

# 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

2 Premature ejaculation (PE) the most common sexual disorder 3 4 among males. Some studies estimated around 25-40% of 5 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, 6 the International Society for Sexual Medicine (ISSM) defines 7 PE as ejaculation that always or nearly always occurs prior 8 to or within about 1 minute of vaginal penetration from the 9 first sexual experience (lifelong PE) or a clinically significant 10 and bothersome reduction in latency time, often to about 11 3 minutes or less (acquired PE) (5). Recently, the American 12 Urological Association (AUA) and the Sexual Medicine 13 Society of North America (SMSNA) guidelines have 14 made a notable adjustment to the definition of ejaculation 15 latency time (ELT), extending it from 1 to 2 minutes. 16 17 This modification was implemented due to the recognition that approximately 20% of men seeking treatment for 18 distressing PE actually have an ELT exceeding 2 minutes (6). 19 Furthermore, the cause of PE is multifactorial between 20 physiology and psychology. 21

The evaluation of the patients suffering from PE 22 includes complete medical and psycho-sexual history. In 23 addition, intravaginal ejaculatory latency time (IELT) 24 can be used to assess patients with PE (7). This sexual 25 dysfunction negatively impacts men's sexual health and their 26 quality of life. Currently, available therapies for PE include 27 behavioral, pharmacological, and surgical therapies. Among 28 these pharmacological treatments, selective serotonin 29 reuptake inhibitors (SSRI) are considered to be the first-30 line treatment in the management of PE and seem to be the 31 most effective (8). However, this type of medical treatment 32 can have some side effects, including nausea, vomiting, 33 diarrhea, headache, and dizziness, which is seen in 60% of 34 patients using dapoxetine (9). Lack of efficacy and compliance 35 to the medical therapy is a changeling for many patients 36 because of the side effects (10). Despite the presence of 37 updated guidelines and the availability of pharmacological 38 treatments, the management of PE continues to pose 39 challenges for many clinicians. Consequently, surgical 40 treatment remains a viable option for individuals who do 41 not respond to medical interventions or for patients who 42 desire a permanent solution (11). 43

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 60

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nerve, and circumcision are widely practiced in Asia (13). 50 As each patient of PE can respond differently and may 51 experience variable side effects to the pharmacological 52 treatment, clinicians must consider all other therapeutic 53 modalities when medical treatment fails (14). This article will 54 discuss the efficacy and safety of the surgical management 55 of PE based on recent guidelines, reviews, and evolving 56 techniques. We present this article in accordance with the 57 Narrative Review reporting checklist (available at https://tau. 58 amegroups.com/article/view/10.21037/tau-23-240/rc). 59

#### Methods

We conducted the search in the PubMed database using the keywords: premature ejaculation, selective dorsal 64 neurectomy, hyaluronic acid, dorsal nerve neuromodulation, 65 cryo-ablation of the dorsal nerve and inner condom 66 technique until May 2023. Eighty-eight records were 67 identified. Comments and reports are excluded (N=15). 68 The full texts that are not related to the topic are excluded 69 (N=56). Full-text original articles of systematic review meta-70 analysis, randomized clinical trials, and prospective studies 71 in English on the surgical treatment of PE were retrieved 72 (N=17) (Figure 1). Author information, year of publication, 73 number of participants, follow-up period, IELT, and 74 complications were collected from eligible studies (Table 1). 75

#### Surgical methods

78 79 Currently, the main surgical approaches for the management of PE include: (I) dorsal nerve neurectomy (DNN); (II) 80 GPA using HA; (III) circumcision; (IV) inner condom 81 technique (Table 2) (15-29). Interventional procedures are 82 also possible such as computed tomography (CT)-guided 83 cryoablation of dorsal nerve ablation and neuromodulation 84 of the dorsal nerve (NMDN) (Table 2) (30,31). Despite 85 the surgical interventions are commonly used in Asia, the 86 guidelines do not recommend any type of intervention for PE 87 because of the absence of long-term efficacy and safety (13). 88

#### 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 98

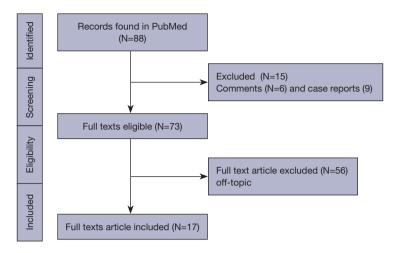


Figure 1 Flowchart describing searching methods.

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 99 trial (RCT) that included 32 SDN and 46 patients who had 100 circumcision. The SDN group had an IELT of 1.1 minutes 101 preoperatively, which increased to 3.8 minutes post-102 operatively (P<0.01), on the contrary, the circumcision 103 group did not show any improvement in the IELT (P>0.005). 104 Postoperatively, no complications were reported such as 105 wound paraesthesia or infection (15). Liu et al. reported that 106 anatomic basis SDN is effective in increasing IELT in those 107 with lifelong PE (0.6±0.2 to 4.2±3.4 minutes) and shared 108 the same opinion as Zhang et al. that SDN is safe and has 109 low complication rates (16). 110

111 Recently an interesting RCT was published by Tang *et al.* 

in 2023 (17), in this study, 120 patients with primary 112 premature ejaculation (PPE) were operated with SDN. The 113 study evaluated the use of intraoperative neurophysiological 114 monitoring (IONM) for penile sensory-evoked potential. In 115 the IONM group (n=55), the SDN technique was found to 116 be significantly effective for 35 patients (63.6%) in achieving 117 an IELT of  $\geq$ 300 seconds, effective for 17 patients (30.9%) 118 with an IELT  $\geq 120$  and < 300 seconds, and ineffective for 119 3 patients (5.5%) with an IELT <120 seconds. On the other 120 hand, in the non-IONM group (n=53), the SDN technique 121 was significantly effective for 18 patients (34.0%) with 122 an IELT  $\geq$ 300 seconds, effective for 31 patients (58.5%) 123 with an IELT  $\geq 120$  and < 300 seconds, and ineffective 124

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#### Table 2 Various studies showing surgical management of premature ejaculation

Modality	Study	Methods	Sample size	Outcome (IELT)	Strength	Complication	Limitations	
SDN	Zhang et al.,	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	
	2012 (15)		46 circ	Mean circ (1.2 to 1.5 min), P>0.05				
	Liu <i>et al.</i> , 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 t 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 <i>et al.</i> , 2023 (17)	RCT	120 patients		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 <i>et al.</i> , 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 <i>et al.</i> , 2004 (19)	Prospective study	Group I (dorsal neurectomy; n=25)	IELT showed no difference between the groups, while at 6 min increased	Patient & partner sexual satisfaction at 6 min increased sig in all groups (group II $>$ III $>$ I)	1 –	Not RCT, single center ) Single center, small simple	
			Group II (dorsal neurectomy with HA; n=49)	in all groups (group II > III > I)				
			Group III (HA; n=65)					
	Alahwany <i>et al.</i> , 2019 (20)	RCT	Groups: control (saline: n=15); Treatment (HA: n=15) Injection dose: HA (25 mg HA ir 2 mL of saline)	Mean baseline IELT: 34 s; 1-month post-op: 120 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		
				3-month post-op: 105.5 s;				
				6-month post-op: 85 s;				
				9-month post-op: 45 s				
	Ahn <i>et al.</i> , 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 <i>et al.</i> , 2021 (22)	RCT	83 patients	Baseline (44.8±8.84 s)	-	Adverse effects: pain, bruising which are disappeared	Single center, small simple	
				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				
	Sakr <i>et al.,</i> 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)

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Table 2 (continued)							
Modality	Study	Methods	Sample size	Outcome (IELT)	Strength	Complication	
	Littara et al.,	RCT	110 patients	Baseline pre-op: 88.34±3.14s	Patient & partner sexual	Not applicable e	
	2013 (24)			6-month post-op: 293.14±8.16s	satisfaction increased at 6 min compared to baseline (1 to 5 min)		
	Perri <i>et al.</i> ,	Pilot study	31 patients	Baselines (mean): 38.65 s	Injection only one at the frenulum, which is a very	Not applicable	
	2022 (25)			30 days: 72.24 s	sensitive area of the glans		
				60 days: 63.75 s			
				90 days: 41.24 s			
	Abdallah <i>et al.,</i> 2012 (26)	RCT	60 patients	1 month (2.12±1.16 to 7.71±7.86 s)	Multicentric	Not applicable	
Circumcision	Tian <i>et al.</i> , 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	
	Yang <i>et al.</i> , 2018 (28)	Systematic review meta-analysis	12 studies	No differences in IELT between the circumcised men and controls	-	-	
Inner condom technique	Wang <i>et al.</i> , 2019 (29)	Prospective	20 patients	Mean pre-op IELT: 0.67 min (range, 0.18–1.1 min)	No nerve resection	No complications reported	
				Mean post-op IELT: 2.37 min (range, 0.828.4 min)			
Neuromodulation of	Basal <i>et al.</i> , 2010 (30) /	Prospective	15 patients	IELT: 9.8 (1–49.5) s	Minimally invasive	No numbness, paresthesia, pain, neuroma erectile dysfunction	
dorsal nerve using pulsed radiofrequency				Median post-op: 119.9 (71.2-239.9)			
Cyo-ablation of dorsal nerves	I David Prologo et al., 2013 (31)	Prospective observational study	24 patients with PE	IELT day 7: 256±104 s (n=11; P=0.241)	Unilateral ablation	No complication	
				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)			

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.

	Limitations
	Single center
	Single center
	Single center
	Low quality studies
	-
	Small sample, unicentric, not randomized, invasive and use of homologous material
na formation, or	Unicentric, small sample, not randomized
	Not RCT, small sample, single center

for 4 patients (7.5%) with an IELT <120 seconds. The 125 clinical efficacy of the SDN technique was significantly 126 better in the IONM group compared to the non-IONM 127 group (P=0.004). Regarding complications, fifteen patients 128 experienced adverse effects, including penile paraesthesia, 129 which involved decreased sensation or varying degrees of 130 numbness or pain, and decreased erectile function. Among 131 these, 12 patients had penile sensory abnormalities (4 132 patients in the IONM group and 8 patients in the non-133 IONM group), and 3 patients in the non-IONM group 134 had mild erectile dysfunction (ED). The difference in 135 complications between the two groups was found to 136 be significant (P=0.043) and patients with IONM were 137 significantly more satisfied with SDN than those in the 138 non-IONM (17). 139

Despite the promising results of SDN in previous 140 studies, concerns were raised against this therapy because 141 of possible ED and post-operative paresthesia (18). The 142 studies conducted by Zhang et al. and Liu et al. were 143 conducted at a single center and had limited sample 144 sizes. These studies faced notable limitations in terms of 145 safety concerns, particularly in determining the optimal 146 number of dorsal nerves to be resected to achieve effective 147 prolongation of IELT while avoiding serious complications 148 such as delayed ejaculation, penile paraesthesia, and ED. 149 On the other hand, the study by Tang et al. reported a 150 significant increase in ED within the non-IONM group, 151 which provides supporting evidence for Anaissie et al.'s 152 that SDN is unsafe (13,15-17). Consequently, far in the 153 West the North American and European associations were 154 against SDN (13). As conducted by Tang et al., IONM is 155 needed at least to be selective and determine how many 156 should be resected but this is technically difficult to apply 157 intraoperatively and costly. 158

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## 160 GPA using HA

161 162 HA is a glycosaminoglycan that finds extensive application 163 in the medical field due to its ability to inhibit the synthesis of pro-inflammatory proteins (33). Existing evidence 164 regarding the use of HA in uro-andrological conditions 165 indicates its potential benefits. Studies have shown that 166 HA can alleviate the acute painful phase associated with 167 Peyronie's disease (34-36) and reduce the frequency of 168 recurrent urinary infection episodes (37). Additionally, HA 169 has been reported to improve pain symptoms and enhance 170 the quality of life in patients with interstitial cystitis (38). 171 The concept behind this technique is the injection of HA 172

gel into the glans of the penis to create a physical boundary 173 between the hypersensitive dorsal nerves and the outside 174 ambiance. The study by Kim et al. was one of the first to 175 study the effect of the HA gel on the glans (19). Included 176 139 patients, divided into 3 groups: (I) DNN group 177 (N=25); (II) DNN with HA gel group (N=49); and (III) 178 HA gel group (N=65). Ejaculation time at the assessment 179 found that preoperative ejaculation times were 89.2±40.29, 180 101.54±59.42, and 96.5±52.32 seconds in Groups I, II, and 181 III, respectively. DNN group with HA gel was significantly 182 longer than the other two groups at 6 months (235.6±58.6, 183 324.24±107.58 and 281.9±93.2 seconds in Groups I, II 184 and III, respectively (P<0.01). Patient and partner sexual 185 satisfaction at 6 months increased significantly in all groups 186 (group II > III > I). The previous results suggest that HA 187 gel is effective. Six- and 12-month follow-ups revealed the 188 effectivity of the HA gel. In contrast to the DNN group, 189 no complications were found in the HA gel group (19). 190 Alahwany et al. (20) in 2019 conducted the first RCT in 191 including 30 patients (Control saline group n=15, HA gel 192 group n=15). The IELT at 3-, 6-, and 9-month intervals 193 in both groups found significant improvement after HA 194 in comparison with saline across the follow-up periods 195 (P=0.001). The drawback of the study of Alahwany et al. is 196 that it has a small sample of patients and was a single-center 197 study. Regarding the complications, during the 1-week 198 follow-up, 6 out of 30 patients (20%) experienced adverse 199 effects such as local discomfort, ecchymosis, and local 200 papule. However, all of these adverse effects were resolved 201 by the 1-month follow-up period (20). Similar findings were 202 reported in studies by Ahn et al., Shebl et al., and Sakr et al., 203 showing that all adverse effects were resolved by the 1-month 204 follow-up (21-23). Many studies have shown that HA is 205 effective and safe and support the findings of Kim et al. and 206 Alahwany et al. (24-26) (Table 2). 207

Moreover, the studies conducted by Kim *et al.*, Littara *et al.*, 208 and Abdallah *et al.* consistently demonstrated a significant 209 increase in patient and partner satisfaction at 6 months 210 (19,24,26). We would share the same opinion as Anaissie 211 *et al.* to consider HA gel as a therapeutic option for lifelong 212 PE, large and multicentric double-blinded RCTs are 213 required to prove the efficacy and safety. 214

#### 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 prepue

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(foreskin) is rich in nerve fibers that account for the 221 hypersensitivity of the human foreskin and its function as 222 erogenous tissue (40). Some studies have shown an increase 223 in IELT from 64 to 731 seconds and a reduction in PE 224 incidence from 32% to 14% (41-43). In two systematic 225 meta-analyses investigating the effects of circumcision on 226 male sexual function after the intervention. Overall, there 2.2.7 was no difference between circumcised and uncircumcised 228 men concerning PE, IELT, ED, or pain during intercourse 229 (27,28). These findings suggest that male circumcision is 230 not an effective modality in patients with lifelong PE. 231

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#### Experimental treatments

# Neuromodulation of dorsal nerve and cryo-ablation ofthe dorsal nerve

Neuromodulation is safe and effective in urology for urinary 237 incontinence associated with bladder hyperactivity (44). To 238 date, the evidence for the treatment of PE based on NMDN 239 is weak as only low-quality studies have been conducted 240 (Table 2) (30). Randomized control studies are necessary to 241 verify the effectiveness and safety of the previous report. 2.42 As with the earlier procedure, the cryoablation of the 243 dorsal nerve is still experimental. David Prologo et al. 244 found promising results in the unilateral removal of the 245 dorsal nerve (Table 2), but the study was a small specimen, 246 unicentric, and was not randomized (31). 247

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#### 249 Inner condom technique

This innovative and experimental surgical technique 250 utilizing an inner condom was first introduced by Wang 251 et al. in 2019. The procedure involved the insertion of 252 acellular dermal matrix (ADM), a biomaterial derived from 253 human skin, beneath the buck's fascia under local anesthesia. 254 In this particular study, a total of 20 men diagnosed with 255 PPE, with an average IELT of 0.67 minutes, underwent 256 this intervention. Following the procedure, the average 257 IELT significantly increased to 2.3 minutes (ranging from 258 0.82 to 8.4 minutes) (P=0.009) (29). The surgical technique 259 employed in this study is characterized by its invasiveness, 260 and the methodology utilized is limited by being a single-261 center study with a small sample size. Additionally, the study 262 lacks randomization, which further necessitates caution in 263 interpreting the results. 264

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#### Limitations

In this narrative review, we recognize that surgical

interventions for the management of PE are common in<br/>Asia, and therefore, relevant studies conducted in non-<br/>English languages may have been excluded. Furthermore,<br/>the variety of surgical procedures, protocols, and follow-up<br/>periods may have led to bias in this review.270<br/>271<br/>272

#### Conclusions

276 277 The mainstay treatment of PE is still pharmaceutical. Among these surgical approaches, HA is minimally invasive 278 and promising in terms of efficacy and safety. However, the 279 current body of evidence on surgical treatments for PE is 280 limited. Men considering surgical therapy for PE should 281 be counseled well for the risks and benefits as there may be 282 chronic disabilities. Further, well-designed trials are needed 283 to establish safety and efficacy for the Surgical treatment. 284

Ac	kno	wle	da	me	nts

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Ethical Statement: The authors are accountable for all304aspects of the work in ensuring that questions related305to the accuracy or integrity of any part of the work are306appropriately investigated and resolved.307

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