Current Sexual Health Reports (2019) 11:115–124
https://doi.org/10.1007/s11930-019-00201-2

UROLOGY, GYNECOLOGY, AND ENDOCRINOLOGY (J SIMON AND M LURIA, SECTION EDITORS)

Chronic Scrotal Content Pain: an Updated Review on Diagnosis and Management

Brijesh G Patel[1] · Laurence A Levine[1]

Published online: 27 April 2019

Abstract

Purpose of Review To provide a review on the diagnosis and management of chronic scrotal content pain (CSCP). We cover the anatomy relevant to the scrotum, pathophysiology related to pain, and discuss medical and surgical options. We investigated the impact this condition has on patients and quantified the significant burden on quality of life.

Recent Findings Our review found that among centers that manage chronic scrotal content pain regularly, medical management consistently includes scrotal rest/ice, NSAIDs, tricyclic anti-depressants, or neuropathic pain modulators. Among surgical options, microdenervation of the spermatic cord in some series provides > 90% relief in scrotal pain. With regard to quality of life, we found that in some series, more than half of patients experience a significant reduction in sexual function and marital relationship. Furthermore, these patients are often caught in a vicious cycle whereby pain and diminished sexual function aggravate each other.

Summary Our findings demonstrate that clinicians who manage this condition regularly are using very similar approaches, thus facilitating a standardized approach for this condition, which carries a significant burden on quality of life.

Keywords Scrotal pain · Spermatic cord block · Microdenervation of spermatic cord · Sexual function

Introduction

Chronic scrotal content pain (CSCP)—or its synonyms chronic orchialgia, testicular pain syndrome, post-vasectomy pain syndrome (PVPS)—is broadly defined as 3 months of constant or intermittent pain identified as coming from structures within the scrotum that causes disturbances in daily activities and prompts a patient to obtain medical attention [1]. This term is felt to be most inclusive as it does not isolate a particular scrotal structure or procedure as the cause for pain. The etiology of CSCP is complex, as evidenced by ~18–50% of cases being idiopathic in nature as well as the number of structures that are implicated in CSCP, including the testicle, epididymis, vas deferens, and paratesticular structures [2•, 3]. A number of medical problems and surgical interventions are associated with CSCP. Similarly, both medical and surgical treatment modalities are available. CSCP has a profound impact on a male patient; however, there needs to be a more precise understanding of the impact this condition has on sexual function so that urologists can optimize management and improve quality of life. Currently, no guidelines exist specifically for CSCP, although the European Urology Association has guidelines for pelvic pain with a limited section on CSCP [4]. With increased awareness of men's health attributed to an aging population and widespread use of social media, urologists are certain to see more CSCP in their clinics. In this review of CSCP, we discuss epidemiology, diagnosis, management options, and relationship to sexual function.

This article is part of the Topical Collection on *Urology, Gynecology, and Endocrinology*

✉ Brijesh G Patel
Brijesh_G_Patel@rush.edu

Laurence A Levine
Laurence_Levine@rush.edu

[1] Division of Urology, Rush University Medical Center, Professional Building, Suite 348, 1725 W Harrison Street, Chicago, IL 60612, USA

Etiology

The etiology of CSCP is best identified via a diagnosis of exclusion approach that starts with a thorough history and physical exam. Among urologic causes, readily reversible ones include spermatocele, tumor, infection, urolithiasis, varicocele, and torsion [5]. CSCP can also develop postoperatively with reported incidences of 6–12% after vasectomy, up to 18% after inguinal hernia repair, 5% after other scrotal surgery, and 1–2% after abdominal surgery [6]. Urologists are most likely to see patients present with post-vasectomy pain syndrome (PVPS) considering some studies have found a 54% incidence rate, even though only 10% of men with PVPS may ultimately seek medical attention. PVPS is attributed to damaged scrotal and/or spermatic cord nerve structures via inflammatory effects, back pressure in the obstructed vas deferens, nerve impingement, and perineural fibrosis [7]. This chronic pain may drive the patient to seek care on average 2 years after the procedure [8, 9].

Not all cases of CSCP may be as simple to identify, contributing to the elusive nature of CSCP. Lai et al. carefully tracked 44 men with mild epididymal tenderness with an otherwise normal GU exam, negative UA, and normal scrotal US. All study subjects were treated with empiric antibiotics and brief cessation of strenuous activity. At the end of study period, all patients experienced complete relief of pain [10]. While some CSCP diagnoses may be subtle yet straightforward, others are part of a larger, more complex pelvic pain syndrome. Wagenlehner et al. found > 60% of patients report testicular pain when inquired about a number of pelvic pain syndromes. This finding underscores the importance of a thorough workup, so as not to misdiagnose and incorrectly treat scrotal content pain rendering the patient without any clinical improvement.

In contrast, several commonly cited non-urologic causes of CSCP must also be addressed including psychiatric illness, peritoneal irritation, incarcerated inguinal hernia, diabetic neuropathy, kidney stones, abdominal aortic aneurysm, polyarteritis nodosa, and low back pain.

When an easily identifiable problem that is amenable to surgery is discovered, surgery ought to be the treatment of choice. Several studies find up to 75% rate of pain relief after surgery [11–13]. For example, in 2015, Kachrilas et al. noted over 90% of patients reporting pain relief after unilateral or bilateral laparoscopic varicocelectomy [14].

Despite the ease of diagnosing CSCP, this entity remains poorly understood. The literature to date includes cohort studies with a limited number of patients, rare placebo controlled trials, and lack of standard evaluation, all of which make formalizing guidelines particularly difficult [5]. However, the European Association of Urology did recently publish guidelines for evaluation and treatment of chronic pelvic pain, although with limited scope on scrotal pain specifically. Nonetheless, Levine, Calixte, Aljumaily, and Parekattil among others have synthesized recommendations for management of CSCP.

Epidemiology

There is an increasing emphasis on men's health attributed to an aging population and wide-spread use of social media. This translates to an estimated 100,000 men per year with a diagnosis of CSCP [15] in the context of approximately 116 million men and women suffering from chronic pain per year in the USA [3]. Typically, patients are in their mid to late 30s [16]. These patients' CSCP care produces a large financial burden on the health care system, considering that it accounts for 2.5% of new patient visits to a urologist's office [1, 17], each patient may see on average 4.5 urologists [18], and ultimately undergo ~ 4–7 diagnostic and 1.6 operative procedures [19]. In sum, chronic pain produces an estimated cost of $635 billion per year worldwide rising from expenses and lost productivity [3].

Pathophysiology

The pathophysiology of CSCP is not well understood, although several plausible mechanisms are proposed with varying degrees of evidence. To further understand these mechanisms, it is imperative to have an understanding of the neuroanatomy of the genitourinary region. Nerve roots L1-L2 and S2-S4 form the iliohypogastric, ilioinguinal, genitofemoral, and pudendal nerves, which supply the testis, epididymis, and scrotum.

As for somatic sensory innervation, the iliohypogastric nerve supplies the skin above the pubis. The ilioinguinal nerve supplies the skin of the inner thigh, penile base, and upper scrotum. The genital branch of the genitofemoral nerve covers the skin of the anterolateral portion of the scrotum and the ilioinguinal nerve covers the anterior scrotal skin. Posterior scrotal skin sensation is carried by the perineal branch of the pudendal nerve.

Further common associations with testicular pain are best understood by analyzing the course of the three branches of the autonomic spermatic nerve, which is responsible for carrying noxious stimuli from the scrotal contents. The superior spermatic nerve from the inter-mesenteric plexus follows the testicular artery to the testis. The middle spermatic nerve arises from the superior hypogastric plexus and passes near the mid-ureter before joining the spermatic cord at the internal ring, contributing to the testicular pain experienced with an obstructing ureteral stone. Finally, the inferior spermatic nerve comes from inferior hypogastric (pelvic) plexus, and some

fibers decussate, which may contribute to sensation of pain in the testicle contralateral to side of injury (Fig. 1).

Recently, Oka et al. obtained 47 spermatic cord biopsies and performed neural staining on samples. They discovered that nearly 50% of nerve distribution in the cord is found around the vas deferens, 20% within spermatic fascia, and the rest distributed throughout the cord. They were comprised of almost all sympathetic and somatic fibers, with few parasympathetic fibers [20•]. The density of nerves in this area and subsequent injury incurred during vasectomy can explain post-vasectomy pain syndrome, among other etiologies of CSCP.

The transition from acute pain, explained via pathways discussed above, to chronic pain is still under investigation. This entity is related to changes in neuronal activity that allows persistent stimulation without inhibitory feedback [21, 22]. In this framework, nociceptors carry noxious stimuli to the dorsal horn via myelinated A delta fibers and unmyelinated C fibers. This information is carried cephalad via lateral and medial spinothalamic tracts. Under normal conditions, noxious stimuli diminish as healing progresses, and pain sensitization diminishes, too. However, persistent intense painful stimuli can cause peripheral and central modulation resulting in lower thresholds to trigger increased neuronal activity manifesting as allodynia and hyperalgesia [23, 24].

Repeated painful stimuli can trigger Wallerian degeneration (WD) whereby neuronal death is triggered distally in the neuron leading to an environment free of inhibitory factors and supportive of axon regrowth. Parekattil et al. reviewed spermatic cord biopsy specimens from 56 men. They identified a median of 25 < 1 mm width nerve fibers in the spermatic cord. Eighty-four percent of specimens showed WD while only 20% of the control group showed the same histological finding [6]. However, these findings have not been further substantiated by other investigators.

Diagnosis

A thorough evaluation of CSCP starts with establishing patient rapport and counseling that appropriate management of CSCP may take several weeks or months [25]. The initial encounter should rule out the previously mentioned etiologies of CSCP. History ought to focus on onset, duration, severity (scale 0–10), location, referral of pain, and exacerbating or alleviating factors. It is prudent to determine whether voiding, bowel movements, or sexual activity have any relationship to scrotal content pain. Neuropathic pain burns, causes numbness, and radiates to the skin while nociceptive pain typically

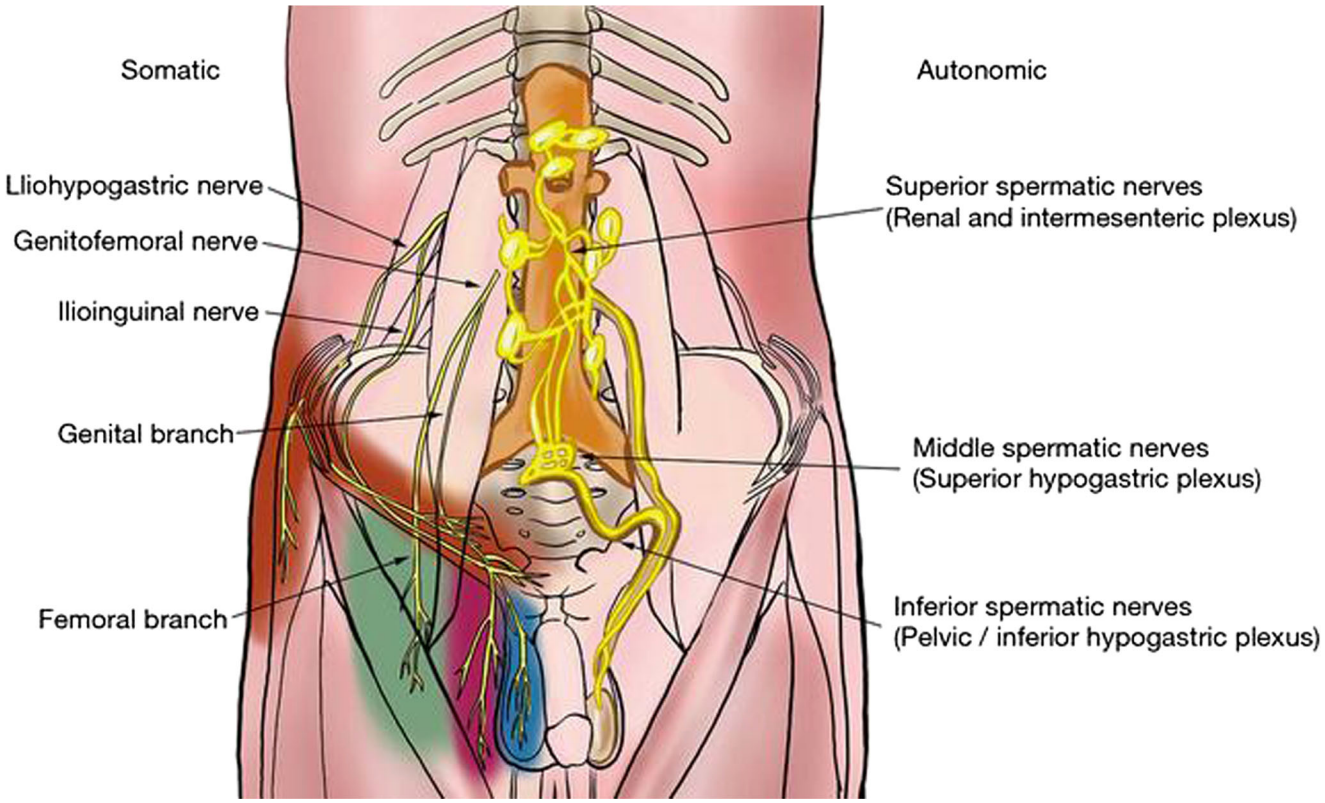


Fig. 1 The course of the autonomic spermatic nerve relative to other intra-abdominal nerve structures. The course of the nerve is highlighted in yellow, and correlates with abdominal pain, flank pain, and testicular pain. 2017 by Dhairya Patel, based on Reynolds LW, Sills SM. Orchialgia. In: Waldman SD. editor. Pain Management, Philadelphia: Elsevier, 2011. Reprinted with permission. http://tau.amegroups.com/article/view/14984/15154

causes a dull aching sensation. A psychiatric history may raise suspicion for malingering or secondary gain [2]. Surgical history ought to focus on groin, scrotal, spinal, or abdominal procedures. Importantly, a relationship between sexual abuse and chronic groin pain has also been described [26].

Physical examination of GU organs must be detailed and performed in both supine and standing positions, starting with the less painful side first. It is prudent to examine suprapubic skin, penis, bilateral spermatic cords with vasa, epididymis, testes, and the perineum. A 360° rectal exam is also indicated to evaluate for pelvic floor dysfunction [27•]. Laboratory studies should include urinalysis in all men and urine and/or semen culture if indicated. Radiologic evaluation can be limited to a scrotal duplex US to assess for anatomic and vascular abnormality [19, 28], although the yield is low. Brannigan et al. reviewed 18,593 scrotal ultrasounds, of which, 7668 (41.2%) were performed for scrotal pain. Of those, only 2.2% demonstrated a finding that was an absolute indication for surgery, while 80.4% showed benign findings or normal exam [29•]. Further imaging can include CT or MRI if patients have had a history of hip or spine surgery or describe musculoskeletal symptoms.

Lastly, a spermatic cord block (SCB) should be performed to determine if the pain originates from the scrotum. We recommend that this block be performed by injecting 20 mL of 0.25% bupivacaine or ropivacaine without epinephrine into the spermatic cord at the level of the pubic tubercle [5]. If the pain is conducted via the nerves running through the spermatic cord, then the patient should experience temporary relief or reduction in pain.

Treatment Options

As with other conditions, CSCP follows a standard treatment paradigm starting with conservative measures including pharmacotherapy and physical therapy leading to surgical options from micro-denervation of spermatic cord (MDSC) to orchiectomy. Granitsiotis and Kirk suggest a multi-disciplinary approach involving a urologist, physical therapist, pain specialist, and possibly a psychologist in select cases [2•].

If any signs or symptoms consistent with epididymitis, cystitis, or orchitis are detected, a 2–4-week course of antibiotic therapy is warranted. Medications of choice include trimethoprim/sulfamethoxazole or a quinolone, as these agents are lipophilic and are highly absorbed in GU tissues. On the contrary, a course of antibiotics is contraindicated in the absence of signs/symptoms suggestive of infection.

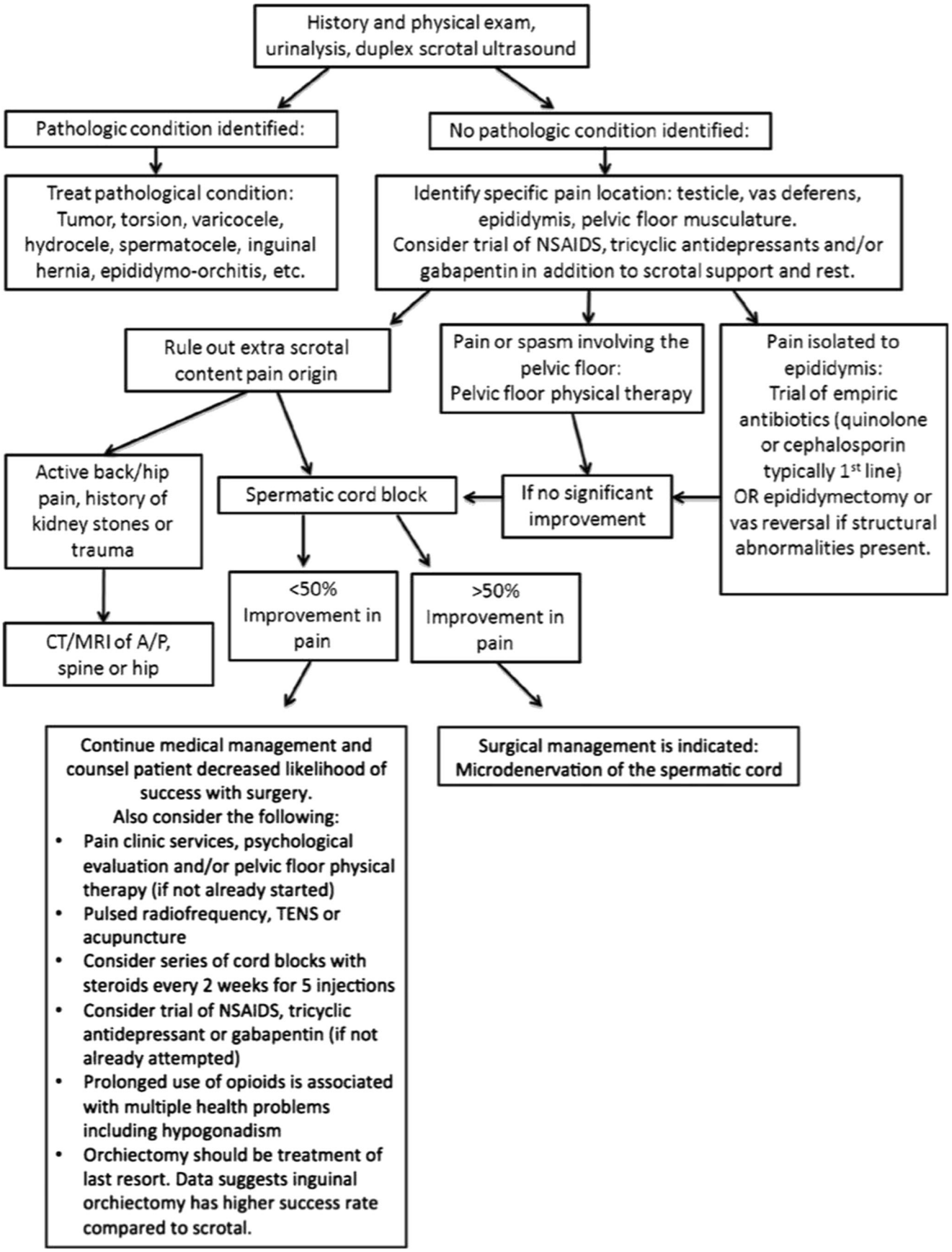
Once infection has been ruled out, pain control is the primary goal. This may be accomplished with non-steroidal anti-inflammatory drugs (NSAIDs) for a period of 4–10 weeks. Celecoxib 200 mg daily and ibuprofen 600 mg TID are first-line choices for NSAID therapy. Oral narcotics may be used to bring acute pain under control, but are not recommended out of concern for addiction, bowel dysfunction, and testosterone dysregulation over the long term.

In the event of NSAID failure, Sinclair et al. found the use of tricyclic anti-depressants (TCA) led to improvement in pain control in 4 out of 6 (66%) patients after 3 months of TCA therapy. If using TCAs, it is important to counsel patients that the drug takes 2–3 weeks to become effective. Another medication directed towards addressing neuropathic pain is pregabalin. Once more, Sinclair et al. found that 61.5% of patients with idiopathic testicular pain showed improved pain after 3 months of gabapentin therapy in a trial of 13 patients [30]. Furthermore, gabapentin has been validated as a treatment for a variety of neuralgias including diabetic neuropathy and post-herpetic neuralgia [31–33].

In addition to pharmacotherapy, pelvic floor physical therapy (PFPT) may be a valuable tool, and administered concurrently with pharmacotherapy, especially if initial history and physical examination indicate its use. PFPT may include biofeedback, trans-rectal pelvic floor massage, and relaxation techniques [34]. Farrell et al. showed that after a mean of 12 PFPT sessions, 50% of patients with CSCP and a positive DRE, indicating a pelvic floor dysfunction, showed improvement in pain, while 13.3% had complete resolution. After PFPT, fewer subjects required pain medication than prior to PFPT (44.0% vs 73.3%, $p = 0.03$, 30). Sinaki et al. also emphasized the importance of PFPT in patients with pelvic floor tension myalgia, often identified via point tenderness in pelvic floor muscle attachment sites on rectal exam [35].

Patients may also benefit from spermatic cord block (SCB) with local anesthetic with or without steroid to alter the afferent pain pathway. This may be utilized as a diagnostic procedure, in that it confirms a neural source of pain, and as a therapeutic procedure as it temporarily provides relief. Masarani and Cox concluded that if pain is testicular and not referred, SCB or division of nerves in the spermatic cord should relieve pain [21]. Patients may receive the SCB in clinic and report their response about 24 h later. Patients expressing satisfaction from SCB may receive 4–5 more SCBs, one every 2 weeks. However, this is not an appropriate long-term pain management solution when the duration of pain exceeds 1 year or when the analgesic effect of the block only lasts as long as the medication itself with no progressive reduction of pain is following each block. Our step-wise progression from commonly used NSAIDs to open surgeries is detailed in Fig. 2.

Fig. 2 Diagnostic Approach to CSCP. Our recommended approach to managing CSCP begins with a thorough H&P followed by immediate treatment of pathologic condition, if identified; subsequently, we try conservative approaches including pain management, physical therapy, and empiric treatment for infection followed by radiologic studies. With continued lack of improvement, a SCB can be performed to determine if a patient is a candidate for microdenervation of spermatic cord


History and physical exam, urinalysis, duplex scrotal ultrasound
Pathologic condition identified:
No pathologic condition identified:
Treat pathological condition: Tumor, torsion, varicocele, hydrocele, spermatocele, inguinal hernia, epididymo-orchitis, etc.
Identify specific pain location: testicle, vas deferens, epididymis, pelvic floor musculature. Consider trial of NSAIDS, tricyclic antidepressants and/or gabapentin in addition to scrotal support and rest.
Rule out extra scrotal content pain origin
Pain or spasm involving the pelvic floor: Pelvic floor physical therapy
Pain isolated to epididymis: Trial of empiric antibiotics (quinolone or cephalosporin typically 1st line) OR epididymectomy or vas reversal if structural abnormalities present.
Active back/hip pain, history of kidney stones or trauma
Spermatic cord block
If no significant improvement
CT/MRI of A/P, spine or hip
<50% Improvement in pain
>50% Improvement in pain
Continue medical management and counsel patient decreased likelihood of success with surgery.
Also consider the following:
• Pain clinic services, psychological evaluation and/or pelvic floor physical therapy (if not already started)
• Pulsed radiofrequency, TENS or acupuncture
• Consider series of cord blocks with steroids every 2 weeks for 5 injections
• Consider trial of NSAIDS, tricyclic antidepressant or gabapentin (if not already attempted)
• Prolonged use of opioids is associated with multiple health problems including hypogonadism
• Orchiectomy should be treatment of last resort. Data suggests inguinal orchiectomy has higher success rate compared to scrotal.
Surgical management is indicated: Microdenervation of the spermatic cord

In addition to the basic therapeutic modalities discussed above, a number of unique options are also available, although their efficacy is not well studied. In 2014, a small open-label study was conducted to investigate usage of botox for spermatic cord injection in men suffering from CSCP. Seventy-two percent of patients reported reduction of pain at 1 month, 56% at 3 months, and the majority of men returned to baseline pain at 6 months [36]. Alternately, transcutaneous electrical stimulation devices have been used in small non-controlled trials. These devices can potentially help release endorphins at the dorsal horn of spinal cord, which may be responsible for disrupting communication between peripheral nerve and spinal cord, thus providing pain relief [37].

Surgical

In the event that medical therapy is unable to control pain, or if obvious pathology (varicocele, epididymal cyst, obstructing stone, etc) is identified, surgical therapy should be pursued. The majority of publications are single-center reviews, with no comparative studies or level 1 evidence [38]. In this section, we discuss several open and minimally invasive surgical options.

MDSC

Microdenervation of spermatic cord (MDSC) is a well-reviewed option, and should be considered if no identifiable, reversible source of testicular pain is present, and if there is a positive response to SCB [2]. This approach was first described in 1978 by Devine and Schellhammer, and since then, this surgery is associated with complete relief of pain in 71–100% of patients [39, 40]. The primary advantage of MDSC over other alternatives is to spare the testis for both psychological and physiologic reasons [2•]. The objective of the surgery is to divide any structure that carries nerve fibers, but to leave intact all arteries (testicular, deferential, cremasteric), lymphatic channels, and the vas deferens. This will minimize testicular atrophy, hydrocele formation, and pain associated with an obstructed vas, assuming it has not been already divided from prior vasectomy. The procedure may be offered to those even with a history of prior inguinal or scrotal surgery [41], but the most important selection factor is a positive response on SCB defined as > 50% reduction in pain, as this has been shown to predict a successful outcome for MDSC [42]. Pre-operative consent must emphasize the risk for persistent, or even in rare cases, worsening pain [2•].

The evidence in support of MDSC is robust and well documented, although it is largely based upon single-center reports. Marconi et al. followed 50 patients who underwent MDSC, and at 6 months after surgery, they found 80% of subjects to be pain free, 12% with improved pain, while 8% had no change in pain [43••]. In another report, Heidenreich et al. found that 34/35 (97%) of patients who underwent MDSC for CSCP had complete resolution of pain while 1/35 (3%) had partial resolution [18]. In one of the more rigorous studies, Oomen et al. conducted a prospective, double blinded pre-operative pain clinic screening before MDSC was offered, and at mean 42.8-month follow-up, 86.2% had > 50% reduction of pain and 51.7% were completely pain free [44]. Strom and Levine analyzed 95 patients who underwent MDSC for CSCP and found that 71% had durable complete relief, 17% with partial relief (< 50% relief), and 12% with no change in pain scores. Notably, no study subject experienced worsening pain [45]. In perhaps the largest review published to date, Parekattil et al. conducted a retrospective review of 772 patients who underwent a targeted robotic MDSC between 2008 and 2016 with primary outcome being pain level assessed by visual analog scale. They found 63% with complete resolution, 22% with > 50% reduction, and notably, few complications: one testicular ischemia, two testicular artery injuries (repaired with no long-term sequel), one vasal injury, 11 hematomas, three seromas, and five wound infections [15]. The targeted robotic approach focuses on dividing tissues with the greatest concentration of nerves around the vas, within the cremasteric fascia, and the tissue posterior to the cord. Their reported success may therefore be a bit lower than the more radical open MDSC. Larsen et al. sought to determine the differential effects of having prior surgical intervention for CSCP on MDSC outcomes. They found a mean post-operative pain score of 2, representing a 79% decline among those who had no prior surgical correction attempts compared with a mean post-operative pain score of 3, representing a 67% decline among those who did have prior attempts at surgical correction. Sixty-four percent of subjects in the no prior intervention group had complete pain relief compared with 50% in those who did have surgery [41].

Epididymectomy

In contrast to MDSC, epididymectomy has a more varied success rate ranging from 10–92% [46–48], with best pain relief achieved among those who had pain localized only to the epididymis pre-operatively [49, 50]. On the contrary, poor outcomes are found among patients who received epididymectomy for pain in adjacent structures and for chronic inflammation [51]. Given the varied success rates and rather narrow indication, this procedure is not commonly performed for CSCP in the USA. In Switzerland, however, a 2005 survey demonstrated that 74% of urologists would perform epididymectomy for CSCP, while 7% would choose inguinal orchiectomy, and only 6% MDSC [17]. We do not perform epididymectomy unless the patient has pain and tenderness limited to the epididymis, and/or sonographic findings of pathology localized to epididymis.

Vas Reversal

Vasectomy is performed 500,000 times annually in the USA, and about 60 million men rely on this form of contraception worldwide [52]. For those that do develop CSCP, vasectomy reversal is associated with 50–69% complete pain relief and up to 100% improvement in pain [53–56]. Calixte et al. performed 57 robot-assisted vas reversals for CSCP. Among those, 60% experienced pain relief if they had reversal for CSCP [57]. Polackwich et al. reported similar findings when they studied 26 vasovasostomies and 7 vasoepididymostomies and found 34% experienced complete resolution of pain, while 59% had improvement in pain scores [58]. The basis for vasectomy reversal is believed to be relieving the obstruction in a congested proximal vas/epididymis. However, Lee et al. published a study of 32 men who underwent vas reversal. Among those with a patent anastomosis, mean drop in pain score was 6 ± 1.25 post operatively, compared with a mean drop of 4.43 ± 0.98 among those did not have patent anastomoses. Since pain scores did decline among the non-patent group, it is reasonable to deduce that pain is attributed to more than just relief of obstruction after vasectomy [59]. In the appropriate setting, vasectomy reversal can work well, but still remains costly as insurance often does not cover the procedure, and more importantly, if successful with regard to patency, it reverses the desired sterility initially pursued. Alternatively, microdenervation of spermatic cord can be performed for therapeutic intent while preserving sterility. In a study by Levine et al., 27 patients had a median (range) preoperative pain score of 7 out of 10 [2•, 3–10], and after MDSC, median score dropped to 0 out of 10 (0–10). Overall, they found a 71% success rate, as defined by a pain score of 1 or less postoperatively [60].

Orchiectomy

When all other previous methods have not ameliorated scrotal content pain, orchiectomy may be considered. It is highly recommended that patients be counseled on the persistence of pain. Success rates are varied, ranging from 20 to 70% [61], with better outcomes among those receiving inguinal versus scrotal orchiectomy. Davis et al. reviewed 24 patients with chronic unilateral or bilateral orchialgia, not just CSCP, for which 15 subjects received inguinal orchiectomy while 9 received scrotal orchiectomy. 11/15 had complete resolution while 4/15 had partial relief in the inguinal orchiectomy group, in contrast to 5/9 having complete relief, 3/9 with partial relief, and 1 with no change in pain in the scrotal orchiectomy group [1]. The rates of persistent pain shown here are in contrast to findings by Costabile et al., who showed that 80% of subjects continued to have pain after orchiectomy [38]. Given varied findings, orchiectomy is recommended as the final attempt at controlling CSCP, and even then, it ought to be offered only to patients who demonstrate a positive response to SCB.

Effect on Sexual Function

Though it is under studied and quantified, it is well established that CSCP carries a negative impact on sexual function, quality of life, and relationships [62]. Further analysis should be performed, as results of such studies can give physicians a deeper appreciation for the magnitude of impact CSCP carries on sexual function and quality of life. In a survey-based study by Jarvi et al., authors found that 71% of men with CSCP were unable to participate in normal social activities as a result of pain, and 61.8% noted a negative impact on sexual function [63••]. Beutel et al. found in a controlled clinical trial study of 770 men that sexual dysfunction was more frequently reported by men with pelvic pain than men without a pain syndrome [64]. More specifically, Ciftci et al. administered the International Index of Erectile Function (IIEF) [65] to 50 patients with CSCP and 50 healthy controls. The study found significantly worse orgasmic function, intercourse satisfaction, sexual desire, overall satisfaction, total IIEF scores, and health-related quality of life scores among those with CSCP. Notably, only erectile function was found to be not significantly different between groups [66]. Not only is there a strong and reasonable correlation between CSCP and sexual dysfunction/quality of life, but there is also a direct dose dependency whereby higher pain intensity predicted a poorer quality of life in patients independent of partner status and age [67]. In another study by Aljumaily et al., the authors explore the possibility of a reciprocal relationship between CSCP and sexual function. They find that 38% and 37% of patients felt sexual activity and orgasm aggravated CSCP, respectively. Sexual function worsens pain, and pain worsens sexual function, alluding to the "double jeopardy" nature of CSCP. Furthermore, the authors note that more severe pain (7–10/10) compared with less severe pain (1–6/10) results in worse outcomes when all parameters of sexual function are considered, including arousal, desire, frequency of coitus, and libido. Thirty-nine percent of men with pain scores 1–6 report no limitations to normal sexual activity while only 10% of patients with pain scores 7–10 report the same to be true ($p < 0.01$) [68••]. The finding of sexual activity worsening CSCP is substantiated by Jarvi et al., who surveyed 131 men presenting to their clinic with CSCP and find that 36.6% and 35.9% experienced exacerbation of CSCP with ejaculation and sex, respectively [63]. The importance of these findings is perhaps best summarized by Flor et al. who found that 67% of patients experienced a negative impact on marital relationship secondary to chronic pain syndrome [69].

In addition to the obvious interconnection between pain and sexual function, two alternate etiologies of worsening sexual function must also be considered. When exogenous opioids are used to control pain, they can exert their effect at the level of the hypothalamus and alter the physiologic pulsatile secretion of gonadotrophin-releasing hormone, which can

cause down-stream effects of decreased luteinizing hormone (LH) and follicle-stimulating hormone (FSH) along with potentially markedly lower testosterone levels. In addition, the use of anti-depressants can trigger delayed orgasm and contribute to sexual dysfunction. Considering Schover et al. found 48 genital pain patients to have a psychological condition like major depression (27%) and somatization disorder (56%) [70], it is not unreasonable to suspect anti-depressant-related sexual dysfunction in the setting of chronic pain.

Conclusion

CSCP is a complex diagnosis of exclusion for whose pathophysiology is not well characterized and whose etiology may be idiopathic in up to 50% of cases. Treatment options are numerous, but not well studied in terms of larger scale evidence-based trials, thus making the generation of formalized management guidelines challenging. Although the EAU has published guidelines on management of chronic pelvic pain, the section covering scrotal pain is limited. Despite that, Levine et al. has proposed an effective and logical algorithm for CSCP, a diagnosis that has a profound negative impact on sexual function, quality of life, and relationships if managed poorly. This underscores the need for further collaboration among leaders in the field to generate management guidelines in the near future. In this review, we have provided several salient principles that ought to be implemented in the management of CSCP.

Compliance with Ethical Standards

Conflict of Interest Brijesh G. Patel declares no conflict of interest.

Laurence A. Levine declares speaking and advising fees from Boston Scientific and Coloplast Corp, with no conflict of interest pertaining to article.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Davis BE, Noble MJ, Weigel JW, Foret JD, Mebust WK. Analysis and management of chronic testicular pain. J Urol. 1990;143:936–9.
2.• Levine LA, Hoeh MP. Evaluation and management of chronic scrotal content pain. Curr Urol Rep. 2015;16:36 **This review performed in 2015 identifies many of the basic strategies clinicians ought to employ in managing CSCP and reiterates the role for MDSC as a valuable technique for refractory cases.**
3. Quallich SA, Arlsanian-Engoren C. Chronic testicular pain in adult men: an integrative literature review. Am J Mens Health. 2013;7(5):402–13.
4. Fall M, Baranowski AP, Elneil S, Engeler D, Hughes J, Messelink EJ, et al. EAU guidelines on chronic pelvic pain. Eur Urol. 2010;57(1):35–48.
5. Levine L. Chronic orchialgia: evaluation and discussion of treatment options. Ther Adv Urol. 2010;2:209–14.
6. Parekattil SJ, Gudeloglu A, Brahmbhatt JV, Priola KB, Vieweg J, Allan RW. Trifecta nerve complex: potential anatomical basis for microsurgical denervation of the spermatic cord for chronic orchialgia. J Urol. 2013;190:265–70.
7. Scherger JE, Ellis AR. Post-Vasectomy Pain Syndrome: Common But Hidden; 2012. p. 1–8.
8. Morris C, Mishra K, Kirkman RJ. A study to assess the prevalence of chronic testicular pain in post-vasectomy men compared to nonvasectomised men. J Fam Plann Reprod Health Care. 2002;28:142–4.
9. Tandon S, Sabanegh E Jr. Chronic pain after vasectomy: a diagnostic and treatment dilemma. BJU Int. 2008;102:166–9.
10. Lai Y, Yu Z, Shi B, Ni L, Liu Y, Yang S. Chronic scrotal pain caused by mild epididymitis: report of a series of 44 cases. Pak J Med Sci. 2014;30(3):638–41.
11. Gray CL, Powell CR, Amling CL. Outcomes for surgical management of orchialgia in patients with identifiable intrascrotal lesions. Eur Urol. 2001;39:455–9.
12. Yaman O, Ozdiler E, Anafarta K, Gogus O. Effect of microsurgical subinguinal varicocele ligation to treat pain. Urology. 2000;55(1):107–8.
13. Park HJ, Lee SS, Park NC. Predictors of pain resolution after varicoclectomy for painful varicocele. Asian J Androl. 2011;13(5):754–8.
14. Kachrilas S, Popov E, Bourdoumis A, Akhter W, El Howairis M, Aghaways I, et al. Laparoscopic varicocelectomy in the management of chronic scrotal pain. JSLS. 2014;18(3):1–4.
15. Parekattil SJ, Cohen MS. Robotic surgery in male infertility and chronic orchialgia. Curr Opin Urol. 2010;20:75–9.
16. Wesselman U, Burnett AL, Heinberg LJ. The urogenital and rectal pain syndromes. Pain. 1997;73:269–94.
17. Strebel RT, Leippold T, Luginbuehl T, Muentener M, Praz V, Hauri D. Chronic scrotal pain syndrome: management among urologists in Switzerland. Eur Urol. 2005;47:812–6.
18. Heidenreich A, Olbert P, Engelmann UH. Management of chronic testalgia by microsurgical testicular denervation. Eur Urol. 2002;41:392–7.
19. Prospective double-blind preoperative pain clinic screening before microsurgical denervation of the spermatic cord in patients with testicular pain syndrome, Costabile R, Hahn M, McLeod D. Chronic orchialgia in the pain prone patient: the clinical perspective. J Urol. 1991;146:1571–4.
20.• Oka S, Shiraishi K, Matsuyama H. Microsurgical anatomy of the spermatic cord and spermatic fascia: distribution of lymphatics, and sensory and autonomic nerves. J Urol. 2016;195:1841–7 **This study identifies the neural anatomy of the spermatic cord and offers rationale for how and why MDSC can be a substantial therapeutic option.**
21. Masarani M, Cox R. The aetiology, pathophysiology and management of chronic orchialgia. BJU Int. 2003;91(5):435–7.
22. Cassidy DJ. Early experience with microsurgical spermatic cord denervation for chronic orchialgia at a Canadian centre. Can Urol Assoc J. 2015;9(1–2):e72–4.
23. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006;367:1618–25.

24. Voscopoulos C, Lema M. When does acute pain become chronic? Br J Anaesth. 2010;105(suppl 1):69–85.
25. Kumar P, Mehta V, Nargund VH. Clinical management of chronic testicular pain. Urol Int. 2010;84:125–31.
26. Heidelbaugh JJ, Llanes M, Weadock WJ. An algorithm for the treatment of chronic testicular pain. J Fam Pract. 2010;59(6):330–6.
27.• Farrell MR, Dugan SA, Levine LA. Physical therapy for chronic scrotal content pain with associated pelvic floor pain on digital rectal exam. Can J Urol. 2016;23:8546–50 **This study explores the role for physical therapy and tremendous therapeutic effect it can have in appropriately selected patients with assistance of DRE. Study subjects significantly reduced narcotic intake following physical therapy.**
28. Williams DH. How to manage testicular/groin pain: medical and surgical ladder Urol Times Aug 2014.
29.• Kashanian JA, Mazur DJ, Hehemann MC, Morrison CD, Oberlin DT, Raup VT, et al. Scrotal ultrasound for pain: low frequency of absolute surgical indications. Urology. 2017;108:17–21 **Study authors reviewed scrotal ultrasounds and found that more than 80% had benign findings, and only 2.2% had findings warranting surgical intervention. This study emphasizes the limited role radiologic studies have in workup of CSCP.**
30. Sinclair AM, Miller B, Lee LK. Chronic orchialgia: consider gabapentin or nortriptyline before considering surgery. Int J Urol. 2007;14:622–5.
31. Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA. 1998;280:1831–6.
32. Rowbotham M, Harden N, Stacey B, Bernstein P, MagnusMiller L. Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial. JAMA. 1998;280:1837–42.
33. Rice AS, Maton S. Gabapentin in postherpetic neuralgia: a randomised, double blind, placebo controlled study. Pain. 2001;94:215–24.
34. Tan WP, Levine L. What can we do for chronic scrotal content pain? World J Men's Health. 2017;35(3):146–55.
35. Sinaki M, Merritt JL, Stillwell GK. Tension myalgia of the pelvic floor. Mayo Clin Proc. 1997;52:717.
36. Khambati A, Lau S, Gordo A, Jarvi KA. OnabotulinumtoxinA (botox) nerve blocks provide durable pain relief for men with chronic scrotal pain: a pilot open-label trial. J Sex Med. 2014;11(12):3072–7.
37. Nnoaham KE, Kumbang J. Transcutaneous electrical nerve stimulation (TENS) for chronic pain. Cochrane Database Syst Rev. 2008;3:CD003222.
38. Kavoussi PK, Costabile RA. Orchialgia and the chronic pelvic pain syndrome. World J Urol. 2013;31:773–8.
39. Levine LA, Matkov TG. Microsurgical denervation of the spermatic cord as primary surgical therapy for the treatment of chronic orchialgia. J Urol. 2001;165:1927–9.
40. Levine LA, Matkov TG, Lubenow TR. Microsurgical denervation of the spermatic cord: a surgical alterative in the treatment of chronic orchialgia. J Urol. 1996;155:1005–7.
41. Larsen SM, Benson JS, Levine LA. Microdenervation of the spermatic cord for chronic scrotal content pain: single institution review analyzing success rate after prior attempts at surgical correction. J Urol. 2013;189(2):554–8.
42. Benson JS, Abern MR, Larsen S, Levine LA. Does a positive response to spermatic cord block predict response to microdenervation of the spermatic cord for chronic scrotal content pain? J Sex Med. 2013;10(3):876–82.
43.•• Marconi M, Palma C, Troncoso P, et al. Microsurgical spermatic cord denervation as a treatment for chronic scrotal content pain: a multicenter open label trial. J Urol. 2015;194:1323–7 **Study authors carefully tracked clinical progress of patients receiving MDSC for CSCP and found 80% of subjects to be pain free and 12% with improved pain. These findings support the therapeutic efficacy of MDSC.**
44. Oomen RJ, Witjens AC, Van Wijck AJ, Grobbee DE, Lock TM. Prospective double-blind preoperative pain clinic screening before microsurgical denervation of the spermatic cord in patients with testicular pain syndrome. Pain. 2014;155(9):1720–6.
45. Strom KH, Levine LA. Microsurgical denervation of the spermatic cord (MDSC) for chronic orchialgia: long-term results from a single center. J Urol. 2008;180:949–53.
46. Calleary JG, Masood J, Hill JT. Chronic epididymitis: is epididymectomy a valid surgical treatment? In J Androl. 2009;32:468.
47. Padmore DE, Norman RW, Millard OH. Analyses of indications for and outcomes of epididymectomy. J Urol. 1996;156:95–6.
48. Siu W, Ohl DA, Schuster TG. Long-term follow-up after epididymectomy for chronic epididymal pain. Urology. 2007;70:333–5.
49. Hori S, Sengupta A, Shukla CJ, Ingall E, McLoughlin J. Long-term outcome of epididymectomy for the management of chronic epididymal pain. J Urol. 2009;182:1407–12.
50. West AF, Leung HY, Powell PH. Epididymectomy is an effective treatment for scrotal pain after vasectomy. BJU Int. 2000;85:1097–9.
51. Terkawi AS, Romdhane K. Ultrasound-guided pulsed radiofrequency ablation of the genital branch of the genitofemoral nerve Curr Urol rep (2015) 16: 36 page 7 of 8 36 for treatment of intractable orchalgia. Saudi J Anaesth. 2014;8(2):294–8.
52. Barone MA, Hutchinson PL, Johnson CH, Hsia J, Wheeler J. Vasectomy in the United States, 2002. J Urol. 2006;176:232–6; discussion 236.
53. Myers SA, Mershon CE, Fuchs EF. Vasectomy reversal for the treatment of the post-vasectomy pain syndrome. J Urol. 1997;157:518–20.
54. Nangia AK, Myles JL, Thomas AT Jr. Vasectomy reversal for the post-vasectomy pain syndrome: a clinical and histological evaluation. J Urol. 2000;164:1939–42.
55. Shapiro EI, Silber SJ. Open-ended vasectomy: sperm granuloma, and postvasectomy orchialgia. Fertil Steril. 1979;32:546–50.
56. Werthman P. Vasectomy reversal for post-vasectomy pain syndrome: a ten-year experience. J Urol. 2010;183(suppl):e752.
57. Kavoussi P, Calixte N, Brahmbhatt J, Parekattil S. Robot assisted microsurgery for chronic orchalgia. Pain Res Manag. 2017;6(Suppl 1):S6–9.
58. Polackwich AS, Tadros NN, Ostrowski KA, Kent J, Conlin MJ, Hedges JC, et al. Vasectomy reversal for postvasectomy pain syndrome: a study and literature review. Urology. 2015;86:269–72.
59. Lee JY, Chang JS, Lee SH, Ham WS, Cho HJ, Yoo TK, et al. Efficacy of vasectomy reversal according to patency for the surgical treatment of postvasectomy pain syndrome. Int J Impot Res. 2012;24:202–5.
60. Tan WP, Tsambarlis P, Levine LA. Microdenervation of spermatic cord for post vasectomy pain syndrome. BJU Int. 2018;121(4):667–73.
61. Holland JM, Feldman JL, Gilbert HC. Phantom orchialgia. J Urol. 1994;152:2291–3.
62. Aubin S, Berger RE, Herman JR, Ciol MA. The association between sexual function, pain, and psychological adaptation of men diagnosed with chronic pelvic pain syndrome type III. J Sex Med. 2008;5:657–67.
63.•• Aljumaily A, Al-Khazraji H, Gordon A, Lau S, Jarvi KA. Characteristics and etiologies of chronic scrotal pain: a common but poorly understood condition. Pain Res Manag. 2017;2017:3829168 **Study authors found that 71% of men with CSCP were unable to participate in normal social activities as a result of pain, and 61.8% noted a negative impact on sexual function.**

Furthermore, more than one-third of patients reported an exacerbation of pain with sex and ejaculation, thus hastening quality of life. The study precisely quantifies the relationship between sexual function, CSCP, and quality of life.

64. Beutel ME, Weidner W, Brahler E. Chronic pelvic pain and its comorbidity. Urology. 2004;43:261–7.
65. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function: a multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822–30.
66. Ciftci H, Savas M, Gulum M, Yeni E, Verit A, Topal U. Evaluation of Sexual Function in Men with Orchialgia. Arch Sex Behav. 2011;40:631–4.
67. Tripp DA, Curtis NJ, Landis JR, Wang YL, Knauss JS, CPCRN Study Group. Predictors of quality of life and pain in chronic prostatitis/chronic pelvic pain syndrome: findings from the National Institutes of Health chronic prostatitis cohort study. Br J Urol Int. 2004;94:1279–82.
68.•• Aljumaily A, Al-Khazraji HA, Gordon A, Lau S, Jarvi KA. Chronic scrotal pain may lead to reduced sexual function and interest, while sexual activity may worsen chronic scrotal pain: double jeopardy. Transl Androl Urol. 2018;7(Suppl 1):S23–8 **This study describes the vicious, reciprocal nature of CSCP. Patients suffering from CSCP often suffer from reduced sexual activity, and rare instances of sexual activity for some patients, with intent to break pain and emotional suffering, often only exacerbate the pain. These findings demonstrate the poor quality of life endured by CSCP patients and underscore the need for better diagnosis and treatment of CSCP.**
69. Flor H, Turk DC, Scholz OB. Impact of chronic pain on the spouse: marital, emotional and physical consequences. J Psychosom Res. 1987;31:63–71.
70. Schover LR. Psychological factors in men with genital pain. Cleve J Med. 1990;57(8):697–700.