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Title: Improving Patient Outcomes in Urology: The Rise of the Robots?**Abstract****1. Introduction**

The ideas of the surgical use of Robots dates almost seven decades back. Today, robots have diffused in many parts of the world and is replacing common surgical practices like open surgeries and minimally invasive laparoscopic surgeries.¹ In regard to Urology, one of the earliest uses of robot and computer in surgeries was reported in 1993, termed as Surgeon Assistant Robot for Prostatectomy (SARP).² With advancements in technology and development of the Da Vinci Robot in the early 21st Century, robot-assisted urological procedures like radical prostatectomy gained popularity. Within 2004 and 2010, over four-thousand robot-assisted radical prostatectomy were performed in the United States.³ While robots may sound like a fancy surgery option, the major incentive for which robots are utilized is their precision and accuracy which leads to many clinically favorable outcomes for the patient and clinicians. Some of the benefits noted in various robot-assisted urological procedures versus laparoscopic and open procedures include significantly less blood loss, nerve sparing, shorter catheterization times, and quicker mean erection return.⁴ In the early years, robot-assisted procedures were limited to a few procedures in Urology, namely prostatectomy and cystectomy.

As of today, literature shows that robot-assisted surgeries have been carried out in procedures like living-donor kidney transplant, partial and total nephrectomy, pyeloplasty, and laparoscopic ureteral anastomosis along with prostatectomy and cystectomy.³⁻⁶ A brief of review various systematic reviews and meta-analyses gives a hint that if appropriate technology and training is present, robot-assisted urological surgeries might be the new future of Urology. In this light, we

have carried out several research studies aiming to explore the clinical outcomes of robot-assisted urological procedures including those mentioned above. The studies were carried out in a multi-center setting in Switzerland and aimed to demonstrate and improve various clinical outcomes of urological pathologies.

1.1 Robots in Urology

The official initiation of robotic surgery in the realm of Urology ensued in 2001. It was done using one of the most renowned surgical robotic systems, da Vinci Surgical Robot, owned by Intuitive Surgical, USA.⁷ Over the last two decades, there have been several modifications to it, and it has improved in various capacities leading to almost 750,000 da-Vinci-assisted surgical procedures performed in 2017.⁸ Despite this long duration of monopoly, several other robotic systems have emerged since 2015; naming Senhance Surgical Robotic System (Transenterix, USA), REVO-I Robotic Surgical System (Meere Company, South Korea), Hinotori (Medicaroid, Japan, USA), Versius (CMR Surgical, England), and Surgenius (X Surgical Robotics, Italy).^{9,10}

1.2 Use of Robots for Prostatectomy

Radical prostatectomy (RP) has been the gold standard surgical procedure for low risk to high-risk prostate cancer.¹¹ This procedure is one of the most performed procedures in urology, owing to prostate cancer being the most encountered cancer in males. Radical prostatectomy roots back to the early 18th century. In 1904-1905, Young, known by many as the founder of modern urology, performed and described the first radical perineal prostatectomy. Almost three decades later (1945), Millin reported a retropubic approach for radical prostatectomy. As mentioned earlier, open radical prostatectomy (ORP) is associated with significant intraoperative and post-operative complications including impotence and urinary incontinence.¹² In the attempts to

minimize surgical complications, laparoscopic radical prostatectomy (LRP) originated in the 1990s.¹³ Although, laparoscopic RP was widely used in Asia and Europe due to being minimally invasive and cheaper (than robot-assisted RP), research eludes that it is difficult procedure to perform and had similar functional outcomes to open RP.¹⁴

With over two decades since the first robot-assisted RP (RARP), many hospitals are shifting towards utilizing robots due to its precision and accuracy, to minimize adverse clinical outcomes, and because of its shorter learning curve. In terms of clinical outcomes, there are several systematic reviews and meta-analyses available to support the use of RARP for prostate cancer patients. Several studies demonstrate that RARP is associated with lower transfusion rate, lower blood volume loss, shorter post-operative hospital stays, earlier continence recovery, earlier return of erectile function, and reduced hospital durations and costs.¹⁵⁻¹⁷ The most important measure of debate is the recurrence of prostate cancer. While recurrence of malignancy, denoted by positive surgical margins (PSM) and biochemical recurrence (BCR), is dependent of various factors like surgeons' expertise, BMI, Gleason score, extra-prostatic diseases, and staging, various trails and cohorts demonstrated superiority of RARP over LRP and ORP. Analysis of various RCTs, prospective, and retrospective studies indicate that PSM and BCR are significantly lower following RARP than LRP and ORP.^{15,16,18}

Lastly, there have been several advancements in RARP including single port RARP versus multiport RARP. Single site procedures are preferred due to their positive post-operative outcomes. In 2018, the FDA approved da Vinci Single Port (SP) system urological surgeries and several systematic reviews and meta-analyses have depicted the comparisons between single port (SP) RARP and multi-port (MP) RARP. Current literature eludes that there is no significant difference between estimated blood loss, operative times, intraoperative complications, PSM and

BCR, and other functional outcomes like return of erectile function. However, there is statistically significant reduction in post-operative pain and opioid use, catheterization time, and duration of hospital stays following SP-RARP procedures.¹⁹⁻²¹

1.3 Robots for Living Donor Nephrectomy

End-stage renal disease (ESRD) is one of the leading diseases requiring organ transplants. According to the United States Renal Data System's (USRDS) 2021 Annual Report, the 2019 prevalence of ESRD in the USA was estimated to be over 809,103. Out of these patients, 239,413 patients have undergone a transplant and nearly 570,000 patients still await a transplant. While dialysis works for a small number of patients, kidney transplant is the treatment of choice for ESRD²², and there has been a 4.5% increase in the number of transplant surgeries performed from 2018-2019.²³ While most kidney transplants used deceased donor kidneys, the increase in need of kidney transplants has increased living donor nephrectomy (LDN) for graft as well. Similar to the surgical advancements in other urological procedures, living donor nephrectomy has also undergone several modifications. In the 1950s, living donor nephrectomy was pioneered as an open procedure and is still in practice in various areas of the world due to its graft-related advantages, especially, low warm ischemia time. Current literature suggests that laparoscopic LDN (LLDN) and open LDN (OLDN) produce similar functional outcomes regarding operating time, donor preoperative renal function, donor and recipient postoperative kidney function, delayed graft function or the incidence of major complications. The consensual deduction from most comparisons is that laparoscopic LDN is superior in terms of reduced post-operative pain, shorter hospital stays, and earlier return to work.²⁴⁻²⁷ Some studies, however, have reported a fewer estimated blood loss.^{28,29}

The first ever cases of robot-assisted LDN (RLDN) were reported by Horgan et al. in 2002, who used da Vinci Surgical System for 12 cases.³⁰ Over the next two decades, several studies have been published demonstrating the feasibility, learning curve, technique, and peri-operative outcomes of RLDN.³⁰⁻³⁴ Similar to other robotic surgeries, RLDN had some proposed benefits described by various early studies. These included: higher dissection facility, easier suturing and knotting (even for anomalous vasculature), more accurate graft preservation, faster learning curve for the surgeons³⁵, and significantly higher surgeon's comfort. These advantages, particularly surgeons' comfort during the procedure, came as a result of a 3D view and magnification during the surgery (versus 2D view in hand assisted LDN), EndoWrist instruments, and console conformation and work station for surgeon positioning.³²

In terms of functional outcomes and peri-operative outcomes RLDN and LLDN are comparable, and both are considered an effective option for kidney transplant. Wang et al. reported that LLDN has several advantages like reduced EBL, shorter warm ischemia time and operative times, and RLDN patients were noted to have significantly lower post-operative pain scores. However, there was no significant difference between the length of hospital stay (LOS), postoperative serum creatinine (SCr) in donors, postoperative estimated glomerular filtration rate (eGFR) of recipients, and postoperative complications between RLDN and LLDN.³⁶ A more recent meta-analysis, from Hinojosa-Gonzalez et al., concluded similar findings and added that robotic approach is apparently superior in terms of shorter LOS and post-operative day 1 pain. However, the latter findings need to be analyzed further.³⁷ When compared to the conventional OLDN, RLDN was determined to be superior in terms of lower surgical site infection, decreased pain, and shorter LOS but is associated with higher warm time and mean operative times.^{38,39}

1.4 Robot-Assisted Partial Nephrectomy

Modern-day (open) partial nephrectomy (PN) pioneered in the mid 20th century by Czerny for localized and small renal tumors. However, it was met with much criticism due to its high complication rate and low 1-year and 5-year survival rate. It was not until the beginning of the 21st century (2000) that elective nephron sparing partial nephrectomy was considered an acceptable and viable procedure by urologists for the treatment of small (<4 cm) and localized renal tumors.⁴⁰⁻⁴²

To date, partial nephrectomy has been used in various conditions. Current literature advocates PN as a gold standard for small, localized renal tumors. The American Urological Association (AUA) recommends PN for cT1a renal masses as it preserves kidney function, minimizes the risks of CKD and CKD progression, and provides excellent local control. The AUA also recommends prioritizing nephron-sparing procedures for patients with solid or Bosniak 3/4 complex cystic renal masses and an anatomic or functionally solitary kidney, bilateral tumors, known familial RCC, preexisting CKD, or proteinuria.⁴³

Laparoscopic partial nephrectomy (LPN) was first introduced in 1992 by Winfield.⁴⁴ In the coming years, several comparative studies took place describing the peri-operative outcomes of LPN versus open partial nephrectomy (OPN). Performed through retroperitoneal and transperitoneal approach, earlier studies hinted that LPN was associated with lower EBL, shorter LOS, and lower post-operative pain and opioid use than OPN.⁴⁵ Recent analyses of 26 studies by You and Du et al. concluded that there was no significant difference between LPN and OPN in terms of operative time, intraoperative complications, recurrence, cancer-specific survival, disease-free survival, and variations of estimated glomerular filtration rate. LPN resulted in significantly lesser EBL, shorter LOS, lower blood transfusion, lower total and post-operative

complications, lesser raise in serum creatinine, and higher overall survival. However, LPN was resulted in significantly higher positive surgical margin than OPN.⁴⁶

Almost four years after the FDA approved da Vinci Surgical System for urological surgeries, in 2004, Gettman et al. reported the first use of robot-assisted partial nephrectomy and implicated its safe use in resection of tumors like renal cell carcinoma and oncocytoma.⁴⁷ Subsequently, robot-assisted partial nephrectomies (RAPN) gained popularity around the world due to its minimally invasive approach, better surgeon experience, shorter learning curve, and comparable-to-better functional outcomes than both open partial nephrectomy and laparoscopic partial nephrectomy.⁴⁸ Currently, there are various studies comparing RAPN with LPN and OPN is available. While there are no randomized controlled trials comparing RAPN with other treatment modalities, there is still some apparent evidence suggesting the future trends of RAPN. When compared to LPN, RAPN is considered equally effective and viable with almost similar peri-operative results. RAPN has some superiority over LPN in terms of short learning curves as the operative times and warm ischemia time was demonstrated to be lower in RAPN⁴⁹⁻⁵². Other functional outcomes have been determined to be comparable in RAPN and LPN with both producing favorable results in patients.^{51,53} In specific cases like renal hilar tumors, Bao and Dong et al., and Chen and Deng et al. have suggested the use RAPN for hilar tumors as it provides more ipsilateral parenchymal volume preservation, reduced warm ischemia time, lower EBL, and hence better functional outcomes for the kidney.^{54,55} When compared with OPN, RAPN has several apparent advantages. RAPN has been seen to offer a lower rate of perioperative complications, less EBL and lower need for transfusion, and shorter LOS than LPN, suggesting that RAPN can be an effective alternative to OPN. However, authors have pointed out the need for more RCTs for a more accurate analyses.⁵⁶⁻⁵⁸

1.5 Robots for Uteropelvic Junction Obstruction (UPJO)

Ureteropelvic junction obstruction (UPJO) has an estimated incidence of 1 in 1000 to 1 in 1500. It is more commonly seen in pediatric population and, nowadays, diagnosed by highly sensitive antenatal ultrasounds. Most cases occur in males and the left kidney is affected twice as much as the right kidney.⁵⁹ For confirmation of anatomical and functional obstruction, contrast-enhanced CT and diuretic renography are used. Treatment for UPJO includes active surveillance, endourological procedures, and surgical interventions, the latter being, when indicated, is the treatment of choice for UPJO.^{59,60}

The first successful case of open pyeloplasty was carried out by Kuster in 1891, followed by popularity of endopyelotomy (1980s), and laparoscopic pyeloplasty by Schuessler et al. (1993).⁶⁰ The introduction of the da Vinci Surgical robot for pyeloplasty was first reported in 2002.^{61,62} It was also notably the first robotic surgery procedure in pediatric urology.⁶³ A review published by Khan et al. described the efficacy of various surgical procedures for pyeloplasty. The review concluded that the highest success rate was achieved by open pyeloplasty, laparoscopic, and robot-assisted pyeloplasty. Robot-assisted pyeloplasty was suggested to be the most effective and safest procedure out of all but due to its cost and unavailability across many parts of the world, open pyeloplasty is considered gold-standard for UPJO.⁶⁴

In terms of drawbacks, open pyeloplasty is associated with significant scarring, post-operative pain, and higher complication rate. Laparoscopic pyeloplasty is considered a complicated procedure and has a difficult learning curve for most surgeons, and therefore requires longer operative times. Robot-assisted pyeloplasty has the limitation of being expensive to acquire.⁶⁴ Several reviews, however, have advocated the use of robot-assisted pyeloplasty to be the gold standard surgical treatment for UPJO in the future.^{64,65}

1.6 Robots for Radical Cystectomy

Radical cystectomy (RC) roots back to the 1800s and was described somewhat meticulously by Whitmore and Marshall in 1962.⁶⁶ Open RC (ORC) is classically indicated for urothelial carcinoma of the bladder (UCB), which include non-muscle invasive bladder cancer (NMIBC), muscle invasive bladder cancer (MIBC), and it has been considered as the ‘gold standard’ for NMIBC and MBIC and select cases of metastatic UCB.⁶⁷ Despite being the standard procedure for invasive UBCs, RC has the classical drawbacks of higher peri-operative complications, higher EBL, more intraoperative and post-operative transfusion, high post-operative pain, and longer LOS.^{68,69}

The first robot-assisted radical cystectomies were reported by Menon et al. in 2003 and also commented similarly on the dexterity and complexity of laparoscopic cystectomy.⁷⁰ Later in the early 21st century, various centers reported feasibility and likely superiority of robot-assisted radical cystectomy over open procedures in terms of reduced blood loss, shorter LOS, and decreased post-operative pain and narcotic use.^{71–73} These studies also proposed the use of RARC over ORC in the future. Fortunately, yet unlike most other robotic surgical procedures, there are several RCTs and their respective meta-analysis available for the comparison of RARC with ORC. The largest trial consisting of 350 randomized patients concluded that RARC is not inferior to ORC in a 2-year survival time. The RCT also eluded that patients undergoing robot-assisted procedure experienced significantly less blood loss, less intra-operative, perioperative and post-operative blood transfusion, and shorter LOS. The operative time was significantly longer than ORC.

Functional outcomes after robot-assisted pyeloplasty for ureteropelvic junction obstruction: A bi-center experience

Mid-term functional outcomes of extraperitoneal robot-assisted simple prostatectomy: a single center experience

Post-kidney Transplant Robot-assisted Laparoscopic Ureteral (Donor-receiver) Anastomosis for Kidney Graft Reflux or Stricture Disease

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