Robotic Surgery for Male Infertility

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KEYWORDS

• Robotic surgical procedures • Infertility • Male • Vasovasostomy • Varicocele

KEY POINTS

- Robotic-assisted approaches to male infertility microsurgery have potential practical benefits including reduction of tremor, 3-dimensional visualization, and decreased need for skilled surgical assistance.
- Several small, retrospective studies have described robotic-assisted vasectomy reversal with comparable clinical outcomes to the traditional microsurgical approach.
- Few studies have described application of the robot to varicocelectomy, testicular sperm extraction, and spermatic cord denervation.
- The use of robotic-assistance for male infertility procedures is evolving, and adoption has been limited. Rigorous studies are needed to evaluate outcomes and cost-effectiveness.

INTRODUCTION

Up to 15% of couples have infertility, with approximately 50% of cases involving a male factor.[1,2] A substantial proportion of men with subfertility have surgically treatable and even reversible etiologies, such as a varicocele or vasal obstruction. The introduction of the operating microscope revolutionized the field of male infertility, dramatically improving visualization of small, complex anatomic structures. The technical precision afforded has improved operative outcomes across the board. For decades, microsurgery has been considered the gold standard for many male infertility procedures.

As robotic-assisted laparoscopic surgery was widely adopted in urology, male infertility surgeons began to explore potential applications of the robotic platform to microsurgical operations. On the one hand, most male infertility procedures are extra-abdominal and extra-corporeal, rendering them less amenable to the benefits of the robotic approach that are best recognized with intraperitoneal and pelvic surgery. On the other hand, many of the theoretic and practical advantages offered by the robotic approach are highly transferrable to surgery for male infertility:

High quality, 3-dimensional visualization is essential for any microsurgical procedure.

Improved surgeon ergonomics are always desirable, particularly given the surgeon morbidity associated with microsurgery.[3]

Filtering of physiologic tremor can improve precision during technically demanding microsurgical operations.

The robotic arm may obviate the need for a skilled surgical assistant that is often required in microsurgical cases (**Table 1**).

This article reviews the application of robotic surgery to each of the 4 primary male infertility procedures: vasectomy reversal, varicocelectomy, testicular sperm extraction, and spermatic cord denervation. For each, a brief historic perspective is presented alongside the data, limited in most cases, examining its use.

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Table 1
Theoretic advantages of the robotic approach for male infertility surgery

Advantage	Description
3-dimensional visualization	High-quality, 3-dimensional visualization is comparable and possibly superior to conventional microscopy in certain anatomic areas.
Ergonomics	Improved surgeon comfort and ergonomics may reduce morbidity associated with conventional microsurgery.
Tremor reduction	Filtering of physiologic tremor can improve precision during technically demanding microsurgical operations.
Minimal assistance	Fourth robotic arm may obviate the need for a skilled surgical assistant, often required for complex microsurgical cases.

ROBOTIC-ASSISTED MICROSURGICAL VASECTOMY REVERSAL

Vasectomy is a commonly used method of contraception with over 500,000 vasectomies performed annually in the United States.[4] It is estimated that up to 6% of these men will eventually pursue vasectomy reversal.[5] In most men, vasectomy reversal is technically feasible; however, long-term success rates with respect to pregnancy and live birth are variable.[6]

From a technical perspective, the vasal anastomosis is the critical operative step. The vasal lumen is exceedingly small, with an average diameter of approximately 1.0 mm.[7] The key surgical principles are the achievement of a tension-free, water-tight, vasal anastomosis, and taking great care to avoid iatrogenic obstruction with placement of a cross-luminal suture. Early vasectomy reversals were performed without magnification; however the introduction of the operating microscope greatly improved both patency and pregnancy rates, and thus microsurgical vasectomy reversal became the standard of care.[8,9] The technique and microsurgical skills require dedicated training experience and often a skilled microsurgical assistant. Robot-assisted microsurgical approaches offer advantages to overcome some of the challenges associated with pure microsurgery for this challenging procedure. As such, vasectomy reversal was the first application of robotic microsurgery to male infertility.

Initial descriptions of robotic vasal surgery were small feasibility studies in ex vivo models.[10–12] In 2003, Schoor and colleagues[10] performed en bloc resection of the spermatic cord and testis in euthanized rats, following which they sharply divided the bilateral vasa and performed a robotic-assisted single-layer vasal anastomosis using 10-0 nylon suture. The authors noted that both surgeons found the robotic instruments sufficiently delicate for manipulation of the vasal tissue and suture material. Other benefits described in this initial report were “complete elimination of tremor, and enhanced comfort.” Soon thereafter, Kuang and colleagues[11] compared vasovasostomy (VV) outcomes of a single surgeon using the robotic versus microsurgical approaches in an ex vivo human model consisting of fresh vasal specimens from radical cystectomy patients. Although operative time was longer using the robotic approach, there was no difference in the number of needle passes, surgeon fatigue, or anastomotic patency between the 2 approaches. The authors also noted that surgeon tremor was substantially reduced with the robotic approach.

The first comparative study of robotic vasal surgery in rats was published by Schiff and colleagues in 2004.[13] The authors performed vasectomy in 24 rats, returning 2 weeks later to perform robotic versus microsurgical VV or vasoepididymostomy (VE). Robotic VV was significantly faster than the conventional microsurgical procedure (68.5 vs 102.5 minutes, P=.002), whereas there was no significant difference for VE (90.3 vs 107.3 minutes, P = .29). Similar anastomotic patency rates were seen between the two groups for both VV (robotic 100% vs conventional 90%, P=.23) and VE (robotic 100% vs conventional 90%, P=.16). Although the study was not designed to assess the surgeon learning curve, the authors noted that experienced microsurgeons were able to adapt their skills to the robotic approach during a short, 6-hour training period before the study, during which they performed robotic-assisted suture placement and knot tying on a practice card.

It was not until almost a decade later that the first retrospective studies of robotic vasectomy reversal in people were published. Parekattil and colleagues reported the largest study to date, comparing 110 robotic and 45 conventional microsurgical cases performed by a single fellowship-trained microsurgeon.[14] Median obstructive interval was similar between the 2 groups (7 vs 6.5 years, respectively; $P=.3$), and 2-layer anastomotic technique was used in both approaches. Median operative time was shorter for the robotic VV compared with the microsurgical VV (97 vs 120 minutes, $P < .001$), although the authors excluded time required for setup of either the robot or the microscope. Patency (defined as sperm concentration >1 million/mL) was higher in the robotic group compared with the microsurgical group (96% vs 80%, $P=.02$), although there was no difference in pregnancy rates (65% vs 55%, *P*-value not reported). Kavoussi reported results from a smaller, retrospective study of 25 men who underwent robotic VV compared with 27 men who underwent conventional microsurgical VV.[15] The author found that there was no difference in operative time, anastomotic patency, or total motile sperm counts between the 2 groups.

Early adopters of the robotic approach also reported their experience with the robotic learning curve. As mentioned previously, Schiff and colleagues[16] found the robotic approach to be easily adoptable with 6 hours of laboratory-based practice, although the authors did not report any subsequent results in human studies. Parekattil and colleagues[17] noted that the initial 10 robotic cases had substantially higher operative times (range 150–180 minutes), needle bending, and suture breakage, all of which improved thereafter. Most recently, Kavoussi and colleagues reported a single-surgeon learning curve experience with robotic vasectomy reversal. The authors divided the surgeon's initial 100 cases into quartiles, finding that while high patency was achieved early in the learning curve, approximately 75 cases were required to achieve optimal operative and anastomotic time.[18] Santomauro and colleagues[19] examined trainee experience with the robotic approach, reporting on 20 patients in whom an experienced staff surgeon performed unilateral vasal reconstruction and a trainee performed the contralateral anastomosis. Mean anastomotic time was lower for staff surgeons compared with trainees, but the difference was not significant (37.6 vs 54 minutes, $P=.13$); however, the study was likely underpowered. In aggregate, these findings suggest that the learning curve for the robotic approach is short, at least for the well-trained microsurgeon. A summary of studies examining robotic-assisted vasal reconstruction is presented in **Table 2**.

From a technical perspective, there is no significant difference between the robotic and microsurgical approach for vasectomy reversal (**Fig. 1**). In either circumstance, conventional open identification, mobilization, and exteriorization of the vas deferens are performed, followed by vasal transection and examination of vasal fluid. The technical aspects of robotic vasal anastomosis are comparable to the microsurgical procedure. Small differences in technique have been described, but all utilize 9-0 and 10-0 suture to perform either single- or 2-layer anastomoses using conventional microsurgical principles.[14,15,20,21]

Procedures involving high or intra-abdominal vasal obstruction may be uniquely suited to the robotic approach, as the conventional microsurgical approach has limited access to the high-inguinal and intra-abdominal vas deferens. Najari and colleagues initially described robot-assisted intra-abdominal mobilization of the vas deferens for a patient with iatrogenic bilateral vasal obstruction secondary to a prior bilateral hernia repair. Abdominal mobilization allowed for a tension-free anastomosis that was externalized and performed microscopically. At 12-month follow-up, the patient had return of sperm to the ejaculate with normal concentration.[22] Trost and colleagues[23] subsequently described a purely intracorporeal robotic vasectomy reversal with an intra-abdominal vasal anastomosis in the setting of bilateral obstruction secondary to prior inguinal hernia repair with mesh. The authors demonstrated technical success with semen analysis at 8-week follow-up demonstrating normal sperm concentration.

At present, there is little consensus among reproductive urologists regarding the role for robotic vasectomy reversal.[24] Although the few retrospective studies demonstrate encouraging results with relatively short learning curves and high patency rates, there are no randomized trials comparing the 2 approaches. And despite the theoretical and subjective advantages of potentially decreased surgeon tremor and increased comfort, these metrics have not been rigorously studied.

ROBOTIC-ASSISTED MICROSURGICAL VARICOCELECTOMY

Varicoceles are found in up to 15% of all men[25] and in up to 35% of men presenting with

Table 2
Summary of animal and human studies examining robotic-assisted vasal reconstruction

Author	Year	Subjects	N	Study Characteristics	Significant Findings
Schoor, R[10]	2003	Rats	8	Ex vivo, combination of experienced and inexperienced microsurgeons performing vasal anastomosis	• Elimination of tremor • Enhanced surgeon comfort • Improved visual acuity • Robotic instruments sufficiently delicate for manipulation of vasal tissue and suture material
Kuang, W[11]	2004	Humans	10	Ex vivo, fresh vasa from radical cystectomy specimens, 5 RAVV vs 5 MAVV	• Mean operating time higher for RAVV • # of adverse haptic events higher for RAVV • Similar # of needle passes • No tremor in RAVV, minimal to moderate in MAVV • Equivalent vasal patency
Fleming, C[12]	2004	Humans	1	Case report of RAVV in a human subject	• Demonstrated feasibility in vivo
Schiff, J[16]	2004	Rats	24	In-vivo, randomized trial, 11 RAVV vs 10 MAVV and 12 RAVE vs 10 MAVE	• Shorter operative time for RAVV • Equivalent anastomotic patency • Fewer sperm granulomas with RAVV vs MAVV
Kuang, W[21]	2005	Rabbits	4	In vivo, 4 RAVV vs 4 MAVV	• Longer operative time for RAVV • Similar # of needle passes • No tremor for RAVV, minimal to moderate in MAVV
Santomauro, M[19]	2012	Humans	20	In vivo, case series of MAVV with either single (n = 17) or double (n = 3) anastomosis	• Mean operative time 187 min • Among 13 men with follow-up, 12 (92.3%) patent • Mean sperm concentration 14 million/mL, motility of 26.4%
Parekattil, S[14]	2012	Humans	155	Retrospective, case series	• Higher patency with RAVV (96%) vs MAVV (80%), P=.02 • No difference in total motile sperm count or pregnancy at 1-y
Trost, L[23]	2014	Humans	1	Case report of intracorporeal robotic vasovasostomy for bilateral vasal obstruction secondary to inguinal mesh	• Total operative time was 278 min. • No intraoperative or post-operative complications
Kavoussi, P[15]	2015	Humans	52	Retrospective, cohort study of RAVR (N = 25) vs MAVR (N = 27)	• No difference in operative time, though RAVR had longer anastomotic time (74 vs 63 min) • Equivalent patency • No difference in total motile sperm count operative time: no difference

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Table 2
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Author	Year	Subjects	N	Study Characteristics	Significant Findings
Marshall, M[20]	2017	Humans	79	Case series of RAVV with single-layer layer anastomosis	• Mean operative time was 192 min • Among men with follow-up (N = 42), 37 (88%) patent

Data from Refs.[10–12,14–16,19–21,23]

infertility.[26] In a proportion of these men, the varicocele may contribute to the impairment of semen parameters. Hypothesized pathophysiologic mechanisms include increased oxidative stress, testicular hypoperfusion, and alteration of the countercurrent heat exchange that is necessary for maintenance of optimal scrotal temperature resultant from the variocele.[27] Studies have shown improvements in semen parameters, pregnancy rate, and live birth rate following varicocele repair, and as such, the diagnosis and treatment of varicoceles have become crucial in the management of male infertility.[28–30]

Varicocele ligation can be performed by a retroperitoneal (high ligation via open incision or laparoscopic), inguinal, or subinguinal, approach. Some evidence suggests that the microsurgical subinguinal approach is associated with lower risks of recurrence and lower rates of postoperative complications including hydrocele and testicular atrophy, compared with other approaches.[31] Thus, rather than translating the laparoscopic approach to a robotic modification, initial reports of robotic-assisted varicocelectomy used the gold-standard subinguinal approach, leveraging the advantages of the robotic platform including excellent visualization and potential reduction of hand tremor in an extracorporeal fashion.[32] Additionally, the fourth robotic arm allows for Doppler mapping of the testicular arteries, minimizing the need for a surgical assistant (Fig. 2). Beyond these differences, the basic principles of robotic-

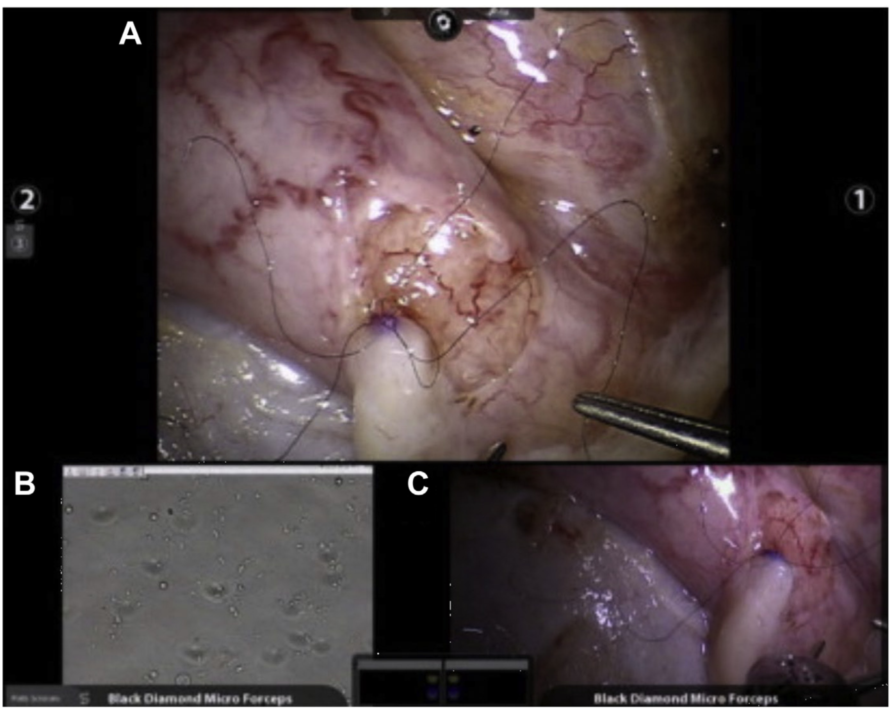

Fig. 1. Surgical technique for robotic assisted vasoepididymostomy.(*A*) Main view from da Vinci robotic platform. (*B*) Live image of andrology optical microscope. (*C*) View from the right side for enhanced magnification. (*From* Gudeloglu A., Brahmbhatt JV., Parekattil SJ. Robot-Assisted Microsurgery in Male Infertility and Andrology. Urologic Clinics of North America. 2014;41(4) 559–566; with permission.)

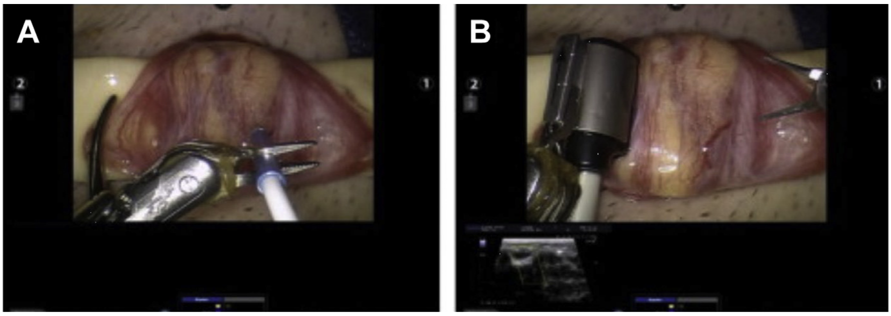

Fig. 2. Surgical technique for robotic assisted varicocelectomy. (*A*) Main view from da Vinci robotic platform of spermatic cord with audio micro-Doppler. (*B*) Video micro-Doppler. (*From* Gudeloglu A., Brahmbhatt JV., Parekattil SJ. Robot-Assisted Microsurgery in Male Infertility and Andrology. Urologic Clinics of North America. 2014;41(4) 559–566; with permission.)

assisted varicocelectomy are essentially unchanged from the conventional microsurgical approach.

Shu and colleagues reported the first series of robotic-assisted subinguinal varicocelectomy in 8 patients, demonstrating no difference in operative time compared with the conventional microsurgical approach, although the authors did not report outcomes such as postoperative complications, recurrence, or changes in semen parameters.[32] Parekattil and colleagues reported outcomes of robotic-assisted varicocelectomy in 154 patients with median follow-up of 22 months. Two patients (1.3%) had recurrences during follow-up; 1 patient (0.6%) developed a postoperative hydrocele, and 2 patients (1.3%) suffered postoperative hematomas.[33]

Most recently, McCullough and colleagues reported a single-surgeon experience in 140 consecutive men who underwent robotic-assisted varicocelectomy for subfertility. Mean operative time for robotic-assisted versus conventional microsurgical approach was 57 plus or minus 16 versus 49 plus or minus 13 minutes per side (no *P*-value provided). However, the authors also noted that mean robotic dock time for bilateral robotic-assisted approach was 39 plus or minus 9 minutes, a substantial addition to operative time that was not included in the operative time for each side. Median follow-up was not reported, but recurrence or failure rate was 9.7%, substantially higher than reported in the literature for the conventional approach. Other observed complications included hematoma (2.7%) and hydrocele (0.8%), with no incidence of testicular loss.[34] Postoperative improvements were noted in serum testosterone (median 145 ng/dL; $P<.01$) and sperm concentration (3.0 million/mL), although pregnancy and birth outcomes were not reported.

These studies are limited by their retrospective nature, single-institution experience, and lack of comparison groups. However, the reported outcomes are roughly comparable to historical data from the conventional microsurgical approach, although the higher recurrence rate reported by McCullough and colleagues does raise some concern. At this time, more rigorous studies are needed to meaningfully compare the robotic approach with the conventional subinguinal microsurgical approach. The authors' anecdotal observation is that the adoption of robot-assisted approaches for varicocele repair is currently limited.

ROBOT-ASSISTED MICRODENERVATION OF THE SPERMATIC CORD

Chronic groin or scrotal content pain (CGSCP) is a common condition, estimated to represent 2.5% of all urology clinic visits.[35] Defined as intermittent or constant pain or discomfort lasting more than 3 months in the groin, scrotum, testis, or epididymis, CGSCP can be frustrating for the patient and provider, as there is no universally accepted treatment algorithm.[36] Although some patients will have an attributable cause such as varicocele, infection, trauma, inflammation, or history of inguinal surgery, up to 50% of cases remain idiopathic.[37] In men refractory to medical management with nonsteroidal anti-inflammatory drugs, antibiotics, and neurotransmitter inhibitors, surgical options may be considered including microdenervation of the spermatic cord (MDSC), epididymectomy, and orchiectomy. Initially described by Levine and colleagues,[38] MDSC offers high success rates with a testis-sparing approach, rendering this an attractive surgical option for these men.

Similar to varicocelectomy, the robotic approach to MDSC is virtually identical to the conventional microsurgical procedure with the exception of robotic in lieu of microsurgical instrumentation. Parekettil and colleagues were first to describe robotic MDSC. In their initial series of 24 cases, they reported a mean operative time of 41 minutes (range 19–80 minutes). Complete resolution of pain was seen in 18 (75%) patients, with an additional 4 (17%) reporting greater than 50% improvement in pain and 2 patients having no benefit. No control group was described.[39] The authors noted that advantages of the robotic approach were elimination of surgeon tremor and decreased dependence on a surgical assistant because of the availability of the fourth robotic arm.

Most recently, the same group reported outcomes of robot-assisted MDSC in a large, single-institutional series of 772 patients with chronic orchalgia.[40] Median patient age was 41 years, and median postoperative follow-up was 24 months. Complete resolution of pain was observed in 426 (49%) cases, improvement in pain in 292 cases (34%), and persistent pain in 142 cases (17%). Complications included hydrocele (2.7%), wound infection (1.5%), and testicular artery injury (0.2%). Overall, these success rates are slightly lower than those with the conventional microsurgical approach, but postoperative complication rates are similar.[41]

ROBOT-ASSISTED MICRODISSECTION TESTICULAR SPERM EXTRACTION

Nonobstructive azoospermia (NOA) affects approximately 10% of men presenting with infertility.[42] As was the case for the aforementioned procedures, the operating microscope revolutionized treatment for NOA with the initial description of the microTESE (microdissection testicular sperm extraction) procedure in 1998 by Schlegel.[43] Under high-power magnification, individual seminiferous tubules more likely to harbor sperm are identified and selectively harvested for further processing, resulting in higher success rates than conventional TESE.[44]

The theoretic advantages of the robotic platform for microTESE are few. Parekattil and colleagues reported the only series of robot-assisted microTESE, which they suggested could facilitate simultaneous visualization of the operative field and the andrology laboratory microscope, thereby allowing the surgeon to continue operating while assessing the testicular tissue, resulting in improved operative workflow and efficiency. The authors also reported easier testicular tissue dissection and tissue handling, along with improved surgeon ergonomics, compared with conventional microTESE, although no objective data or comparisons were performed.[33] In their small series of 12 procedures, no complications were observed, and the authors found that robot-assisted microTESE was safe and effective. Patient characteristics, operative time, and sperm retrieval rates were not reported.

Certainly, additional studies are needed to assess the robotic approach to microTESE and determine its value added. The ability of the robotic platform to integrate video and imaging inputs from other sources does open the possibility for easy adoption of advanced imaging techniques for visualization of seminiferous tubules and sperm, should these become clinically available. For now, the data supporting this approach are limited.

THE FUTURE OF ROBOTIC SURGERY FOR MALE INFERTILITY

Although the robotic platform has been rapidly adopted by other urologic subspecialties, it has not yet taken hold among reproductive urologists. The paucity of data on robot-assisted male infertility surgery and the authors' anecdotal experience suggest that the robotic approach is rarely utilized by most reproductive urologists. Despite the theoretic benefits of robotic surgery, the outcomes to date have not justified its widespread use.

The reasons for low utilization of robotic surgery in this field are likely multifactorial. First, as mentioned previously, the data examining the approach are sparse. For each of the procedures described, the data are limited to case series. Where advantages of the robotic approach are posited (eg, better visualization or surgeon ergonomics), no studies have attempted to measure these outcomes rigorously. The few studies that have shown equivalent outcomes to the conventional microsurgical approaches will, at best, lead toward noninferiority of the robotic platform. However, this is an insufficient impetus for a paradigm shift in surgical approach for male infertility.

Second, traditional microsurgeons have remained skeptical regarding the delicate tissue handling capabilities of the robotic approach. Some have pointed to the lack of haptic feedback and dedicated microsurgical robotic instruments as limitations of the robotic approach, and additional studies are needed to examine the difference in tissue handling across platforms. Additionally, although early studies suggest relatively quick learning with the robotic approach, surgeon experience and comfort with the traditional microscope may limit widespread adaptability of the robot.

Third, costs have also been touted as a substantial drawback of robotic surgery. Initial capital investment for acquisition of a surgical robot can exceed that of an operating microscope by a factor of 10, which does not account for the high disposable costs of the robotic platform that are virtually nonexistent with the operating microscope.[45] Parekattil and colleagues[33] noted that the only path toward financial viability for the robotic model is to dramatically increase case volume. The authors found that the robotic platform almost doubled their operative efficiency, which justified the increased robotic costs. However, operative efficiency is not the only driver of patient volume. Some urologists may not have sufficient case volume (whether because of the nature their practice, size of catchment area, or other factors) to increase operative volume. In such instances, the robotic investment may not be financially viable. Alternatively, some reproductive urologists may operate within a health care system already in possession of a surgical robot, in which case the added use costs would be substantially less.

Beyond these concerns, the more recent arrival of video microsurgery for male infertility, although in its infancy, has the potential to undermine and outpace the potential advantages of robotic surgery in this specialty. Video microsurgery employs a heads-up approach, combining 3-dimensional imaging with 4K video output to provide a laparoscopy-like experience with high magnification and high-quality visualization.[46] This approach maintains the haptic feedback and delicate tissue-handling capabilities of traditional microsurgery while improving surgeon ergonomics and visualization. Like the robotic platform, it has the potential to integrate advanced imaging techniques with simultaneous video input, should these technologies arise. Although video microsurgery does not reduce surgeon tremor or obviate the need for a surgical assistant, it does have the potential to substantially improve on the conventional microsurgical experience. Importantly, the initial capital investment and ongoing disposable costs for video microsurgery are substantially lower than those for robotics.[45]

In order for robotic surgery to take hold and gain widespread adoption, multicenter, randomized trials are needed. The obstacles to performing these trials are many, not the least of which is the small number of centers currently performing this type of surgery. Moreover, other techniques, such as video microsurgery, that offer greater technical advantages have the potential to leapfrog robotic surgery for male infertility. Although the robotic platform offers potential added benefits for male infertility, rigorous clinical trials are needed to compare outcomes and costs to those of other surgical platforms with validated outcomes. In the meantime, the evidence does not support the postulated incremental technical benefits justifying the substantial barriers to adoption.

DISCLOSURE

The authors have nothing to disclose.

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