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Platelet rich plasma: New therapy for erectile dysfunction

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Abstract
Background: Erectile Dysfunction (ED) is characterized by the inability to attain and/or sustain an erection of a quality necessary to engage in sexual activity to satisfaction. Our objective was to evaluate the safety and efficacy of Platelet-Rich Plasma (PRP) intracavernosal injection as a novel regenerative therapy for males with.
Methods: This placebo-controlled, prospective, single-blind, randomised clinical trial involved 120 patients with mild to moderate ED as measured by the International Index of Erectile Function (IIEF). The blinded patients were divided into two groups at random: group A (PRP group) and group B (placebo group) (group B). Every patient underwent the following assessments: personal history, sexual history, physical examination (including genital and general examination), laboratory investigations, imaging, and IIEF-5.
Results: Regarding patient satisfaction, neither of these variables exhibited a statistically significant increase over the course of the three time periods examined in the study. With regard to IIEF, there was no statistically significant difference in the treatment group over time. Regarding IIEF, there was no statistically significant difference in the placebo group. There was no statistically critical difference observed between the two groups in terms of evaluation data following treatment for 1, 3, and 6 months.
Conclusions: Treatment of mild to moderate ED with two intracavernosal PRP injections separated by one month is safe, but not more effective than placebo, according to the findings of our clinical trial. Further investigation into patient selection and treatment protocols is required in order to reevaluate these initial findings.

Keywords: Platelet rich plasma, therapy, erectile dysfunction, international index of erectile function

Introduction
Erectile dysfunction (ED) is a multifaceted and intricate condition that primarily arises from endothelial dysfunction, diminished penile blood flow, and arterial insufficiency or stenosis. While enhancing penile hemodynamics, the majority of recommended treatments improve erectile function without reversing the pathophysiologic mechanisms that cause ED [1].
Among adult males, ED is one of the most prevalent conditions, impacting an approximate one-fifth (4.3 million men) in the United Kingdom (UK). It is anticipated that by 2025, 322 million men globally will be impacted by ED, with prevalence rates reaching as high as 48%. The prevalence of this condition escalates as men age, rising from 5% among those aged 20-39 to 70 percent among those aged > 70 [1]. ED can arise from a variety of factors, including psychogenic and organic causes that have been thoroughly examined in other sections. Endothelial and nerve dysfunction, as well as decreased penile arterial blood flow, are the causes of ED [2, 3].
Platelet-rich plasma (PRP) is an autologous plasma fraction generated through the centrifugation of whole blood. It differs from whole blood in that it contains a mean platelet concentration that is three to seven times greater. 3 By virtue of the advantageous characteristics exhibited by growth factors present in significant concentrations within this fraction, a multitude of medical specialties have incorporated PRP injections into their repertoire of treatment alternatives [4].

After a decade, maxillofacial surgeons began utilising PRP, and it is now utilised in a variety of fields, including Orthopedics/musculoskeletal injuries, cardiac surgery, plastic surgery, and dermatology, albeit with mixed results [5, 6]. PRP promotes healing by increasing the number of cells (Mitogenesis) and stimulating vascular ingrowth (angiogenesis) [7]. Platelets possess not only hemostatic characteristics but also a profusion of growth factors (GFs) and cytokines, which exert influence over cellular proliferation, angiogenesis, and inflammation. Platelet activation triggers the release of various cytokines and growth factors, with platelet-derived GF (PDGF), fibroblast GF (FGF), transforming GF beta-1 and beta-2 (TGF-b1/2), insulin-like GF (IGF-1, IGF-2), epidermal GF (EGF), hepatocyte GF (HGF), interleukin 8, and matrix metalloproteinases 2,9 being among the most significant GFs [8]. PRP injections may modify key pathophysiologic mechanisms that contribute to ED via anti-inflammatory, reparative, Neuroprotective, and neurotrophic effects, according to studies [9].

Recently, PRP intracavernosal injections have surfaced as a regenerative, angiogenic, and vasculogenic treatment option for ED. PRP injections may ameliorate critical components of the pathophysiologic mechanisms that contribute to ED via anti-inflammatory, reparative, Neuroprotective, and neurotrophic effects, according to ten animal studies. 11-14 However, these mechanisms have not been sufficiently investigated nor fully comprehended as of yet [10].

The purpose of this study was to compare the safety and efficacy of PRP injections to a placebo in the treatment of ED in patients.

Patients and Methods

This prospective, single-blinded, randomized, placebo-controlled clinical trial performed on 120 patients with mild to moderate ED degree according to International Index of Erectile Function (IIEF). The participants in question had an ED diagnosis for a minimum of six months, had discontinued oral medication (PDE5i) or any other treatment for ED at least one month prior to the study, and met the necessary inclusion criteria. Between April 2022 and April 2023, in the outpatient clinic of the Andrology unit of the Urology department at Tanta University Hospitals.

Written informed consent was obtained from the patient or their legal guardians. Following registration on clinicaltrials.gov and approval from the Ethical Committee of Tanta University Hospitals (no.35403/4/22), and registration of clinicaltrials.gov (ID).

Sexually active married heterosexual males between the ages of 20 and 75 who have had mild to moderate ED for a minimum of six months meet the inclusion criteria.

Exclusion criteria were previous major penile surgery or radiation; history of priapism, penile fracture, peyronie's disease, abnormal morning serum testosterone levels (lower than 300 ng/dL or greater than 1197 ng/dL); previous major pelvic surgery or trauma; penile curvature or any other anatomical disorder affecting erectile function; psychogenic ED; history of any severe medical and psychiatric condition impairing participation in the study and; participants whose partners disclosed sexual dysfunction or any other significant medical condition that restricted sexual activity during the study period, in addition to those who presented with an age below 18 years, were breastfeeding, or were pregnant.

Randomization and blindness

These blinded patients were randomly divided into 2 groups: PRP group (Group A) and placebo group (group B). Randomization was performed according to a computer-generated sequence developed by the study coordinating team. To ensure allocation concealment and minimize selection bias, assignment to groups.

Patients' assessment

Physical examination (General examination and genital examination), sexual history, personal history, and investigations (Imaging and laboratory).

International Index of Erectile Function-5 (IIEF-5)

Each of the five items comprising this questionnaire is evaluated using a five-point ordinal scale; lower values indicate inferior sexual function. Based on IIEF-5 scores, ED is categorised into four groups: Severe (scoring 5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25). Individuals who have IIEF-5 (12 -21).

PRP Preparation and Administration

Administration and Preparation of PRP a blood sample was collected from each patient using a 60 mL syringe containing 8 mL of anticoagulant. Injections of placebo and PRP were prepared in an isolated room. Patients randomised to receive PRP were subjected to processing using an FDA-approved autologous platelet separator (Magellan Autologous Platelet Separator; Arteriocyte Medical Systems, Hopkinton, MA) to obtain an approximate volume of 10 mL of PRP. Samples of patients randomised to receive placebo were discarded. While processing, minimal intervention is necessary due to the closed loop, fully automated nature of the Magellan Separator. PRP, specifically, is dispensed into a distinct sterile syringe after being automatically isolated from anticoagulated whole blood within circa 15 minutes. The Magellan system provides PRP of superior quality, according to a comparison of commercially available PRP separation systems. 23 While the remaining aliquot is prepared for intracorneal administration, one millilitre of PRP is utilised for quality control. Patients were positioned in a supine position and a penile tourniquet was affixed to the base of the penis subsequent to the preparation of the injection. To reduce platelet cell damage, a volume of 5 mL was infused into each corpus cavernosum while the needle was gradually retracted over a 2-minute duration to ensure improved distribution of PRP into the erectile tissue. Without anaesthesia, the entire procedure was conducted under sterile conditions. After administration, further penile compression was achieved by encircling the shaft of the penis with a dressing. Twenty minutes following the injections, the penile tourniquet was removed and the patients were discharged. Four hours subsequent to the injection, every patient was directed to remove the compression bandage at their residence.

Mode of injection

Following the completion of injection preparation, the patient was positioned in a supine position. Applying a topical anaesthetic cream to the injection site was performed. A tourniquet was affixed to the penile region at its base. The injection was administered at the 3 or 9 o'clock position in the mid-penile region. A volume of 5 mL was

injected gradually into each corpus cavernosum for a duration of 2 minutes in order to mitigate the risk of platelet cell injury. The entire procedure was executed in an absolutely sterile environment.

After administration, further penile compression was achieved by encircling the shaft of the penis with a dressing. Twenty to thirty minutes after injection, patients were observed in the clinic in order to document any early complications. Twenty minutes after the injection, the penile tourniquet was removed. Four hours following the procedure, every patient was directed to remove the compression bandage at their residence.

The Experimental group: received 2 sessions of autologous PRP penile injection, each administered 1 month apart±7 days.

The placebo group: subjected to the same protocol using normal saline rather than PRP.

Patients' follow up

All patients were followed up after 1, 3 and 6 months of the procedure aiming at assessing safety and efficacy of the technique.

The safety of the method was assessed through the documentation of any adverse events, whereas its effectiveness was evaluated by observing alterations in the IIEF and penile duplex. Furthermore, the satisfaction of the patients was evaluated on a Likert scale ranging from 1 to 5. A rating of 1 indicated extreme dissatisfaction, 2 indicated dissatisfaction, 3 indicated neither dissatisfaction nor satisfaction, 4 indicated satisfaction, and 5 indicated very satisfaction.

The primary outcome of our study was the proportion of patients in each group attaining MCID in the IIEF-EF domain from baseline to 6 months after the final treatment.

Statistical analysis

SPSS v27 was utilised for the statistical analysis (IBM2, Armonk, NY, USA). Histograms and the Shapiro-Wilks test were utilised to assess the normality of the data distribution. A unpaired student t-test was utilised to analyse quantitative parametric data presented as mean and standard deviation (SD). The Chi-square test was employed to analyse qualitative variables, which were presented in the form of frequencies and percentages (%). Considered statistically significant was a two-tailed P value below 0.05.

Results

In this study, 163 patients were assessed for eligibility, 25 patients did not meet the criteria and 18 patients refused to participate in the study. The remaining 120 patients were randomly allocated into two groups (60 patients in each). All allocated patients were followed-up and analysed statistically (Figure 1).

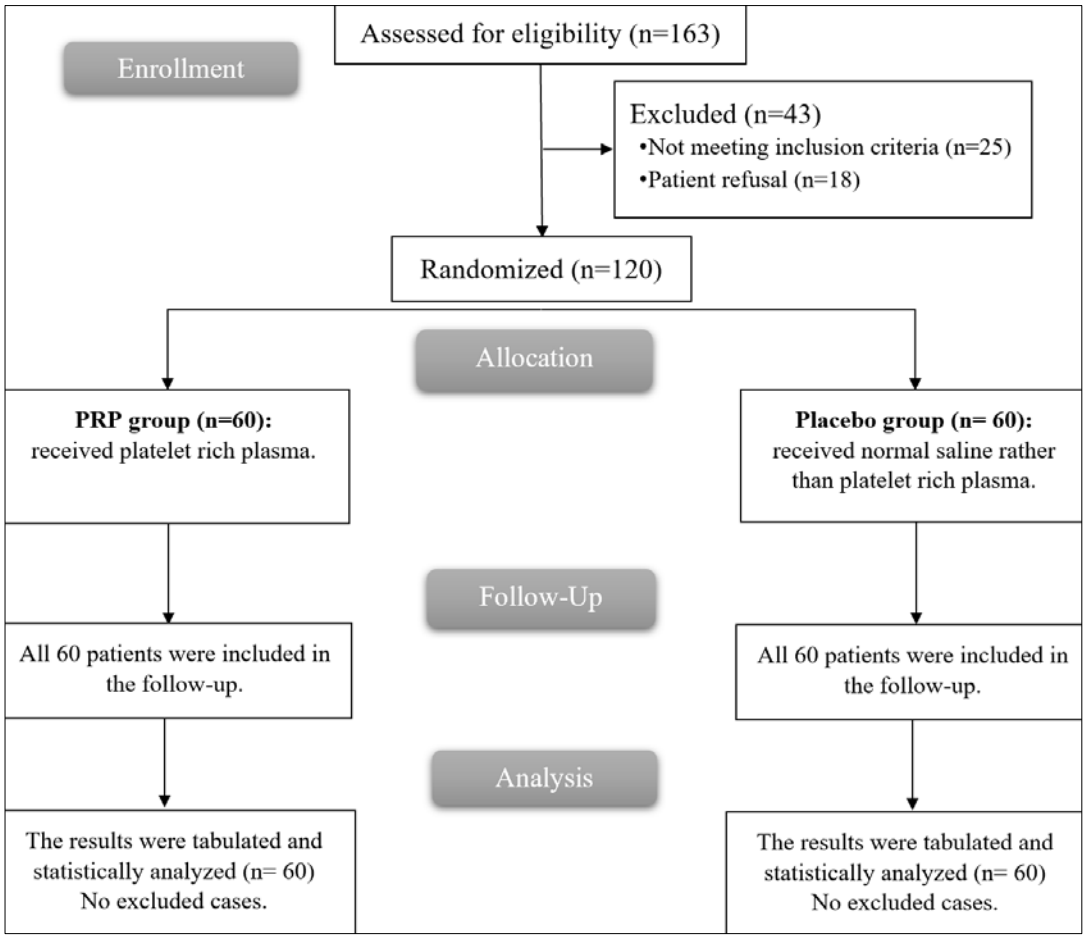

Fig 1: CONSORT flowchart of the studied groups

Regarding the initial data, no statistically significant distinction was observed between the two groups. Table 1

Table 1: Baseline data of the study population

	Treatment group (N = 60)	Placebo group (N = 60)	P. Value
Age (Years)	53.2±5.33	51.5±5.3	0.8048
Duration of ED (months)	13.87±5.05	12.8±3.7	0.28507
Co-morbidities			
DM	20 (33.33%)	14 (23.33%)	0.3900
HTN	14 (23.33%)	8 (13.33%)	0.32511
Dyslipidemia	8 (13.33%)	4 (6.67%)	0.39801
HbA1C	5.3±0.79	5.44±0.69	0.2466
IIEF (Pre)	15.97±1.38	15.83±1.72	0.5642

Data are presented as Mean ± SD and number (%). ED: Erectile Dysfunction, DM: Diabetes Mellites, HTN: Hypertension, HbA1C: Hemoglobin A1C, IIEF: International Index of Erectile Function

In relation to the satisfaction of patients, neither of these variables exhibited a statistically significant increase over the course of the three time periods utilised in the research. With respect to IIEF, there was no progression of time that was statistically significant within the treatment group. Concerning IIEF, the placebo group exhibited no statistically significant difference, Table 2.

Table 2: Efficacy of treatment

	Treatment group (N=60)	Placebo group (N=60)	P. Value
1 month			
IIEF	17.12±1.35	16.99±1.47	0. 538
Likert Score	1.63±0.70	1.56±0.66	0.627
3 months			
IIEF	16.78±1.22	16.31±1.28	0. 547
Likert Score	1.51±0.49	1.43±0.49	0.298
6 months			
IIEF	16.45±1.49	16.55±1.28	0.7333
Likert Score	1.45±0.59	1.42±0.49	0.711

Data are presented as Mean ± SD. IIEF: International Index of Erectile Function

Evaluation data at the 1, 3, and 6 months of treatment did not reveal any statistically significant differences between the two groups (Figure2).

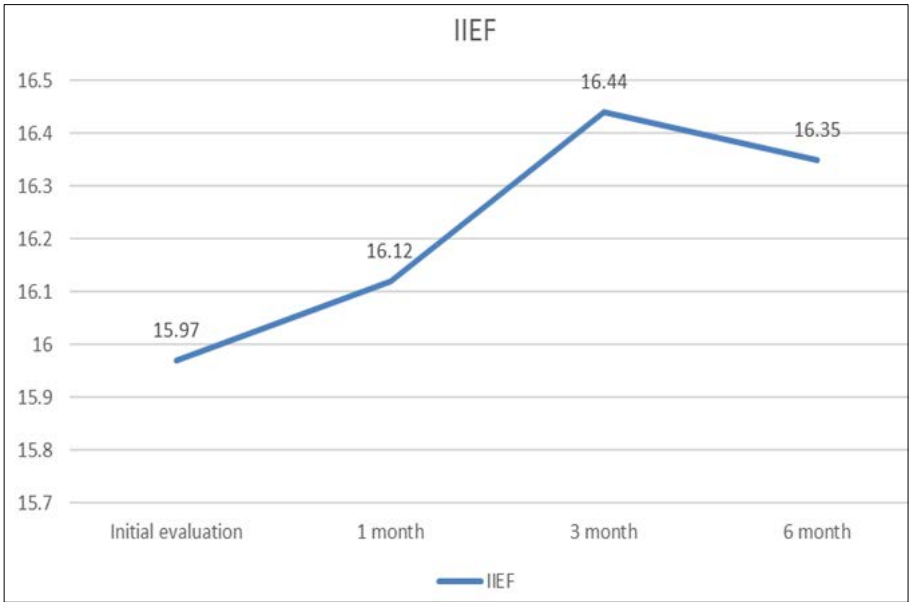

Fig 2: IIEF in Treatment group through time

Discussion

PRP treatment was found to be safe but ineffective in mild to moderate ED patients when compared to placebo, according to the findings of the present study.

An exhaustive literature search was conducted to identify comparable studies examining the safety and efficacy of PRP treatment in ED patients. Masterson *et al* [11] who examined the effect of PRP prospectively on ED patients (28 in the PRP group and 33 in the placebo group), reached the same conclusion as we did: PRP was safe, but not more effective than placebo in treating patients with mild to moderate ED. Notwithstanding the IIEF score attaining statistical significance, it remained analogous to a placebo. Nevertheless, male participants were permitted to maintain PDE5 inhibitor usage without adjusting the dosage during the course of the study. Consequently, this research should be approached with prudence [12].

Some clinical trials, two of which were published in 2021, demonstrated the safety and efficacy of PRP treatment in these patients, contrary to our findings. The first was a case series by Tas *et al.* [13] that included 31 men with ED and metabolic syndrome. Three injections of 3.0 mL intracavernosal PRP were evaluated each injection was administered at 15-day intervals. Nineteen (61 percent) participants had improved IIEF-EF scores at the six-month follow-up, indicating possible efficacy. In Greece, 60 men with mild to moderate ED were randomised to receive either two intracavernosal injections of 10 mL PRP or 10 mL normal saline separated by one month. Poulios *et al.* [14] published their double-blind, randomised, placebo-controlled clinical trial. At the 6-month mark, they discovered that 22/29 (76%) patients in the PRP group achieved the IIEF minimum clinically important difference (MCID), while only 7/28 (25%) in the placebo group did so. MCIDs, which are patient-derived scores that indicate significant improvements in a clinical intervention, are predicated on the IIEF-EF score. For instance, patients with mild ED (baseline IIEF-EF score of 17-25) are defined as having an increase of ≥ 2, whereas patients with moderate ED have an increase of ≥ 5. (Score of 11-16). ED classifications according to the IIEF-EF score: no ED (26-30), mild (17-25), moderate (11-16), and severe (26-30). (0-10) [15].

Shaher *et al.* [16] published an additional study in 2023 that comprised 100 patients in both groups (PRP and placebo). Significant improvement was observed at the one-month and three-month follow-ups, but it declined marginally at the six-month mark. 76% of the PRP group demonstrated an enhanced IIEF with MCID, compared to 18% of the saline group [17].

Certain authors have hypothesised that PRP and Li-SWT could potentially facilitate enhanced PDE5i efficacy. In 2019, Ruffo *et al.* [18] conducted a prospective randomised trial to evaluate the efficacy of PRP injections in conjunction with Li-SWT for ED (abstract only). The trial compared Li-SWT alone (Two weekly sessions) for six weeks or Li-SWT (two weekly sessions) plus PRP injection (once per week for 6 weeks). The researchers demonstrated a substantial increase in the mean IIEF scores for both groups: in group 1, they rose from 14.6 to 17.3 (p<0.03), and in group 2, they rose from 13.7 to 20.2 (p<0.001). This substantial increase persisted in Group 2 during the twenty-four weeks of follow-up. The findings indicate a favourable reaction when PRP was combined with Li-SWT [19, 20].

The limitation is the outcome data may be impacted by the small sample size and relatively brief follow-up period. Additionally, our protocol of two injections separated by one month may not produce optimal results, given that it was developed on the basis of previous PRP studies. Significant variations in IIEF could have been caused by administering additional injections or varying the interval between injections. Further investigation is therefore required regarding patient selection, protocol optimization, and PRP dosing.

PRP samples were not subjected to qualitative or quantitative analysis in the course of this research. A greater degree of dependability would have been compromised had this analysis been conducted. As of the present moment, neither the precise mechanism of action of PRP nor the optimal concentration of PRP required to treat ED are agreed upon.

Conclusions

Two intracavernosal PRP injections administered every one month to treat mild to moderate ED are safe, but do not outperform placebo, according to the findings of our clinical trial. Re-evaluating these primary results requires additional investigation regarding patient selection and treatment protocols.

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Conflict of Interest: Nil

References

1. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, *et al*. Erectile dysfunction: AUA guideline. J Urol. 2018;200:633-41.
2. Liu Z, Yuan X, Fernandes G, Dziak R, Ionita CN, Li C, *et al*. The combination of nano-calcium sulfate/platelet rich plasma gel scaffold with BMP2 gene-modified mesenchymal stem cells promotes bone regeneration in rat critical-sized calvarial defects. Stem Cell Res Ther. 2017;8:122-9.
3. Strazzulla LC, Avila L, Lo Sicco K, Shapiro J. An overview of the biology of platelet-rich plasma and microneedling as potential treatments for alopecia areata. J Investig Dermatol Symp Proc. 2018;19:21-4.
4. Oates J. Urological aspects of perineal surgery and reconstruction. Perineal reconstruction: Principles and practice. 6: Springer; c2023. p. 33-41.
5. De Souza ILL, Ferreira EDS, Vasconcelos LHC, Cavalcante FA, Da Silva BA. Erectile Dysfunction: Key Role of Cavernous Smooth Muscle Cells. Front Pharmacol. 2022;13:89-94.
6. Tavakoli MR, Faraji M, Sam S, Ghasempour A, Rezaei M, Langarizadeh MA, *et al*. Erectile dysfunction from mechanisms to medicines with a focus on the application of topical Minoxidil. Sex Med Rev. 2023;11:114-23.
7. Lewis FM. The normal vulva. Ridley's The Vulva. 2022;9:19-35.
8. Wang Q, Qin H, Deng J, Xu H, Liu S, Weng J, *et al*. Research progress in calcitonin gene-related peptide and bone repair. Biomolecules. 2023;13:45-9.
9. Olabiyi AA, Ajayi K. Diet, herbs and erectile function: A good friendship! Andrologia. 2022;54:144-9.
10. Campbell JD, Milenkovic U, Usta MF, Albersen M, Bivalacqua TJ. The good, bad, and the ugly of regenerative therapies for erectile dysfunction. Transl Androl Urol. 2020;9:252-61.
11. Masterson TA, Molina M, Ledesma B, Zucker I, Saltzman R, Ibrahim E, *et al*. Platelet-rich plasma for the treatment of erectile dysfunction: A prospective, randomized, double-blind, placebo-controlled clinical trial. J Urol. 2023;210:154-61.
12. Mettawi A. Anatomy and embryology of male and female reproductive systems; c2020. p. 1-38.
13. Taş T, Çakıroğlu B, Arda E, Onuk Ö, Nuhoğlu B. Early clinical results of the tolerability, safety, and efficacy of autologous platelet-rich plasma administration in erectile dysfunction. Sex Med. 2021;9:100313.
14. Poulios E, Mykoniatis I, Pyrgidis N, Zilotis F, Kapoteli P, Kotsiris D, *et al*. Platelet-Rich Plasma (PRP) Improves Erectile Function: A double-blind,

randomized, placebo-controlled clinical trial. J Sex Med. 2021;18:926-35.
15. Hadidi AT. Surgical anatomy of the penis and urethra. Hypospadias surgery: An illustrated textbook: Springer; 2022. p. 105-26.
16. Shaher H, Fathi A, Elbashir S, Abdelbaki SA, Soliman T. Is Platelet Rich Plasma Safe and Effective in Treatment of Erectile Dysfunction? Randomized Controlled Study. Urology. 2023;175:114-9.
17. Golovko S, Gybalo R, Lurin I, Taraban I, Kobirnichenko A, Ganiuk V, *et al*. Penetrating gunshot wounds to the penis: a case report of combat patient injured in the war in Ukraine. Int J Emerg Med. 2023;16:5-16.
18. Ruffo A, Franco M, Illiano E, Stanojević N. Effectiveness and safety of Platelet Rich Plasma (PRP) cavernously injections plus external shock wave treatment for penile erectile dysfunction: First results from a prospective, randomized, controlled, Inter-ventional study. Europ Urol Suppl. 2019;18:1622-3.
19. Aubé M, Chua M, McCammon K. Principles of Urethral Stricture Reconstruction and Its Instrumentation; c2020. p. 67-79.
20. Buckley J. Urologic reconstructive surgery, an issue of urologic clinics, E-Book: Elsevier Health Sciences; c2022.

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