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Original Article RADIOLOGY

Predictive value of machine learning-based T2-weighted MRI radiomics in the diagnosis of polycystic ovary syndrome

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ABSTRACT

OBJECTIVE: This study aims to explore the predictive performance of machine learning-based radiomic features extracted from T2-weighted magnetic resonance imaging (MRI) in differentiating between women with polycystic ovary syndrome (PCOS) and healthy counterparts.

METHODS: The study included patients diagnosed with PCOS who had undergone pelvic MRI in the endocrine department between 2014 and 2022, along with an age-matched control group. The ovaries were manually segmented from T2-weighted images using the 3D Slicer software. Both first- and second-order features, including wavelet filters, were extracted from the images. Utilizing the Python 2.3 programming language and the Pycaret library, various machine learning algorithms were employed to identify highly correlated features. The optimal model was selected from the 15 algorithms assessed.

RESULTS: The study involved a total of 202 ovaries from 101 patients with PCOS (mean age 23±4 years) and 78 ovaries from the control group comprising 40 individuals (mean age 24±5 years). In the training set, the machine learning models displayed accuracy and area under the curve (AUC) values ranging from 72% to 83% and 0.50 to 0.81%, respectively. Notably, the Light Gradient Boosting Machine (LightGBM) model emerged as the most effective model among the various machine learning algorithms, exhibiting an AUC of 0.81 and an accuracy of 83%. When evaluated on the test set, the AUC, accuracy, recall, precision and F1 values of the LightGBM model were 0.80, 82%, 91%, 86%, 88%, respectively.

CONCLUSION: Machine learning-based T2-weighted MRI radiomics seems viable in differentiating between individuals with and without PCOS.

Keywords: Artificial intelligence; machine learning; magnetic resonance imaging; polycystic ovary syndrome; radiomics.

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Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder that affects 6–15% of women in their reproductive years, resulting in oligo-anovulation and hyperandrogenism. It stands as the foremost cause of infertility among women [1–3]. The clinical manifestations comprise oligo-amenorrhea, infertility, weight gain, hirsutism, and acne. The presentation of these symptoms, however, varies in intensity, creating a heterogeneous profile [1, 2].

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Although the etiology remains elusive, insulin resistance plays a pivotal role in PCOS. Elevated levels of insulin, coupled with a skewed luteinizing hormone (LH) to follicle-stimulating hormone (FSH) ratio, drive an increased release of androgens from the ovaries [2–4]. These intricate endocrine disruptions set the stage for a range of health problems. PCOS is linked to a range of comorbidities that pose substantial public health concerns, including insulin resistance, type 2 diabetes, cardiovascular diseases, dyslipidemia, hypertension, non-alcoholic fatty liver disease, infertility, endometrial cancer, as well as depression, anxiety, and eating disorders [4–10].

The diverse characteristics of this syndrome underscore the importance of establishing standardized diagnostic criteria. Based on the consensus of numerous experts, the diagnostic criteria involve identifying clinical or biochemical hyperandrogenism, chronic anovulation, and ruling out other potential disorders. Diagnosis typically requires fulfilling at least two criteria outlined by the Rotterdam European Society of Human Reproduction and Embryology (ESHRE)/American Society of Reproductive Medicine (ASRM)–Sponsored PCOS Consensus Workshop Group in 2003. These encompass oligo-anovulation, clinical or biochemical hyperandrogenism, and the presence of polycystic ovary morphology (PCOM) visualized through ultrasound (US) imaging [5]. In 2009, the Androgen Excess and PCOS Society introduced a modified definition, which incorporates both hyperandrogenism (hirsutism and hyperandrogenemia) and ovarian dysfunction (oligo-anovulation or polycystic ovary appearance on US), building upon the 1990 National Institutes of Health (NIH) criteria [1].

In PCOS, the failure of a dominant follicle to develop results in the accumulation of immature follicles at the periphery of the ovaries. Magnetic resonance imaging (MRI) has been proposed as a valuable diagnostic tool for PCOS, particularly for obese and virgin patients who may not attain satisfactory image quality via abdominal US [11].

Radiomics is a technique through which an extensive array of imaging characteristics is derived from a specific region of interest, allowing the correlation of these features with diagnostic or prognostic insights [12]. These extracted attributes include volume, shape, surface, density and intensity, texture, spatial location, and associations with adjacent tissues. First-order features offer insights into the distribution of pixel intensities. Histograms depicting the intensity of pixel distribution are analyzed using diverse statistical measures, such as variance, skewness, and kurtosis. Second-order features, on the other hand, are derived from the average interrelation among pixels/voxels [13].

Highlight key points

- Machine learning-based T2-weighted MRI radiomics features are useful in distinguishing patients with polycystic ovary syndrome from healthy individuals.
- Among the machine learning models, Light Gradient Boosting Machine (LightGBM) was the most successful, with an AUC value of 0.81 and an accuracy value of 83%.
- MRI-based radiomics features may be particularly helpful in obese patients who cannot undergo transvaginal US.

The aim of this study is to investigate the predictive potential of machine learning-based T2-weighted MRI radiomic features in differentiating those with PCOS from healthy women.

MATERIALS AND METHODS

Ethics

This retrospective study received ethical approval from the Kartal Dr. Lutfi Kirdar Training and Research Hospital Clinical Research Ethics Committee (date: 27.04.2022, approval no: 2022/514/224/23). The study was conducted in accordance with the Declaration of Helsinki.

Participants

We identified female patients who had undergone pelvic MRI examinations at our hospital's endocrinology department from January 2014 to June 2022. The records of these patients were meticulously scrutinized, and those with a PCOS diagnosis were categorized into the patient group. The control group consisted of age- and body mass index (BMI)-matched healthy women without any medical conditions who had been examined for euthyroid multinodular goiter within the endocrinology department.

The diagnosis of PCOS disease was made by endocrinologists with 10 and 7 years of experience. The patient group's diagnosis adhered to the Rotterdam criteria [14], whereby individuals who met a minimum of two conditions (oligo or anovulation, clinical or biochemical hyperandrogenism, and the presence of polycystic ovary morphology (PCOM) observed via US were classified as having PCOS.

For the assessment of biochemical hyperandrogenism, the criteria included elevated serum androgen levels (testosterone ≥60 ng/dl) and/or a high free androgen index (FAI≥49) [15]. Patients with a modified Ferriman-Gallwey (FG) score of ≥7 were considered to have hirsutism [16]. Exclusion criteria incorporated conditions such as non-classical congenital adrenal hyperplasia, hyperprolactinemia, thyroid dysfunction, Cushing's syndrome, and androgen-producing tumors—each of which could lead to hyperandrogenism and oligo-ovulation/anovulation. Conversely, the control group lacked clinical or biochemical hyperandrogenism and demonstrated regular menstrual cycles. Ovaries with cysts exceeding 20 mm in size and lesions like endometriomas or hemorrhagic cysts were excluded from the study. Pelvic MRI was performed for reasons other than PCOS, such as abdominal and pelvic pain, bowel diseases.

MRI Acquisition Protocol

The MRI examinations were conducted using a 1.5 Tesla (1.5T) MRI device (Philips Ingenia, Philips Healthcare, Best, The Netherlands) equipped with a dedicated 32-channel phased array body coil. MRI examinations were performed after 8 hours of fasting. During the imaging procedure, participants were positioned in the supine position and instructed to hold their breath. The acquisition process included non-fat-saturated turbo-spin-echo axial T2W (Field of View (FOV): 311x311 mm, Matrix: 224x206, Flip Angle (FA): 90 degrees, Repetition Time (TR): 7181 ms, Echo Time (TE): 90 ms, Slice thickness: 6.00 mm, Slice gap: 5.00) and sagittal T2W (FOV: 288x288 mm, Matrix: 292x273, FA: 90 degrees, TR: 2558, TE: 90, 90 ms, Slice thickness: 5.00 mm, Slice gap: 5.00) images.

Feature Extraction

T2-weighted MRI images of both PCOS patients and the control group were imported into the 3D Slicer software in DICOM format (version 4.10.2; https://www.slicer.org). These images underwent resampling to achieve a uniform size of 1x1x1 mm and were subsequently normalized. Manual segmentation was independently executed by two experienced radiologists, each possessing 8 and 10 years of expertise in abdominal radiology. These professionals were blinded to the participants' diagnoses. All axial sections containing ovaries were meticulously segmented, precisely delineating the volume of interest. The Slicer-Radiomics tool (PyRadiomics v.3.0.1) facilitated the extraction of a spectrum of features, including first-order, second-order, and wavelet-based texture features (Fig. 1). To gauge the interobserver consistency, the reproducibility of radiomic features was assessed. This was achieved by independently segmenting 40 ovaries from a randomly selected pool of 20 patients, with each segmentation being performed by both radiologists. Interobserver agreement of radiomics features was calculated with intraclass correlation coefficient (ICC) values.

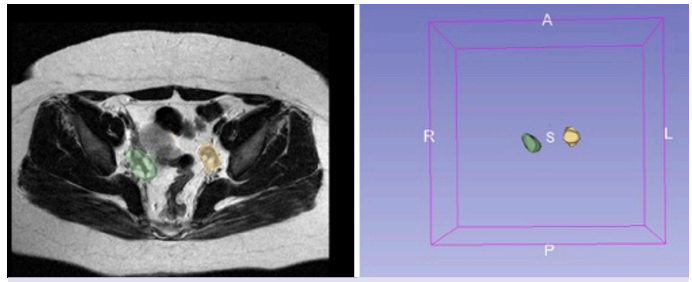

FIGURE 1. Manual segmentation of ovaries on T2-weighted axial images.

Data Processing and Machine Learning Analysis

The data processing and subsequent machine learning analysis were conducted using Python version 2.3 through Jupyter Notebook, with the assistance of the Pycaret Library. During the feature selection process, we employed Random Forest, Lasso regression, and correlation-based techniques. For feature selection, the threshold value was set at 0.7.

The textural feature data were randomly divided into sets of training and test sets. The datasets were divided into a training set (196, 70%) and a test set (84, 30%). To counteract the possibility of overfitting, a 10-fold cross-validation strategy was implemented for the trained models.

The predictive performances of the machine learning (ML) algorithms were assessed by comparing mean AUC, accuracy, recall, precision, and F1 scores. The performance evaluation of the best model, determined based on accuracy and AUC, was carried out on the test set. To represent predictive performance, a Receiver Operating Characteristic (ROC) curve and learning curve were generated. The AUC, accuracy, recall, precision, and F1 scores were calculated using the confusion matrix. Subsequently, the best model underwent tuning and finalization processes to enhance its performance.

Table 1. Examination findings and biochemical results of patient and control groups

Parameters	Patient group (n=101)	Control group (n=40)	p
Age (mean±SD)	23±41	24±53	0.586
BMI (mean±SD)	28±12	29.06±16	0.541
Oligo-amenorrhea (%)	76.9	1.1	<0.001
Hyperandrogenism (%)	62.9	9.9	<0.001
FG score ≥7 (%)	75.8	4.3	<0.001
FG score (median, Q1–Q2)	10 (6.15)	0 (0.1)	<0.001
Testosterone (median, Q1–Q2, ng/dl)	60 (45.75)	38 (27–47)	<0.001
DHEAS level (mean±SD, ng/dl)	377.72±16	145.50±5	0.041
LH/FSH ratio (median, Q1–Q2)	0.94 (0.64–1.70)	0.87 (0.56–1.08)	0.014
PCOM (%)	85.2	24.1	<0.001

BMI: Body mass index; SD: Standard deviation; n: Number; FG: Ferriman-Gallwey; DHEAS: Dehydroepiandrosterone sulfate; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone; PCOM: Polycystic ovary morphology.

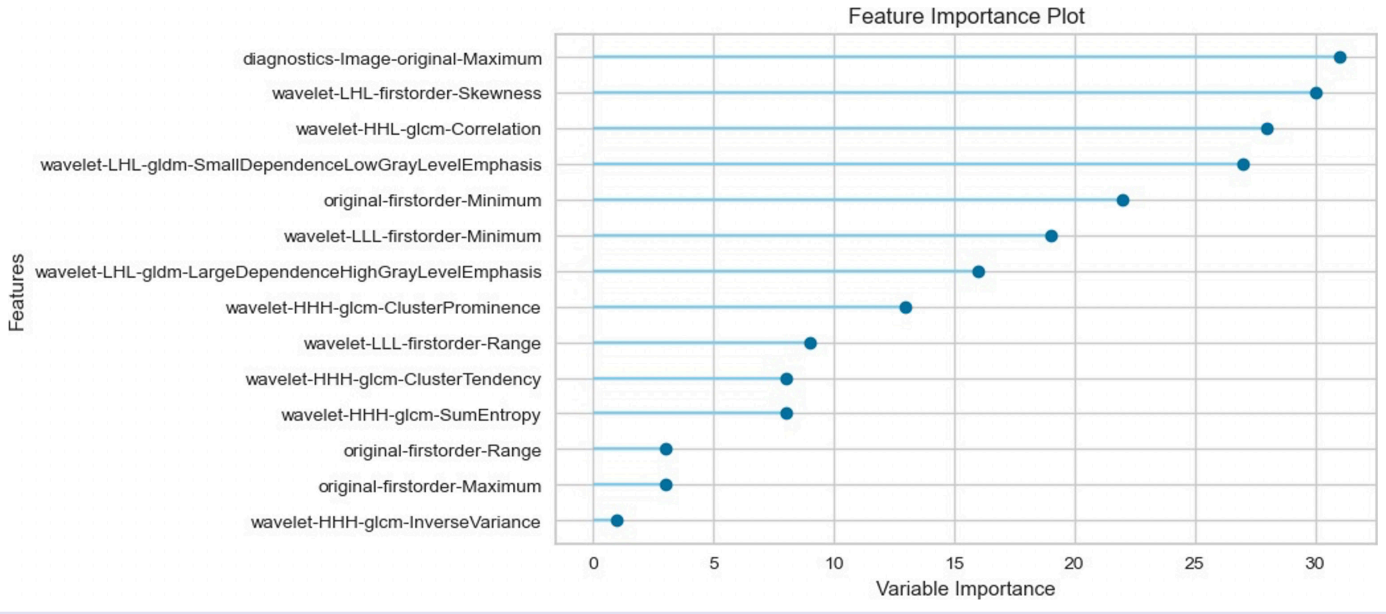

Figure 1. Feature importance plot of the texture features selected by algorithms.

Statistical Analysis

The analysis of study data was conducted using the Statistical Package for Social Sciences (SPSS) version 25.0.0.0 software (IBM Corp., Armonk, N.Y., USA). Descriptive results were summarized using percentages, means, and standard deviations. The one-sample Kolmogorov-Smirnov test was conducted to assess whether the data in the groups followed a normal distribution. Continuous variables demonstrating a normal distribution were presented as mean (±standard deviation [SD]). The assessment of interobserver agreement for the extraction of radiomic features was based on ICC values. A p-value less than 0.05 was considered the threshold for determining statistical significance.

RESULTS

The study enrolled 102 patients with PCOS and 42 women in the control group. One PCOS patient was excluded due to poor image quality caused by artifacts, along with the ex-

TABLE 2. Predictive performance of machine learning-based T2-weighted MRI radiomics for PCOS diagnosis

Model	Accuracy	AUC	Recall	Precision	F1 score
K neighbors classifier	0.8276	0.8017	0.9433	0.8412	0.8877
Extra trees classifier	0.8271	0.7978	0.9505	0.8389	0.8890
Light gradient boosting machine	0.8266	0.8109	0.9214	0.8573	0.8845
Random forest classifier	0.8224	0.7926	0.9643	0.8254	0.8872
Ridge classifier	0.8218	0.0000	0.9505	0.8344	0.8856
Linear discriminant analysis	0.8218	0.8097	0.9362	0.8419	0.8836
Logistic regression	0.8168	0.8069	0.9433	0.8314	0.8810
Gradient boosting classifier	0.8166	0.8000	0.9286	0.8417	0.8787
Ada boost classifier	0.7963	0.7878	0.8786	0.8571	0.8596
Naive bayes	0.7916	0.7233	0.9295	0.8154	0.8668
SVM - linear kernel	0.7558	0.0000	0.8586	0.8162	0.8345
Decision tree classifier	0.7245	0.6655	0.8010	0.8188	0.8064
Quadratic discriminant analysis	0.7245	0.7142	0.9643	0.7353	0.8339
Dummy classifier	0.7197	0.5000	1.0000	0.7197	0.8369

AUC: Area under curve; SVM: Support vector machines; PCOS: Polycystic ovary syndrome.

clusion of two participants from the control group. This led to the inclusion of 202 ovaries from 101 PCOS patients, with a mean age of 23±4 years, and 78 ovaries from 40 controls, with a mean age of 24±5 years. Comprehensive examination findings, biochemical, and MRI results for both the patient and the control groups are detailed in Table 1.

In total, 851 features were extracted and subjected to analysis across 15 ML algorithms. 18 radiomic features selected by the ML algorithms (Fig. 2). The interobserver agreement for these radiomic features yielded ICCs ranging from 0.742 to 0.873, indicating a robust level of agreement.

The ML algorithms in the training set showcased accuracy and AUC values ranging between 72% and 83%, 0.50 and 0.81, respectively (Table 2). Of the ML algorithms evaluated, the Light Gradient Boosting Machine (LightGBM) emerged as the optimal model. AUC, accuracy, recall, precision values, and F1 score of LightGBM model were 0.80, 82%, 91%, 86%, and 88%, respectively. The predictive performance is further illustrated by the confusion matrix and classification report in Figure 3.

DISCUSSION

Transabdominal US might be a preferred imaging modality for diagnosing PCOS in virgin patients unable to undergo transvaginal US. However, when it comes to obese patients, the image quality provided by transabdominal US may not be sufficient for effective ovarian assessment. In such cases, interpretations primarily rely on ovarian volume calculations rather than antral follicle counts [17]. In contrast, certain studies have investigated MRI as an alternative for diagnosing PCOS. MRI has effectively depicted ovarian volume and morphology in adolescent girls with PCOS [17–22]. Our study demonstrated the efficacy of radiomic features extracted from MRI in differentiating between PCOS patients and healthy women. Notably, the LightGBM model achieved high AUC and accuracy values in the context of distinguishing PCOS patients from the control group.

The radiomic features chosen in our study primarily focused on the internal signal characteristics of the ovaries, encompassing both first- and second-order features. Intriguingly, volume-related features were not identified as predictive by the machine learning models. This observation aligns with findings from prior research suggesting that follicle number per ovary (FNPO) holds greater diagnostic value than ovarian volume in the context of PCOS diagnosis. For instance, Pereira-Eshraghi et al. [21] highlighted the increased sensitivity of FNPO values in MRI for PCOS diagnosis compared to ovarian volume. This study further unveiled a correlation between FNPO and androgen levels, while no such relationship was identified between ovarian volume and androgen levels. Likewise, Ali et al.'s [22] ultrasound-based study

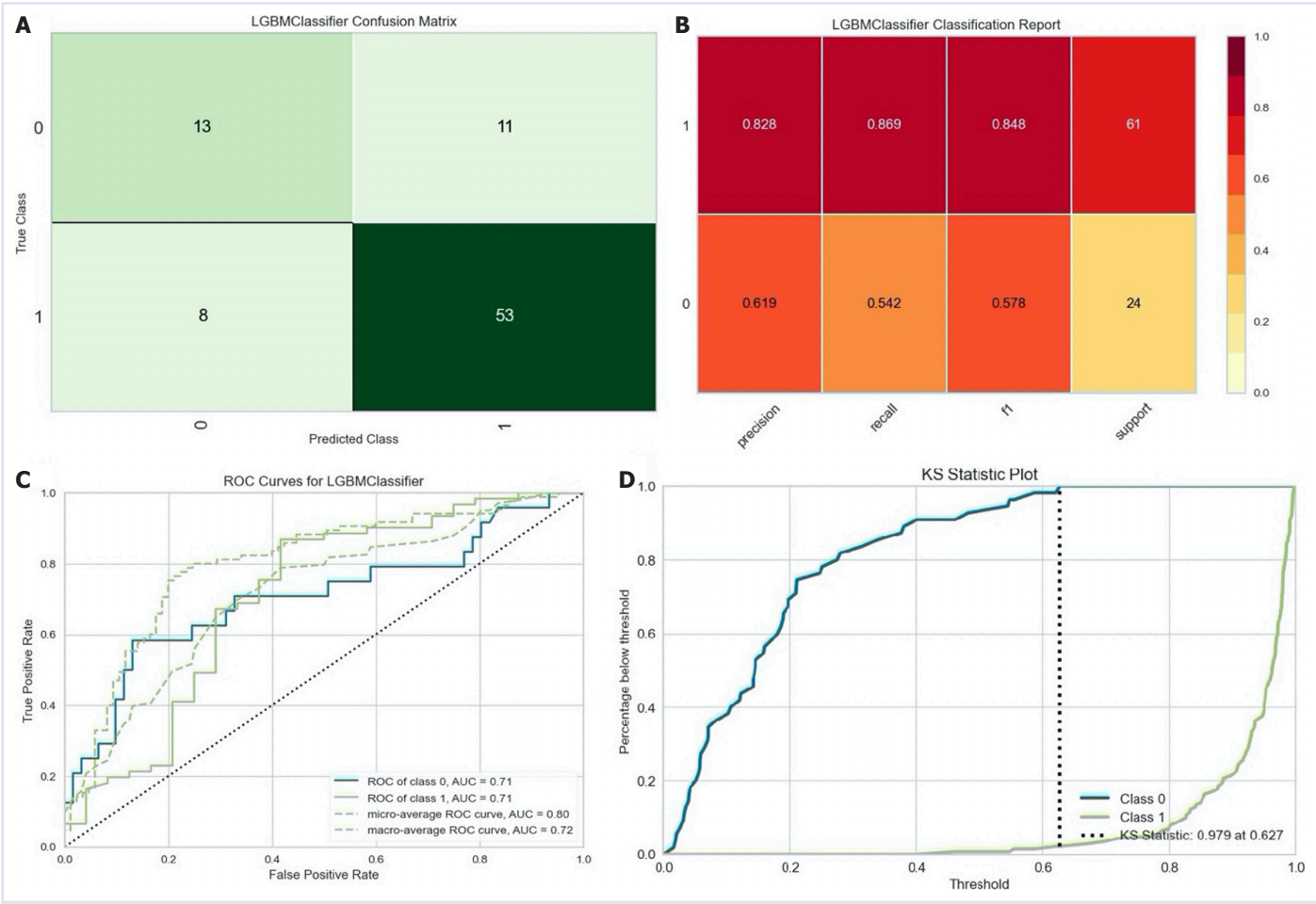

FIGURE 3. **(A)** Confusion matrix, **(B)** classification report for Light Gradient Boosting Machine model in T2-weighted image texture analysis.

underscored the enhanced reliability of ovarian morphological features over ovarian volume in diagnosing PCOS.

In MRI-based investigations, previously reported AUC values have ranged from 0.77 to 0.87. However, these studies were constrained by limited patient cohorts [18–21]. While interobserver agreement was not consistently reported across these studies, the study by Fondin et al. [20] indicated moderate agreement. Remarkably, our study's AUC value of 0.80 fell within this range. It is worth noting that our study featured a larger patient sample size and demonstrated improved interobserver agreement compared to previous reports.

Pelvic MRI has emerged as a valuable tool for diagnosing PCOS, offering the advantage of being operator-independent in contrast to US. Similarly, the radiomic features extracted from MRI remain unaffected by the operator or reader variability. Furthermore, T2-weighted sequences, commonly employed in MRI protocols, obviate the requirement for contrast agents. An added benefit of MRI lies in its radiation-free nature, which is particularly relevant when evaluating the younger age group affected by PCOS. However, the cost associated with MRI remains a significant constraint. Given the significance of early and accurate diagnosis, especially for obese and young patients, the utilization of MRI has been strongly advocated [11, 22].

Our study has limitations, including its retrospective design and the relatively small patient cohort. Manual segmentation is another limitation of our study, as it may cause interobserver variability. Additionally, manual segmentation is a time-consuming method for practitioners.

Alongside clinical manifestations, radiomic features derived from T2-weighted MRI hold the potential for enhancing PCOS diagnosis. These objective features offer valuable support for PCOS diagnosis through MRI. To further bolster our results, future investigations with a larger sample size are warranted.

Conclusion

In conclusion, radiomic features obtained from T2W sequences are useful in the diagnosis of PCOS. The advantages of T2W sequences are that they are noninvasive and do not require contrast material. Although MRI is a high-cost and not easily accessible examination, it may be useful in diagnosis in a selected group of patients who are obese and cannot undergo transvaginal US.

Ethics Committee Approval: The Kartal Dr. Lutfi Kirdar Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 27.04.2022, number: 2022/514/224/23).

Authorship Contributions: Concept – GR, NF, TAS, MA, MBE, SO, KA; Design – GR, NF, KA; Supervision – GR, NF, KA; Fundings – GR, NF, TAS, MA, MBE, SO, KA; Materials – GR, NF, SO, KA; Data collection and/or processing – GR, NF, MA, SO, KA; Analysis and/or interpretation – GR, TAS, MBE, SO, KA; Literature review – GR, NF, TAS, MA, MBE, SO, KA; Writing – GR, NF, KA; Critical review – GR, NF, SO, KA.

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