

### ORIGINAL ARTICLE

# Male Fertility

# Real-time transrectal ultrasound-guided seminal vesiculoscopy for the treatment of patients with persistent hematospermia: a single-center, prospective, observational study

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This study aimed to describe endoscopic anatomy of the seminal tract and summarize our experience of transutricular seminal vesiculoscopy (TSV) guided by real-time transrectal ultrasonography (TRUS) in managing persistent hematospermia. A total of 281 consecutive patients with persistent hematospermia who underwent TSV with or without real-time TRUS were enrolled in this single-center, prospective, observational study. The median follow-up period was 36.5 (range: 8.0–97.5) months. TSV was successfully performed in 272 (96.8%) patients. The approach of a 4.5/6 F rigid vesiculoscope entering the seminal tract was categorized into four types on the basis of endoscopic presentation of the ejaculatory duct orifice and verumontanum. Seven (2.6%), 74 (27.2%), 64 (23.5%), and 127 (46.7%) patients had Types I (through the ejaculatory duct in the urethra), II (through the ejaculatory duct in the prostatic utricle), III (transutricular fenestration through a thin membrane), and IV (real-time transrectal ultrasound-guided transutricular fenestration) approach, respectively. In patients who successfully underwent surgery, bleeding occurred in the seminal vesicle in 249 (91.5%) patients. Seminal vesicle cysts, and seminal vesicle cysts were observed in 213 (78.3%), 96 (35.3%), 22 (8.1%), 81 (29.8%), 25 (9.2%), and 11 (4.0%) patients, respectively. Hematospermia was alleviated or disappeared in 244 (89.7%) patients 12 months after surgery. Fifteen patients had recurrent hematospermia, and the median time to recurrence was 7.5 (range: 2.0–18.5) months. TSV guided by TRUS may contribute to successful postoperative outcomes in managing persistent hematospermia.

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#### INTRODUCTION

Hematospermia is a common clinical symptom in the fields of urology and andrology, and it mainly occurs in patients <40 years of age.<sup>1</sup> The etiology of hematospermia may be classified into inflammation, infection, tumor, ductal obstruction, cyst formation, iatrogenic causes, and systemic conditions, such as severe hypertension or hematological diseases.<sup>2</sup> Hematospermia can last from a few weeks to several years, although it is generally benign and self-limiting.<sup>3</sup> However, symptoms in a portion of patients with hematospermia cannot be improved after medication and hematospermia persists. This condition is called persistent hematospermia. In addition, consistent symptoms of hematospermia often cause great psychological distress to patients, and all types of conservative treatment can fail, posing a challenge to doctors.

Transrectal ultrasonography (TRUS) and magnetic resonance imaging (MRI) are routine noninvasive diagnostic modalities for evaluating hematospermia. However, limitations in spatial resolution and soft tissue contrast with these methods may not permit complete evaluation of the seminal vesicle and ejaculatory duct.<sup>4</sup> Furthermore, these limitations might even result in a false negative result if there are small lesions. Transutricular seminal vesiculoscopy (TSV) provides a direct visual examination for the interior of the seminal tract and obtains a therapeutic benefit concurrently. However, detailed procedures for this surgery have not been clearly illustrated, particularly regarding gaining access to the ejaculatory duct and seminal vesicle.<sup>5</sup> Therefore, TSV is a challenging procedure for surgeons just beginning to use this procedure.<sup>6</sup> Even for experienced surgeons, the success rate of TSV ranges from 90.9% to 93%.<sup>4–8</sup>

TRUS is the most widely used tool for examining hematospermia because of its convenience and nonradiation exposure characteristics. TRUS can provide real-time images with good resolution in the process of TSV. The combination between images of spatial structure from

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TRUS and direct observation in TSV might enable more accurate diagnosis and treatment for hematospermia.

In this study, we performed TSV guided by real-time TRUS in patients with persistent hematospermia. The present study summarizes our experience of patients with hematospermia by illustrating detailed surgical techniques, clinical outcomes, intraoperative findings, and approaches to enter the seminal tract.

#### PATIENTS AND METHODS

#### Study cohort

This prospective, observational study enrolled consecutive patients who had persistent hematospermia between January 2010 and January 2018 in the Department of Urology, The Second Hospital of Shandong University, Jinan, China. Persistent hematospermia was defined as consistent hematospermia with a duration exceeding 3 months, regardless of medical treatments (including antibiotics with or without nonsteroidal anti-inflammatory medication). All patients underwent physical examination, urinalysis, and blood tests. All patients received at least one type of imaging examinations, including transrectal ultrasound and MRI, before surgery.

Exclusion criteria included poorly controlled hypertension, cirrhosis or deteriorated liver function, anticoagulant therapy, a history of trauma to the urogenital tract, and acute urinary tract infections. Patients with known hematological malignancy were also excluded.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. We received ethics committee approval of the Second Hospital of Shandong University with written informed consent obtained from each participant before enrollment.

#### Surgical procedures

Patients were placed in the dorsal lithotomy position under spinal or general anesthesia. The operating room was arranged so that the monitor was on one side of the patient, while the TRUS (Sonicaid 9900, Medison, Seoul, Korea) and Endovision monitor (Image 1 hub HD, Karl Storz GmbH & Co. KG, Tuttlingen, Germany) were on the other side. A flowchart of the procedure is shown in **Figure 1**. Cystoscopy was initially



Figure 1: Flowchart of the surgery. DRE: digital rectal examination.

performed to investigate the position of the verumontanum, orifice of the prostatic utricle, and bilateral ejaculation duct orifices. Under direct visualization, we then located the source of hematospermia from the orifice of the prostatic utricle or unilateral/bilateral ejaculation orifices by squeezing the bilateral seminal vesicles through a digital rectal examination (**Figure 2**). A vesiculoscope (4.5/6 F; Wolf, Richard Wolf GmbH, Beijing, China) was then inserted into the urethra. There are four approaches for applying TSV to enter the seminal vesicles and these approaches are described below.

#### Type I: through the ejaculatory duct in the urethra

The first approach for applying TSV was through an opening of bilateral ejaculatory ducts located at a position lateral to the verumontanum in the urethra. Under the guidance of a Zebra guide-wire (Urovision, Oberbayern, Germany), a vesiculoscope was inserted directly into the ejaculatory ducts. This was performed with the assistance of hand-controlled intermittent perfusion dilatation with a 30-ml syringe using normal saline (**Figure 2**). The seminal vesicle and the opening of the vas deferens were subsequently examined.

#### Type II: through the ejaculatory duct in the prostatic utricle

In some patients, the opening of the ejaculatory duct could not be identified on the surface of the verumontanum. In such a situation, a vesiculoscope was initially inserted into the prostatic utricle through the verumontanum. The orifice of the ejaculatory duct was then observed in the lateral wall of the prostatic utricle neighboring the orifice of the prostatic utricle (**Figure 2**).

#### Type III: transutricular fenestration through a thin membrane

In other patients, the orifice of the ejaculatory duct could not be indentified under direct visualization. In this situation, a surgical fenestration was established. A vesiculoscope was initially inserted into the orifice of the prostatic utricle. The junctions between the prostatic utricle and the seminal vesicles are mainly a thin layer of membrane-like tissue and are typically located on the lateroposterior



Figure 2: Endoscopic view of verumontanum: (a) prostatic utricle orifice and ejaculation duct orifices by cystoscopy; (b) hematospermia from the ejaculation duct orifice by squeezing seminal vesicle; (c) hematospermia from the prostatic utricle orifice by squeezing seminal vesicle; and (d) posterior urethral bleeding while squeezing seminal vesicle.

aspect of the utricular wall (**Figure 3**). Under pulsatile low-pressure saline flushing, the membranous tissue often appeared in a periodic motion of sinking and bulging, which was driven by pulsatile flow. Subsequently, the vesiculoscope was punctured through the center of the thin membrane into the seminal vesicles.

## *Type IV: real-time transrectal ultrasound-guided trans-utricle fenestration*

Sometimes, the surgical path could not be established in patients with a nonmembranous junction because of a longer separation in the distance between the seminal vesicle and prostatic utricle. In addition, the orifice of the ejaculation duct was sometimes inaccessible because of a narrow opening of ejaculation and was sometimes covered with membranous tissue. In these cases, the position between the prostatic utricle and seminal vesicles was initially detected by axial and sagittal TRUS images (Toshiba SSA-270 A; Toshiba, Tokyo, Japan) with 6-MHz and 7.5-MHz biplane transducers. Under real-time TRUS guidance, a vesiculoscope was inserted into the prostatic utricle. In the sagittal plane, the vesiculoscope tip with a strong echo then penetrated into the seminal vesicle through the most suitable surgical path (**Figure 4**). Finally, the surgical path between the prostatic utricle and seminal vesicle was expanded using the scope body or a holmium laser incision to prevent possible stenosis and recurrence.



**Figure 3:** (a) Right ejaculation duct orifice could be observed in the urethra; (b) under the guidance of a Zebra guide-wire to enter ejaculation duct in Type I patients; the orifice of the ejaculatory duct was observed in the (c) right and (d) left lateral walls of prostatic utricle in Type II patients; the seminal vesicle and the prostatic utricle were only separated by a thin layer of membrane-like tissue located (e) in the anterior lateral wall of the prostatic utricle and (f) on the lateroposterior aspect of the utricle wall in Type III patients.

After these approaches, close observation and treatments were performed according to endoscopic findings. Typically, the seminal vesicles contained a honeycomb-like structure, congested walls, and a milky or pink seminal vesicle fluid filled with flocculent turbidity and blood clots (**Figure 5**). Seminal vesicle fluid was collected for bacterial culture. In cases of stones in the seminal vesicles, a holmium YAG laser (SRM-H2B, Raykeen, Shanghai, China) or grasping forceps (WF-180GL020, Olympus, Shinjuku, Tokyo) were applied. The seminal vesicles were repeatedly flushed using normal saline to clear out the seminal plasma fluid, blood, and small calculi. A 0.50% (*w*/*v*) levofloxacin (3 mgl<sup>-1</sup>, Zhejiang Medicine, Shaoxing, China) solution was then injected into the seminal vesicles. A catheter (F-22, Angel Medical Equipment, Jinhua, China) was placed after surgery and removed on the next day.

#### Data collection

We prospectively recorded demographic and operative data, including age, baseline symptoms, and other clinical parameters. Patients were asked to refrain from ejaculation for 2 weeks after surgery. The patients returned for the first follow-up 1 month after the procedure. Patients then received regular follow-up every 3 months up to 12 months and then yearly after surgery.

#### Statistical analysis

Numerical variables were presented as the mean (range). All analyses were performed with PASW Statistics for Windows, version 18.0 (IBM SPSS Inc., Chicago, IL, USA).

#### RESULTS

#### Patients' characteristics

A total of 281 consecutive patients with persistent hematospermia were eligible for inclusion in the study. The median disease



**Figure 4:** The surgical path was established under real-time TRUS guidance in Type IV patients. (a) Nonmembrane-like junctions between the prostate utricle and seminal vesicle; (b) endoscopic view in prostatic utricle postoperatively; (c) image of real-time TRUS during operation. TRUS: transrectal ultrasonography.





Figure 5: Perioperative findings in transutricular seminal vesiculoscopy. (a) Normal seminal vesicle; (b) inflammatory changes in the seminal vesicle; (c) calculus in the seminal vesicle; (d) calculus in the ejaculatory duct.

duration was 8.0 (range: 3.0–36.0) months and the mean time of follow-up was 36.5 (range: 8.0–97.5) months. TSV was successfully performed in 272 (96.8%) patients. Hematospermia was alleviated or disappeared in 56 (20.6%) and 188 (69.1%) patients, respectively, by 12 months after surgery. A total of 15 (5.5%) patients experienced recurrence after surgery, and the median time to recurrence was 7.5 (range: 2.0–18.5) months. Hematospermia was usually alleviated or resolved by 3–4 months after surgery. The patients' characteristics are shown in **Table 1**.

#### Approaches for the vesiculoscope entering the seminal tract

The approaches of the vesiculoscope entering the seminal tract were Types I, II, III, and IV in 7 (2.6%), 74 (27.2%), 64 (23.5%), and 127 (46.7%) patients, respectively.

#### Intraoperative findings and complications

In patients who successfully underwent surgery, bleeding in the seminal vesicle occurred in 249 (91.5%) patients. Seminal vesiculitis, calculus in the prostatic utricle, calculus in the ejaculatory duct, calculus in the seminal vesicle (Figure 5), prostatic utricle cysts, and seminal vesicle cysts (Figure 6) were observed in 213 (78.3%), 96 (35.3%), 22 (8.1%), 81 (29.8%), 25 (9.2%), and 11 (4.0%) patients, respectively (Table 1). Irrigation was applied to flush out blood clots and small calculi in the prostatic utricle, ejaculatory duct, or seminal vesicle. Clavien I complications (fever >38.5°C) were found in 14 (5.1%) patients and Clavien II complications were found in 3 (1.1%) patients (postoperative epididymitis was treated successfully with a 2-week standard regimen course of antibiotics). No seminal vesicle perforation, rectal injury, retrograde ejaculation, or other severe complications were observed. Nine patients failed to receive bilateral transurethral seminal vesiculoscopy, even under TRUS guidance. These nine patients were all characterized by seminal dysplasia in MRI/TRUS.

#### DISCUSSION

Hematospermia is usually benign and self-limiting. In our study, we found that the most important causes of persistent hematospermia



Figure 6: (a) Endoscopic view of prostatic utricle cyst; (b) preoperative magnetic resonance imaging of prostatic utricle cyst; (c) endoscopic view of seminal vesicle cyst; (d) preoperative magnetic resonance imaging of seminal vesicle cyst.

Table	1:	Preoperative	and	postoperative	characteristics	in	the	study
popula	atic	on ( <i>n</i> =281)						

Projections	Patients with hematospermia (n=281)
Age (year), median (range)	42 (22–72)
Duration of disease (month), median (range)	8.0 (3.0–24.0)
Urine routine, n/total (%)	
Hemopyuria	10/281 (3.6)
Microscopic hematuria	25/281 (8.9)
Pyuria	5/281 (1.8)
Normal	251/281 (89.3)
Semen analysis, n/total (%)	
Red blood cell	201/228 (88.2)
White blood cell	47/228 (20.6)
Normal	21/228 (9.2)
Not tested	53/281(18.9)
Intraoperative findings, <i>n</i> /total (%)	
Bleeding	249/272 (91.5)
Prostatic utricle calculus	96/272 (35.3)
Ejaculatory duct calculus	22/272 (8.1)
Seminal vesicle calculus	81/272 (29.8)
Seminal vesiculitis	213/272 (78.3)
Prostatic utricle cyst	25/272 (9.2)
Seminal vesicle cyst	11/272 (4.0)
Follow-up period (month), median (range)	36.5 (8.0–97.5)
Complications, n/total (%)	
Fever (>38.5°C)	14/272 (5.1)
Epididymitis	3/272 (1.1)
Retrograde ejaculation	0 (0)
Seminal vesicle perforation	0 (0)
Rectal iniury	0 (0)

were inflammation, stenosis, and calculi. These disorders are usually associated and influence each other.<sup>9</sup> If infection is suspected, at least

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4-week empiric treatment with antibiotics should be performed.<sup>10</sup> However, symptoms in most patients cannot be improved after medication. Subsequently, medicines, including antibiotics and steroid hormones, are injected into dilated seminal vesicles under TRUS guidance, and the disorder transiently resolves for a maximum of 3 months.<sup>11</sup>

Persistent hematospermia related to cystic lesions and tumors of the prostate, seminal vesicles, ejaculatory ducts, or embryological remnants, including the Müllerian duct, should be treated with surgery instead of conservative treatment. Managing persistent hematospermia in the absence of any obvious underlying pathology or significant benefits from conservative treatment is challenging. TSV can directly observe the urethra, ejaculatory ducts, and seminal vesicles to identify the anatomical causes of hematospermia. TSV has been introduced in clinics since 2002; Asian andrologists have explored the application of TSV as a diagnostic and treatment tool for hematospermia and performed this procedure in several centers in China, Japan, and other countries. As a diagnostic and therapeutic approach, many reports have shown that TSV is an effective and safe tool for hematospermia.<sup>7,12-16</sup> Liu et al.<sup>7</sup> reported a 93% success rate and 8.5% recurrence rate in a prospective, observational study on 114 patients with intractable seminal vesiculitis. Hu and Chen<sup>6</sup> also reported a similar success rate (92.1%) with a semirigid ureteroscope introduced into the intractable hematospermia, and 4 (11.8%) of 33 patients had recurrent hematospermia. Xing et al.8 reported a 92.3% success rate and an effective rate of 84.7% with a ureteroscope introduced into the seminal vesicles.

However, TSV is a challenging procedure, especially for surgeons just beginning to use this procedure. As demonstrated by Chen *et al.*,<sup>5</sup> there are several issues preventing wide application of this procedure. First, detailed surgical procedures for TSV are currently nonstandardized. Second, endoscopic presentation of the ejaculatory duct orifice and the verumontanum are complicated. This makes identifying the ejaculatory duct orifice or establishing a surgical path difficult. Third, the surgical path cannot be established in one case (Type IV), leading to failure of the procedure. Under these conditions, there are no explicit instructions that we can follow to identify the proper surgical path.

TRUS can clearly show the positional relationships among the prostatic utricle, ejaculatory ducts, and seminal vesicles. This technique is useful for diagnosing seminal vesicle diseases, such as cysts and stones,<sup>17-19</sup> and persistent hematospermia.<sup>20</sup> TRUS can provide real-time images with good resolution and thus can be used for intraoperative monitoring. In some patients with anatomical abnormalities, vas deferens/seminal vesicle puncture and injection of methylene blue, combined with transurethral endoscopy, can aid in observations of the ejaculatory duct openings in patients with ejaculatory duct obstruction.<sup>21,22</sup>

Under the combination of real-time TRUS and TSV, the ejaculatory ducts and the seminal vesicle can be successfully located, which enables the surgeon to determine the surgical path. Because the penetration position between the wall of the prostatic utricle and seminal vesicle is easily established by real-time TRUS and endoscopic images, this procedure is much safer, and risks, such as rectal injury, can theoretically be avoided. This procedure can decrease surgical morbidity and minimize the risk of further complications. Obviously, this technique requires advanced ultrasonographic machines and a radiologist for a multidisciplinary approach.

In our study, although ureteroscopy and seminal vesiculoscopy achieved approximately 90% efficiency in treating patients with hematospermia, there were still many patients who experienced failure in the procedure or recurrence. The native opening of the ejaculatory duct is extremely narrow and sometimes covered with membranous tissue. This situation makes visualization difficult, even under low-pressure saline irrigation. In contrast, the transutricular approach is relatively straightforward because of the large utricular opening. In our experience, among 272 patients with TSV, only seven had introduction through the ejaculatory duct, whereas most (127 patients) patients had transutricular fenestration. Especially in the situation of Type IV, the surgical path could not be established in other studies,<sup>5,6</sup> leading to failure of the procedure. In the present study, under real-time transrectal ultrasound guidance, the success rate of TSV was 96.8%, which is superior to similar previous studies. In fact, the nine cases of failure were not suitable for TSV because of dysplasia of the ejaculatory duct orifice or seminal vesicle. We advise that surgeons should strictly choose indications. Moreover, real-time transrectal ultrasound can also be effectively applied in other clinical scenarios, including managing seminal tract obstruction or midline prostatic cysts for male infertility, prostatic cancer staging to exclude seminal vesical invasion, removal of seminal vesical stones, and drainage of seminal fluid in patients with refractory seminal vesiculitis.

Complications of TSV that might occur include epididymitis caused by ascending infection, painful ejaculation, seminal vesicle perforation, and rectal damage. Therefore, operations must be gentle to avoid rectal damage, vesicle perforation, and aggravated bleeding, which may cause a blurred visual field. Epididymitis was observed in three patients in our study. These patients were treated with a standard regimen course of antibiotics and recovered in 2 weeks. No retrograde ejaculation, seminal vesicle perforation, or rectal injury was observed in all 272 patients.

Although our outcomes are encouraging in a relatively long-term follow-up period, there are some limitations in the present study. Notably, hematospermia is usually self-limiting and might spontaneously improve without aggressive treatment.<sup>23</sup> TSV should only be performed in patients with persistent or recurrent symptoms who have received medical treatments, but these treatments have not been successful. In addition, the present surgical approach may damage the natural anatomical tract of the seminal vesicle, which may cause potential adverse effects. Furthermore, because of the limited sample size, further multicenter, clinical trials with a larger sample size are required.

#### CONCLUSION

TSV is an effective and safe procedure for managing persistent hematospermia. Real-time transrectal ultrasound applied in the surgical process may contribute to better outcomes for surgery.

#### **AUTHOR CONTRIBUTIONS**

MZY and LQG participated in the design and coordination of the study, and directed others to conduct the experimental investigation. XSW and ZM conceived the idea of the study and drafted the manuscript. XSW and XLZ revised the manuscript. ZYX and WDS performed the statistical analysis. ML and GFS collected the data. All authors read and approved the final manuscript.

#### **COMPETING INTERESTS**

All authors declared no competing interests.

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