Post-Vasectomy Pain Syndrome: Common but Hidden

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Anthony R. Ellis, M.D.
Assistant Clinical Professor
Department of Psychiatry
Michigan State University

Joseph E. Scherger, M.D., M.P.H.
Clinical Professor
Department of Family & Preventive Medicine
University of California, San Diego

Address correspondence to:
Joseph E. Scherger, MD, MPH
2658 Del Mar Heights Rd. #604
Del Mar, CA 92014
scherger@ucsd.edu
858-232-8858

Authors Note:
The Internet has created new ways for patients and doctors to learn from each other and help solve clinical problems. JES became interested in PVPS when afflicted men began to ask questions of him as the Men's Health expert on Revolution Health. Despite more than 20 years of teaching and performing vasectomies, JES was unaware of the problem of long-term pain and other symptoms after vasectomy. The anonymity provided by the Internet helps to expose problems like PVPS that are otherwise embarrassing for patients to talk about. ARE, a psychiatric physician became interested in learning about the problem and helping other men with similar symptoms find relief. Besides frequently contributing to the discussion on Revolution Health, he answers questions about PVPS on Yahoo Answers and has constructed a website dedicated to expanding knowledge about PVPS VasectomyPain.org. We hope this clinical review of the literature helps to illuminate this problem for primary care physicians and their patients.

Abstract:
Post-Vasectomy Pain Syndrome (PVPS) refers to a variety of distressing and painful symptoms that can develop after vasectomy. These include pain or dull ache in the epididymides or testes, discomfort with sexual intercourse or after vigorous activity, and pain during or after ejaculation. The incidence of PVPS in post-vasectomy surveys varies widely but symptoms persist longer than 3 months in 15-20% of men and can become chronic. The available studies indicate that 1-5% of men are severely affected and report pain during sex or pain affecting quality of life. Conservative measures such as scrotal support, heat or cold therapy, and anti-inflammatory medications help in mild cases. Surgical treatment for cases failing conservative management has included conversion to open vasectomy, microsurgical denervation of the spermatic cord, vasovasostomy, epididymectomy, and inguinal orchiectomy. Vasovasostomy (vasectomy reversal) is an effective intervention in up to 85% of persistent cases. Informed consent for vasectomy should include a discussion of PVPS so that the patient and their partner are prepared for this outcome, as PVPS is the most common vasectomy outcome affecting quality of life.

Introduction:
Pain and discomfort after vasectomy are a source of concern to prospective vasectomy

candidates and the physicians who perform this effective and permanent surgical birth control method. There are two broad types of post-vasectomy pain: acute post-surgical pain, and delayed or chronic pain. The acute post-vasectomy infection or bleeding complications seen in one to six percent of patients rarely requires subsequent procedural intervention, but may contribute to short-term pain after vasectomy [1].

The nomenclature of delayed or chronic pain after vasectomy has been evolving since it became an area of clinical focus. It has been referred to as post-vasectomy orchialgia [2], congestive epididymitis [3], a late post-vasectomy syndrome [4], chronic post-vasectomy testicular pain (CPTP) [5] and post-vasectomy pain syndrome (PVPS) [6]. The latter term seems to have gained some popularity and is widely used, but it is not entirely clear what is being referred to in terms of symptoms, incidence, course, and etiology. Post-vasectomy pain syndrome (PVPS) is usually characterized by chronic or intermittent testicular and/or epididymal pain and is frequently worsened by intercourse or ejaculation. PVPS can be exacerbated by vigorous physical activity, and is frequently accompanied by tender or full epididymides [7]. Symptoms may be unilateral or bilateral and the pain may radiate into the groin or abdomen along the course of the spermatic cord structures.

Definition of PVPS:
Any definition of PVPS should be flexible enough to account for individual differences in presentation, and would include a statement regarding appropriate diagnostic testing and examination excluding other causes for the pain. Several studies have concluded that a discussion of chronic post-vasectomy testicular pain is imperative and should be included in the informed consent process [8,9]. The study by Choe and Kirkemo concluded that chronic scrotal pain was the most common post-vasectomy complication that can adversely affect quality of life [10]. A lack of diagnostic consensus and difficulties estimating true incidence may have delayed inclusion of the risk of developing PVPS as a routine part of the vasectomy consent process.

The American Urological Association has addressed PVPS in their patient information for prospective vasectomy candidates: "Post-vasectomy pain syndrome is a chronic pain syndrome that follows vasectomy. The cause of this syndrome and its incidence are unclear. It is generally treated with anti-inflammatory agents. Occasionally, patients will elect to undergo vasectomy reversal in an attempt to alleviate this syndrome. Unfortunately, the response to surgical intervention is unpredictable." [11]

We propose a definition of PVPS based on the literature and the experience of author (ARE) in counseling men with this condition: Post-Vasectomy Pain Syndrome is the new onset of unilateral or bilateral testicular, epididymal, or scrotal pain greater than three months duration following vasectomy with one or more of these associated symptoms: pain with erection, pain during or after intercourse or orgasm, pain that may radiate into the groin or abdomen, decreased libido, or decrease in erection. The associated physical findings of tender or full epididymides, tender proximal vas, or evidence of sperm granuloma may be found on exam. History, physical exam, and diagnostic testing have ruled out tumor, infection, varicocele, hydrocele, inguinal hernia, or prostate pathology as likely causes for the pain. The pain is not better accounted for by post vasectomy neuralgia or intermittent testicular torsion.

How Common is PVPS?
Despite the number of studies to date, the actual incidence of PVPS is hard to state reliably and can only be estimated from retrospective survey data. The available studies suggest an

incidence of any persistent post-vasectomy scrotal or testicular pain of approximately 14 to 33% [5, 8-10, 12]. The only prospective study available surveyed men preoperatively, and again six months later [13]. In this study, 488/593 (82.2%) completed both surveys and 65 (14.7%) reported new onset scrotal pain with an average visual analog score of 3.4/10. Four men (0.9%) reported pain "quite severe and noticeably affecting their quality of life." Given the mean time to PVPS onset of two years [7], an obvious limitation as to eventual incidence was this study's duration of only six months.

Many of these survey studies have incomplete response rates and there is a possibility that men with symptoms are over represented in responses. In a large retrospective mail survey study of PVPS (560 surveys sent, 71% response rate), they reported an incidence of any testicular pain of 27.2%, but when using pain duration of three months or greater, the incidence was 19% [5]. A smaller unfortunate group of patients have more severe pain that affects quality of life or sexual function. This outcome has been reported in 1-5% of patients [10, 12, 13]. When using a more rigorous definition as proposed, the incidence would be in this lower range. Well-designed prospective studies with duration substantially greater than two years would be required to gain a better estimate of the actual incidence of PVPS.

Etiology of PVPS:
The etiology of PVPS is still uncertain but there is some understanding of possible mechanisms for the pain. The currently available evidence suggests that several processes lead to the histological findings seen in PVPS. There may be a final common pathway leading to chronic testicular or epididymal pain that involves damage to scrotal nervous structures via immune system inflammatory effects, back pressure affects in the post-vasectomy closed system, or via perineural fibrosis from either of these processes.

Postulated etiologies for PVPS have included pressure from epididymal congestion, inflammation, or compression of paravasal nerves by sperm granuloma, interstitial fibrosis in the epididymides, or perineural fibrosis [14]. Studies of epididymectomy specimens from patients with post-vasectomy pain have shown evidence of pathological changes possibly related to longstanding obstruction. This interstitial fibrosis and perineural fibrosis seen in the epididymides of affected men could explain the pain [15].

In a study by Nangia, et al, patients with PVPS were treated with vasovasostomy after a variety of failed conservative treatments that had included NSAIDS, narcotic pain medications, antibiotics, oral steroids, biofeedback and psychiatric evaluation. Five of the thirteen patients had also had regional nerve blocks or lumbar sympathectomy. Of the thirteen patients in the series, four had palpable vasal nodules, of which two were painful and three were found to be sperm granulomas. All four of these patients had vasitis nodosum, chronic inflammation, or significant fibrosis. In four other patients with a tender vasectomy site they found chronic inflammation, sperm granuloma, fibrosis, suture granuloma, or vasitis nodosum. In the pain-free control group, there were similar findings of vasitis nodosum, inflammation, and nerve proliferation. It was noted that three patients (23%) needed a second surgical intervention (repeat vasovasostomy or epididymectomy) to become pain free. The authors suggested that this implied an obstructive etiology in these cases [7].

Chronic neuropathic pain or painful neuroma is possible after vasectomy due to injury of spermatic cord nervous structures. This type of post-surgical pain has been described with nerve damage after other pelvic or inguinal surgery [16]. Injury of a pelvic nerve can cause testicular pain (17), but treatment options differ for these patients as was noted in a six case series of this presentation of testicular pain after inguinal herniorrhaphy (18). These patients

typically present earlier than PVPS patients and usually lack the pain on arousal or ejaculation that is seen with PVPS.

Vasectomy affects structures proximal to the testicular end of the vas and damages the blood-testes and blood-epididymus barriers either via inflammation or pressure related changes [14]. The compromise of these physiologic barriers and "epididymal blowouts" cause extravasation of sperm and the formation of a variety of antibodies, some of which have been studied [19]. The animal and human literature on the post-vasectomy formation, types, and effects of anti-sperm antibodies is extensive and beyond the scope of this paper [20]. The available animal studies lead to the conclusion that the autoimmune response to vasectomy is species specific and perhaps even strain specific in its effects [21]. Many of these antibodies have not been fully characterized and their effects may play a role in the inflammatory damage seen in PVPS patients via the individual expression of immune response genes.

Testicular damage has been described in most mammalian studies of the histological changes after vasectomy. These findings have included degeneration of spermatids, reduced spermatogenesis (22), testicular interstitial fibrosis, and loss of Sertoli cells [23], decreases in depth of the epithelium and increases in thickness of the basement membrane or peritubular fibrosis [24]. It has been postulated that these changes are due to the increased pressure proximal to the testicular end of the vas, or are inflammatory or autoimmune in nature. The interstitial fibrosis can affect pregnancy success after reversal of vasectomy [25]. Inflammation severe enough to cause testicular fibrosis could cause orchialgia.

The epididymides are frequently enlarged or tender on physical examination of PVPS patients. Physical examination and ultrasound of scrotal contents of men with PVPS shows evidence of sperm granulomas in some, but not all patients. The role of sperm granulomas in the pathophysiology of PVPS is controversial. Some postulate a protective role for sperm granuloma at the testicular end of the vas as a "pressure valve" which could help prevent backpressure related damage [2]. Other studies focus on pain caused by sperm granulomas that require excision [26]. In addition, the sperm granuloma is the immune system lesion where sperm are broken down and presented to the immune system resulting in antibody formation that may drive some of the inflammation related damage that could contribute to PVPS. Some studies suggest an increase in antisperm antibodies in men with granulomas [27]. Whether a sperm granuloma is preventative or potentially causative may depend on the size, location, and proximity to nervous structures or amount of associated paravasal inflammation. Removal of sperm granuloma has led to resolution of symptoms in some patients with persistent pain [26].

The specific symptom complex of PVPS, similarity of reported symptoms, and consistency of histological specimens in affected patients argue against a psychological cause. There are no studies that reliably point to a psychogenic cause for PVPS. The contribution of psychological factors is unclear. In a study by Schover, somatization disorder, depression, and chemical dependency were noted in men with chronic genital pain with no organic findings [28]. The study population was not typical of vasectomized men as only half were married despite a mean age of forty-one and a third of the patients in the study were socially isolated. In a review of chronic testicular pain the authors concluded, "some of these patients are undoubtedly depressed" [29]. Chronic pain can cause depression in many patients and the depression may require separate treatment. The presence of depression in patients with PVPS is likely a consequence of the pain and its effects on sexual function, rather than the cause of the syndrome.

Diagnosis of PVPS:
The diagnosis of PVPS is based on a history of vasectomy, symptoms consistent with the diagnosis, a physical exam confirming the presence of associated findings, and the exclusion of other urogenital tract pathology with appropriate laboratory or sonographic studies. The most common symptoms and signs of PVPS are presented in Table 1.

The differential diagnoses for patients with post-vasectomy pain include neuralgia or neuroma, varicocele, hydrocele, infection, tumor, intermittent testicular torsion, inguinal hernia, and psychogenic causes [14]. With neuropathic pain, the character and location of the pain may be different and present earlier with localized sharp, burning, intense pain for neuralgia versus a dull testicular aching (with or without intermittent sharp testicular pain) for PVPS, allowing diagnosis and treatment to follow the appropriate route. Traumatic neuromas following nervous injury from vasectomy are also sensitive to light pressure. The association of pain with orgasm or after sex in patients with PVPS helps differentiate neuroma or neuropathic pain from congestive pain.

Treatment options for PVPS:
Transient mild pain after vasectomy is expected but any severe pain requires evaluation and physical exam. In any post-vasectomy patient with persistent testicular or epididymal pain for more than three months, PVPS should be considered. Conservative treatment may include scrotal support, heat or cold therapy, limiting vigorous physical activity or sexual activity, and analgesic medications such as acetaminophen or NSAIDS if there are no contraindications. Antibiotics have not been used successfully in the absence of overt infection. Anti-inflammatory medications have been used and the recent review article by Tandon, et al, suggests conservative management and NSAIDS for three months before other more invasive treatments [30].

If conservative treatments fail to provide relief, pain management strategies may be used while considering more definitive treatment. Nerve blockade via the spermatic cord may be attempted especially in cases where neuralgia is expected based on the patient's symptoms and physical exam, but relief would seem to be transient and this would not address the underlying inflammatory process. A third of the patients in the Nangia et al series had nerve block procedures and yet their pain persisted and required vasovasostomy [7]. Using chronic pain approaches with antidepressants or anticonvulsants has produced poor results in post-vasectomy pain patients while helping others with idiopathic orchialgia [31].

Definitive treatment of PVPS that fails conservative management is primarily surgical. A variety of procedures have been tried with varying degrees of success. They are listed here in increasingly aggressive order: conversion to open vasectomy, microsurgical denervation of the spermatic cord, vasovasostomy, epididymectomy, and inguinal orchiectomy [29]. Conversion to open vasectomy reduces the pressure buildup in the closed system and encourages the formation of a sperm granuloma to relieve this pressure over time. There is a small series in the literature showing resolution of "pain on ejaculation after vasectomy" by this technique [32]. Microsurgical denervation of the spermatic cord has been used to treat chronic orchialgia of any cause with good results in over 70% of patients in some series, but was associated with testicular atrophy in a small percentage of cases [33]. One series reported achieved success in 96% of patients [34]. The results may not directly apply to PVPS patients as these studies involved chronic testicular pain patients, with or without a history of vasectomy.

Vasovasostomy (reverse vasectomy) has been effective in up to 75% to 85% of patients and

has been studied specifically with PVPS patients, but restores unwanted fertility [35]. In the Myers, et al, series, eight of thirty-two patients had continued symptoms and six underwent a second reversal procedure, eventually leading to resolution of pain in twenty-seven of thirty-two patients in the series. In another series, vasovasostomy resulted in complete resolution of pain in nine of thirteen patients with PVPS [7]. In this series, when complete cure or significant improvement was used as an endpoint, there was success with 85% of patients. 23% of the patients in the Nangia, et al, series [7] and 19% of those in the Myers series [35] required a second surgical intervention; generally repeat vasovasostomy, for pain relief. Several patients had relief that lasted months for years, only to have reoccurrence of symptoms, possibly from loss of patency. Despite its success, insurance carriers do not usually cover vasovasostomy for PVPS and cost of the procedure can be a barrier for some patients.

Epididymectomy was effective in 50% of patients in a small series of ten patients with PVPS [15]. In another series, 14 of 16 patients improved with epididymectomy and factors associated with poor outcome included testicular or groin pain, erectile dysfunction, and normal ultrasound appearance of the epididymides [36]. These factors suggest that PVPS treatment success could be substantially lower. These results should be tempered with the findings of Sweeney, et al, which concluded that epididymectomy has a limited role in PVPS after a very poor response rate in their series [37]. As a tragic last resort, inguinal orchiectomy has been used to treat refractory PVPS with varying success [29].

Discussion:
Persistent testicular pain (PVPS) is the most frequent vasectomy complication that can adversely affect quality of life. Because of this, it should be included in the vasectomy consent process. Due to a lack of prospective data and differing definitions for post-vasectomy pain, consensus on incidence has not been reached. In available studies, a wide range of incidence from 14-33% is reported for any testicular pain after vasectomy. A smaller group of patients, 1-5%, have severe pain that affects quality of life or sexual function. A conservative estimate for chronic PVPS of 1-5% of vasectomized men may be warranted based on available data, but the overall incidence may be higher.

Pathologic specimens from patients with PVPS point towards perineural inflammation and fibrosis as a possible cause for persistent pain. Whether this pain is due to pressure related effects in the post-vasectomy closed system alone or inflammation from the genetically determined individual autoimmune response to vasectomy, or both, is still controversial and requires further study. Traumatic neuroma or neuralgia related to surgical injury of nervous structures represents a separate entity that can be distinguished from PVPS by history and physical exam and requires a more individualized treatment approach.

The chronic pain and sexual effects of PVPS may cause depression that requires separate treatment. If a three-month trial of conservative treatment fails, the patient should be offered pain management referral versus definitive treatment based on the severity of symptoms and individual case findings. Microsurgical testicular denervation has been used with high success rates in some series. Vasovasostomy (reverse vasectomy) studies suggest complete or significant resolution of pain can be seen in up to 85% of well-selected patients. Results vary widely with surgical treatment of PVPS.

Since PVPS causes significant morbidity in affected men, some warning about this complication should be part of the informed consent for vasectomy. Future research should focus on the role of different vasectomy techniques on the incidence of PVPS, the effects of

early vasovasostomy on the course of PVPS, risk factors for PVPS, and the development of more effective therapies. Advocacy for insurance coverage for treatment of PVPS with vasovasostomy may help more affected men obtain relief.

Table 1: Signs and symptoms of PVPS:*

Symptoms
Orchialgia (pain or pressure)
Epididymal pain
Pain with intercourse or erection
Pain with ejaculation (can persist for hours or days)
Pain that radiates into the groin or abdomen
Decrease in libido or decrease in erection
Pain increases with vigorous exercise

Signs
Tender proximal vas
Tender vasectomy site
Full epididymus
Tender epididymus
Palpable granuloma (painful or non-painful)

** Adapted from Nangia, et al, [7]*

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