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Acute and Chronic Pain Management of the Urologic Patient

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Abstract

Objectives: Here, we review opioid-sparing or opioid-free anesthesia and pain management for urologic procedures and pathologies–urological pain syndromes, kidney stone pain management, development of post-surgical pain syndromes, and prevention. We explore acute management of perioperative pain during and after urologic procedures; additionally, we review the pathophysiology of various urologic pain syndromes along with a variety of interventions, including pharmacologic management, nerve blocks, neurolysis, and neuromodulatory therapies in hopes of educating providers who treat the urologic patient.

Methods: Relevant literature on various topics related to acute and chronic urologic pain was reviewed and incorporated into this comprehensive overview. Relevant clinical treatments and treatment guidelines for managing pain related to various urological conditions and syndromes are discussed, compared, and contrasted and conclusions are drawn.

Results and Discussion: Urological pathologies, procedures, pain syndromes and their pharmacologic and interventional pain management strategies are discussed.

Conclusion: Acute and chronic pain remain essential components of postoperative morbidity, both in the urologic patient and otherwise. The opioid epidemic has further complicated perioperative management, but effective pain control is vital to improving patient outcomes. Close collaboration between urologists, anesthesiologists, and pain specialists is critical in improving patient care.

Keywords: Urologic pain, Multimodal opioid-sparing approach, Pain management

Introduction

Effective pain management is a vital part of the perioperative process that influences the preoperative evaluation, patient satisfaction, and postoperative outcomes. Acute and chronic pain can contribute significantly to postoperative morbidity, and coordination among urologists and anesthesiologists is critical in improving patient outcomes. Clinically, pain can be classified as nociceptive or neuropathic. Nociceptive pain is directly linked with noxious stimuli and is caused by damage to body tissues. Neuropathic pain results from a lesion to the peripheral or central nervous system and may not be associated with a specific stimulus to the body [1]. Pain can be further classified as acute or chronic pain. Acute pain is defined as an expected response to a noxious mechanical, thermal, or chemical stimulus, while pain is considered chronic when it lasts longer than the expected normal healing time [2]. Acute and chronic pain management of the urologic patient requires

an understanding of preventative and multimodal analgesia, intraoperative anesthetic approaches, and postoperative care. Additionally, while the breadth of urologic procedures and pain syndromes are vast, each presents itself with a unique and specific pain management approach. Kidney stone pain management, for example, will require a much different framework than prostatic cancer pain. This review summarizes acute and chronic pain management for both urologists and anesthesiologists for the urological patient population and provides the framework to approach the varied urologic patient.

Methods

Search strategy

A comprehensive search was conducted across multiple electronic databases including PubMed, Cochrane Library, Embase, Scopus, Google Scholar, and UpToDate up to the year 2024. The search was performed using a combination of keywords and Medical Subject Headings (MeSH) terms relevant to urological pain syndromes. Various search terms were utilized, including the following: "urologic pain syndromes", "chronic pelvic pain", "renal colic pain management", "urolithiasis pain management", "coccygodynia", "pudendal neuralgia", "chronic prostatitis pain", "epididymitis pain", "scrotal pain", and "chronic orchialgia".

Inclusion criteria

Articles were included if they met the following criteria:

- Investigated pain management strategies in urological pain syndromes.
- Included both retrospective and prospective study designs.
- Involved adult human subjects.
- Published up to the year 2024.

Exclusion criteria

Studies were excluded if they:

- Were not relevant to pain management in urological pain syndromes.
- Were not available in full-text.
- Were not written in English.

Study selection

Two independent reviewers screened the titles and abstracts of the retrieved records to identify potentially eligible studies. Full texts of potentially eligible studies were then assessed for final inclusion. Any discrepancies were resolved through discussion and consensus between the reviewers.

Data extraction

Data extraction was performed independently by two reviewers using a standardized data extraction form. Extracted data included study characteristics (e.g., author, year of publication, study design), participant characteristics (e.g., sample size, demographics), interventions or treatments evaluated, outcomes assessed, and key findings relevant to pain management in urological pain syndromes.

Data synthesis

Due to the anticipated heterogeneity of included studies in terms of study design, interventions, and outcomes assessed, a narrative synthesis approach will be employed to summarize the findings. Results will be organized and presented according to the specific urological pain syndromes investigated and the effectiveness of various pain management strategies evaluated in the included studies.

Results and Discussion

Acute pain management

Preoperative considerations:

Opioid dependence and overdose in the urological population: Patients requiring anesthesia for renal and genitourinary surgery are often a more comorbid, elderly population. Renal dysfunction, for example, is commonly seen, and has implications for metabolism and excretion of opioids such as morphine and meperidine. Although opioids such as fentanyl are less affected by kidney dysfunction, heightened awareness of opioid side effect profiles and addictive potential has increased the use of multimodal, opioid-sparing anesthetic plans. Recent studies have elucidated risk factors for opioid dependence and overdose after urological surgery. Overall, the rate of opioid dependence and overdose (ODO) is low at 0.09% and affects approximately 1 in 1,111 patients within one year postoperatively, consistent with rates in other surgical populations. The highest rates were in patients who underwent kidney stone procedures or major renal surgery. Patients with ODO were typically younger (median age 50), more likely to be Caucasian or African American, and less likely to have undergone ambulatory surgery. Preoperative depression and tobacco use were significant comorbidities associated with opioid dependence and overdose [3]. Understanding the risk factors specific to this patient population can help physicians tailor perioperative pain regimens to improve patient outcomes.

Methadone and buprenorphine: It is common for urological patients to have chronic pain prior to urological surgery, making it challenging to avoid opioid regimens. Methadone

has become a common mainstay for maintenance therapy in opioid use disorder and should be continued in the perioperative period [4]. For major open surgeries, methadone may be helpful given its longer-lasting effects compared to other opioids [5].

The management of acute perioperative pain in patients on buprenorphine as opioid maintenance therapy can be challenging, as buprenorphine's high receptor binding affinity, long half-life, and antagonism of analgesic actions of traditional opioids complicate postoperative pain for both anesthesiologists and urologists. For surgeries expected to have minimal postoperative pain, guidelines suggest continuing the same dose of buprenorphine without supplemental opioids and instead considering multimodal adjuncts. For surgeries expected to have moderate to severe postoperative pain, the patient should return to their buprenorphine provider and be placed on a short-acting opioid or be weaned off before surgery. These patients should also have close follow-up with their buprenorphine provider [6].

Preoperative pain relief strategies: The vast majority of preoperative urologic pain is related to obstruction of the urinary tract due to calculous disease or extrinsic compression of the upper tracts. Conservative management with NSAIDs or short-term narcotics can be used. Prompt intervention to those not responding to conservative measures can be resolved with removal of the obstructive stone providing a negative urine culture. Stenting or placement of a percutaneous nephrostomy can be undertaken if primary treatment of the obstruction cannot be performed in the cases of infected urine or extrinsic compression. Acute urinary retention is another significant source of preoperative pain and will easily be relieved with catheterization or suprapubic tube placement in the case of the impassable urethra. Infiltrative malignancies of the pelvis can involve the pelvic floor or pelvic nerves and is often treated with either neoadjuvant chemotherapy, radiation, or surgical extirpation.

Intraoperative considerations: Over the last few decades, there has been an increase in the use of laparoscopic and robotic urological surgical procedures which have improved patient-related outcomes for various complex urological procedures [7,8]. While laparoscopic and robotic surgeries may be associated with decreased pain compared to open surgery, patients still experience moderate pain from incision sites [9].

Several types of pain are associated with laparoscopic and robotic surgery: incisional port site pain, pain from peritoneum distended with carbon dioxide, visceral pain, and referred shoulder tip pain. Rapid insufflation of the peritoneum with carbon dioxide causes tearing of blood vessels, traumatic traction of nerves, and release of inflammatory mediators. Residual gas post-procedure causes shoulder tip pain, back pain, and upper abdominal pain by diaphragmatic stretching and phrenic nerve irritation [10].

A range of multimodal strategies has been proposed to reduce postoperative pain and opioid use. One of the main strategies relies on using long-acting local anesthetic-based regional analgesic techniques. Administering central or regional neural blockade reduces opioid use and facilitates early enteral feeding and mobility [11].

TAP blocks: The Transversus Abdominal Plane (TAP) block provides analgesia to the anterolateral abdominal wall. The analgesic effect usually targets the anterior rami of the intercostal nerves T7-T11, subcostal nerve T12, and the ilioinguinal and iliohypogastric nerves L1. These nerves run in the TAP plane and provide sensory innervation to the skin, muscles, and parietal peritoneum of the anterolateral abdominal wall [12]. TAP blocks have been shown to improve postoperative pain scores and reduce opioid consumption after minimally invasive surgery. These benefits translate into reduced postoperative delirium, pneumonia, urinary retention, and falls [13]. A recent meta-analysis has shown that preoperative administration of TAP blocks before minimally invasive surgery controls postoperative pain and opioid consumption more effectively than a postoperative block [14]. TAP blocks have also provided better pain control postoperatively than local wound infiltration [15].

The TAP block is an effective pain control modality for early pain and has been shown to reduce postoperative opioid consumption after minimally invasive urological surgery. Compared to other neuraxial and analgesic techniques, TAP blocks are associated with fewer episodes of hypotension and a reduced length of stay [16].

QL blocks: The Quadratus Lumborum block (QLB) is an effective analgesic modality that lowers opioid consumption after lower abdominal surgeries [17]. The QL block is an emerging truncal block technique that involves injecting local anesthesia into the thoracolumbar fascia surrounding the QL muscle. The analgesic effect is produced by the local anesthetic spreading along the thoracolumbar fascia into the thoracic paravertebral space and transversalis fascia [18]. Based on the different injection sites, there are four types of QLB: lateral, posterior, transmuscular, and intramuscular. The transmuscular or QLB3 includes the local injection between the QL and psoas major muscle and can provide the appropriate sensory blockage for open urological procedures, with reliable coverage for T6-L1 [19].

Neuraxial anesthesia: Spinal anesthesia has been used for urologic operations because it allows for early recognition of symptoms caused by overhydration, transurethral resection of prostate (TURP) syndrome, and bladder perforation [20]. Clinical symptoms appeared as abdominal pain, bradycardia, loss of consciousness, nausea, vomiting. Therefore,

maintaining consciousness during surgery for early detection was a significant advantage over general anesthesia [21]. In addition, short-acting spinal anesthesia may help prevent complications associated with delayed immobilization [22]. Spinal anesthesia typically includes a local anesthetic such as hyperbaric bupivacaine with or without an opioid adjunct such as fentanyl can provide sufficient sensory block, a short duration of sensory blockade, and reliable postoperative analgesia.

Other nerve blocks: The Ilioinguinal and Iliohypogastric nerves (L1) provide sensation to the skin of the pubic region and are targeted in groin surgeries, orchiopexies, or surgeries in the anterior scrotum. Dorsal penile blocks are used in circumcision, urethral surgery, priapism, and penile laceration repairs targeting the pudendal nerve (S2-S4) as it divides into the right and left dorsal nerves that pass under the pubis symphysis and travel below Buck's fascia to supply sensory innervation to the penis.

Postoperative considerations: Although the importance of pain control has become increasingly emphasized, acute postoperative pain continues to be undermanaged [23]. Effective postoperative pain management leads to increased patient satisfaction, reduced hospital costs, earlier mobilization, reduced postoperative morbidity, and shorter hospital stay [24]. Inadequate control of acute postoperative pain increases morbidity and mortality, decreases the quality of life, and increases the likelihood of developing persistent postoperative pain [25].

Insufflation related pain: There is a correlation between the amount of residual intraperitoneal gas and pain scores postoperatively. Therefore, using lower abdominal pressures during insufflation and aspirating residual gas may reduce postoperative pain at the end of the procedure [26]. A Cochrane database systematic review of 15 trials also demonstrated less shoulder tip pain and reduced analgesic requirement with lower pressure pneumoperitoneum [27].

Postoperative urinary retention: Postoperative urinary retention should be considered as a source of postoperative pain after urologic surgery. Left untreated, postoperative urinary retention can result in bladder distention and has adverse effects on long-term urodynamics. Prompt diagnosis, either clinically or via ultrasound and bladder catheterization if indicated, can prevent sequelae [28].

Education of nursing staff is crucial to diminish the effects of this complication and we encourage the liberal use of bladder scanning. Pre-operative discussion and education should be undertaken with patients at increased risk for post-operative retention regarding the possible need for intermittent catheterization. Teaching can occur in a short period of time and the skills are retained for application in the post-operative period [29].

Post-surgical pain syndromes: Post-surgical pain, particularly in oncologic surgeries of prostate, kidney, and bladder, is an important consideration. Retropubic radical prostatectomy for definitive treatment of localized prostate cancer can be performed open, robotically, or laparoscopically and minimally invasive techniques are now more frequently used and have led to smaller incisions, reduced blood loss, and shorter hospital stays. Cancer control, urinary continence, and preservation of sexual function are the main goals for radical retropubic prostatectomy, however there are still risks associated with various types of laparoscopic surgery that could lead to post-operative pain including nerve entrapment and nerve injury resulting in pain, weakness, paresthesia, and loss of sensation. Nerve injury following radical cystectomy for muscle-invasive urothelial cancer has a similar risk of nerve injury as compared to other major pelvic surgeries.

Nerve entrapment: The incidence of nerve injury following pelvic surgery is approximately 2 percent. Neuropathies associated with pelvic surgery are often due to patient positioning or retractor blades than direct operative injuries. The lithotomy position may result in sciatic, femoral, and peroneal neuropathies [30]. Fascial closure and pelvic reconstruction surgery are mechanisms that can result in nerve entrapment, resulting in partial or complete loss of function of the nerve involved. Symptoms can occur soon after surgery or months to years later [31]. Ureterosacral ligament suspensions have been associated with nerve entrapment and sensory pain most commonly involving the visceral fibers of the S2/S3 nerve roots [32]. Meticulous surgical technique regarding the placement of sutures can help diminish this.

Iliohypogastric/Ilioinguinal nerve injury: Trauma to the Iliohypogastric or Ilioinguinal nerves can be characterized by the triad of sharp, burning pain radiating from 1) the incision to the suprapubic area, labia/scrotum, or thigh, 2) paresthesia over the area, and 3) pain relief after infiltration with a local anesthetic [33]. If a selective nerve block produces a substantial decrease in pain, neurectomy and excision of the excised nerve should be considered. Studies have shown that more than 90% of patients had a resolution of symptoms after the neurectomy. Release of the entrapped nerve can restore normal sensory and motor function [34].

Pudendal nerve injury: Pudendal nerve injury can occur during pelvic reconstructive procedures. Pudendal nerve injury or entrapment symptoms include clitoris/penis, distal urethra, labia/scrotum, perineum, and anus pain worsened in the sitting position and resolution of pain with a selective pudendal nerve block. Treatment options include surgical decompression, pudendal nerve stimulation, and the use of cushioned pads to avoid excessive perineal pressure while seated [35].

Kidney stone pain management: Nephrolithiasis is an extremely common problem in urology, usually presenting

with renal colic symptoms and gross hematuria, however, some patients may present with more atypical symptoms including abdominal pain, vague flank pain, testicular pain, nausea, or urinary urgency/pain [36]. Patients who present with colic symptoms are initially managed with fluids, medical expulsive therapy, and pain medications. The most common supportive measures for pain control include nonsteroidal anti-inflammatory drugs (NSAIDS), including intravenous or intramuscular ketorolac (Toradol) or oral NSAIDs most commonly diclofenac, indomethacin, or ibuprofen. A recent systematic review comparing NSAIDs, opioids, and paracetamol for the treatment of acute renal colic shows that NSAIDs were equivalent to opioids or paracetamol for the relief of acute pain at 30 minutes and patients had fewer episodes of vomiting and requirements for rescue analgesia [37]. They may also act to decrease smooth muscle tone enhancing medical expulsive therapy with alpha blockers [38].

Pain after stone passage or surgical treatment for kidney stones can also be a significant problem. Several types of pain patterns can be seen after stones have passed. Persistent edema of the upper tract or the passage of clots either post-operatively or after spontaneous stone passage can result in colicky pain and can easily be treated with NSAIDs. On rare occasions, a stent may need to be reinserted to resolve the problem, especially in a febrile patient. Bladder irritability or pain can be relieved with the use of anti-cholinergic agents. Dysuria, which will also be short-lived can be helped with either prescription or over the counter urinary tract anesthetics.

Chronic urologic pain conditions and management

Chronic pelvic pain represents many complex, potentially debilitating disorders defined as nonmalignant pain for at least six months [39]. Chronic pelvic pain includes various diagnoses, including neuropathic symptoms such as paresthesia, numbness, burning. Pain often occurs when sitting, urinating, defecating, and during sexual activity. An initiating stimulus, such as infection, reflux of immunologic urine substances, perineal or pelvic trauma results in a local response of inflammation or neurogenic injury. A multimodal approach to treatment is often necessary for patients with chronic pelvic pain. Interventional and neuromodulatory procedures can be applied for diagnostic evaluation and treatment, often once more conservative measures have failed to provide relief [40,41].

Approach to the male patient with chronic urogenital pain: The most common clinical urologic pain syndrome in males is termed chronic prostatitis/chronic pelvic pain. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is defined as pain or discomfort in the pelvic region that is often accompanied by urologic storage or voiding symptoms and/or sexual dysfunction. It is commonly defined and clinically termed "prostatitis", however the term represents a broad constellation of symptoms and the prostate gland itself may or may not be the source of the problem [42]. The prevalence rate of pelvic pain and prostatitis-type symptoms has a mean prevalence of 8.2% over a man's lifetime [43]. The National Institutes of Health (NIH) consensus definition is the most commonly used international definition of CP/CPPS. It categorizes prostatitis symptoms into four categories including acute bacterial, chronic bacterial, CP/CPPS, and asymptomatic prostatitis respectively. The majority of patients who present with prostatitis symptoms are thought to have CP/CPPS versus acute or chronic bacterial prostatitis [44].

The etiology of CP/CPPS is still unknown and includes a variety of potential non-infectious causes including inflammation due to trauma, neurogenic pain, and the interplay between somatic and psychological factors [45]. Because of the heterogenous clinical presentation and complex pathophysiology, the appropriate diagnosis and management of patients with CP/CPPS remains a challenge. For the clinician, identification of symptoms and obtaining a thorough clinical history is paramount to treatment decision making. Use of quantitative questionnaires including the NIH-chronic prostatitis symptom index (NIH-CPSI), the International Prostate Symptom Score (IPSS), the International Index of Erectile Function (IIEF), and the phenotypic classification system known as UPOINT, are quite helpful. Physical exam of the abdomen and urogenital system are necessary and should include evaluation of myofascial trigger points of the small pelvis. Laboratory analysis should include urinalysis and urine culture, as well as the two-glass test, semen culture, PSA. Procedural testing should include transrectal ultrasound, cystoscopy, and urodynamic studies– while not routine, they should be considered for patients with storage and voiding symptoms or with a higher suspicion for other differential diagnoses like prostate cancer.

The treatment algorithm for CP/CPPS is a heterogeneous, ill-defined one, and thus a multidisciplinary approach is necessary. Beyond initial antibiotic therapy, the treatment options for CP/CPPS male urogenital pain include use of an alpha blocker with or without an anti-inflammatory medication, pain and neuromodulatory medications such as gabapentin, pregabalin, and amitriptyline, as well as various interventional neuromodulatory therapies including acupuncture, electroacupuncture, pelvic floor physical therapy, trigger point injections, and nerve blocks. Patients are encouraged to make behavioral changes including limiting or eliminating alcohol, caffeine, and spicy foods, taking warm daily baths, and voiding in the bath while maximally relaxed, and partaking in regular sexual activity. We also suggest the use of homeopathic agents with anti-inflammatory products such as quercetin and bee pollen extract. Botox has been investigated for the treatment of chronic pelvic pain, and its use into the prostate has been shown to be associated with significant decreases in pelvic pain [46]. Finally, psychological support including cognitive behavioral therapy is also recommended as an important treatment of this complex syndrome.

Chronic orchialgia: Chronic orchialgia is defined as at least 3 months of intermittent or constant testicular pain. Innervation of the testes, epididymis and scrotum arise from the iliohypogastric, ilioinguinal, genitofemoral and pudendal nerves which come from the L1-L2 and S2-S4 nerve roots. This effects approximately 100,000 men in the US yearly, and results in approximately 2.5-4% of urology consultations [47]. It is estimated that over $55 million are spent yearly to evaluate and manage chronic testicular pain [48]. Limitations of daily activities, work and decreased sexuality are reported by over 50% of patients [49].

Idiopathic cases with no clear etiology are common for chronic orchialgia. However, many patients presenting with chronic orchialgia are found to have obvious causes such as a hernia or intra-scrotal pathology such as varicocele, hydrocele, epididymal cysts, or torted appendages. Surgical correction of these entities will usually result in complete resolution. Referred pain can be caused by tumors of the retroperitoneum, abdominal aneurysms, spinal cord pathology, and inguinal hernias.

In the US, 1-2% of the 500,000 patients undergoing vasectomy will experience chronic testicular pain [50], known as post-vasectomy pain syndrome. There are competing theories as to the cause of this syndrome including the presence of anti-sperm antibodies, nerve entrapment, proximal back pressure on the cut vasal end, and fibrosis. Vasectomy reversal (vasovasostomy) can often alleviate the discomfort seen with the post-vasectomy syndrome [50].

Initial conservative management should consist of a course of anti-inflammatories and elimination of any inciting factors. Although antibiotics are encouraged by some for cases failing to respond to conservative therapy, we are very hesitant to advocate their indiscriminate usage without a positive culture given the increasing prevalence of antibiotic resistant microbes. When an underlying anatomic variation is not found, conservative management with NSAIDs can be moderately successful or orchialgia.

Anticonvulsants such as gabapentin have demonstrated an ability to alleviate chronic pain likely by modulating the alpha-2 delta subunits of voltage-gate calcium channels [51]. Tricyclic anti-depressants such as amitriptyline or nortriptyline can also be used for the treatment of chronic orchialgia. The use of tricyclics or anticonvulsants has been reported to show a greater than 50% improvement in pain [52]. When conservative management fails, we rely on interventional treatment for chronic pain.

Approach to the female patient with chronic pelvic pain: Chronic pelvic pain (CPP) in females is defined as pain in the pelvic area for at least 3 months that is unrelated to pregnancy and is further categorized based on location, duration, and not inclusive of pain only during menstruation. Common somatic neuropathic pain in the female can occur from trauma such as childbirth or laparoscopic surgery, or nerve stretch/compression injury. Common nerve entrapments seen in female CPP include nerve entrapments of the sacral plexus, the pudendal nerve and its branches, clitoral phimosis, and nerves that innervate the vulva and perineum including the ilioinguinal nerve, genital branch of the genitofemoral nerve, and perineal branch of the posterior femoral cutaneous nerve [53]. While there is a paucity of research in the treatment of female CPP, multimodal approaches should be considered including medical therapies such as anticonvulsants and tricyclic drugs, interventional treatments, other neuromodulatory therapies, and pelvic floor physical therapy.

Interventional treatments for chronic pelvic pain:

Superior hypogastric block: The superior hypogastric plexus (SHP) is a collection of nerves located in the retroperitoneal space at the bifurcation of the aorta and lies directly in front of the L5-S1 intervertebral disc. It provides innervation to most of the structures of the pelvic region, including the bladder, urethra, vagina, vulva, ovaries, prostate, penis, testicles, uterus, ureter, pelvic floor, descending colon, and rectum. Under radiographic guidance, a needle is inserted through the skin and advanced toward the anterolateral L5 vertebra [41]. A blockage of the SHP has been reported to decrease pelvic pain associated with malignancy by 70% [54].

Ganglion of impar block: The Ganglion of Impar is located at the level of the sacrococcygeal junction (SCJ) and is the most caudal of the sacral sympathetic chain between the SCJ and the lower segment of the first coccygeal segment. The Ganglion of Impar provides nociceptive and sympathetic supply from the perineum, distal rectum, anus, distal urethra, distal vagina, vulva, coccyx, and scrotum. The Ganglion of Impar is often involved in pain in the pelvic and perineal structures. The injection may be highly effective in treating pain originating from the cervix, colon, bladder, rectum, and endometrium [55]. One common indication is coccydynia, be it from trauma, infection, degenerative changes, or subluxation [56,57]. Some studies have reported 70-100% pain relief from this procedure [58,59].

Epididymectomy: Surgical excision of the epididymis has been used to relieve chronic epididymal pain. Its efficacy in patients with evidence of radiological tubal obstruction after vasectomy has been reported to be 63 % [60]. Eliminating the possibility of vasectomy reversal in those who ultimately decide to do this is a concern with this procedure, however, with the exceptional results that are now obtained with in vitro techniques, the concern is diminishing. When compared with other techniques to treat post-vasectomy pain syndrome such as vasectomy reversal, there has not been any significant differences detected with regards to satisfaction with surgical outcomes [61]. When the outcome of this procedure compares patients who have post-vasectomy syndrome with those who

have not undergone vasectomy and have other etiologies for their testicular pain, it has been shown that epididymectomy is more effective in patients who are experiencing pain with a prior history of vasectomy [62]. Patients who have undergone epididymectomy for non-vasectomy related pain also report satisfaction with this technique with up to 75% of patients reporting less or zero pain post-operatively [63], and 90% expressing satisfaction having undergone the procedure [64].

Spermatic cord block: Spermatic cord blocks can effectively be used in patients who have failed conservative management of chronic orchialgia. This technique can prove to be both diagnostic and therapeutic for some patients – 4 mg of dexamethasone (2 mg/ml) and 8 mg of 0.25% bupivacaine with a 27g needle can be used. The patient is asked to identify their maximal point of tenderness and 5 cc are initially targeted there. An additional 10 cc are then administered medial to the external ring. Patient responses can either be durable, but most patients will require up to three injections to achieve the desired result. Patients identified with a non-durable response typically have neuropathic pain, as this is suggestive that the afferent nerve fibers are involved. These patients are most likely to respond to other interventional techniques.

Neurolysis and ablation: In many cases, an interventional block will only provide temporary relief. In these cases, neurolysis or neuroablation can be utilized to provide longer-term relief. Chemodenervation involves injecting small amounts of either alcohol or phenol onto a target nerve to block the nociceptive tissue pathways through the destruction of neural tissue. This can be performed on the Ganglion of Impar and Superior Hypogastric Plexus [65].

Pulsed radiofrequency ablation (RFA) is a nondestructive variant of thermal RFA for providing long-term pain relief. It is not temperature-dependent and is safer to use when targeting peripheral nerves known to contain motor fibers. Pulsed radiofrequency is delivered in short bursts, followed by a quiet phase in which no current is delivered, allowing for the cooling of the electrodes. The average temperature does not reach neurodestructive ranges, and the risk of destroying nearby structures is reduced [66].

Spermatic cord microsurgical denervation: Denervation of the spermatic cord has been found to decrease or eliminate chronic orchialgia. The microsurgical spermatic cord denervation is a well-described intervention, aimed at transecting all nerves within the cord, including autonomic and somatic branches of the genital and ilioinguinal nerves with some centers now performing this robotically as well [67-69]. Resolution of pain has been reported in 49% of patients and at least a significant reduction in 83% [68,69]. The nerve supply that is transected during this procedure is associated with Wallerian degeneration in reproducible patterns which likely explains the effect of the denervation procedure and its resultant efficacy [70]. Risks of this procedure, which should be thoroughly discussed with the patient, include atrophy of the testicle, hydrocele formation, bleeding, infection, infertility, and persistent pain.

Neuromodulatory therapies:

Spinal cord stimulation: Spinal cord stimulation (SCS) is a minimally invasive, interventional surgical procedure useful in refractory chronic pain syndromes. An SCS system is made up of electrodes, implantable pulse generators, and charging/programming systems. SCS has demonstrated the ability to treat neuropathic and sympathetically associated pain. Sacral Neuromodulation (SNM) involves electrode placement, targeting S2-S4 with minimally invasive placement. Through continuous or intermittent electrical stimulation, SNM has been used to treat both overactive and underactive bladder activity as well as chronic pelvic and bladder pain [71]. There are reports of the use of SCS to relieve testicular pain in patients who received temporary relief from repeat genitofemoral nerve blocks [72].

Peripheral nerve stimulators (PNS) work similarly to spinal cord simulators but are targeted to selective nerves outside of the spinal cord. In a similar fashion, a pulse generator sends electrical pulses to the nerves and interferes with pain transmission [73]. SNM and PNS are thought to be based on the gate-control theory of pain, in which the patient can control the delivery of non-painful electrical pulses to specific nerves, which "gates" or closes the nerve to transmitting pain sensation to the CNS. Stimulation of either the dorsal horn or the dorsal nerve roots activates large AB fibers and reduces the spontaneous firing of neurons with neuropathic injuries [74].

Acupuncture: Acupuncture has been established as a neuromodulatory pain treatment by the NIH for numerous conditions. The physiologic mechanisms of acupuncture include both central and peripheral mechanisms. Central mechanisms have been demonstrated in several studies, which have shown that acupuncture needling affects functional cortical activity as well as stimulates the release of endogenous neurotransmitters [75,76]. Peripheral mechanisms of action are related to changes in the connective tissue and physiologic responses to acupuncture needling at the site of the needle, namely local inflammatory pathway signaling [77]. In urology, high quality clinical trials have demonstrated that acupuncture is an effective neuromodulatory strategy for the treatment of CP/CPPS and cancer related pain [78,79].

Miscellaneous alternative therapies:

Intrathecal drug administration: Intrathecal drug administration has been used to treat a variety of refractory painful conditions. Continuous intrathecal infusions reduce fluctuations of drug levels in CSF and allow for significant analgesia and the use of spinal adjuncts such as local

anesthetics or ziconotide. Ziconotide is derived from the toxin of the cone snail and is 1000 times as potent as morphine. There is Level 1 evidence for the use of intrathecal ziconotide to treat refractory nociceptive and neuropathic pain conditions [80]. It is thought to reduce central sensitization through the blockade of presynaptic N-type voltage-gated calcium channels, reducing afferent input to the dorsal horn ganglion [81].

Onabotulinum toxin: Onabotulinum toxin (Botox) has been studied as a means to create chemical denervation of the spermatic cord. Uncontrolled studies have shown pain relief however a double-blinded, controlled study demonstrated no increased efficacy in reducing pain when compared to a local anesthetic [82].

Pelvic floor rehabilitation: Increased pelvic floor resting tone has been identified in patients with chronic testicular pain [83]. Pelvic floor physical therapy has demonstrated pain improvement in 50% of patients, complete resolution in 13% of patients, and minor residual pain in 44% of patients [84]. Up to 10% of patients with chronic testicular pain frequently have associated musculoskeletal pain which localizes to the adductors and pelvic floor [85]. These findings suggest that pelvic floor physical therapy with biofeedback training and relaxation exercise would be useful as an adjunct to treat patients, especially those without an otherwise obvious pathophysiologic cause.

Conclusion

Acute and chronic pain remain essential components of postoperative morbidity, both in the urologic patient and otherwise. The opioid epidemic has further complicated perioperative management, but effective pain control is vital to improving patient outcomes. Close collaboration between urologists, anesthesiologists, and pain specialists is critical in improving patient care.

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None.

Authors' Contributions

Dr. Varghese and Dr. Chang have given substantial contributions to the conception and design of the manuscript, Dr. Mirman and Ms. Capodice to the analysis and interpretation of data/references, and Dr. Shehebar to the overview, finetuning, and conception of the manuscript. All authors have participated in drafting the manuscript and Dr. Mirman and Dr. Varghese revised it critically.

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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