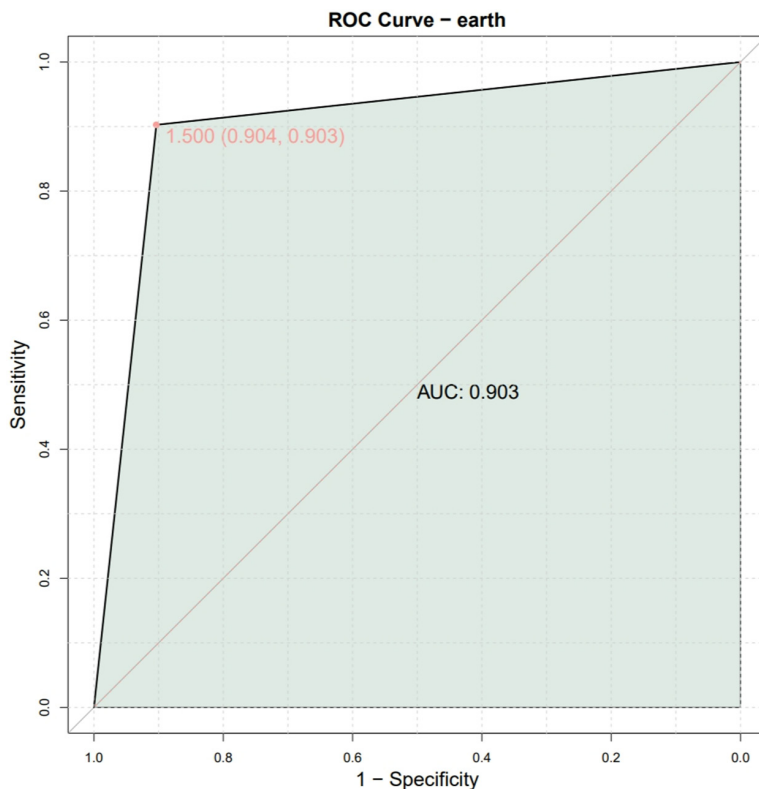
est odds ratio, while testosterone levels exhibited a substantial odds ratio. Moreover, LH and FSH levels displayed notable odds ratios, indicating their predictive value. Additionally, SWE parameters, including SWV Max, SWV Min, SWV Mean, SWV SD, and SWV Coefficient of Variation, demonstrated substantial odds ratios, further highlighting their use as predictive markers for differentiating CPP with breast development.

### ROC

In evaluating the predictive value of SWE parameters and sex hormone levels for genuine precocious puberty breast development, the analysis revealed varying sensitivities, specificities, AUCs, and Youden indices (**Table 6**). Estradiol demonstrated a sensitivity of

0.283 and a specificity of 0.868, yielding an AUC of 0.578 and a Youden index of 0.151, while testosterone exhibited a sensitivity of 0.319, a specificity of 0.851, an AUC of 0.583, and a Youden index of 0.17. Notably, LH and FSH displayed higher sensitivities (0.611 and 0.646, respectively) and AUCs (0.741 and 0.762, respectively) along with substantial Youden indices (0.374 and 0.409, respectively), indicating their potential as predictive markers for genuine precocious puberty breast development. Additionally, SWE parameters, including SWV Max, SWV Min, SWV Mean, and SWV Coefficient of Variation, demonstrated noteworthy sensitivities and specificities, yielding AUCs ranging from 0.576 to 0.783 and Youden indices ranging from 0.143 to 0.47. These results underscore the potential of both sex hormone levels and SWE parameters for

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**Figure 1.** Predictive value of a combined model of shear wave ultrasound elastography parameters for genuine precocious puberty breast development.

predicting genuine precocious puberty breast development.

### *Combined model of shear wave ultrasound elastography parameters*

Finally, this study combined SWE parameters with significant predictive value to construct a joint model for predicting genuine precocious puberty breast development (**Figure 1**). The results revealed an AUC value of 0.903, indicating that the joint model of SWE holds significant predictive value for genuine precocious puberty breast development.

### **Discussion**

Central precocious puberty (CPP) is a condition characterized by the premature development of secondary sexual characteristics due to the early activation of the hypothalamic-pituitary-gonadal axis [18-20]. It is essential to accurately diagnose CPP, particularly in cases involving breast development, to ensure timely intervention and management. In this study, we aimed

to investigate the potential of shear wave elastography (SWE) in differentiating CPP with breast development and its correlation with sex hormone levels.

The findings of this study provide valuable insight into the potential of SWE as a diagnostic tool for differentiating CPP with breast development and its correlation with sex hormone levels. Precocious puberty, characterized by premature development of secondary sexual characteristics, poses diagnostic and management challenges. Identifying genuine precocious puberty breast development is crucial for appropriate intervention and management.

Significant differences were observed in sex hormone levels between the two groups, highlighting the utility of hormonal assays in the diagnosis of precocious puberty.

Specifically, estradiol, testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin levels exhibited significant differences between the non-CPP and CPP groups. These findings are consistent with previous research that has established the pivotal role of LH [21, 22], FSH [23, 24] and prolactin [25] in the pathophysiology of precocious puberty. The correlation analysis further illuminated the relationships between sex hormone levels and SWE parameters, demonstrating significant correlations between LH, FSH, estradiol, and testosterone levels with various SWE parameters. These results provide valuable evidence of the interplay between sex hormones and breast development in the context of precocious puberty.

The notable predictive associations identified through logistic regression analysis underscore the use of sex hormone levels and SWE parameters as predictive markers for differentiating genuine precocious puberty breast development. The substantial odds ratios observed for testosterone, LH, FSH, and SWE parameters

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emphasize their clinical relevance in the evaluation of precocious puberty. A combination of hormonal assays and SWE parameters can contribute to improved diagnostic accuracy in differentiating CPP with breast development.

The evaluation of the predictive value of sex hormone levels and SWE parameters through receiver operating characteristic (ROC) analysis revealed varying sensitivities, specificities, area under the curve (AUC) values, and Youden indices. Although individual sex hormone levels exhibited moderate to high AUC values and sensitivities, the combined model of SWE parameters demonstrated an impressive AUC of 0.903, indicating its robust predictive value for genuine precocious puberty with breast development. This finding highlights the use of SWE as a non-invasive imaging modality to complement hormonal assessments in the diagnostic algorithm for precocious puberty. The combined model's superior predictive performance suggests that SWE parameters, when integrated, may offer enhanced discriminatory power in identifying genuine precocious puberty breast development. SWE provides precise and quantitative measurements of tissue stiffness and elasticity [12, 26]. In the context of CPP with breast development, this allows for the objective assessment of the changes in breast tissue biomechanics associated with early development. These quantitative data can aid in distinguishing genuine precocious puberty breast development from non-genuine causes by detecting subtle, yet significant, differences in tissue elasticity.

As a non-invasive imaging modality free of ionizing radiation, SWE is well-suited for pediatric and adolescent populations [27, 28]. This non-invasive nature enhances patient comfort and safety, making SWE an attractive option for diagnostic evaluation in the context of precocious puberty [29-31]. The strengths of this study lie in its comprehensive approach to evaluate the diagnostic utility of SWE in conjunction with sex hormone levels in the context of precocious puberty. The inclusion of a sizeable study population and rigorous statistical analyses enhance the validity and reliability of the findings. The precise documentation of the methods employed, including the imaging techniques, hormonal assays, and statistical analyses, contribute to the reproducibility and translatability of the study outcomes. Furthermore,

the integration of multiple parameters, including hormonal assays and SWE, offers a multifaceted approach to diagnostic evaluation, reflecting the multifactorial nature of precocious puberty.

Despite the notable strengths of this study, several limitations warrant consideration. The study's retrospective design introduces inherent biases and limits the establishment of causal relationships. Prospective longitudinal studies are warranted to validate the findings and assess the long-term prognostic implications of the diagnostic modalities evaluated. Additionally, the generalizability of the findings may be influenced by the single-center nature of the study and the specific demographic characteristics of the study population. Multi-center studies encompassing diverse demographic and ethnic backgrounds are essential to enhance the applicability of the findings.

### Conclusion

This study highlights the use of SWE as a non-invasive imaging modality for differentiating CPP with breast development. The correlations identified between sex hormone levels and SWE parameters provide valuable insight into the pathophysiology of precocious puberty and suggest the complementary roles of hormonal assays and SWE in the diagnostic workup. The superior predictive performance of the combined model of SWE parameters emphasizes the value of integrated SWE assessments in improving the accuracy of diagnosis. SWE is a promising diagnostic adjunct in the comprehensive evaluation of precocious puberty. Future research endeavors should focus on prospective, multi-center studies to validate the findings and elucidate the long-term implications of SWE in the management of precocious puberty. Additionally, investigations into the cost-effectiveness and accessibility of SWE in diverse clinical settings are warranted to facilitate its integration into routine clinical practice.

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All patients provided informed consent before enrollment.



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## Disclosure of conflict of interest

None.

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