ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:

‘’ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,

ΡΟΜΠΟΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ ΚΑΙ ΤΗΛΕΧΕΙΡΟΥΡΓΙΚΗ’’

ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ: ΡΟΜΠΟΤΙΚΑ ΥΠΟΒΟΗΘΟΥΜΕΝΗ ΜΙΚΡΟΧΕΙΡΟΥΡΓΙΚΗ ΣΤΗΝ ΑΝΔΡΟΛΟΓΙΑ: ΜΙΑ ΣΥΣΤΗΜΑΤΙΚΗ ΑΝΑΣΚΟΠΗΣΗ

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ROBOTIC-ASSISTED MICROSURGERY IN ANDROLOGY: A SYSTEMATIC REVIEW

POSTGRADUATE STUDENT:

DOUROUMIS KONSTANTINOS

A.M.: 20181024

SUPERVISOR: PROFESSOR KONSTANTINOS STRAVODIMOS

ATHENS

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Περίληψη

Η ρομποτική χειρουργική είναι η πρώτη επιλογή σε πολλούς τομείς της ουρολογίας. Σε αυτή τη συστηματική ανασκόπηση, στοχεύουμε να αναφέρουμε τη χρήση της στην ανδρολογία και να αξιολογήσουμε τυχόν πλεονεκτήματα. Διεξήχθη μια συστηματική αναζήτηση των βάσεων δεδομένων PubMed και Cochrane Library, προκειμένω να εντοπιστούν άρθρα που αναφέρονται στη ρομποτικά υποβοηθούμενη μικροχειρουργική στην ανδρολογία. Η στρατηγική αναζήτησης ήταν σύμφωνη με τις κατευθυντήριες οδηγίες των Προτιμώμενων Στοιχείων Αναφοράς για Συστηματικές Ανασκοπήσεις και Μετα-αναλύσεις (PRISMA) και το Εγχειρίδιο Cochrane. Στη συνέχεια, τα άρθρα εξετάστηκαν από δύο συγγραφείς. Πραγματοποιήθηκε ποιοτική ανάλυση των άρθρων που πληρούσαν τα κριτήρια συμπερίληψης. Τριάντα ένα άρθρα που πληρούσαν τα κριτήρια συμπερίληψης εξετάστηκαν. Τα πρώτα αποτελέσματα για την ρομποτικά υποβοηθούμενη αναστόμωση του σπερματικού τόνου (RAVV) είναι ενθαρρυντικά καθώς επιτεύχθηκαν εξαιρετικά ποσοστά βατότητας, σύντομοι χρόνοι επέμβασης και καμπύλες εκμάθησης. Είναι ενδιαφέρον ότι τα ποσοστά βατότητας ήταν μεγαλύτερα σε ορισμένες σειρές περιπτώσεων για τη RAVV παρά για τη μικροχειρουργική αναστόμωση του σπερματικού τόνου, με στατιστικά σημαντική διαφορά. Επιπλέον, το ρομποτικό σύστημα έχει αποδειχθεί ότι είναι πολύ χρήσιμο στην παράκαμψη των ινωτικών αλλαγών των ιστών σε περιπτώσεις ιατρογενών τραυματισμών των αγγείων, δυσκολίες που εμφανίζονται με την παραδοσιακή μικροχειρουργική. Επιπλέον, η εφαρμογή της ρομποτικά υποβοηθούμενης μικροχειρουργικής έχει αποδειχθεί δυνατή για την αποκατάσταση κιρσοκήλης και τη μικροχειρουργική απονεύρωση του σπερματικού τόνου, με αποδεκτή βελτίωση στις παραμέτρους του σπέρματος και στον πόνο, αντίστοιχα. Τα τρέχοντα στοιχεία δείχνουν ότι υπάρχουν πιθανά πλεονεκτήματα από τη χρήση των ρομποτικών συστημάτων στην ανδρολογία. Ωστόσο, για να ενσωματωθεί η ρομποτική χειρουργική στην καθημερινότητα των ανδρολόγων, απαιτούνται μεγάλες, πολυκεντρικές τυχαιοποιημένες μελέτες. Όσο τα συστήματα ρομποτικής χειρουργικής χρησιμοποιούνται όλο και περισσότερο στην καθημερινή ουρολογική πρακτική, είναι λογικό να πιστεύει κανείς ότι θα βρουν τη θέση τους και στην ανδρολογία.

Λέξεις κλειδία: ανδρολογία, ανδρική υπογονιμότητα, ρομποτικές χειρουργικές επεμβάσεις, κιρσοκήλη, αναστόμωση σπερματικού πόρου

Abstract

Robot-assisted surgery is the gold standard of treatment in many fields of urology. In this systematic review, we aim to report its usage in andrology and to evaluate any advantages. A systematic search of the PubMed and Cochrane Library databases was conducted to identify articles referring to robotic-assisted microsurgery in andrology. The search strategy was in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook. The articles were then reviewed by two authors. A qualitative analysis of the articles that met the inclusion criteria was performed. Thirty-one articles that met the inclusion criteria were reviewed. The first results for robot-assisted vasovasostomy (RAVV) are encouraging as excellent patency rates, short operative times, and learning curves were achieved. Interestingly, patency rates were greater in some case series for RAVV than for microsurgical vasovasostomy, with a statistically significant difference. In addition, robot has been shown to be of great use in bypassing fibrotic changes in cases of iatrogenic vasal injuries, difficulties encountered with traditional microsurgery. In addition, the feasibility of robot-assisted microsurgery has been proven for varicocelectomy and microsurgical denervation of the spermatic cord, with acceptable improvement in sperm parameters and pain, respectively. The current evidence suggests that there are potential advantages of the use of robots in andrology. However, for robotic surgery to become incorporated into the daily use of the andrologists, large, multicenter randomized trials are needed. As robotics systems are becoming standard in urology practice, it is reasonable for one to believe that they will also find their place in andrology.

Keywords: andrology; male infertility; robotic surgical procedures; varicocele; vasovasostomy

Ευχαριστίες

Ευχαριστώ θερμά όλους τους καθηγητές, διδάσκοντες και το προσωπικό του Π.Μ.Σ. ‘’Ελάχιστα Επεμβατική Χειρουργική, Ρομποτική Χειρουργική και Τηλεχειρουργική’’ για την ευκαιρία να εμβαθύνω στην ελάχιστα επεμβατική χειρουργική και να αποκτήσω ένα ικανό επίπεδο γνώσης, τόσο θεωρητικό όσο και πρακτικό.

Θα επιθυμούσα να ευχαριστήσω ιδιαιτέρως τον επιβλέποντα της διπλωματικής Καθηγητή Ουρολογίας κ. Κωνσταντίνο Στραβοδήμο, τον Καθηγητή Χειρουργικής κ. Νικόλαο Νικητέα, τον Καθηγητή Χειρουργικής κ. Δημήτριο Δημητρούλη, τον Αναπληρωτή Καθηγητή Χειρουργικής κ. Γεράσιμο Τσουρούφλη, τον επιστημονικό συνεργάτη της Α’ Ουρολογικής Κλινικής ΕΚΠΑ κ. Παναγιώτη Λεβή και τον συντονιστή του Π.Μ.Σ κ. Ελευθέριο Σπάρταλη για τη συμβολή τους στην ανάπτυξη και ολοκλήρωση αυτής της διπλωματικής εργασίας.

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Επίσης, ευχαριστώ τους δασκάλους μου, τα μέλη ΔΕΠ της Α’ Ουρολογικής Κλινικής ΕΚΠΑ: Μητρόπουλο Διονύσιο, Στραβοδήμο Κωνσταντίνο, Αλαμανή Χρήστο, Αναστασίου Ιωάννη, Αδαμάκη Ιωάννη και Φραγκιάδη Εύαγγελο που συμβάλλουν καθημερινά στην εξέλιξη μου ως άνθρωπος, ουρολόγος και επιστήμονας.

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Introduction

Male infertility is a significant factor in infertile couples, as it accounts for the sole cause in one-fifth of cases. In addition, in almost 40% of cases, both male and female disorders cause infertility.[1] Although in nearly one-third of the cases, no male factor is found (idiopathic male infertility), a significant number of these patients have surgically correctable disorders, such as varicocele and vasal obstruction.[2] In these patients, the microsurgical approach is the standard of care.[2,3] Microsurgery has also revolutionized the treatment of patients with nonobstructive azoospermia with the development of microsurgical testicular sperm extraction (micro-TESE).[4]

Robotic surgery is used on a large scale in urology, with prostatectomy being the first procedure to be performed in 2000.[5] Radical cystectomy and partial nephrectomy followed.[6,7] Robotic surgery has been utilized in some other fields of microsurgery, such as ophthalmology and plastic surgery.[8,9] Potential advantages of the incorporation of robotic platforms in microsurgery are the elimination of surgeon's tremor and stability improvement, better surgeon ergonomics, scalability of motion, multi-input visual interphases with up to three simultaneous visual views, enhanced magnification, and the ability to manipulate three surgical instruments and cameras simultaneously.[10] These potential advantages led to the initial robot-assisted andrological procedures.

The first reported procedure was performed by Kuang et al. [11] in 2004 in an ex vivo vasovasostomy model, which highlighted the feasibility of robot-assisted vasovasostomy (RAVV). The first randomized prospective study was reported by Schiff et al.,[12] who compared RAVV and pure microsurgical vasovasostomy (MVV) in a rat model. The results show decreased operation time and sperm granuloma formation at the anastomosis, showing superiority for RAVV. After these advances, robotic microsurgery for vasovasostomy,[13] subinguinal varicocelectomy, and microsurgical denervation of the spermatic cord (RMDSC) for chronic orchialgia in vivo have been reported.[14,15]

This review aims to identify up-to-date reported literature on the use of robotic assistance in andrology. The study also aims to compare robotic and standard microsurgery in urology, evaluating any possible advantages and its feasibility.

Materials and Methods

The search strategy was constructed in line with the Cochrane Handbook[16] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17] A database search was conducted to identify articles describing robot-assisted andrological procedures.

PubMed (1996–present) and Cochrane Library (1989–present) electronic databases were reviewed up to May 2021.

Using the Medical Subject Headings (MeSH) database of PubMed, we found the MeSH terms for the keywords. All synonyms as free text and MeSH terms for each component were combined using the Boolean operator "OR". Then, the different terms were combined using the Boolean "AND". The search strategy can be found in Table 1 and Box 1.

Search results from the databases were uploaded to Mendeley Reference Management Software (version 2.75.0, Elsevier, Amsterdam, The Netherlands), and duplicate records were removed. Two independent reviewers (KD and PKL) examined all search results, and according to their titles and abstracts, 780 articles were excluded. The authors examined the full texts of relevant titles and abstracts independently. Of the 87 articles assessed, 31 were included in the qualitative synthesis. Disagreements between authors were resolved by a third reviewer (KS). References were checked and added if appropriate (Figure 1).

The criteria for a study to be considered eligible for qualitative synthesis were as follows: (1) publication in the English language; (2) adult participants-patients (age ≥18 years); (3) study types including case reports, case–control studies, case cohorts and randomized control trials, both prospective and retrospective; (4) no limitation on the publication date; (5) only clinical applications (exclusion of articles with applications involving animal and ex vivo models); and (6) studies reporting the use of a robotic surgical system for andrology cases. From the included studies, data were collected regarding the authors, publication date, type and number of operations performed, and outcomes. All data were extracted and organized using Microsoft Office (Microsoft, Redmond, Washington, DC, USA).

Results

A total of 31 papers were included in this review. The studies were divided into groups based on the surgical procedure.

Robot-assisted microsurgical vasovasostomy and vasoepididymostomy

Obstructive azoospermia is defined as the absence of spermatozoa in the sediment of a centrifuged sample of ejaculate due to obstruction.[2,18] It accounts for 20%–40% of patients with azoospermia.[19] Obstruction can be congenital (i.e., congenital bilateral absence of the vas deferens, idiopathic epididymal obstruction, etc.) or acquired (vasectomy, infection, trauma, iatrogenic injury, etc.).[20] Treatment options are (1) MVV or microsurgical vasoepididymostomy (MVE) for epididymal or vasal obstruction, respectively (in case the female partner's ovarian reserve is good), or (2) sperm retrieval techniques in all other cases.[2] The patency rates of MVV and MVE are 99% and 65%, respectively.[21] However, these procedures are technically challenging, as they demand manual dexterity, steadiness of movement and coordination,[22] along with a skilled microsurgical assistant.

Robot-assisted microsurgery was introduced to overcome these challenges. Initial reports included ex vivo and animal models. These reports highlighted a short learning curve with an easy transition for microsurgeons, significantly less operation time, and less formation of sperm granuloma on the vasovasostomy anastomosis site than conventional microsurgery. Furthermore, the elimination of hand tremors and excellent patency rates was observed.[11,12,23,24]

Fleming first reported RAVV in two cases of bilateral robot-assisted vasovasostomies.[13] The author reported the elimination of normal physiological hand tremor, a greater ease and precision of suture placement, a shorter learning curve than microsurgical techniques and excellent patency results.[13] In 2007, De Naeyer *et al*.[25] reported a case of robot-assisted vasectomy reversal without intraoperative problems (no loose stitches, no broken sutures, etc.) or postoperative complications. In the 3-month follow-up period, semen analysis showed 120×10^6 viable spermatozoa per ml, which confirmed patency.

Parekattil *et al*.[26] reported their first cases in 2009, with excellent results for the RAVV group, even in patients with many years (7, 18, and 19 years) postvasectomy. The same group compared, in 2010, 20 RAVV and 7 MVV cases performed by a single microsurgeon.[27] The operation time for RAVV decreased significantly after the first nine cases (150–180 min to 65–120 min). The authors also highlighted the significant (P = 0.04) improvement in early semen analysis and decrease in the mean operative time with the assistance of the Da Vinci® robotic system.[27]

Parekattil and Brahmbhatt followed with a prospective control study of a clinical database, with 123 patients undergoing vasectomy reversal (78 of robot assisted and 45 of microsurgery).[28] Thirty of these cases were robot-assisted vasoepididymostomies (RAVE), and seventeen were MVE. The operative time was significantly shorter for both RAVV and RAVE than MVV and MVE. The setup time for the robot, after a certain number of cases, was comparable to that of the microscope. The need for a skilled microsurgical assistant was eradicated because the surgeon could utilize the additional robotic arm.[28]

The same group reported similar results in another study comparing robotic and microsurgical vasectomy reversal. They documented a significant difference in operation time for both vasovasostomy (97 min vs 120 min, P = 0.0003) and vasoepididymostomy (120 min vs 150 min, *P* = 0.0008) in favor of robotic assistance. A significant difference was reported for postoperative sperm count recovery but not for the mean postoperative total mobile sperm count. Patency rates were significantly greater for RAVV (96% vs 80%, *P* = 0.002). Pregnancy rates 1 year after surgery were 65% for the RAVV group and 55% for the MVV group.[29] Gudeloglu *et al.*[30] and Kavoussi[31] reported similar results. In addition, Gudeloglu *et al.*[30] reported 55% patency rates after RAVE. It should be noted that patency rates for MVE range from 39% to 92%. The level at which MVE is performed and the technical experience of the surgeons are two major factors for its success.[32,33]

Santomauro *et al.*[34] performed robotic vasovasostomy using both one-layer and two-layer techniques. The anastomosis was performed by experienced staff on one side, followed by the resident on the opposite side. There was no statistically significant difference in the mean operation time between the two groups (37.6 min for experienced surgeons and 54 min for residents, *P* = 0.13). Twelve of the 13 patients were patent (92.3%) in the follow-up (as evidenced by sperm in the ejaculate). That study showed the feasibility and effectiveness of the one-layer technique, along with a relatively fast learning curve.[34] Furthermore, in 2017, Marshall *et al.*[35] reported similar results for single-layer RAVV. Sixty patients underwent single-layer anastomosis. Eighty-eight percent of anastomoses were patent, and 11% of operations (7/60) had low-grade complications.

Furthermore, robotic-assisted microsurgery enables the surgeon to operate in body locations that are difficult to access with open microsurgery. Trost *et al.*[36] reported the first intracorporeal RAVV for the treatment of a patient with vasal obstruction following bilateral inguinal hernia repair with mesh placement. Robotic assistance helped surgeons bypass fibrotic changes that developed in the inguinal canal after herniorrhaphy. In addition, through RAVV, surgeons were able to perform minimal incisions instead of the standard extended bilateral inguinal incisions required for this procedure.[36] Another novel application of RAVV was described by Barazani *et al.*,[37] who performed intra-abdominal RAVV in a case of obstructive azoospermia following laparoscopic vasectomy. Robot-assisted laparoscopy was used for the mobilization of the vas deferens and robotic microsurgery for vasovasostomy.

Finally, Brahmbhatt *et al.*[38] evaluated the use of RAVV for postvasectomy pain syndrome (PVPS). The group used a pain impact questionnaire (PIQ-6; range: 40–78) and visual analog pain scale (VAPS; range: 0–10) to assess the pain. They performed 22 RAVV and 2 RAVE procedures for PVPS. The patency rate was 94.1% (16 of 17 patients), and improvement in the PIQ-6 score was found in 85.0% (17 of 20 patients), with a mean follow-up of 4.5 (standard deviation [s.d.]: 0.6) months. A significant decrease was found in PIQ-6 and VAPS scores immediately after surgery and at the 6-month follow-up.[38] This study shows that RAVV is a possible technique for PVPS management. A summary of the studies referring to robotic-assisted vasovasostomy is provided in Table 2.

Robot-assisted microsurgical varicocelectomy

Varicocele is considered a major factor of male infertility. A 1992 study showed a clear association between varicocele and impairment in testicular function.[39] Varicocelectomy leads to significant improvements in semen parameters, regardless of the surgical technique applied, as shown in a 2007 meta-analysis.[40] Çayan *et al.*[41] compared various treatment approaches for varicocele repair in 2009. They concluded that the microsurgical subinguinal approach (MVx) has higher spontaneous pregnancy rates, fewer recurrences, and lower complication rates than other techniques.

The first varicocelectomy performed with the assistance of the Da Vinci® robotic system was performed by Corcione *et al.*[42] in 2004. They performed two robot-assisted laparoscopic intra-abdominal varicocelectomies among 32 various robot-assisted laparoscopic procedures in an effort to report preliminary data about the advantages and limitations of robot-assisted laparoscopy. Shu *et al.*[14] first described robot-assisted microsurgical inguinal varicocelectomy (RAVx) in 2008. The group compared it with microsurgical varicocelectomy. No significant differences were found in operating time (even with their limited experience in RAVx). They also described the elimination of hand tremors as an advantage of RAVx.[14]

Parekattil and Brahmbhatt[28] performed a prospective randomized controlled trial of microsurgery versus robotic-assisted subinguinal varicocelectomy in a canine model. Significant differences were found in operation times (per side) in favor of RAVx (9.5 min vs 12 min, $P = 0.04$). The robot and microscope setup times were comparable. No vessel injuries or knot failures were reported. The same group published five updates of reviews of their prospective clinical database. Patients treated with varicocelectomy were men with grade two or three varicocele and one of the following: (1) azoospermia, (2) oligospermia, or (3) chronic orchialgia with or without oligospermia who failed all conservative management options. The median operation time was gradually shorter after the initial case, with 20 min reported in their fourth (181 cases) and fifth (238 cases) updates.[10,15,28,30,43,44] The median follow-up was 22 (range: 1–48) months, as stated in the fourth paper. The percentage of oligospermic men with significant improvement in sperm parameters (count and/or motility) was 75%–77% in all studies, even in the initial cases. Twenty-eight percent of patients with azoospermia presented with oligospermia after repair. Ninety-two percents of patients who underwent RAVx for testicular pain (along with robotic denervation of the spermatic cord in some cases) presented a significant reduction in pain. Only three complications occurred after 181 procedures, two scrotal hematomas and one hydrocele, both being treated conservatively. Only two varicocele recurrences or persistence were reported.[10,15,28,30,43,44] Furthermore, the same group published the results of RAVx in addition to robot-assisted microsurgical denervation of the spermatic cord in 319 patients with varicocele and orchialgia. Improved sperm parameters were found in 65% of patients, and a significant reduction in pain was reported by 73% of them.45 The above studies indicate the feasibility, efficacy, and safety of robot-assisted microsurgical subinguinal varicocelectomy.

McCullough *et al.* [46] published a retrospective review of 258 RAVx procedures (in 140 patients), reporting the effect of RAVx on semen parameters and testosterone levels. The (mean ± s.d.) operative time per side was 49 ± 13 min for robotic varicocelectomy and 57 ± 16 min for microsurgical varicocelectomy. A learning curve was reached after 15 cases. A statistically significant increase was observed in the median total and free testosterone levels ($P < 0.0001$), median sperm concentration ($P < 0.03$), and median testicular volume at the 3-month follow-up ($P < 0.0006$ for right testicle volume and $P < 0.0001$ for left testicle volume). Recurrence of varicocele was reported in 9.6% of cases, higher than that in previous reports. The authors noticed that this higher recurrence was due to the way they defined recurrence (any measurable postoperative retrograde flow).[46] A summary of the studies referring to robotic-assisted varicocelectomy is provided in Table 3.

Robot-assisted microsurgical denervation of the spermatic cord

Chronic orchialgia is intermittent or constant, unilateral or bilateral testicular pain that significantly interferes with patients' daily activities and lasts more than 3 months.[47] This pain may involve the epididymis, paratesticular structures, and the spermatic cord.[48] Etiological factors include trauma, infection, hydrocele, torsion, varicocele, vasectomy, and hernia repair. In almost 25% of patients, no etiological factor can be found (idiopathic).[47,49,50] First-line treatment consists of a combination of antibiotics, analgesics, and anti-inflammatory drugs. Surgical treatment is indicated after conservative management has failed. Microsurgical denervation of the spermatic cord (MDSC) has emerged as the treatment of choice over orchiectomy and epididymectomy. MDSCs allow testicular preservation and offer high success rates.[51,52] Furthermore, Parekattil *et al.* [53] identified Wallerian degeneration in nerve bundles located at the cremaster muscle, perivasal, and periarterial/lipomatous area tissues. These findings help to minimize the ligation area and preserve the bulk of the spermatic cord without compromising MDSC efficacy.

Parekattil *et al.*[10,15] developed a targeted approach involving robot-assisted microsurgical denervation of the spermatic cord (RMDSC). They have published seven updates of their results (Table 4).[10,15,28,30,43,54,55] Patient selection criteria were chronic testicular pain (>6 months), failure of conservative pain management treatments, no findings on neurologic and urologic workup, and complete temporary resolution of pain after spermatic cord block with local anesthetic agents. In the latest published report of their clinical database, the group reviewed

860 RMDSC cases (October 2008–July 2016). The median robotic console time was 20 (range: 15–80) min. Complete resolution of pain was achieved in 462 cases (49%), and a decrease above 50% (using PIQ-6 and VAS scores) was achieved in 292 (34%) cases. In 142 (17%) patients, the pain persisted. A remarkable finding was a significant reduction in pain at follow-up (67% of patients at 6 months, 68% at 1 year, 77% at 2 years, 86% at 3 years, and 83% at 4 years). The median operative time was 41 min and 37 min for the initial cases and decreased to 20 min in the final update. Complete resolution of pain was significantly lower in the final update (49%) than in previous reports (70.5%–75%). The complications were 2 cases of testicular artery injury, 1 case of testicular ischemia, 1 case of vasal injury, 4 cases of seroma, 23 cases of hematoma, 24 cases of wound infection and dehiscence, 2 cases of penile swelling/pain, 1 case of pulmonary embolus, 1 case of hydrocele, 1 case of urinary retention, 1 case of port site pain, 1 case of referred leg pain, and 1 case of port site bleeding. Testicular artery injuries were identified and repaired intraoperatively, with no long-term testicular atrophy identified. Testicular ischemia was noted in a case with multiple previous pelvic and groin injuries and surgeries. The work of this group[10,15,28,30,43,54,55] illustrates the feasibility and effectiveness of targeted RMDSCs in the treatment of chronic testicular and scrotal pain.

In addition, Parekattil and Cohen[43] performed robotic microsurgical ligation of the genitofemoral and inferior hypogastric nerve fibers above the internal inguinal ring in 30 patients with persistent pain after microsurgical denervation of the spermatic cord and patients with phantom groin pain following orchiectomy. The operation was performed using an abdominal approach, and five of the cases were conducted using a single-port approach. Pain was eliminated in 60% (18/30) of the cases and was reduced by more than 50% in 13% (4/30) after 1 month of follow-up. The mean operative time was 10 (range: 5–30) min.

Robot-assisted microscopic testicular sperm extraction

Nonobstructive azoospermia (NOA) is the absence of sperm in a semen analysis after centrifugation in at least two consecutive sperm analyses.[56] NOA is caused by primary testicular dysfunction or dysfunction of the hypothalamus–pituitary–gonadal axis. Sperm retrieval is considered in men who are candidates for assisted reproductive technology (ART) protocols. The gold standard surgical approach is testicular sperm extraction (TESE).[2] Microsurgical TESE (mTESE) is performed under a surgical microscope and has 1.5 higher retrieval rates than conventional TESE.[57]

When conducting our search, only two references regarding robot-assisted TESE (ROTESE) were published, one of which was an animal model study. In the animal model study, ROTESE appeared comparable to open TESE in color spot detection (canine testicles were injected with different color dye spots at random locations).[28] Parekattil and Gudeloglu[10] performed 12

ROTESE procedures between 2009 and 2012 without any reported complications. The authors reported that tissue handling and dissection were slightly easier and ergonomic with robotic assistance.

Discussion

Robotic surgery is being performed on a great scale in urology. Its advantages have been well reported and include reduced blood loss, reduced postoperative pain, and a shorter hospital stay. This is not the case for its use in andrology, with only a handful of centers reporting robot-assisted surgical procedures for male infertility and chronic orchialgia. This situation may be due to the high cost of the robot. Parekattil and Gudeloglu[10] found that the cost of robotic vasovasostomy can be reduced by 40%–50% in comparison to standard microscopic surgery. The enhanced surgical efficiency and decrease in surgical fatigue allowed the authors to perform 3–4 procedures with robot assistance in contrast to 1–2 microsurgical cases in the same amount of time. The authors highlighted that this model is applicable only in high-volume centers. It is important to keep in mind that the robotic system can be shared by all surgical units in a medical center, and hence, the cost is allocated accordingly. On the other hand, the microscope is used less frequently unless there is a high-volume infertility practice. In addition, the microscope as a unit is less expensive than the robotic system and is independent of expensive consumables. Furthermore, its cost can be shared by other departments (ophthalmology and neurosurgery). The aim of this article, however, is not to compare head-to-head the costs of robotic microsurgery versus conventional microsurgery but to examine the feasibility and potential advantages of the robotic systems in the field of andrology. This subject can therefore be addressed in more detail in the future.

Elimination of tremors and greater ease of suture placement allows for a short learning curve. Fleming mentions that the learning curve is shorter than that of traditional microsurgery. For experienced microsurgeons, the curve is nonexistent.[13] This evidence is strengthened by the comparison in vasectomy reversal anastomosis between experienced surgeons and residents.[34] From an examination of the available studies, we could not find a precise number of operations a surgeon has to perform for the robotic microsurgery expertise to be achieved. As an increased number of residents are now trained in robotic systems and are familiar with them, it is safe to believe that the learning curve will be shorter for them than that for traditional microsurgery.

The first results of RAVV are encouraging, as excellent patency rates, short operative times, and short learning curves were achieved. In addition, robots have been shown to be of great use in bypassing fibrotic changes in cases of iatrogenic vasal injuries. In addition, varicocelectomy and microsurgical denervation of the spermatic cord seems feasible with robotic assistance, with acceptable improvement in sperm parameters and pain, respectively. For micro-TESE, we found only one article about the in vivo application of the Da Vinci® robotic system, which showed the feasibility of the procedure.

Our review comes with limitations. The protocol was not registered in any database before it was conducted. In addition, the search was conducted only in the PubMed and Cochrane Library databases.

This is a systematic review of the role of robotic surgery in andrology. As one can notice, the data are limited. In addition, all included articles were case reports or series. Another point is that the last reported cases were published in 2017, 2018, and 2018 for RAVV, RAVx, and RMDSC, respectively.[10,46,55]

In conclusion, the current evidence suggests that there are potential advantages in the use of robots in andrology. However, for robotic surgery to become incorporated into the daily use of the andrologist large, multicenter randomized trials are needed. As robotics systems are becoming a standard in urology practice, it is reasonable for one to believe that they will also find their place in the andrology, as more urologists are becoming familiar with these devices.

Author contributions

KD conceived the study, performed the search, reviewed the search results, and drafted the manuscript. PKL reviewed the search results and helped draft the manuscript. KS resolved disagreements between the two reviewers and participated in their design and coordination. ES participated in its design and helped draft the manuscript. GT, DD, and NIN participated in its design and coordination. All authors read and approved the final manuscript.

Competing interests

All authors declare no competing interests.

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Appendix

PICO component	*Term*	*Synonym*	*MeSH term*
Patient	Andrology	Male infertility Chronic orchialgia Orchialgia Varicocele Varicocelectomy Vasectomy reversal Vasoepididymostomy Vasovasostomy Testicular sperm retrieval TESE Micro-TESE Spermatic cord Spermatic cord denervation Sperm retrieval	Male infertility Andrology Varicocele Vasovasostomy Testicular diseases Spermatic cord Sperm retrieval Vas deferens
Intervention	Robotic surgery	Robotics Robot Robot-assisted Da Vinci® Robotic surgery	Robotics Robotic surgical procedures

PICO: patient, intervention, comparison, and outcome; MeSH: Medical Subject Headings; TESE: testicular sperm extraction; Micro-TESE: microsurgical testicular sperm extraction

Table 1: The search strategy

Search query

(((male infertility) OR chronic orchialgia)) OR Orchialgia)) OR varicocele)) OR varicocelectomy)) OR vasectomy reversal)) OR vasoepidydimostomy)) OR vasovasostomy)) OR testicular sperm retrieval)) OR TESE)) OR micro-TESE)) OR spermatic cord)) OR spermatic cord denervation)) OR sperm retrieval)) OR male infertility[MeSH])) OR andrology[MeSH])) OR varicocele[MeSH])) OR vasovasostomy[MeSH])) OR Testicular Diseases[MeSH])) OR spermatic cord[MeSH])) OR sperm retrieval[MeSH])))) OR vas deferens[MeSH])))) AND (((((((((((((robotics) OR robot)) OR robot-assisted)) OR Da-Vinci)) OR robotic surgery)) OR Robotic[MeSH])) OR Robotic Surgical Procedures[MeSH]))

Box 1: The search query in this review. MeSH: Medical Subject Headings; TESE: testicular sperm extraction.

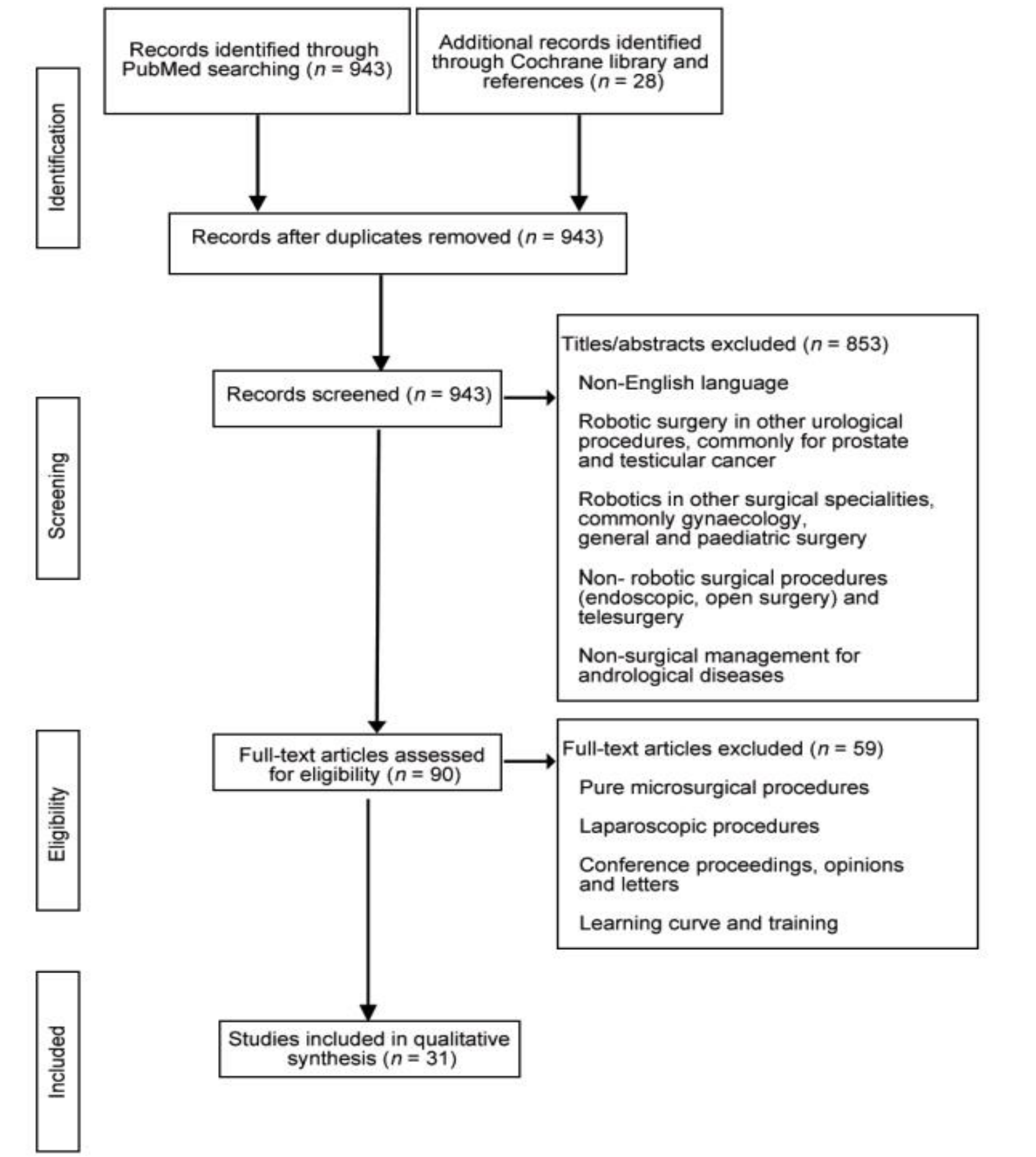

Figure 1: PRISMA flow diagram. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Study	Year	Study design	Operations performed	Outcomes reported
Fleming[13]	2004	Case series	2 bilateral RAVV	First *in vivo* human cases Elimination of tremor Ease and precision of suture placement Shorter learning curve Excellent patency rates
De Naeyer *et al.*[25]	2007	Case report	1 RAVV	OT: 120 min (80 min robotic time) No intraoperative or postoperative complications Patent anastomosis
Parekattil *et al.*[26]	2009	Case series	3 RAVV and 1 RAVE	RAVV successful 1 RAVV patient: 102×10^6 motile sperm per ml 1 month postoperation RAVE patient a few nonmotile sperm 6 months postoperation Better ergonomics and suture control
Parekattil *et al.*[27]	2010	Case series	20 RAVV and 7 MVV	Mean OT: RAVV 109 min *vs* MVV 128 min (P=0.09) All patients patent 2 months' postoperation Mean sperm count: RAVV 54×10^6 *vs* MVV 11×10^6 (P=0.04)
Parekattil and Brahmbhatt[28]	2011	Case series	78 robotic, 45 microsurgery 48 cases bilateral RAVV, 30 cases RAVE on at least one side 28 cases bilateral MVV and 17 cases MVE on at least one side	96% patency in RAVV, 80% in MVV (>1×10^6 sperm per high-power field) OT: RAVV 90 (range: 40–180) min, MVV 120 (range: 60–180) min, RAVE 120 (range: 60–180) min, MVE 150 (range: 120–240) min, set up not included Mean postoperative total motile sperm counts were not significantly higher in RAVV/RAVE versus MVV/MVE Rate of sperm return to the ejaculate after surgery was greater in RAVV/RAVE RAVV: 13×10^6 motile sperm per month (the slope of the mean sperm counts 2, 5, 9, and 12 months postoperatively), MVV: 3×10^6 motile sperm per month
Santomauro *et al.*[34]	2012	Case series	20 RAVV two-layer repair, 17 one-layer repair bilaterally and 2 epididymovasotomies on one side with a one-layer vasovasostomy on the contralateral side	Mean OT for vasal reconstruction: 37.6 min Mean OT: 185.8 min Two-layer repair mean operative time: 238 min One-layer anastomosis mean operative time: 182 min Mean sperm density: 14×10^6 ml^{-1}, with motility of 26.4%
Parekattil *et al.*[29]	2012	Case series	110 with robotic assistance, 45 pure microsurgical. 66 cases bilateral RAVV, 44 cases RAVE on at least one side, 28 cases bilateral MVV, and 17 cases MVE on at least one side	Patency rate (>1×10^6 sperm per ejaculate): RAVV 96% *vs* MVV 80% (P=0.02) Pregnancy rates (within 1 year postoperation): RAVV 65% *vs* MVV: 55% OT: RAVV 97 (range: 40–180) min *vs* MVV 129 (range: 60–180) min (P=0.0003) RAVE 120 (range: 60–180) min *vs* MVE 150 (range: 120–240) min (P=0.0008) Mean postoperative total motile sperm counts not significantly higher in RAVV/RAVE *vs* MVV/MVE Rate of postoperative sperm count recovery significantly greater in RAVV/RAVE
Brahmbhatt *et al.*[38]	2013	Case series	22 RAVV and 2 RAVE procedures for PVPS	Patency rate: 94.1% (16/17) Improved PIQ-6: 85.0% (17/20)
Gudeloglu *et al.*[30]	2014	Case series	RAVV (n=106), RAVE (n=74)	Median OT: RAVV 120 (range: 40–180) min, RAVE 150 (range: 60–210) min Patency rate (>1×10^6 sperm per ejaculate): RAVV 97%, RAVE 55%
Trost *et al.*[36]	2014	Case report	RAVV for the treatment of bilateral vasal obstruction occurring following bilateral inguinal hernia repairs with mesh placement	OT: 278 min No intraoperative or postoperative complications Semen analysis 8 weeks' postoperation demonstrated successful result
Barazani *et al.*[37]	2014	Case report	Robotic intra-abdominal vasectomy reversal	3 months' postoperation: sperm concentration of 30×10^6 sperm per ml Near complete resolution of the patient's chronic intermittent pelvic pain Physical examination demonstrated bilaterally flat epididimydes
Kavoussi[31]	2015	Cohort study	27 MVR and 25 RAVR procedures	0–8 years from the time of vasectomy: no statistically significant difference in patency rates at 6 weeks' post-VR, robotic group 100% patency rate, microsurgical group had an 89% patency rate No statistically significant difference in patency rates in men who were 9–15 years from the time of vasectomy, in the >15 years' postvasectomy group, or in overall patency rates regardless of obstructive interval All vasoepididymostomies were patent in both groups No difference between the microsurgical and robot-assisted groups in mean sperm concentration or total motile count upon semen analysis 6 weeks' post-VR There were no men in either group who presented immotile sperm in the semen, indicative of stricture Mean OT: MVR 141 min *vs* RAVR 150 min (P=0.3) Mean anastomosis time: MVR 64 min *vs* RAVR 74 min (P=0.009) Vasoepididymostomy mean anastomosis time: MVR 74 min *vs* RAVR 72 min
Marshall *et al.*[35]	2017	Case series	RAVV using a single-layer anastomosis	Mean OT: 192 min 88% (37/42) had return of sperm

RAVV: robot-assisted vasovasostomy; OT: operation time; RAVE: robot-assisted vasoepididymostomy; MVV: microsurgical vasovasostomy; MVE: microsurgical vasoepididymostomy; PIQ: pain impact questionnaire; MVR: microsurgical vasectomy reversal; VR: vasectomy reversal; PVPS: postvasectomy pain syndrome

Table 2: Studies referring to the use of robotics in vasectomy reversal

Study	Year	Study design	Operations performed	Outcomes reported
Corcione *et al.*[42]	2005	Case series	2 robot-assisted laparoscopic varicocelectomies among 32 various robot-assisted laparoscopic procedures	Robotic surgery is feasible and safe The main advantage of robotic assistance is the 3D vision and better instrument manipulation More ergonomic position for the surgeon
Shu *et al.*[14]	2008	Case series	Microscopic: 9 (7 left-sided, 1 bilateral) Robotic: 9 (7 left-sided, 1 bilateral)	Mean (s.d.) OT: microscopic inguinal varicocelectomy 73.9 (12.2) min, robot-assisted 71.1 (21.1) min Robot-assisted varicocelectomy can be safely and effectively performed Added benefit of eliminating hand tremor No intraoperative, postoperative complications of varicocele recurrence on both groups
Parekattil and Cohen[15]	2010	Case series	25 RAVx procedures	Mean OT per side: 41 (range: 25–80) min 3-month follow-up (11 patients): 7 with oligospermia had a significant improvement in sperm counts (2 achieved pregnancy) and 2 with azoospermia unchanged All testicular pain patients had complete resolution of pain The fourth robotic arm allowed the surgeon to control one additional instrument, decreasing reliance on the microsurgical assistant
Parekattil *et al.*[44]	2011	Case series	46 RAVx procedures	Mean OT per side: 38 (range: 25–80) min
Parekattil and Brahmbhatt[28]	2011	Case series	97 RAVx procedures	Median OT per side: 30 (range: 10–80) min 3-month follow-up (81 patients): 75% with oligospermia had a significant improvement in sperm count or motility, 1 with azoospermia was converted to oligospermia, and 92% of patients with testicular pain had complete resolution of symptoms (targeted neurolysis of the spermatic cord had been performed in addition to varicocelectomy) There was 1 recurrence or persistence of a varicocele, 1 patient developed a small postoperative hydrocele, and 2 patients had small postoperative scrotal hematomas
Parekattil and Gudeloglu[10]	2013	Case series	181 RAVx procedures performed on 154 patients	Median OT per side: 20 (range: 10–80) min In total, 77% of patients with oligospermia had significant improvement in sperm count or mobility, 18% (3 patients) with azoospermia were converted to oligospermia, and 96% of the testicular pain/orchialgia patients had a significant reduction in pain (85% of these patients had targeted denervation of the spermatic cord in addition to varicocelectomy) There were 2 cases of recurrence or persistence of varicocele, 1 patient developed a small postoperative hydrocele, and 2 patients had postoperative scrotal hematomas
Gudeloglu *et al.*[30]	2014	Case series	238 RAVx procedures	Median OT: 20 min In total, 76% of patients with oligospermia had a significant improvement in sperm count and/or motility, and 28% of patients with azoospermia were converted to oligospermia. 92% of patients with testicular pain had a significant reduction in their pain scores (84% of them had robot-assisted-targeted microsurgical denervation of the spermatic cord procedure at the same time)
Etafy *et al.*[45]	2018	Case series	319 RMDSC and RAVx procedures for varicocele with pain	65% improvement in sperm parameters (sperm count and motility) 73% significant reduction in pain
McCullough *et al.*[46]	2018	Case series	140 patients with varicocele: 118 bilateral (84.3%) + 22 unilateral (15.7%) repairs = 258 total RAMV procedures	Median T and free T increased by 44.3% (*P*<0.001) Testicular volume increased bilaterally by at least 12.5%, median sperm concentration increased by 37.3% (*P*<0.03) Mean (s.d.) OT per side: TMV 49 (13) min *vs* RAMV 57 (16) min Mean (s.d.) robot-docking time: 39 (9) min 9/258 (3.5%) complications: 7 (2.7%) hematomas and 2 (0.8%) hydroceles No injuries to the vas deferens or testicular artery on any of the testicular units Persistent venous flow on postoperative ultrasound was seen in 9.7% (25), although reduced Intraoperatively, one testicular artery was identified on 80.7% of testicular units, 2 arteries on 15.2%, and 3 arteries on 4.1% Postoperatively, 37.3% of patients used pain medications >24 h

OT: operation time; s.d.: standard deviation; RAVx: robot-assisted microsurgical inguinal varicocelectomy; RMDSC: robot-assisted microsurgical denervation of the spermatic cord; TMV: traditional microscopic varicocelectomy; RAMV: robot-assisted microscopic varicocelectomy

Table 3: Summary of studies referring to robotic-assisted varicocelectomy

Variable	Parekattil and Cohen[15]	Parekattil and Moran[54]	Parekattil and Brahmbhatt[28]	Parekattil and Cohen[43]	Parekattil and Gudeloglu[10]	Gudeloglu et al.[30]	Calixte et al.[55]
Time period	October 2008 to June 2009	October 2008 to November 2009	October 2008 to April 2010	October 2008 to September 2010	October 2008 to June 2012	October 2008 to October 2013	October 2008 to July 2016
Number of cases (*n*)	24	62	151	230	401	546	872
Operative duration (min), median (range)	41 (19–80)	37 (5–95)	25 (10–150)	20 (7–150)	15 (10–150)	15 (10–150)	20 (15–80)
Decrease in pain (%) (PIQ-6 ≤50%)	92	87	85	85	86	84.8	83
No change (%)	8	13	15	15	14	15.2	17
Complete resolution (%)	75	Not mentioned	Not mentioned	77	72	70.5	49
Complications	Not mentioned	Not mentioned	1 hydrocele 2 testicular artery injuries and 1 vasal injury	Not mentioned	1 case of testicular ischemia 9 hematomas 2 seromas 2 testicular artery injuries and 1 vasal injury	1 case of testicular ischemia 10 hematomas 3 seromas 5 wound infections 2 testicular artery injuries and 1 vasal injury	1 case of testicular ischemia 23 hematomas 4 seromas 13 wound infections 2 testicular artery injuries and 1 vasal injury 1 pulmonary embolus 2 cases of penile swelling/pain

PIQ: pain impact questionnaire

Table 4: Updates on the results from robot-assisted microsurgical denervation of the spermatic cord