Review Article

The role of surgical therapy in the management of premature ejaculation: a narrative review

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Background and Objective: Premature ejaculation (PE) is a common sexual disorder among male adults and negatively impacts a man's sexual life. Currently, the mainstay treatment of PE is still medical therapy which has drawbacks among patients as a consequence of side effects. Despite the new definitions, the evolution of medical therapy, and the consensus for the management of PE, it remains challenging to treat for many clinicians especially when medical treatment fails. However, the International Society for Sexual Medicine (ISSM) and the American Urological Association (AUA) guidelines ignored surgical therapy due to conflicting medical reports and doubts about the safety of surgical management. This article discusses the surgical management of PE based on recent guidelines, reviews, and evolving techniques.

Methods: We reviewed the literature using PubMed and searched for the following keywords: premature ejaculation, selective dorsal neurectomy, hyaluronic acid, dorsal nerve neuromodulation, cryo-ablation of the dorsal nerve and inner condom technique until May 2023. Seventeen studies were found.

Key Content and Findings: Even though the widespread use of many surgical modalities in Asia such as glans penis augmentation (GPA) using hyaluronic acid (HA) selective dorsal neurectomy (SDN), cryo-ablation of the dorsal nerve, neuromodulation of the dorsal nerve (NMDN), and circumcision are still considered as controversial for the guidelines.

Conclusions: The mainstay treatment of PE is still pharmaceutical. However, the current body of evidence on surgical treatments for PE is limited. Men considering surgical therapy for PE should be counseled well for the risks and benefits as there may be chronic disabilities. Further, well-designed trials are needed to establish safety and efficacy for the surgical treatment.

Keywords: Premature ejaculation (PE); selective dorsal neurectomy (SDN); hyaluronic acid (HA); dorsal nerve neuromodulation

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Introduction

Premature ejaculation (PE) the most common sexual disorder among males. Some studies estimated around 25–40% of men suffer from PE at any point in their lives (1-3). PE was first reported in the medical literature in 1887 (4). In 2014, the International Society for Sexual Medicine (ISSM) defines PE as ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration from the first sexual experience (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE) (5). Recently, the American Urological Association (AUA) and the Sexual Medicine Society of North America (SMSNA) guidelines have made a notable adjustment to the definition of ejaculation latency time (ELT), extending it from 1 to 2 minutes. This modification was implemented due to the recognition that approximately 20% of men seeking treatment for distressing PE actually have an ELT exceeding 2 minutes (6). Furthermore, the cause of PE is multifactorial between physiology and psychology.

The evaluation of the patients suffering from PE includes complete medical and psycho-sexual history. In addition, intravaginal ejaculatory latency time (IELT) can be used to assess patients with PE (7). This sexual dysfunction negatively impacts men's sexual health and their quality of life. Currently, available therapies for PE include behavioral, pharmacological, and surgical therapies. Among these pharmacological treatments, selective serotonin reuptake inhibitors (SSRI) are considered to be the first-line treatment in the management of PE and seem to be the most effective (8). However, this type of medical treatment can have some side effects, including nausea, vomiting, diarrhea, headache, and dizziness, which is seen in 60% of patients using dapoxetine (9). Lack of efficacy and compliance to the medical therapy is a changeling for many patients because of the side effects (10). Despite the presence of updated guidelines and the availability of pharmacological treatments, the management of PE continues to pose challenges for many clinicians. Consequently, surgical treatment remains a viable option for individuals who do not respond to medical interventions or for patients who desire a permanent solution (11).

The guidelines of the ISSM of 2014, don't include surgical therapies for PE because of their invasiveness and the possible permanent complications (12). Surgical therapies such as glans penis augmentation (GPA) using as hyaluronic acid (HA), selective dorsal neurectomy (SDN), cryo-ablation of the dorsal nerve, neuromodulation of dorsal nerve, and circumcision are widely practiced in Asia (13). As each patient of PE can respond differently and may experience variable side effects to the pharmacological treatment, clinicians must consider all other therapeutic modalities when medical treatment fails (14). This article will discuss the efficacy and safety of the surgical management of PE based on recent guidelines, reviews, and evolving techniques. We present this article in accordance with the Narrative Review reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-240/rc).

Methods

We conducted the search in the PubMed database using the keywords: premature ejaculation, selective dorsal neurectomy, hyaluronic acid, dorsal nerve neuromodulation, cryo-ablation of the dorsal nerve and inner condom technique until May 2023. Eighty-eight records were identified. Comments and reports are excluded (N=15). The full texts that are not related to the topic are excluded (N=56). Full-text original articles of systematic review meta-analysis, randomized clinical trials, and prospective studies in English on the surgical treatment of PE were retrieved (N=17) (*Figure 1*). Author information, year of publication, number of participants, follow-up period, IELT, and complications were collected from eligible studies (*Table 1*).

Surgical methods

Currently, the main surgical approaches for the management of PE include: (I) dorsal nerve neurectomy (DNN); (II) GPA using HA; (III) circumcision; (IV) inner condom technique (*Table 2*) (15-29). Interventional procedures are also possible such as computed tomography (CT)-guided cryoablation of dorsal nerve ablation and neuromodulation of the dorsal nerve (NMDN) (*Table 2*) (30,31). Despite the surgical interventions are commonly used in Asia, the guidelines do not recommend any type of intervention for PE because of the absence of long-term efficacy and safety (13).

Discussion

SDN

SDN is commonly used in Asia, especially in Korea. A survey conducted in 2013 by Yang *et al.* stated that 73% of Korean urologists have an experience with SDN while around 96% of the patients who undergone SDN were satisfied (32). In 2012, Zhang *et al.* (15) published that

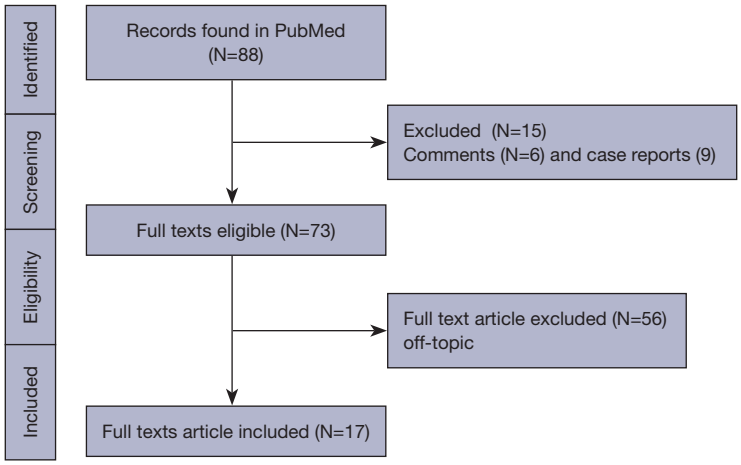

Figure 1 Flowchart describing searching methods.

Table 1 The search strategy summary

Items	Specification
Date of search	February 2023 to May 2023
Databases and other sources searched	PubMed
Search terms	Premature ejaculation, selective dorsal neurectomy, hyaluronic acid, dorsal nerve neuromodulation, cryo-ablation of the dorsal nerve and inner condom technique
Timeframe	No limitation on publication year
Inclusion and exclusion criteria	Inclusion criteria: original articles of systematic review meta-analysis, randomized clinical trials and prospective studies, retrospective, review articles in English
	Exclusion criteria: comments, case reports
Selection process	The selection process was conducted by Hamed Ambusaidi, Muaath Alshuaibi and independently. The author involved in the process individually screened the articles based on predefined inclusion and exclusion criteria. Any discrepancies or uncertainties were resolved through discussions and consensus among the authors in the review

SDN is effective and safe based on a randomized controlled trial (RCT) that included 32 SDN and 46 patients who had circumcision. The SDN group had an IELT of 1.1 minutes preoperatively, which increased to 3.8 minutes post-operatively (P<0.01), on the contrary, the circumcision group did not show any improvement in the IELT (P>0.005). Postoperatively, no complications were reported such as wound paraesthesia or infection (15). Liu *et al.* reported that anatomic basis SDN is effective in increasing IELT in those with lifelong PE (0.6±0.2 to 4.2±3.4 minutes) and shared the same opinion as Zhang *et al.* that SDN is safe and has low complication rates (16).

Recently an interesting RCT was published by Tang *et al.* in 2023 (17), in this study, 120 patients with primary premature ejaculation (PPE) were operated with SDN. The study evaluated the use of intraoperative neurophysiological monitoring (IONM) for penile sensory-evoked potential. In the IONM group (n=55), the SDN technique was found to be significantly effective for 35 patients (63.6%) in achieving an IELT of ≥300 seconds, effective for 17 patients (30.9%) with an IELT ≥120 and <300 seconds, and ineffective for 3 patients (5.5%) with an IELT <120 seconds. On the other hand, in the non-IONM group (n=53), the SDN technique was significantly effective for 18 patients (34.0%) with an IELT ≥300 seconds, effective for 31 patients (58.5%) with an IELT ≥120 and <300 seconds, and ineffective

Table 2 Various studies showing surgical management of premature ejaculation

Modality	Study	Methods	Sample size	Outcome (IELT)	Strength	Complication	Limitations
SDN	Zhang *et al.*, 2012 (15)	RCT	32 SDN	Mean SDN (1.1 to 3.8 min), P<0.001	Evaluation of sexual function by BMFSI	No post-op wound pain	No long-term data, small sample single center
			46 circ	Mean circ (1.2 to 1.5 min), P>0.05			
	Liu *et al.*, 2019 (16)	RCT	48 SDN	SDN (0.65±0.26 to 4.29±3.42 min)	RCT Full anatomic comparison based on both the number of branches of the dorsal penile nerve and the effect	No significant difference was found in the abnormal sensation in the glans and retardation of ejaculation between the two groups	Cannot determine how many dorsal nerves should be selectively resected for each person to achieve optimal IELT prolongation
			46 circ	Circ (0.62±0.22 to 0.82±0.43 min)		None of the patients experienced permanent glans numbness, wound infection, or hematoma	Single center
	Tang *et al.*, 2023 (17)	RCT	120 patients	SDN-non IONM median (1 to 4.7 min)	Classification of patients according to neuro-physiological test results Utilizing IONM to minimize irreversible damage to neural tissue	12 patients with penile sensory abnormalities (4 patients in the IONM group and 8 patients in the non-IONM group) and 3 patients with mild erectile dysfunction (all in the non-IONM group), P=0.043	Unicentric
				SDN-INOM median (0.8 to 4.93 min)	Determine how many dorsal nerves must be selectively resected for each individual in order to obtain optimal IELT elongation Maximum resection of nerves is respected by leaving one nerve on each side		Longer operative time
	Kwak *et al.*, 2008 (18)	Prospective observational study	25 SDN	Mean baseline IELT increased from 1.5 to 4 min	–	5% of patient had numbness	Not RCT, single center, small sample size
GPA using as HA	Kim *et al.*, 2004 (19)	Prospective study	Group I (dorsal neurectomy; n=25) Group II (dorsal neurectomy with HA; n=49) Group III (HA; n=65)	IELT showed no difference between the groups, while at 6 min increased in all groups (group II > III > I)	Patient & partner sexual satisfaction at 6 min increased sig in all groups (group II > III > I)	–	Not RCT, single center
	Alahwany *et al.*, 2019 (20)	RCT	Groups: control (saline: n=15); Treatment (HA: n=15) Injection dose: HA (25 mg HA in 2 mL of saline)	Mean baseline IELT: 34 s; 1-month post-op: 120 s; 3-month post-op: 105.5 s; 6-month post-op: 85 s; 9-month post-op: 45 s	RCT with cross over	Complications: At 1-week follow-up, 6/30 patients (20%) had adverse effects, including local discomfort, ecchymosis, local papule. All adverse effects were resolved at 1-month follow-up	Single center, small simple
	Ahn *et al.*, 2022 (21)	RCT multicenter trial	64 patients	IELT (5.36±3.51 to 7.86±4.73 min)	Patient and partner satisfaction was significant	Inflammation and pain that disappeared in 6.3% of the patients	Single center, small simple
	Shebl *et al.*, 2021 (22)	RCT	83 patients	Baseline (44.8±8.84 s) 1-month post-op: 277±123.86 s 3-month post-op: 305.14±125.36 s 6-month post-op: 242.97±132.75 s	–	Adverse effects: pain, bruising which are disappeared	Single center, small simple
	Sakr *et al.*, 2023 (23)	Prospective	30 patients	IELT (37.83±11.01 s at baseline to 323.03±42.06, 281.07±41.05, 241.03±43.09 and 235.6±41.87 s after 1, 3, 6 and 12 months	–	Adverse effects: 3 patients with discomfort, 2 patients with bullae, and 1 patient with ecchymosis disappeared	Single center, not randomized, small sample

Table 2 (*continued*)

Table 2 (*continued*)

Modality	Study	Methods	Sample size	Outcome (IELT)	Strength	Complication	Limitations
	Littara *et al.*, 2013 (24)	RCT	110 patients	Baseline pre-op: 88.34±3.14 s 6-month post-op: 293.14±8.16 s	Patient & partner sexual satisfaction increased at 6 min compared to baseline (1 to 5 min)	Not applicable	Single center
	Perri *et al.*, 2022 (25)	Pilot study	31 patients	Baselines (mean): 38.65 s 30 days: 72.24 s 60 days: 63.75 s 90 days: 41.24 s	Injection only one at the frenulum, which is a very sensitive area of the glans	Not applicable	Single center
	Abdallah *et al.*, 2012 (26)	RCT	60 patients	1 month (2.12±1.16 to 7.71±7.86 s)	Multicentric	Not applicable	Single center
Circumcision	Tian *et al.*, 2013 (27)	Systematic review meta-analysis	10 studies	No differences in IELT between the circumcised men and controls	–	No difference in adverse effects between the circumcised men and controls	Low quality studies
	Yang *et al.*, 2018 (28)	Systematic review meta-analysis	12 studies	No differences in IELT between the circumcised men and controls	–	–	–
Inner condom technique	Wang *et al.*, 2019 (29)	Prospective	20 patients	Mean pre-op IELT: 0.67 min (range, 0.18–1.1 min) Mean post-op IELT: 2.37 min (range, 0.82—8.4 min)	No nerve resection	No complications reported	Small sample, unicentric, not randomized, invasive and use of homologous material
Neuromodulation of dorsal nerve using pulsed radiofrequency	Basal *et al.*, 2010 (30)	Prospective	15 patients	IELT: 9.8 (1–49.5) s Median post-op: 119.9 (71.2–239.9) s	Minimally invasive	No numbness, paresthesia, pain, neuroma formation, or erectile dysfunction	Unicentric, small sample, not randomized
Cyo-ablation of dorsal nerves	David Prologo *et al.*, 2013 (31)	Prospective observational study	24 patients with PE	IELT day 7: 256±104 s (n=11; P=0.241) IELT at 3 months: 182.5±87.8 s (n=6; P=0.0342) IELT at 6 months: 182.5±27.6 s (n=23; P<0.0001) IELT at 1 year: 140.9±83.6 s (n=22; P<0.001)	Unilateral ablation	No complication	Not RCT, small sample, single center

IELT, intravaginal ejaculatory latency time; SDN, selective dorsal neurectomy; Circ, circumcision; RCT, randomized controlled trial; BMFSI, brief male sexual functioning inventory; post-op, postoperative; IONM, intraoperative neurophysiological monitoring; HA, hyaluronic acid; pre-op, preoperative; PE, premature ejaculation.

for 4 patients (7.5%) with an IELT <120 seconds. The clinical efficacy of the SDN technique was significantly better in the IONM group compared to the non-IONM group (P=0.004). Regarding complications, fifteen patients experienced adverse effects, including penile paraesthesia, which involved decreased sensation or varying degrees of numbness or pain, and decreased erectile function. Among these, 12 patients had penile sensory abnormalities (4 patients in the IONM group and 8 patients in the non-IONM group), and 3 patients in the non-IONM group had mild erectile dysfunction (ED). The difference in complications between the two groups was found to be significant (P=0.043) and patients with IONM were significantly more satisfied with SDN than those in the non-IONM (17).

Despite the promising results of SDN in previous studies, concerns were raised against this therapy because of possible ED and post-operative paresthesia (18). The studies conducted by Zhang *et al.* and Liu *et al.* were conducted at a single center and had limited sample sizes. These studies faced notable limitations in terms of safety concerns, particularly in determining the optimal number of dorsal nerves to be resected to achieve effective prolongation of IELT while avoiding serious complications such as delayed ejaculation, penile paraesthesia, and ED. On the other hand, the study by Tang *et al.* reported a significant increase in ED within the non-IONM group, which provides supporting evidence for Anaissie *et al.*'s that SDN is unsafe (13,15-17). Consequently, far in the West the North American and European associations were against SDN (13). As conducted by Tang *et al.*, IONM is needed at least to be selective and determine how many should be resected but this is technically difficult to apply intraoperatively and costly.

GPA using HA

HA is a glycosaminoglycan that finds extensive application in the medical field due to its ability to inhibit the synthesis of pro-inflammatory proteins (33). Existing evidence regarding the use of HA in uro-andrological conditions indicates its potential benefits. Studies have shown that HA can alleviate the acute painful phase associated with Peyronie's disease (34-36) and reduce the frequency of recurrent urinary infection episodes (37). Additionally, HA has been reported to improve pain symptoms and enhance the quality of life in patients with interstitial cystitis (38). The concept behind this technique is the injection of HA gel into the glans of the penis to create a physical boundary between the hypersensitive dorsal nerves and the outside ambiance. The study by Kim *et al.* was one of the first to study the effect of the HA gel on the glans (19). Included 139 patients, divided into 3 groups: (I) DNN group (N=25); (II) DNN with HA gel group (N=49); and (III) HA gel group (N=65). Ejaculation time at the assessment found that preoperative ejaculation times were 89.2±40.29, 101.54±59.42, and 96.5±52.32 seconds in Groups I, II, and III, respectively. DNN group with HA gel was significantly longer than the other two groups at 6 months (235.6±58.6, 324.24±107.58 and 281.9±93.2 seconds in Groups I, II and III, respectively (P<0.01). Patient and partner sexual satisfaction at 6 months increased significantly in all groups (group II > III > I). The previous results suggest that HA gel is effective. Six- and 12-month follow-ups revealed the effectivity of the HA gel. In contrast to the DNN group, no complications were found in the HA gel group (19). Alahwany *et al.* (20) in 2019 conducted the first RCT in including 30 patients (Control saline group n=15, HA gel group n=15). The IELT at 3-, 6-, and 9-month intervals in both groups found significant improvement after HA in comparison with saline across the follow-up periods (P=0.001). The drawback of the study of Alahwany *et al.* is that it has a small sample of patients and was a single-center study. Regarding the complications, during the 1-week follow-up, 6 out of 30 patients (20%) experienced adverse effects such as local discomfort, ecchymosis, and local papule. However, all of these adverse effects were resolved by the 1-month follow-up period (20). Similar findings were reported in studies by Ahn *et al.*, Shebl *et al.*, and Sakr *et al.*, showing that all adverse effects were resolved by the 1-month follow-up (21-23). Many studies have shown that HA is effective and safe and support the findings of Kim *et al.* and Alahwany *et al.* (24-26) (*Table 2*).

Moreover, the studies conducted by Kim *et al.*, Littara *et al.*, and Abdallah *et al.* consistently demonstrated a significant increase in patient and partner satisfaction at 6 months (19,24,26). We would share the same opinion as Anaissie *et al.* to consider HA gel as a therapeutic option for lifelong PE, large and multicentric double-blinded RCTs are required to prove the efficacy and safety.

Circumcision

Circumcision has been one of the most common surgical interventions in the world for decades for medical, religious, cultural, social, and several other reasons (39). The prepuce

(foreskin) is rich in nerve fibers that account for the hypersensitivity of the human foreskin and its function as erogenous tissue (40). Some studies have shown an increase in IELT from 64 to 731 seconds and a reduction in PE incidence from 32% to 14% (41-43). In two systematic meta-analyses investigating the effects of circumcision on male sexual function after the intervention. Overall, there was no difference between circumcised and uncircumcised men concerning PE, IELT, ED, or pain during intercourse (27,28). These findings suggest that male circumcision is not an effective modality in patients with lifelong PE.

Experimental treatments

Neuromodulation of dorsal nerve and cryo-ablation of the dorsal nerve

Neuromodulation is safe and effective in urology for urinary incontinence associated with bladder hyperactivity (44). To date, the evidence for the treatment of PE based on NMDN is weak as only low-quality studies have been conducted (*Table 2*) (30). Randomized control studies are necessary to verify the effectiveness and safety of the previous report. As with the earlier procedure, the cryoablation of the dorsal nerve is still experimental. David Prologo *et al.* found promising results in the unilateral removal of the dorsal nerve (*Table 2*), but the study was a small specimen, unicentric, and was not randomized (31).

Inner condom technique

This innovative and experimental surgical technique utilizing an inner condom was first introduced by Wang *et al.* in 2019. The procedure involved the insertion of acellular dermal matrix (ADM), a biomaterial derived from human skin, beneath the buck's fascia under local anesthesia. In this particular study, a total of 20 men diagnosed with PPE, with an average IELT of 0.67 minutes, underwent this intervention. Following the procedure, the average IELT significantly increased to 2.3 minutes (ranging from 0.82 to 8.4 minutes) (P=0.009) (29). The surgical technique employed in this study is characterized by its invasiveness, and the methodology utilized is limited by being a single-center study with a small sample size. Additionally, the study lacks randomization, which further necessitates caution in interpreting the results.

Limitations

In this narrative review, we recognize that surgical interventions for the management of PE are common in Asia, and therefore, relevant studies conducted in non-English languages may have been excluded. Furthermore, the variety of surgical procedures, protocols, and follow-up periods may have led to bias in this review.

Conclusions

The mainstay treatment of PE is still pharmaceutical. Among these surgical approaches, HA is minimally invasive and promising in terms of efficacy and safety. However, the current body of evidence on surgical treatments for PE is limited. Men considering surgical therapy for PE should be counseled well for the risks and benefits as there may be chronic disabilities. Further, well-designed trials are needed to establish safety and efficacy for the Surgical treatment.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-23-240/rc

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-23-240/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-23-240/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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