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Review

Robotics in Urology: No More Shadows?

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Abstract: Robotic surgery saw unprecedented success throughout the world, with urology as a key discipline. Robotic-assisted radical prostatectomy (RARP) and partial nephrectomy (RAPN) were the frontline procedures. Many other urologic procedures have since been standardized over time. However, there is no universal consensus in current research on the recognition of robotics as the standard of care. Although better operative outcomes have been reported for most robotic procedures compared to open and laparoscopic surgery, no superiority has been proven as far as oncologic outcomes are concerned. This review aims to describe current research on robotic surgery concerning each urologic procedure, showing its applications and limits. The non-classic parameters in part responsible for the planetary success of robotics, such as the shorter learning curve, improved ergonomics, and surgeon's comfort, as well immersive three-dimensional vision, are further areas of focus.

Keywords: robotic; surgery; robotic-assisted radical prostatectomy; robotic-assisted partial nephrectomy; robotic-assisted radical nephrectomy; robotic-assisted pyeloplasty; robotic-assisted radical cystectomy; robotic retroperitoneal lymph node dissection; robotic-assisted inguinal lymphadenectomy; standard; state-of-the-art; immersive tridimensional vision

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1. Introduction

Robotic surgery has seen a tremendous evolution since the launch of the first robotic platform. Urologists have been at the forefront of the adoption of robotics. Since the 2001 Food and Drugs Administration (FDA) approval for da Vinci-assisted prostate surgery, robotic prostatectomy has become the most commonly performed robotic oncologic procedure in the United States [1]. By 2003, robotic prostatectomy had an approximately 22% market share in the USA, which rose to 85% in 2013 [2]. Similarly, the proportion of procedures conducted as RARPs increased from 53.2% in 2013 to 92.6% in 2018 in England. This accelerated implementation placed urology at the center of Intuitive Surgical's strategy, prompting the use of da Vinci in other genitourinary oncologic procedures—robotic partial nephrectomy in 2002, radical cystectomy in 2003, retroperitoneal lymph node dissection in 2006, and inguinal lymphadenectomy in 2009 [3]. Although robotics' relative share of the total number of procedures has seen a decline, due to the rise of other disciplines, urology remains a major field of application for robotic surgery.

This review aims to describe the current state of robotic surgery research in each urologic procedure, presenting its applications and limits. The final chapters are dedicated to factors that are unrelated to classic operative and oncologic outcomes that might drive the adoption of robotic platforms in medical settings.

2. Robotic-Assisted Radical Prostatectomy (RARP): Towards a New Standard?

The increasing availability of PSA and prostate cancer diagnoses [4], with 1.3 million new cases of prostate cancer worldwide [5] and 140,000 radical prostatectomies performed annually in the USA alone [2], along with the accessibility to robotic platforms [6], combined to make RARP a popular and safe form of cancer surgery.

The outcomes of RARP were presented and compared extensively with retropubic (RRP) and laparoscopic radical prostatectomy (LRP) in a series of systematic reviews and meta-analyses by Ficarra and Novara. Although it is specified that the data are influenced by patient characteristics, surgeon experience, surgical technique, and the methods used to collect and report data, a statistically significant advantage in favor of RARP in comparison with both RRP and LRP was demonstrated in terms of 12 months urinary continence and potency recovery, and blood loss and transfusion rates [7]. The data on biochemical recurrence-free survival were considered promising but not mature, and significant data on cancer-specific mortality were not available at the time [7]. These reviews were published in 2012.

The rate of transfusion in contemporary robotic series has been confirmed at about 2%, and the reoperation rate about 2%, a quarter of which are for bleeding complications [8–10]. However, it should be considered that these data derive from top robotics institutions with very high surgical volumes. Although the relative proportion of bleeding complications is higher, bleeding complications remain the most common and life-threatening reason for reoperation even at a regional level, with 120–140 procedures performed annually [11].

A recent randomized study failed to demonstrate the superiority of RRP or RARP for positive surgical margin rates as an early oncologic outcome [12], and various population and cohort analyses suggest at least an early oncologic equivalence [13,14]. On the other side, the risk of biochemical recurrence (BCR) versus RRP was initially higher for RARP and was 35% lower after a long learning curve in a prospective single-surgeon cohort of 2206 consecutive cases after 3.5 years; the functional and quality-of-life outcomes followed a similar trend. Furthermore, a large European single-center cohort of RARPs with a median 10 Year follow-up identified overall BCR-free, cancer-specific, and overall survival rates of 82%, 98.5%, and 93.0%, respectively. They observed only 167 BCRs (17.6%), translating to 110 salvage therapy (12.4%) and 16 (1.8%) deaths from prostate cancer: these results compare very well with the open series. The authors highlight the sustained long-term impact of preoperative and postoperative clinicopathologic parameters on BCR and salvage therapy.

3. Robotics-Assisted Partial Nephrectomy (RAPN)

Laparoscopic partial nephrectomy (LPN) was first performed in 1993 [15] and improved over the next 20 years. Partial nephrectomy (PN) has become the gold standard in the treatment of T1 renal neoplasia over the past 10 years [16]. PN features the same oncological outcomes as radical nephrectomy (RN), which results in greater mortality and a greater risk of renal failure [17]. Although LPN and robot-assisted partial nephrectomy (RAPN) are technically more challenging, they have gained greater application. Minimally invasive partial nephrectomy (MIPN) is now the most effective treatment for small kidney masses, but also for tumors larger than cT1a. MIPN has become the gold standard for the better preservation of renal function, with the same risk of positive surgical margin (PSM) [18].

In the RAPN, excellent results have been demonstrated for renal neoplasms with greater sizes of cT1b, with a satisfactory total complication rate. Long-term oncological findings and renal function findings have yet to be confirmed, but comparing data on open partial nephrectomy and LNP, long-term outcomes should also be acceptable [19]. With the development of the technique of LNP, novelties in the field of imaging, and developments regarding the renal anatomy, tumors presenting increasing levels of technical challenge for surgeons, such as hilar [20] and endophytic or large lesions, are operated [21]. MIPN is also technically feasible in patients with intrarenal neoplasms [22], in the treatment of kidney stones [23], and in pathology of the ureteropelvic junction [24]. Simultaneous bilateral RAPN has also been described [25], following the expanding indications of simultaneous bilateral endurologic procedures [26].

Recently, Zhang et al. evaluated LPN and RAPN in fully endophytic renal tumors, which were shown to be comparable in terms of operation time, estimated blood loss (EBL), WIT, PSM rate rates, and postoperative complications; a lower cost in LRP was shown [22]. In a meta-analysis by Raghi et al. [27] comparing LPN and RAPN, similar results were shown for perioperative outcomes, such as WIT and complications. Abumarzouk et al. [28] performed a similar study, including seven non-randomized observational studies on patients treated with RAPN (>300) and LPN (>400). In conclusion, RAPN demonstrated a shorter WIT; however, it did not demonstrate significant differences in terms of blood loss, operative time, conversion, complications, or hospitalization (LOS) [29,30]. These advantages of the robotic technique must be attributed to image magnification, improved 3D imaging, seven-degree-of-freedom wrist devices and tremor filtering [31].

In order to preserve maximum renal function, the zero-ischemia technique has been used over the years, avoiding the ischemic damage secondary to clamping of the main renal artery. The selective clamping of renal arteries and veins and distal branches has also recently been termed a “zero-ischemia technique”.

The zero-ischemia technique was first applied by Gill et al. [32], with the intention of leaving the perfused healthy renal parenchyma during dissection maneuvers. The first results are promising. A lower postoperative bleeding rate has been demonstrated in cases of selective arterial clamping, due to bleeding that is more easily diagnosed than complete clamping. The main advantages of this technique are seen in patients with chronic kidney disease or solitary kidney. Recently, Mattevi et al. demonstrated that the use of fluorescence to guide selective arterial clamping during RAPN offers better early functional results than standard clamping [33]. The development of intraoperative imaging techniques has also improved the results of RAPN and LPN. The most frequently used and well-established technique is ultrasound. Ultrasound can demonstrate kidney ischemia during surgery and confirm renal vessel anatomy, as described in a New York University study [34]. At the same time, laparoscopic Doppler ultrasound can reduce the isolation time of the renal hilum and improve the detection of renal hilar vessels [35]. On the other hand, the use of fluorescence during MIPN has been widely used and appears to aid in the identification of renal neoplasm, as well as in guiding selective ischemia and assessing margins. Furthermore, developments in the field of augmented reality have offered surgeons the possibility of superimposing previously processed images onto real vision during surgery [36].

Through the development of technology, RAPN appears to have improved perioperative outcomes in comparison with LPN. To standardize tumor study and tumor assessment bias, many preoperative scoring systems for kidney cancers have been developed. A significant amount of research and substantial practices have been carried out to obtain the “trifecta” of MIPN, which consists in the complete removal of tumors, the maximum conservation of function, and the lowest complication rates.

4. Robotics-Assisted Radical Nephrectomy (RARN)

Minimally invasive radical nephrectomy is now the preferred treatment for renal tumors not amenable to partial nephrectomy, as supported by a growing body of research supporting nephron-sparing surgery over the last two decades. While there is a well-described experience with complex radical nephrectomy treated laparoscopy, robot-assisted surgery has shortened the learning curve and facilitated the greater uptake of minimally invasive surgery in difficult scenarios traditionally performed with open surgery. Following the first reports of robotic-assisted radical nephrectomy (RARN) in 2005, the safety, feasibility, and efficacy of this approach compared to standard laparoscopic radical nephrectomy (LRN) [37–40] have been established by several small single-arm and comparative series.

Jeong from Johns Hopkins compared 243 LRNs with 76 RARNs. Equivalent operative times (136 vs. 139’), intraoperative complications (2.8% vs. 2.0%), and lengths of stay (2 vs. 2 days) were found [41]. RARN cases were more likely to include lymph node dissection (LND) (12% vs. 24%), greater estimated blood loss (50 vs. 100 mL), and no differences in hospital charges ($14,900 vs. $16,200, P = 0.17). The utilization of RARN increased from

1.5% in 2003 to 27.0% in 2015. There were no differences in the rate of minor and major complications between the two groups. However, the RARN group exhibited a higher proportion of prolonged operating time (>4 h) and higher mean 90 days direct hospital costs, which were attributed to higher operating room and supply costs. Cost–benefit evaluations of RARN are considered simplistic and overlook several important factors [42].

Most centers performing RARN feature one or more robotic systems and there is no additional capital cost involved. Finally, robotic technology has significant implications for surgical education, training, and assessment. Contemporary urological training in the US facilitates greater exposure to robotic surgery compared to laparoscopy, which may translate to greater levels of proficiency and expertise in using the robotic platform. Furthermore, an objective assessment of surgical skills is allowed by robotics in a way that is unparalleled in previous eras of training [43].

In other words, RARN is not among the front-line procedures of robotic platforms. However, it is a perfect example of how an evaluation of standard perioperative, oncologic, and costs measures once again might not say everything on this topic. Subtle surgical market, and education factors either on a local and global scale complicate an objective evaluation of the value of RARN.

Minimally invasive robotic surgery, which is considered more aesthetic and less traumatic, has also been applied in recent years in pediatric surgery [44,45] The search for limited manipulation of tumors, the difficulties associated with the vascular involvement of neuroblastic tumors, and the risk of leakage have raised many concerns over the application of minimally invasive surgery in pediatric oncology [46,47]. It is mainly applied to neuroblastic tumors that can be fragmented [48–51]. Duarte et al., in 2004, presented the first series of Wilms tumors (WT) treated with an MIS approach, in children undergoing neoadjuvant chemotherapy [52]; a similar study was published in 2009 by Barber et al. [53]. The largest cohort of MIS-treated WTs was presented in 2014 by the Renal Tumor Strategy Group of the International Society of Pediatric Oncology (SIOP). The first review was published by Bouty et al. in 2018, in which 88 articles were analyzed for a total of more than 100 laparoscopic nephrectomies for WT worldwide. The advantages of robotics-assisted laparoscopy (RAL) are also reflected in pediatric surgery, through the ability to perform and reproduce difficult operations, especially when there is a deep and narrow field and when fine dissection is necessary for the manipulation of delicate tissues. The lack of tactile feedback can be considered a potential limitation, especially in cancers that cannot be fragmented, such as WT. The first applications of RAL were described in a partial transperitoneal nephrectomy in 2012 [54] and, in 2014, in a nephrectomy on an adolescent with WT [55].

5. Robotic-Assisted Pyeloplasty (RAP)

Favorable outcomes of RAP for uretero-pelvic junction obstruction (UPJO) in the pediatric population were reported in a meta-analysis by Masieri in a recent review: the success rate for primary RAP was found to be >90% in 21 of 22 studies involving 1448 patients, with a low complication rate [56]. RAP was associated with a significantly higher success rate and a shorter length of hospital stay compared with laparoscopic pyeloplasty in a meta-analysis of 14 observational studies on 2254 pediatric patients with UPJO, who underwent LP (n = 1021) or RALP (n = 1233). Moreover, non-significant reductions in postoperative complications (3.9% vs. 8%) and re-intervention (1.7% vs. 5.9%) were found in favor of RAP. There was no difference in procedure time between the two approaches [57]. RAP was associated with a 10 min operative time reduction and significantly shorter hospital stays compared with laparoscopic pyeloplasty; there were no differences between the approaches with regard to the rates of complication (including urinary leaks and readmission) and success [58]. In a single-center series on open, laparoscopic, and robotic pyeloplasty, a similar success rate and efficacy was recorded, irrespective of the technique utilized [59]. Operative outcomes were more favorable for

RAP compared to laparoscopy and open surgery, although such differences were not universally reported.

6. Robotic-Assisted Radical Cystectomy (RARC)

Radical cystectomy is one of the urological surgeries characterized by the highest morbidity [60–62]. The gold standard for the treatment of invasive muscle bladder cancer (MIBC) and high-risk non-muscle invasive bladder cancer (NMIBC) refractory to intracavitary treatments is open radical cystectomy (ORC) associated with extended pelvic lymphadenectomy (PLND) [63]. Robot-assisted radical cystectomy (RARC), such as radical prostatectomy and partial nephrectomy, is also performed in many urological surgery centers [64,65]. The robotic technique offers greater ergonomic advantages and a three-dimensional view [66]; however, there is some debate over the oncological safety of RARC versus ORC [67].

The oncological equivalence of RARC and ORC has been demonstrated through randomized clinical trials [68–71], although further consistent level 1 evidence is needed before confirming the superiority of RARC over ORC.

In order to reduce its considerable comorbidity, urinary derivation, used mostly at the beginning of the learning curve, is performed extracorporeally; however, even in medium-volume centers, the adoption of the fully intracorporeal approach has seen an 11% increase per year since 2005 [72]. Studies on RARC with comparative extracorporeal urinary diversion (ECUD) vs. intracorporeal urinary diversion (ICUD) have been published from centers with heterogeneous volumes [73–83].

The benefits include a shorter length of stay (LOS), reduced physiological stress and reduced use of analgesics, as well as an advantage in terms of blood loss and faster recovery of bowel function. A recent analysis showed that RARC offers a shorter operating time (OT) than ORC. It must be stressed that RARC with ICUD is not without its disadvantages and the debate is still open as to whether or not ICUD offers the same advantages as ECUD [84].

In two recent RCT (randomized clinical trial)-based meta-analyses [85], RARC was associated with a reduced incidence of perioperative transfusions, although ORC was associated with shorter operative times. There is no statistically significant difference in terms of PSM (positive surgical margins) [86]. These results were confirmed by another meta-analysis, performed on a subset of these RCTs [84].

Another systematic review and meta-analysis that included RARC case series and prospective or retrospective comparisons between RARC and ORC found similar results [87]. Patients undergoing RARC exhibited less blood loss, fewer transfusions, less hospitalization, and longer operating times but with a lower risk of complications at 90 days. There were no differences in the 30 day complication rates, nor in the 30 and 90 day mortality rates [88].

7. Robotic Retroperitoneal Lymph Node Dissection (Robotic RPLND)

Open retroperitoneal lymph node dissection is the gold standard for the surgical management of testicular cancer, associated with excellent oncologic outcomes and acceptable operative outcomes. Minimally invasive RPLND, starting with laparoscopic RPLND in 1992 and robotic RPLND in 2006, endeavor to decrease the morbidity of open RPLND while maintaining excellent oncologic outcomes. The early outcomes of primary robotic RPLND are promising and comparable to the recurrence-free rates of open (92.5%) and laparoscopic RPLND (95.4%), with no reported retroperitoneal recurrences [89]. Unfortunately, comparisons between techniques are challenging due to the different surgical techniques and adjuvant chemotherapy protocols, as well as the short follow-up time. Post-chemotherapy robotic RPLND is an even more difficult setting, with high complication rates and concomitant surgery (including vascular repair, bowel resections, nephrectomy, etc.). The existing research regarding post-chemotherapy robotic RPLND is most notable for the high reported rates of chylous ascites and short follow-up. The recommendation is that this type of surgery only be performed by experts in testicular cancer, RPLND, and robotic surgery [90].

8. Robotic-Assisted Inguinal Lymphadenectomy (RAIL)

The significant morbidity associated with open inguinal lymphadenectomy led to attempt to develop minimally invasive approaches. A review by Rodrigues analyzing 75 patients undergoing RAIL in three major studies found a mean operative time of 88 min, blood loss of 37 mL, and drain removal after 17 days; the major complication rate was only 5% in these series. Initial series reported lower cutaneous complications compared to conventional approaches, without compromising oncological outcomes: after 33 months of follow-up, the recurrence-free survival rate was 96%. Such promising results are counterbalanced by the relatively short follow-up and higher costs when compared to historical series using the open approach [91]. More robust long-term results are required.

9. Robotics-Assisted Laparoscopic Augmentation Ileocystoplasty and Mitrofanoff Appendicovesicostomy (RALIMA)

The use of the robotic technique is also developing in minimally invasive pediatric surgery [92], where these techniques are beginning to be applied in more complex cases, such as robotics-assisted laparoscopic augmentation ileocystoplasty and Mitrofanoff appendicovesicostomy (RALIMA). Historically, ileocystoplasty and Mitrofanoff appendicovesicostomy (IMA) were performed in an open manner, but in children, the robotic approach produces the benefits of minimally invasive surgery; this includes decreased incisional pain, shorter hospital stays and improved cosmetic outcomes [93]. The first robotics-assisted laparoscopic appendix was performed in 2004 and the first completely intracorporeal RALIMA was performed in 2008 [94]. Historical difficulties, such as a preference for open techniques in children, a lack of standardized training in pediatric robotic surgery, and inherently smaller workspaces, have made the broad application of robotic approaches in pediatric surgery more difficult. Although the open approach for IMA remains the most common technique, RALIMA has established itself as a viable option for pediatric urologists with considerable robotics experience. The main indication for bladder augmentation is attributable to pathologies that compromise bladder function, such as the reduced capacity compliance associated with high-pressure urination. The potential underlying anomalies affecting bladder function include neurogenic spina bifida bladder, non-neurogenic bladder, bladder exstrophy, plum belly syndrome, and posterior urethra valves. Mitrofanoff appendix bladder simplifies and facilitates clean intermittent catheterization (CIC) as catheterization through the urethra becomes inoperable due to discomfort, trauma, urethral stricture disease, disability, or non-compliance. Early case reports have demonstrated safety and efficacy, with outcomes and complication rates that compare favorably with those of open techniques. The benefits of minimally invasive surgery include decreased incisional pain, potentially decreased length of stay in hospital, and improved cosmetic outcomes. These benefits must be weighed against the steep learning curve, cost, and operative time [95,96].

10. Non-Medical Factors

The reasons for the rapid and widespread diffusion of robotic surgery worldwide can be divided into two categories: market-oriented reasons and scientifically oriented reasons. An analysis of the cost-effectiveness of robotic surgery should take both into account. According to the Everett Rogers's model Diffusion of Innovation from 1962, a technology can sustain itself at a point of critical mass with an adoption rate of about 50% [97]. Shah identified three levels of participation in the market leading to this unprecedented success: the surgeon, the hospital administrator, and the patient. (1) Unlike cholecystectomy, the steeper learning curve of laparoscopic radical prostatectomy favored the adoption of robotic technology by the average surgeon. (2) Despite the lack of level 1 evidence, the decreased length of stay associated with robotic prostatectomy allowed da Vinci to gain significant momentum among hospital administrators. Since length of stay is a variable cost and device installation is a fixed cost, robotic prostatectomy was theorized to be cost-effective at high case volumes. (3) The patient is the third unintentional participant, subjected in turn to two modern phenomena: the inevitable enthusiasm for robotics in the era of smart technology, and unregulated advertising campaigns (unlike pharmaceuticals, the FDA does not require a randomized controlled trial for medical devices).

11. The "Impalpable" Factors

In addition to the pressure exerted by market-oriented factors, robotic surgery offers exclusive advantages that are not easily classified into common scientific outcomes.

(1) Robotic surgery implies a much shorter learning curve compared to both open and laparoscopic surgery. In Yaxley's randomized study comparing RARP and RRP, the robotic surgeon with 200 previous robotic procedures achieved the same outcomes as the open surgeon with previous 1500 open procedures.

(2) The EndoWrist articulation provides surgeons with improved ergonomics. A study comparing the musculoskeletal ergonomic parameters of open, laparoscopic and robotic prostatectomy showed that neck and/or back pain was reported by 50% and 56% of surgeons after open and laparoscopic approaches, respectively, but by only 23% of surgeons operating robotically [98]. Similarly, it has been shown that compared to its open and laparoscopic counterparts, robotic pyeloplasty improved surgeons' quality of life and fatigue scores. Notably, an overall high risk of musculoskeletal disorders was observed among surgeons performing vesicoscopic ureteric reimplantation. However, the associated risk was significantly lower with the robotic (medium risk) versus laparoscopic approach (very high risk) [99]. In turn, this reduced human "consumption" might be useful in order to complete some important short- and long-term tasks: a greater number of procedures can be scheduled in the same session and, further surgeon longevity can be better preserved over time.

(3) The optics of robotic platforms, particularly the newest da Vinci systems, provide a visual environment that differs from laparoscopic magnified 3D systems [100]. The robotic surgeon does not observe the anatomy on a screen as in 3D laparoscopy; rather, he interacts with the anatomy based on the immersive three-dimensional vision enveloping the surgeon himself inside the operative field. With or without distraction (i.e., deviation from standardized operative routine), this immersive aspect of 3D may improve performance in the operating room, offering surgeons greater levels of focus and greater acuity.

(4) Robotics research is more recent than laparoscopic and above all open research. The history of radical prostatectomy is paradigmatic. First described as an open procedure by Walsh in 1982, the first series of laparoscopic prostatectomy was then presented by Schuessler 10 years later, and in 2000, the first RARP was described [101,102]. Many other surgical procedures followed a similar trend. Although some series in pioneering centers report more long-term follow-up data, the experience and the oncologic outcomes in the robotic series are inevitably more limited than with the other approaches.

12. Conclusions

Tumor biology and a surgical procedure performed according to the standard of care—regardless of the approach—are the most important determinants of patients' prognosis. Based on the available data, robotic surgery implies better operative outcomes for most procedures; on the other hand, no clear oncologic superiority has been demonstrated for robotic surgery over open and laparoscopic surgery, although these feature longer follow-up data. It is possible that the shorter learning curve, the improved ergonomics and surgeon comfort, and the immersive three-dimensional vision associated with robotics might help to explain the widespread success of robotics and influence further improvements in oncologic and non-oncologic outcomes.

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