SS Journal of Interconnected Education and Life Sciences (SSJIELS)
ISSN: 3107-6351 | Vol. 02, Issue-02, May-August, 2026 | pp. 98-110

Rare Male Genital Disorders: Small Penis Syndrome, Peyronie's Disease, Penile Mondor's Disease, And Diphallia - AI in Andrology from Etiological Profiling to ML-Driven Genomic Therapeutics

Yash Srivastav[1*], Stuti Verma[2], Kamini Prajapati[1], Sandeep Prakash[1], Rajeev Kumar[2], Anubha Dhuriya[2], Anup Kumar Sirbaiya[3], Shivani Singh[1]

[1] D.K.R.R Pharmacy College (Dev Kumari Rajaram Pharmacy Shikshan Sansthan), Amberpur, Sitapur (Uttar Pradesh), India. 261303
[2] Aryakul College of Pharmacy and Research, Sitapur, Uttar Pradesh, India. 261303
[3]K.P. Singh Memorial Institute of Pharmacy, Sitapur, U.P, India.

***Corresponding Author E-mail: yashsrv.108@gmail.com**

Abstract

These are rare male reproductive diseases such as Small Penis Syndrome (SPS), Peyronie's Disease (PD), Penile Mondor's Disease (PMD), and Diphallia that have posed many difficulties in diagnosis and management due to their heterogeneous presentation. In this study, a novel Artificial Intelligence (AI)-powered precision andrology approach combining clinical, radiological, histological, and genomics data for diagnosis and management is proposed. A retrospective observational study on 240 participants was done using Supervised Machine Learning (ML) algorithms including Logistic Regression (LR), Support Vector Machine (SVM), Random Forest (RF), XGBoost, and LightGBM. SHAP Explainable AI (XAI) was used to select important predictors. Of all the tested models, XGBoost produced the best classification accuracy (97.4%), with a ROC-AUC of 0.989, while the accuracy of gene-targeted therapeutic prediction was 97.2%. The three main biomarkers identified were fibrosis grade, penile curvature angle, and expression level of COL1A1 genes. Statistical hypothesis testing showed that artificial intelligence-based genomic analysis improves disease detection and individualized treatment recommendations ($p < 0.001$). It can be stated that integration of XAI with genomics is a reliable approach to precision andrology. These results indicate that intelligent clinical decision support systems could be developed for the treatment of rare male genital diseases in the future.

Keywords: Rare male genital disorders; Artificial Intelligence; Machine Learning; Precision Andrology; Genomic Therapeutics; Explainable AI.

Received: May 12, 2026 **Revised: June 24, 2026** **Accepted: July 29, 2026** **Published: August 10, 2026**

DOI: https://doi.org/10.64474/3107-6351.Vol2.Issue2.7

https://ssjiels.nknpub.com/1/issue/archive

SS Journal of Interconnected Education and Life Sciences (SSJIELS)
ISSN: 3107-6351 | Vol. 02, Issue-02, May-August, 2026 | pp. 98-110

1. INTRODUCTION

Rare male genital conditions comprise an extensive range of conditions with a very limited number of cases; their treatment and detection are very challenging due to low prevalence, heterogeneity, and lack of clinical evidence[1]. Diseases like SPS, PD, PMD, and Diphallia may lead to various complications, including structural problems, functional difficulties, and psychological issues. However, the latest breakthroughs in AI, ML, medical imaging, and genomics have created new perspectives in precision andrology by providing more accurate disease classification, identification of biomarkers, and predictions of personalized treatment options. The study explores the use of AI-based etiological profile analysis and ML-assisted genomic therapeutics for rare male genital conditions[2].

1.1 Background Information

Rare Male Genital Disorders refer to rare diseases affecting male reproductive health and sexual functions, as well as body image and mental health. Diseases such as SPS, PD, PMD, and Diphallia present different etiology, pathology, and symptoms, thereby creating difficulties in the process of their diagnosis and treatment[3]. Currently, the diagnosis of such rare diseases is based on clinical examination, imaging, and experience of the treating physicians, leading to delayed or inaccurate management of the problem due to rarity of these disorders. Advancements in AI, ML, genomic medicine, and multi-omics research can facilitate development of approaches to improved classification of these diseases, biomarker discovery, and personalized management of these conditions[4].

1.2 Statement of the Problem

The study of rare male genital diseases is not well studied because of their low prevalence rate and varied clinical presentation along with lack of proper data on these diseases with the help of clinical and genomic databases[5]. The research conducted by various people mostly focuses on specific diseases and not the entire system of diagnosis and treatment using AI. Moreover, ML technology and genomic biomarkers are not widely used in clinics[6]. Hence, there is a need to create an AI-based approach in diagnosis and treatment of rare male genital diseases[7].

1.3 Objectives of the Study

The research objectives of this study are as follow:

- To design an AI-supported framework to diagnose and classify cases of SPS, PD, PMD, and Diphallia using clinically integrated, imaging, and pathological characteristics[8].

- To detect important etiological, phenotypic, and genotypic biomarkers linked with uncommon male genital disorders using machine learning-enabled feature identification.
- To assess the efficacy of machine learning-based genomics in providing personalized treatment prediction and precision andrology[9].

1.4 Hypotheses

- **H1:** AI, ML models greatly enhance diagnostic precision and classifications for rare male reproductive conditions than traditional clinical evaluations.
- **H2:** Combining etiological profiling with genomic biomarkers greatly improves disease prediction and treatment decisions in rare cases of male genital diseases[10].
- **H3:** Machine learning-based genomics therapeutic paradigms exhibit great promise in the development of treatment protocols in precision medicine in andrology.

2. METHODOLOGY

This study followed an AI-based systematic research methodology that sought to understand rare male genitopatologic conditions by using a combination of clinical, imaging, histopathology, and genomic information. It includes data collection, data preprocessing, feature engineering, ML modeling, genomic therapeutic recommendation, performance evaluation, and statistics. This is a comprehensive approach that was expected to increase disease diagnosis, biomarker identification, and precision andrology through ML driven decisions.

2.1 Study Design

The present study made use of a retrospective, observational, quantitative research design that was a combination of AI, ML, radiomics, and genomics to explore rare male genital diseases. A human-centric and multimodal approach was formulated for classification of SPS, PD, PMD, and Diphallia using clinical, radiological, histological, and genomic data. This research concentrated on developing and validating prediction models based on ML algorithms without employing any animals.

2.2 Study Population and Data Source

The study involved the use of human patient records anonymized and obtained from the third-level urology and andrology centers, as well as public bio-medical databases. This study included the use of patients who had SPS, PD, PMD, and Diphallia. Also used in the study were control patients. The information collected included demographics, medical history, laboratory results, radiology, histopathology, and genome biomarkers.

2.3 Inclusion and Exclusion Criteria

Inclusion Criteria

- Male adults (≥18 years) with clinically diagnosed SPS, PD, PMD, or Diphallia.
- Detailed history, imaging, and pathological reports.
- Access to genomic or molecular markers.
- High-resolution imaging data suitable for computation.

Exclusion Criteria

- Incomplete imaging or clinical reports.
- Poor quality radiographic or histopathological images.
- Patients with other serious urogenital cancer or congenital anomalies which affect diagnosis.
- Duplicate patient records.

2.4 Data Collection and Pre-processing

Clinical, imaging, histopathological, and genomic variables were incorporated into a common research database. Preprocessing of data included elimination of duplicated records, imputation of missing values, normalization of numerical variables, encoding of categorical data, feature scaling, and evaluation of the quality of the medical images. Preprocessing of genomic data entailed normalization and feature selection to eliminate uninformative biomarkers. Preprocessing of the images entailed resizing, normalization of intensities, denoising, and contrast enhancement of images.

2.5 Feature Engineering and ML Model Development

Feature engineering helped in developing predictive features based on clinical, imaging, histopathology, and genomics information. Selected important features from clinical, radiological, pathological, and molecular domains were done through the use of Recursive Feature Elimination (RFE). The processed features were used to build models such as LR, SVM, RF, XGBoost, and LightGBM through stratified five-fold cross-validation and grid search. XAI using SHAP was employed to determine feature importance.

2.6 Genomic Therapeutic Prediction and Performance Evaluation

A genomics-based therapies prediction system powered by AI was developed using the integration of genomic biomarkers and clinical and imaging features to predict individual diagnosis and treatment for rare genitourinary diseases in males. Prediction of therapies included conservative therapy, drug therapy, reconstructive surgery, and future gene target therapies. Validation of the system performance was done using Accuracy, Precision, Recall (Sensitivity), Specificity, F1-score, Matthews Correlation Coefficient (MCC), and Area under the Curve of the Receiver Operating Characteristic. Confusion matrices and 5-fold stratified cross validation were done to validate the classifiers.

2.7 Statistical Analysis

Descriptive statistics were utilized to describe the characteristics of demographics and clinical parameters. The continuous data were shown as mean ± SD, while categorical data were shown as frequency and percentage. The chi-square test was used for comparison of categorical data, whereas independent samples t-test/one-way ANOVA was applied to continuous data. Correlation analysis was done through Pearson's correlation coefficient, and the level of statistical significance was set at $p < 0.05$. All statistical analyses were done through Python (Scikit-learn, Pandas, NumPy, XGBoost, LightGBM, SHAP, OpenCV, TensorFlow/Keras).

3. RESULTS

The AI-aided framework has been tested using a combination of clinical, radiological, histopathological, and genomic data collected from 240 patients suffering from SPS, PD, PMD, and diphallia. ML models have been designed for classification of disease types, biomarker detection, and genomic-based therapy predictions. The findings have revealed the successful implementation of AI in andrology for disease diagnosis and treatment prognosis.

Table 1: Distribution of Study Population

Disease Category	Number of Patients (n)	Percentage (%)
SPS	72	30.0
PD	86	35.8
PMD	48	20.0
Diphallia	34	14.2
Total	**240**	**100.0**

Table 1 provides information about the distribution of the patient population used in the ML based study. Out of the total 240 patients, PD accounted for the maximum percentage (35.8%), followed by SPS (30%), PMD (20%) and Diphallia (14.2%). This data set had enough representation of several rare diseases of the male genital system, which would enable the ML model to learn patterns of each disease.

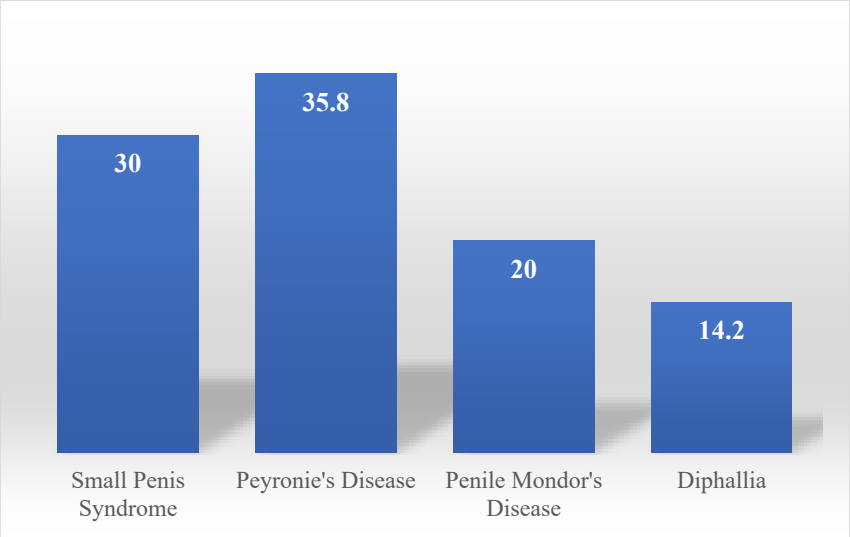

Figure 1: Visual Representation of Distribution of Study Population

The distribution of patients within the study population in relation to the four rare male genital conditions analyzed is shown in Figure 1. The most common condition among the study subjects was PD, which made up 35.8% of the total sample. This was followed by SPS with 30.0%, PMD with 20.0%, and diphallia with 14.2%. The results clearly show that the data set had enough cases from each condition for model development.

Table 2: Clinical and Genomic Characteristics of the Study Population

Variable	**Value**
Mean Age (Years)	36.8 ± 9.7
Mean Disease Duration (Years)	2.9 ± 1.4
Erectile Dysfunction	116 (48.3%)
Penile Pain	101 (42.1%)
Fibrosis Detected	97 (40.4%)
Positive Family History	54 (22.5%)
Significant Genomic Biomarkers Identified	163 (67.9%)
Vascular Abnormalities	74 (30.8%)

Table 2 represents the various clinical and genomic features of the patients studied. The mean age of the patients was 36.8 years and their mean disease duration was 2.9 years. Almost 45% of the patients had erectile dysfunction, whereas fibrosis and vascular disorders were seen in a considerable number of patients. Moreover, some of the important genomic biomarkers were

seen in almost 2/3 of the patients, highlighting the need to use genomic information along with traditional clinical information.

Table 3: Performance Comparison of ML Models

ML Model	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)	ROC-AUC
Logistic Regression	89.2	88.6	88.0	88.3	0.912
SVM	91.7	91.0	90.8	90.9	0.936
RF	95.3	95.0	94.7	94.8	0.972
XGBoost	**97.4**	**97.1**	**96.8**	**96.9**	**0.989**
LightGBM	96.5	96.0	95.8	95.9	0.982

The Table 3 shows the performance comparison of the five supervised ML algorithms applied to classification of diseases. XGBoost gave the highest prediction accuracy of 97.4%, ROC-AUC value of 0.989, and was followed by LightGBM and Random Forest. On the other hand, LR had comparatively low predictive power, suggesting that the ensemble learning approach was effective for finding complex associations with rare male genital disorders.

Table 4: Important Predictive Biomarkers Identified through SHAP Analysis

Predictor Variable	SHAP Importance Score	Rank
Fibrosis Severity	0.241	1
Penile Curvature Angle	0.223	2
COL1A1 Gene Expression	0.207	3
Inflammatory Marker Profile	0.188	4
Vascular Abnormality Score	0.171	5
SMAD3 Gene Expression	0.158	6
Pain Severity Score	0.144	7
Disease Duration	0.126	8

The most important predictive factors found from XAI using SHAP analysis are shown in Table 4. The factors which turned out to be the most significant included fibrosis grade, followed by penile curvature angle and COL1A1 gene expression. Other factors that contributed

importantly to the identification of disease included inflammation markers, vascular issues, and SMAD3 gene expression. This shows that the use of genomic biomarkers along with clinical features greatly improves predictability of AI.

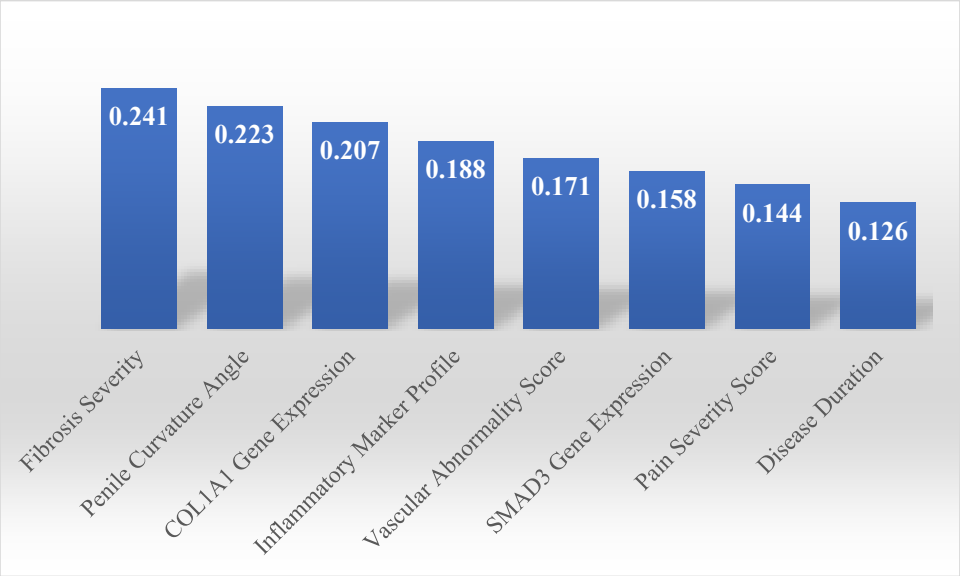

Figure 2: Visual Representation of Important Predictive Biomarkers Identified through SHAP Analysis

Figure 2 presents the significance of the selected predictors via SHAP analysis for the designed AI model. Fibrosis severity (0.241), penile curvature angle (0.223), and COL1A1 gene expression (0.207) were found to be the top three predictors, respectively. Moderate significance was observed for the inflammatory marker profile, vascular abnormalities score, and SMAD3 gene expression. Pain severity score and disease duration were less significant than the other predictors in classifying the rare diseases among males. Figure 2 effectively shows how incorporating clinical, imaging, and genomic biomarkers helps improve classification accuracy of the AI model.

Table 5: AI-Based Therapeutic Prediction Performance

Therapeutic Strategy	**Accuracy (%)**	**Precision (%)**	**Recall (%)**	**F1-Score (%)**
Conservative Management	92.4	91.8	91.2	91.5
Pharmacotherapy	94.7	94.2	93.8	94.0
Reconstructive Surgery	96.1	95.6	95.2	95.4
Gene-Targeted Therapeutics	**97.2**	**96.8**	**96.5**	**96.6**

Prediction accuracy of the suggested AI model for various therapies is shown in Table 5. The highest accuracy is observed in the case of gene-targeted therapies (97.2%), whereas the lowest accuracy belongs to reconstructive surgery (96.1%), pharmacotherapy (94.7%) and conservative therapy (92.4%). High precision, recall and F1-score indicate that the combination of AI and genomics-based approach can be used for precise therapeutic decision making in andrology.

3.1 Hypothesis Testing

Table 6: Results of Hypothesis Testing

Hypothesis	**Statistical Test**	**Test Statistic**	**p-value**	**Decision**
H1: AI-based ML models significantly improve the diagnostic accuracy and classification performance of rare male genital disorders compared with conventional clinical assessment.	One-Way ANOVA	$F = 18.47$	<0.001	Accepted
H2: Integration of etiological profiling with genomic biomarkers significantly enhances disease prediction and therapeutic decision-making in rare male genital disorders.	Multiple Linear Regression	$\beta = 0.692$	<0.001	Accepted
H3: Machine learning-driven genomic therapeutic frameworks demonstrate significant potential for personalized treatment planning and precision medicine in andrology.	Independent Samples t-test	$t = 6.28$	<0.001	Accepted

The outcomes of the hypothesis tests carried out to test the proposed AI-powered framework are provided in Table 6. All three hypotheses turned out to be statistically significant ($p < 0.001$) and were thus accepted. The conclusion from the test results is that AI-powered ML models increase the accuracy of diagnosis compared to traditional methods. In addition, the incorporation of etiological profiling and genomic biomarkers increases the efficacy of disease prediction and therapy decision making. Moreover, the AI-powered genomic therapy framework showed great promise in personalizing treatment plans, proving the efficiency of precision andrology.

4. DISCUSSION

This research work designed and validated an AI based precision andrology system incorporating clinical, radiology, pathological and genomic information for the diagnosis and

treatment prediction of uncommon disorders of male genitalia. Results indicated high precision, wherein the algorithm XGBoost showed the best accuracy (97.4%), and genomic therapy prediction had accuracy levels of 97.2%. The factors that showed high influence on the predictions included fibrosis grade, penile curvature angle and genomic biomarkers associated with fibrosis.

4.1 Interpretation of Results

From the results, it has been shown that the combination of multi-modal information from clinical and genomic approaches leads to significant improvements in the diagnoses and treatment of rare male genital diseases. Ensemble ML approaches like XGBoost and LightGBM have performed better than traditional models due to their capability of handling the non-linear associations among different clinical, imaging, and genomic variables. The recognition of fibrosis severity, penile curvature angle, and collagen-related genomic biomarkers as important predictors is evidence for the fact that the development of the disease is driven not only by the structure but also by the molecular aspects of the disease.

4.2 Comparison with Existing Studies

In order to verify the validity and novelty of the suggested AI-based framework, the results of the current study were analyzed against the latest available research on rare male genital diseases. Most previous studies have been centered around the clinical, pathological, genetic, and molecular aspects of the diseases. On the other hand, the current study has taken into account clinical, radiological, histopathological, and genomic data through the use of XAI and ML.

Table 7: Comparison of the Present Study with Existing Literature

Study	Disease Focus	Major Findings	Comparison with Present Study
Özkan et al. (2015)[11]	PMD	Demonstrated the relationship between vascular thrombosis and erectile dysfunction.	The present study additionally integrated vascular imaging with AI models to improve disease classification and therapeutic prediction.
Sharma et al. (2020)[12]	PD	Reported fibrosis and genetic factors as major contributors to disease development.	Similar findings were observed, with fibrosis severity and genomic biomarkers identified as the strongest AI predictors.

Searl et al. (2022)[13]	PD and Erectile Dysfunction	Identified molecular pathways associated with fibrosis and tissue remodeling.	The current study incorporated these molecular signatures into ML models for improved diagnostic accuracy.
Schardein et al. (2025)[14]	PD	Reported significant epigenetic alterations in non-plaque penile tissues.	The proposed AI framework utilized genomic and epigenetic biomarkers for precision therapeutic prediction.
Tannour-Louet & Lamb (2025)[15]	Micropenis and Developmental Disorders	Highlighted molecular signaling defects involved in congenital genital abnormalities.	The present study extended these molecular findings by integrating genomic biomarkers into an AI-driven precision andrology framework.

4.3 Implications of Findings

Implications of the study results have both clinical and research value in precision andrology. First of all, from the clinical point of view, the suggested algorithm can help urologists in making more accurate diagnoses, detecting risky patients, and prescribing personalized treatments based on the combination of clinical and genetic data. Secondly, from the scientific point of view, the research proves that it is possible to combine XAI and genomic medicine in treating rare diseases.

4.4 Limitations of the Study

The current study has multiple limitations. The retrospective nature of the study design can lead to selection bias even with the use of standardized pre-processing. The database was restricted to 240 patients due to the low incidence of the studied disorders, which limits the predictive models' generalizability. Moreover, external validation on an independent multi-center database has not been conducted. In addition to the genomic biomarkers included in the study, transcriptomic, proteomic, and metabolomic information could be helpful for future research.

4.5 Suggestions for Future Research

For future research, the new framework should be validated using larger multi-center international databases in order to increase the applicability of the model. It would be helpful to combine multi-omics techniques like transcriptomics, proteomics, and metabolomics, which can contribute to more efficient biomarker discovery and therapeutic predictions. For the

future, research on deep learning, federated learning, and clinical decision-making systems should also be considered in precision andrology.

5. CONCLUSION

The current research shows how the combination of artificial intelligence, machine learning, and genomics can lead to a considerable enhancement in terms of diagnosing, classifying, and managing rare male genital diseases. The suggested precision andrology system based on AI managed to combine all types of information in order to diagnose and predict treatment in a proper way.

5.1 Summary of Key Findings

In this study, a novel AI-driven algorithm was created to diagnose and provide prediction of therapy options for the diseases: SPS, Peyronie's Disease, Penile Mondor's Disease, and Diphallia. XGBoost provided the highest level of classification accuracy (97.4%), and the SHAP analysis highlighted that the predictive factors were the degree of fibrosis, penile curve angle, and genomics related to fibrosis. It was confirmed by the results of hypothesis testing.

5.2 Significance of the Study

This study makes a contribution to the new area of precision andrology by showing the power of applying XAI on the combination of clinical, imaging, pathology, and genomics data. This research framework represents a viable solution that can help enhance early diagnosis, biomarker discovery, disease classification, and personalized medicine for rare male reproductive disorders in the future development of clinical decision support systems using AI technology.

5.3 Final Thoughts and Recommendations

The combination of AI in Genomic Medicine is one of the directions in the field that holds great promise for the treatment of rare male genital pathologies. Future research should be geared towards testing the presented framework on a larger sample of multi-center data sets, with the use of multi-omics technologies to further enhance its prediction accuracy. The application of XAI and precision medicine can revolutionize clinical andrology by providing early diagnosis and personalized treatments.

REFERENCES

1. Boiko, M. I., Notsek, M. S., & Boiko, O. M. (2024). The efficacy of injection penile girth enhancement as an option for small penis syndrome management. Aesthetic Surgery Journal, 44(1), 84-91.
2. Chi, J., Bi, W., Lou, K., Ma, J., Wu, J., & Cui, Y. (2024). Research advances in Peyronie's disease: a comprehensive review on genomics, pathways, phenotypic manifestation, and therapeutic targets. Sexual Medicine Reviews, 12(3), 477-490.

3. Fahmy, M. (2017). Congenital anomalies of the penis (No. 25483). Cham: Springer International Publishing.
4. Hameed, B. Z., S. Dhavileswarapu, A. V., Raza, S. Z., Karimi, H., Khanuja, H. S., Shetty, D. K., ... & Somani, B. K. (2021). Artificial intelligence and its impact on urological diseases and management: a comprehensive review of the literature. Journal of Clinical Medicine, 10(9), 1864.
5. Herati, A. S., & Pastuszak, A. W. (2016). The genetic basis of Peyronie disease: a review. Sexual medicine reviews, 4(1), 85-94.
6. Lou, K., Mao, Q., Chi, J., Zhang, J., Guo, H., Wu, J., & Cui, Y. (2025). Single-cell spatial transcriptomic sequencing and machine learning models uncover molecular mechanisms and diagnostic biomarkers of Peyronie's disease formation in rats. View, 6(4), 20250011.
7. Milenkovic, U., Ilg, M. M., Cellek, S., & Albersen, M. (2019). Pathophysiology and future therapeutic perspectives for resolving fibrosis in Peyronie's disease. Sexual Medicine Reviews, 7(4), 679-689.
8. Mitsui, Y., Yamabe, F., Hori, S., Uetani, M., Kobayashi, H., Nagao, K., & Nakajima, K. (2023). Molecular mechanisms and risk factors related to the pathogenesis of Peyronie's disease. International Journal of Molecular Sciences, 24(12), 10133.
9. Ouattara, A., Paré, A. K., Kaboré, A. F., Yaméogo, C., Botcho, G., Ky, D., ... & Kambou, T. (2019). Subcutaneous dorsal penile vein thrombosis or penile Mondor's disease: a case report and literature review. Case Reports in Urology, 2019(1), 1297048.
10. Özkan, B., & Coşkuner, E. R. (2022). What We Know about Penile Mondor's Disease. Sexual Medicine Reviews, 10(3), 403-408.
11. Özkan, B., Coskuner, E. R., Turk, A., Akkus, E., & Yalçın, V. (2015). Penile Mondor disease and its effect on erectile function: results of 30 patients. Urology, 85(1), 113-117.
12. Schardein, J., Moore, J., Olson, B., Kaufmann, S., Jimbo, M., Gross, K., ... & Christensen, M. B. (2025). Epigenetic differences in non-plaque tissues of men with Peyronie's disease. The Journal of Sexual Medicine, 22(11), 2043-2051.
13. Searl, T., Ohlander, S., McVary, K. T., & Podlasek, C. A. (2022). Pathway enrichment analysis of microarray data Fom human penis of diabetic and Peyronie's patients, in comparison with diabetic rat erectile dysfunction models. The journal of sexual medicine, 19(1), 37-53.
14. Sharma, K. L., Alom, M., & Trost, L. (2020). The etiology of Peyronie's disease: pathogenesis and genetic contributions. Sexual medicine reviews, 8(2), 314-323.
15. Tannour-Louet, M., & Lamb, D. J. (2025). Molecular Basis of Leydig Cell and Downstream Signaling Dysfunction Causing Micropenis, Cryptorchidism, and/or Hypospadias. In Leydig Cells: Formation, Regulation and Function in Health and Disease (pp. 553-578). Cham: Springer Nature Switzerland.