Male Sexual Dysfunction

High Inguinal Microsurgical Denervation of the Spermatic Cord for Chronic Scrotal Content Pain: A Novel Approach for Adult and Pediatric Patients

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OBJECTIVE
To improve the technique and results of microsurgical denervation of the spermatic cord (MDSC) for men with chronic scrotal content pain, we describe a novel approach at the level of the internal inguinal ring for the complete transection of the nerves running both inside and outside the spermatic cord for adults and children.

METHODS
A retrospective review of 52 patients (64 testicular units) who underwent high inguinal MDSC was performed. Visual analogue scale (VAS, 1-10) scores were compared with before and every 3 months after the surgery. Depressive symptoms were assessed by the Beck Depression Inventory. Hormonal evaluations were performed before and 6 months after the surgery.

RESULTS
The average patient age was 52.4 years (12-78); including 6 pediatric cases. The mean operative time was 67 minutes per testicular unit, and there were no major complications. The mean pre- and post-MDSC VAS scores were 8.3 and 2.5, respectively (P < .0001). Forty-six (88%) cases showed positive responses after MDSC, and multivariate analysis showed that pain outside the scrotum and depressive symptoms were predictors of MDSC failure (P < .05, odds ratio: 15.27 and 12.56, respectively).

CONCLUSION
For both adult and pediatric patients, high inguinal MDSC is an effective and safe management option, including testicular function, for the chronic scrotal content pain that is refractory to medical management. We find that the high inguinal approach is easier in our experience than the subinguinal approach because of fewer divisions of veins, a larger diameter of the spermatic artery.

CHRONIC ORCHIALGIA, RECENTLY NAMED CHRONIC SCROTAL CONTENT PAIN (CSCP), IS DEFINED AS UNILATERAL OR BILATERAL, INTERTINENT OR CONSTANT TESTICULAR PAIN LASTING FOR MORE THAN 3 MONTHS THAT DISTURBS THE PATIENT’S QUALITY OF LIFE (QOL).1 IT IS A VERY FRUSTRATING PROBLEM FOR BOTH PATIENTS AND DOCTORS BECAUSE A MAJORITY OF CASES ARE IDIOPATHIC, AND NO DEFINITIVE TREATMENT ALGORITHM HAS BEEN ESTABLISHED. THE EXACT EPIDEMIOLOGY IN THE GENERAL POPULATION IS NOT KNOWN, BUT THE CONDITION IS NOT UNCOMMON BASED ON OBSERVATIONS THAT THE PREVALENCE AT OUTPATIENT CLINICS IS AS HIGH AS 4.8%.2

Conservative treatments such as analgesics, anti-inflammatory agents, antidepressants, antibiotics, physical therapy, biofeedback, acupuncture, spermatic cord block (SCB), and psychotherapy should be tried as first-line therapies; however, these treatments are frequently ineffective.1 Orchietomy is a drastic approach that impair testicular function and may cause psychological consequences. The use of MDSC to treat patients with CSCP was first reported in 1978 by Devine and Schellhammer.3 Since then, a number of single-center experiences have reported the effectiveness of MDSC, with success rates from 71% to 96%4-6 with variable follow-up of 20-30 months. An international, multi-institutional study showed complete resolution of pain in 80% of patients7 and recommended MDSC for the treatment of CSCP.

There are several unsolved problems regarding the use of MDSC for CSCP management. First, one reason for the differences in effectiveness among institutions is the indication criteria used. Information that can be applied to select the best candidates for MDSC is warranted. Second, an easy and safe technique for completing MDSC should be established because the need for microsurgical
steps prevents general urologists from becoming familiar with the procedure. Third, there is no information regarding endocrine and spermatogenic functions after MDSC. Lastly, there is a paucity of data describing the effectiveness of MDSC for the treatment of pediatric CSCP. The objectives of this study are to investigate the above problems by establishing high inguinal MDSC, a newly developed approach for CSCP, and including patients with a variety of backgrounds in terms of age, complaint, and etiology.

MATERIALS AND METHODS

This study was approved by the Yamaguchi University Institutional Review Board. (approval number: H29-244). From January 2010 to August 2014, 52 consecutive CSPC patients who underwent high inguinal MDSC were included in this study. A patient history was taken that included type of pain; duration of pain; previous genital infection; any urinary complaints; pain on ejaculation; back injury, pain or trauma; psychiatric disorders; analgesics use; and prior surgery in the pelvis, inguinal region, or scrotum. A detailed examination of all patients in a standing and supine position was performed to evaluate the abdomen and pelvis, testis, epididymis, and vas deferens. All patients underwent duplex scrotal ultrasonography to observe the abdominal and pelvic organs and exclude structural abnormalities. If a comorbidity which may cause CSCP was observed, its treatment was proceeded. A 360-degree digital rectal exam did not show any signs of pelvic floor dysfunction. If patients prefer, semen examination was performed before and after the surgery.

Pain was assessed by a subjective visual analogue scale (VAS) from 0 to 10. This measure was administered preoperatively and every 3 months postoperatively. Complete resolution was defined as a VAS score of 0 or 1 postoperatively, and partial resolution was defined as more than 50% reduction in pain by VAS. The Beck Depression Inventory (BDI), which consists of 21 items measuring the severity of depressive symptoms,8 was administered, and sum scores over 17 indicated suspected depression. Endocrinological evaluations were conducted before and 6 months after the surgery.

Surgical Indication and Procedure

As medical therapies, patients were treated with nonsteroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitor, pregabalin, antidepressant and/or Chinese medicine at least for 6 months. SCB was performed if these medical therapies are ineffective. Sixteen of 22 patients (73%) who underwent SCB responded but desired surgical therapy. A total of 64 testicular units in 52 men with a mean age of 52.4 years (12-78), including 6 pediatric cases, were treated. The mean duration of pain was 15.7 months, ranging from 6 to 33 months. The mean operative time was 67.4 minutes (range 42-88) per testicular unit. The mean patient follow-up time was 31.7 months (range 12-66). No scrotal hydrocele or testicular atrophy occurred during the follow-up period after the pain was improved. One patient who took warfarin after valve surgery developed scrotal hematoma, but it improved with conservative treatment.

The mean preoperative VAS score was 8.5 (range 7-10); it was significantly improved to 2.5 and 2.1 3 and 6 months, respectively, after the surgery (P < .0001, Fig. 2). No significant change in VAS was observed during the follow-up period. A total of 46 men (88%) showed complete or partial resolution. Twenty-seven (52%) showed complete resolution, and 19 (36%) showed partial resolution (Supplementary Table 2). In adult idiopathic cases, there was 85% improvement, while pediatric cases and adults with etiologies of postinguinal hernia repair, postretroperitoneal nephrectomy and scrotal trauma showed 100% responses. For bilateral cases, there was no difference in the improvement between right and left sides. Univariate analysis showed significant differences in the effectiveness of SCB, pain outside the scrotum (eg, lower abdomen, perineum, and femoral region) and depressive symptoms between the groups with and without improvement (P < .05, Table 1). A multivariate analysis showed that the presence of pain outside the scrotum or depressive symptoms were independent predictors of improvement (P < .05), with odds ratios of 15.27 and 12.56, respectively (Table 1). No patients presented prolonged wound pain and scrotal edema. Eight patients (15%) showed slight sensory deficit around inguinal region after surgery, which causes no impact on patients’ QOL.

Table 2 indicates the changes in gonadotropins and testosterone before and after surgery, with the patients categorized into boys (under 15 years old) and adults. In the boys, there were no changes in gonadotropins, while the serum testosterone concentration was significantly higher 6 months after surgery (P < .05). In the adults, there were no changes in luteinizing hormone and serum testosterone concentrations, while follicle-stimulating

Statistical Analysis

The statistical analyses were conducted using JMP software (SAS Institute). Data are presented as the mean ± standard deviation. The statistical significance of the differences in the means and proportions was tested using 1-way analysis of variance and Pearson χ² tests, respectively. All tests were 2-sided, and a P value of <.05 was considered statistically significant. Factors associated with pain improvement were evaluated by multivariate logistic regression analysis.

RESULTS

Supplementary Table 1 shows the demographics of the patients. All the patients failed medical therapies. Sixteen of 22 patients (73%) who underwent SCB responded but desired surgical therapy. A total of 64 testicular units in 52 men with a mean age of 52.4 years (12-78), including 6 pediatric cases, were treated. The mean duration of pain was 15.7 months, ranging from 6 to 33 months. The mean operative time was 67.4 minutes (range 42-88) per testicular unit. The mean patient follow-up time was 31.7 months (range 12-66). No scrotal hydrocele or testicular atrophy occurred during the follow-up period after the pain was improved. One patient who took warfarin after valve surgery developed scrotal hematoma, but it improved with conservative treatment.

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hormone (FSH) significantly decreased 6 months after the surgery ($P < .05$). Results of semen examination were obtained from 8 men. The mean value of semen volume, sperm concentration, and sperm motility pre and 3 months after the surgery were 1.9 and 2.0 mL, 1934 $\times 10^6$ and 2567 $\times 10^6$/mL ($P < .05$), 37 and 51% ($P < .05$), respectively.

**COMMENT**

Our results show the significant improvement of pain and the safety of high inguinal MDSC for both adults and boys with CSCP. MDSC has been established through the subinguinal level, but the majority of the results are reported from high volume centers; consequently, not all urologists can perform MDSC. As we have shown that microsurgical varicocelectomy is easier through a high inguinal approach than a subinguinal approach for beginning microsurgeons, MDSC using a high inguinal approach will be accepted among many urologists who do not have enough experience to perform microsurgery. Another novel finding regarding the safety profile includes testicular endocrine and spermatogenic functions, as evaluated by gonadotropin and testosterone levels.

Hypersensitivity of the pain sensory fibers may exist due to neural plasticity, and Wallerian degeneration in these peripheral nerves is often observed in these fibers of peripheral nerves. A study found a high density of nerves with Wallerian degeneration in 3 main areas: (1) the cremasteric muscle fibers, (2) the perivasal tissues, and (3) the posterior periarterial lipomatous tissue, which together have been called the “trifecta nerve complex.”

Using spermatic cords from men who underwent orchiectomy for testicular cancer, we also observed that 50% of all identified nerves stained with PGP9.5 were located along the vas deferens, and a majority of them

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**Figure 1.** Operative findings during high inguinal microsurgical denervation of the spermatic cord. (A) skin incision, (B) transection of ilioinguinal nerve, (C) transection of iliohypogastric nerve, (D) electrocoagulation of inside area of inguinal canal, (E) preservation of spermatic artery, lymphatics, and vas, (F) electrocoagulation of perivasal area. (Color version available online)
contained calcitonin gene-related peptide-positive nerve fibers, which are sensory nociceptor fibres. The ablation of these nerve complexes is postulated as the possible rationale for the success of MDSC. Furthermore, expert microsurgical skills are required to perform MDSC at the subinguinal level because of the complexity of the vessels near the external inguinal rings. A major merit of the high inguinal approach is that preservation of the spermatic artery is easy and quick. Compared with the literature reports regarding an MDSC operative time of 77 minutes, our results of 67 minutes of operative time, including the coagulation of the internal inguinal ring and perivasal area and closing the external oblique fascia, suggest that the microsurgery step may be shorter in the high-inguinal approach. Judging from the fact that no patient presented prolonged wound and inguinal pain after MDSC, opening the inguinal fascia does not affect patients’ morbidity. We have previously shown that a less-frequent need for a Doppler probe to identify the spermatic artery with the high-inguinal approach, and indeed, we used a Doppler probe in 3 cases (6%) in this series. The ablation of nerves around the spermatic cord, the genital branch of the genitofemoral, ilioinguinal, and iliohypogastric nerves, is another important step for pain improvement; however, all nerves are difficult to visualize, and the branches of the nerves are often spread out away from the spermatic cord below the external inguinal ring, resulting in incomplete ablation when the subinguinal approach is used. A high inguinal approach enables complete ablation of these nerves by coagulating all

![Figure 2. Mean changes of visual analogue scale before and after the surgery. *P < .0001 compared with preoperative value (paired t test).](image)

| Table 1. Univariate and multivariate analyses to predict post-operative improvement |
|----------------------------------|---------------------|---------------------|
| **Univariate Analysis**          | **Multivariate Analysis to Predict Improvement** |
| Improved (n = 46)                |                   |                   |
| Age (mean ± SD)                  | P Value        | Odds Ratio  | 95% CI      |
| 51.9 ± 18.7                     | 0.573          | 0.941       | 0.853-1.039 |
| Preoperative VAS                 | 0.789          | 1.226       | 0.379-3.966 |
| 8.48 ± 1.28                     | 0.612          | 0.916       | 0.059-14.228|
| Laterality (right/left/bilateral) | 0.046          | N/A         |             |
| SCB effective                    | 0.048          | 15.270      | 1.019-22.875|
| Pain outside scrotum             | 0.024          | 12.556      | 1.388-11.956|
| Depressive symptom               | 0.021          | 6.270       | 1.588-24.116|

Unilateral vs bilateral.
SCB, spermatic cord block; VAS, visual analogue scale.

| Table 2. Hormonal changes before and after microsurgical denervation |
|--------------------------|--------------------------|--------------------------|
| **Pediatrics (n = 6)**   | **Adults (n = 46)**      |
| Preoperative             | Postoperative            | Preoperative             | Postoperative            |
| LH (IU/L)                | 1.6 ± 0.4                | 1.7 ± 0.4                | 5.2 ± 1.4                | 5.1 ± 1.3                | n.s. |
| FSH (IU/L)               | 1.9 ± 0.3                | 2.0 ± 0.2                | 8.9 ± 3.1                | 8.4 ± 2.9                | <.05 |
| Testosterone (ng/dL)     | 327 ± 78                 | 450 ± 71                 | 439 ± 120                | 450 ± 116                | n.s. |

n.s., not significant.
around the inguinal canal (Fig. 1D). In the case of orchiectomy for CSCP, an inguinal approach appears to have a higher success rate than a scrotal approach, further indicating that a high inguinal approach is reasonable for MDSC. The safety of the high inguinal approach has also been shown by comparing the complication rates of this approach to the rates for other cohorts of MDSC.

Heidenreich et al reported a 96% success rate in 35 CSCP cases. Strom and Levine reported 71% complete durable relief and 17% partial relief in a sample of 95 testicles, and Oliveira et al achieved 70% complete and 20% partial relief in 60 cases. These results establish MDSC as a promising treatment for CSCP; furthermore, they indicate that approximately 90% of CSCP cases may show significant improvement as a result of MDSC. Consistent with these publications, our results demonstrated that complete or partial resolution rate was 88%, but the rate could be improved up to 95% after excluding men with pain outside the scrotum and/or depressive symptoms. Needless to say, patient selection is an important factor in predicting effectiveness. The etiologies of CSCP are complex, and its pathophysiology is not completely understood. Approximately 25%-50% of cases reveal no specific causes, and the majority of cases are classified as idiopathic. In our experience, 64% of cases were categorized as idiopathic because we never encountered post-vasectomy pain, and the effectiveness of the approach, especially for adults, was inferior (85%) when the patients were subdivided by etiology (Supplementary Table 2). In contrast, despite the small numbers in these subgroups, pediatric patients, postinguinal hernia repair patients, nephrectomy patients, and trauma patients responded dramatically to MDSC (Supplementary Table 2).

Patients who respond to temporary pain relief after SCB are generally considered good candidates for MDSC. In contrast, patients with bilateral pain, pain on ejaculation, and less than 12 hours of relief following an SCB are unlikely to benefit from MDSC. One possible reason for this is the sensitization of the central nervous system after persistent activation of pain receptors and/or a pelvic floor disorder: an overlap with chronic prostatitis/chronic pelvic pain syndrome. Taken together, our results regarding etiologies again show that pediatric patients, whose duration of sensitization may be shorter than that of adults, and patients with no depressive symptoms responded well to MDSC. The purpose of using the BDI in our CSCP practice is not to precisely diagnose depression but to effectively screen potential psychogenic causes, presumably ones that share the same phenotypes as depression. In 12 men with BDI score over 17 (Table 1), 2 and 4 patients were diagnosed as depression and anxiety disorder, respectively. Patients with bothersome symptoms outside the genitourinary tract should be managed using a multidisciplinary approach (eg, psychiatric evaluation). By briefly evaluating psychogenic symptoms using the BDI, we can evaluate the potential role of the psychogenic aspects of CSCP and prescribe tricyclic antidepressants or antianxiolytics prior to SCB and MDSC. Complete resolution rate (52%) will be improved by selecting the candidate for MDSC based on the results of SCB and psychological informations.

Previously, the youngest patients to undergo MDSC were 17 years old, as reported by Strom and Benson. We report for the first time pediatric cases younger than 15 years. Scrotal pain is a common complaint in pediatric urologic clinics, but there are only 2 reports that have focused on pediatric scrotal pain. Kalisvaart et al reported an approximately 80% success rate with conservative measures alone. In contrast, Ching et al reported that 78% of pediatric CSCP patients failed conservative management, including analgesics and scrotal support, and that while pediatric anesthesia-based approaches, including the prescription of amitriptyline and gabapentin and SCB, were effective for 70% of patients, the effective duration was transient. Failure to respond to conservative management often produces frustration and desperation, causing a potentially significant disruption of school and home life. In fact, 4 of our 6 pediatric cases could not go to school because of scrotal pain. MDSC for pediatric cases, especially boys without complete genital development, is technically challenging because of the smaller diameter of the spermatic artery below the subinguinal ring. For this reason, the use of high inguinal MDSC for pediatric cases has great merit for detecting and preserving the spermatic artery, and we have never experienced testicular atrophy. Another issue related to pediatric MDSC is preserving future reproductive function. We could not evaluate the spermatogenic function with an average 3-year follow-up, but preserved or even improved testicular function is likely because there was no apparent increase in FSH, and the serum level of testosterone was significantly increased (Table 2). Significant improvements in sperm concentration and motility were observed in selected patients but further investigation is needed to confirm the safety and usefulness on reproductive function.

This study also evaluated testicular function after MDSC for the first time. For men who do not need future fertility, we can perform a vasectomy to completely ablate the perivascular nerve complex; however, a number of CSCP patients need to ensure future fertility, and all patients need to maintain serum testosterone levels, irrespective of their fertility concerns. As a limitation of the clinical study, we could not perform a semen examination; instead, we measured gonadotropin and testosterone levels as surrogates for testicular function (Table 2). As was demonstrated in the pediatric cases, gonadotropins elevation was not observed in adults (Table 2). In contrast, FSH was significantly decreased 6 months after MDSC, indicating that simultaneous ligation of the internal spermatic veins is beneficial for spermatogenesis, especially for men who will plan to conceive a child.

There are several limitations of this study. First, to demonstrate that high inguinal MDSC is superior to the subinguinal approach, direct comparisons via an randomized
control trial (RCT) that includes both surgical procedures is necessary. Second, we did not evaluate the nature (e.g., burning, stabbing, and aching) of the pain. The VAS detects overall improvement, but patients’ subjective claims are difficult to evaluate. Evaluations of patients’ QOL are needed to evaluate surgical procedures. Third, the number of patients who underwent SCB prior to MDSC was small. Because a majority of patients prefer radical treatment to diagnostic merit and transient pain relief, we continue to let the patients choose MDSC rather than SCB after the failure of medical management.

CONCLUSION
For both adult and pediatric patients, high inguinal MDSC is an effective and safe treatment for CSCP that is refractory to medical management; furthermore, this approach preserves testicular function. High inguinal MDSC is easier to perform because it requires fewer divisions of veins and provides access to a larger diameter of the spermatic artery. This procedure will become widely used by many urologists, and it is hoped that as a result, many CSCP patients will be effectively free from pain.

SUPPLEMENTARY MATERIALS
Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.05.013.

References