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Outcomes of Minimally Invasive Urologic Surgery in the Elderly Patient Population

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Abstract The elderly patient is generally counseled with caution regarding open surgical procedures because of the relatively high morbidity and mortality associated when compared with similar procedures in younger patients without comorbidities. However, there is an ever-increasing utilization of minimally invasive surgical approaches to urological conditions with demonstrable benefits over open surgery in all patient populations, irrespective of age. We explore and present the various applications of minimally invasive surgery in urology, looking at the outcomes and current trends specifically as it applies to urologic surgery in elderly patients.

 $\label{eq:Keywords} \textbf{Keywords} \ \ \textbf{Complications} \ \cdot \textbf{Age} \ \cdot \textbf{Laparoscopic} \ \cdot \textbf{Robotic} \ \cdot \\ \textbf{Cystectomy} \ \cdot \textbf{Nephrectomy} \ \cdot \textbf{Nephroureterectomy} \ \cdot \\ \textbf{Prostatectomy} \ \cdot \textbf{Oncologic}$

Introduction

Minimally invasive surgery (MIS) has become a preferred management approach to various urological conditions, whether benign or malignant. MIS in urology began to take shape in 1990, when Clayman and colleagues reported performing the first successful laparoscopic nephrectomy [1]. In 1994, McDougall et al. reported their experience with laparoscopic procedures specifically in octogenarians [2]. Since then, the application of laparoscopy has become more and more popular in the field of urology, across all age

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groups and patient risk categories. Improvements in laparoscopic techniques, the development of the da Vinci robotic surgical system, and the relatively improved outcomes of these operative techniques have further popularized MIS compared to conventional open surgery.

Some of the reported advantages of laparoscopy as compared to an open surgical approach for the same procedure includes: reduced postoperative pain, less analgesic requirement, early postoperative ambulation, faster return of bowel function, reduced length of hospital stay, improved cosmesis, and overall decreased convalescence period [3-5]. These benefits are especially welcomed in the management of the elderly patient population who are generally counseled with caution regarding open operative procedures given the relatively higher rates of morbidity and mortality associated with these procedures and the typically more tenuous baseline nutritional, pulmonary, and cardiovascular status of the elderly compared to their younger counterparts. Furthermore, advances in MIS techniques, anesthesia, and perioperative care have led to a reduction of operative risks and complications that has rendered surgery, even major operations a safer option in elderly patients. This is especially important given the rising need for operative interventions in this specific patient population. The average life expectancy in United States was estimated to be 78.2 years in 2009 [6]. Also, it is expected that by 2020, the number of individuals 70 years or older will approach 30 %; hence the proportion of elderly patients needing urological surgery will increase as a function of the aging population. Moreover, with the rising incidence of urological cancers in the elderly patient population, the need for surgery is expected to also increase [7, 8]. Hence, MIS with its benefits may be a valuable approach to surgical intervention in the elderly patient population.

However, some hemodynamic changes related to CO₂ insufflation in elderly men undergoing laparoscopy have

been reported [9]. Though the mean arterial blood pressure rises during laparoscopy, the cardiac output remains unchanged as systemic vascular resistances increases. These changes are especially critical in the elderly in who at baseline are more likely to harbor underlying cardiac or pulmonary comorbidities. Be that as it may, the reduced use of narcotic analgesics may reduce the sedative and respiratory depressive effects that often accompany open surgery. Also, given that the incisions are smaller with MIS, the absence of large muscle splitting or dividing incisions may yield improved pulmonary function postoperatively.

In this article, we review the various applications of MIS in urology. We examine the outcomes and current trends as it applies to minimally invasive urologic surgery in elderly patients.

Partial Nephrectomy

With the goal of nephron preservation, partial nephrectomy is a preferred management option for small renal masses (SRMs) [10]. This can be approached using MIS or open technique. Laparoscopy with or without the use of robotic assistance has become the standard approach to the management of SRMs, even in the elderly.

In a retrospective analysis of 115 patients aged > 75 years who underwent renal laparoscopic renal surgery, Guzzo and colleagues reported a median estimated blood loss (EBL) of 300 mL, transfusion rate of 16.1 %, median length of hospital stay of 4 days, and complication rate of 29 %, in a subset of patients who had partial nephrectomy (n=31). This data supports the safety and feasibility of laparoscopic partial nephrectomy in the elderly [11•].

With the introduction of the da Vinci robotic system in MIS, Hillyer et al. evaluated the functional, perioperative, and oncological outcomes of partial nephrectomy in the elderly patient population [12•]. In a retrospective matched (1:1) case-control analysis of 76 patients who underwent robotic-assisted laparoscopic partial nephrectomy (RAPN) for a single kidney tumor (median size=2.65 cm), they found no difference in the perioperative and postoperative outcomes between patients ≥ 70 years and those ≤ 70 years. Postoperative complication (mostly Clavien grade I and II) rates of 31.6 % and 21 %, respectively, were reported but this was not found to be statistically significant. With respect to oncological outcome, one patient had a positive margin in the younger age group versus none in the older; and each group had one patient with recurrence during follow-up. Also, there were five deaths reported, three of which occurred in patients ≥ 70 years at a median duration of 22 months following surgery, but this again was not statistically significant.

MIS thus remains a valuable option for elderly patients who are considered fit and eligible for partial

nephrectomy for management of their renal masses suspicious for malignancy.

Radical Nephrectomy and Nephroureterectomy

Like most other urological conditions, radical nephrectomy or radical nephroureterectomy can be approached with MIS or open technique. In an initial and early report, McDougall and Clayman described their experience in performing laparoscopic nephrectomy and nephroureterectomy in five patients over the age of 80 years, most with ASA score of 3 or 4 [2]. Although the mean duration of surgery was 8.3 hours, the mean EBL was 270 mL. There were no intraoperative complications reported. However, during a mean length of hospital stay of 7 days (range=4–11 days), the postoperative complications reported were: atrial fibrillation in a patient with coronary artery disease, and two patients requiring transfusion for a drop in hematocrit which was later understood to be due to hemodilution, given no CT evidence of bleeding [2]. Over the years with experience of surgeons, the duration of surgery has been significantly shortened and now compares with open surgery as shown below.

In their analysis of 249 patients comparing open (via subcostal or intercostal incision) versus laparoscopic approach to nephrectomy for benign disease, Fornara and colleagues reported that laparoscopic nephrectomy offers comparable perioperative outcomes when compared to open surgery [3]. Specifically, it was found that there was no difference between operative time, pre- and postoperative hemoglobin levels, even after stratifying by age (65-74, 75-84, and \geq 85 years). Furthermore, some of the reported benefits of laparoscopy included reduced analgesic use and length of hospital stay. Regardless of age, patients in the laparoscopy group were found to have less blood loss and no transfusion requirement whereas 75 % of patients in the open nephrectomy group required transfusions. However, although complication rates were similar between the laparoscopic and open nephrectomy groups, an increase was observed for patients aged between 75 and 84 years indicating the comparability of outcomes between MIS versus open approach to radical nephrectomy in the elderly population.

As would be expected, perioperative outcomes of MIS in the elderly patient population are expected to improve with surgical experience. In a retrospective analysis of 158 patients who underwent simple or radical nephrectomy and nephroureterectomy, Lai et al. reported no significant difference in the intraoperative or perioperative complication rates in the elderly patient population (≥ 70 years; n=45) [13•]. Patients who were ≥ 70 years were more likely to have a longer postoperative hospital stay, but this was attributed to those who underwent hand-assisted nephrectomy



as opposed to conventional laparoscopic surgery. In another analysis of 33 patients \geq 75 years and 28 patients \leq 75 years who underwent laparoscopic nephrectomy, Varkarakis et al. reported no significant difference in outcome [14].

In a recent retrospective analysis of 115 patients aged > 75 years old who underwent laparoscopic partial or radical nephrectomy, Guzzo et al. found that the median estimated blood loss was 200 mL, transfusion rate was 9.6 %, median length of hospital stay was 4 days, and overall complication rate was 22.6 %. In a subgroup analysis, the complication rate was reported to be 13.7 % in those > 80 years, and patients with a Charlson Comorbidity Index (CCI) \geq 2 were more likely to experience a perioperative complication as compared to those with a CCI \leq 1 (35 % vs 16 %; P < 0.034). The overall conversion-to-open rate was 3.5 % [11•]. The authors mentioned that this complication rate is comparable to what had been previously reported in the literature for laparoscopic radical nephrectomy overall irrespective of patient age (9 %-37 %) [15–19].

The results from the different studies presented above indicate that in a carefully selected cohort of elderly patients, minimally invasive renal surgery is safe and feasible.

Radical Prostatectomy

The standard treatment for clinically localized prostate cancer is radical prostatectomy, with or without nerve sparing, with or without pelvic lymph node dissection. However, based upon most recommendations available for the management of prostate cancer, surgery is indicated for clinically localized prostate cancer that can be completely excised in patients with no contraindications to surgery, a life-expectancy estimated at > 10 years, and who do not qualify for active surveillance. Hence, patients especially elderly men considering radical prostatectomy as treatment for their prostate cancer should be carefully selected. This section is focused on patients > 65 years with prostate cancer seeking definitive therapy and who qualify for radical prostatectomy.

While laparoscopy has been used for radical prostatectomy, robotic-assisted laparoscopic prostatectomy (RALP) is now widely accepted as the MIS procedure of choice at specialized centers as well as a large proportion of community hospitals. Compared with laparoscopy, RALP offers improved visualization, increased surgical dexterity, and a 3-D (three-dimensional) camera system that offers a more global view of the operative field both for the surgeon at the console and the operative assistant at the bedside [20].

In an initial report looking at the feasibility and efficacy of laparoscopy for prostatectomy, Schuessler and colleagues reported a mean operative time of 9.4 hours and mean length of hospital stay of 7.3 days [21]. Of the nine patients

operated on with a mean age of 65.6 years, only one had positive surgical margin involving the urethra on final pathological examination. Postoperatively, six patients were completely continent of urine, and 50 % of had their erections preserved. As experience with this procedure grew and surgical technique is perfected, there has been further improved perioperative outcomes reported [22–24].

Some authors have examined the utility of robotic assistance in performing laparoscopic radical prostatectomy, hypothesizing that the da Vinci robotic system may enhance precision of the anatomic dissection or periprostatic tissues important for postoperative quality of life measures. Menon et al. in an early report prospectively compared conventional radical retropubic prostatectomy (RRP) and RALP with 30 patients in each group [25]. They reported a mean operating time of 2.3 hours for RRP and 4.8 hours for RALP (P <0.001), with an additional 0.95 hours needed to set up for RALP and one patient who required conversion to open RRP for failure to progress with the robotic MIS approach. However, notable was a significant difference in mean EBL: 970 mL for RRP and 329 mL for RALP (P < 0.001) but this study was limited by the small sample size in each arm and the study center is not known for high volume open prostatectomy. Other significant findings included less postoperative pain and shorter duration of postoperative hospital stay in the RALP group. In terms of oncological outcome, the pathologic stage, margin status, and prostate-specific antigen values were not different between the two groups.

After the first 20 patients in the RALP group as reported by Menon et al. above, there was a significant reduction in the setup time, operative time, EBL, and time to Foley catheter removal [25]. In another report, after 6 months of follow up, the same group reported an 82 % and 75 % return of sexual function in patients < 60 and > 60 years respectively. Also, at 6-months follow up, 96 % of patients were continent [26]. These results demonstrate a fairly comparable outcome of sexual function and continence between men < 60 and > 60 years of age. Hence, over the years with standardization of surgical technique (transor extra-peritoneal approach) [22, 27–29, 30••], the outcomes of RALP including sexual function and continence, have improved significantly and the outcomes compare with RRP [31–35]

When pure laparoscopic radical prostatectomy was compared with RALP, there were no differences in surgery and outcome. However, RALP was significantly more costly [36]. On the hand, Hu et al. reported lower complication rate and operative time with RALP as compared with LRP but this may be attributable to surgeon's experience [37]. The feasibility and efficacy of a single-port laparoscopic approach to radical prostatectomy has equally been reported [38], including the use of robotic assistance [39].



Hence, in the hands of experienced surgeons, the outcomes of laparoscopic prostatectomy and RALP compare with open prostatectomy. Moreover, high-volume surgeons at high-volume centers generally provide better outcomes.

Radical Cystectomy

Radical cystectomy and pelvic lymph node dissection remains the standard treatment for muscle-invasive and recurrent urothelial carcinoma of the bladder [40]. Given the high incidence and prevalence of bladder cancer in the elderly, radical cystectomy accounts for a greater majority of urological procedures in this age group [41, 42]. However, radical cystectomy has been reported to be associated with high incidence of morbidity and mortality [41–49]. For example, Gregg et al. estimated the overall 90-day mortality rate at 7.3 % (16.5 % in patients with nutritional deficiency and 5.1 % in others) following radical cystectomy [49].

Moreover, like most other surgical procedures, advanced age has been identified as a risk factor for perioperative morbidity and mortality following radical cystectomy [50]. But MIS, combining laparoscopic and robotic-assisted laparoscopic surgery, has been demonstrated to improve overall perioperative outcome when compared with open radical cystectomy: decreased blood loss and transfusion requirement, early ambulation, shorter hospital stay, and early return of bowel function [51, 52, 53•, 54, 55, 56•]. Can these benefits of MIS apply to the population of older patients who might be candidates for cystectomy? Coward et al. reported comparable perioperative outcomes, specifically estimated blood loss, time to discharge, and complication rate, stratifying patients who were < 70 years and those ≥ 70 years of age. Also, they found no difference in immediate oncologic outcome: organ-confined disease rate (62 % vs. 71 %, p=0.6805) and lymph node yield (19.5 vs. 18.1, p=3502) [56•].

Recently, Guillotreau et al. compared the perioperative outcomes of laparoscopic radical cystectomy in patients who were < 70 years and those ≥ 70 years of age in a retrospective analysis of 146 patients. They found no difference in perioperative complication rate (39.2 % vs. 38.9 %, p=N.S.) and positive margin rate (5 % in each group). Although the 5-year overall survival was 75 % as compared to 87 % for the older and younger patient cohorts, respectively (p=0.03), there was no significant difference observed in the 5-year cancerspecific survival (51 % vs. 54 %, p=0.7) [57].

In the robotic era, with enhanced dexterity and 3-D visualization, the outcomes of cystectomy in the elderly have equally been investigated. Kauffman and colleagues analyzed the short- and long-term complications following robotic-assisted radical cystectomy in 79 patients with mean age of 71 years [58]. They found that 49 % of patients had

one or more complications within 90 days of surgery, which were mostly low grade (79 %). Some of the high-grade complications encountered were urinary obstruction, abscess, enteric fistula, gastrointestinal bleeding and venous thromboembolism. Predictors of high-grade complications identified included age of \geq 65 years, EBL of \geq 500 mL and intraoperative intravenous fluids of > 5000 mL. However, these high-grade complications were infrequent, and are similar in nature to high-grade events after open radical cystectomy [59–61].

Similarly, in a prospective randomized noninferiority trial comparing robotic (n=21, mean age=67.4 years) versus open (n=20, mean age=69.2 years) radical cystectomy, Nix et al. found no difference in overall complication rate (50 % vs. 33 %, p=0.2789) or mean length of hospital stay (5.1 days vs, 6 days; p=0.239) [62]. When compared with the open approach, the authors reported robotic cystectomy to be associated with longer operating room time 4.2 vs. 3.5 hours, p<0.001), lower EBL (258 vs. 575 mL; p<0.001), shorter time to flatus (p=0.001), shorter time to bowel movement (p=0.001), and less analgesic requirement (p=0.019) demonstrating the noninferiority of robotic cystectomy to open cystectomy.

On the other hand, Lau et al. specifically examined the elderly patient population looking at outcomes following robotic-assisted laparoscopic radical cystectomy [63]. Twenty-four patients with a mean age of 84.7 years were identified, most of whom have an ASA classification of ≥ 3 (82.6 %) and a CCI of ≥ 3 (95.6 %). In this cohort, there was one open conversion and two patients had positive surgical margins. There were five patients who had no complications, and two patients died due to multi-organ failure. At 24 months, the overall, diseasefree and disease-specific survivals were 51.1 %, 64.3 %, and 79 %, respectively. These data highlighted the fact that octogenarians undergoing robotic-assisted radical cystectomy have a significant risk of morbidity and mortality that needs to be balanced with the anticipated benefits. However, in carefully selected patients and in the hands of experienced surgeons, the outcomes of laparoscopic or robotic-assisted radical cystectomy compares with open radical cystectomy.

Pelvic Lymph Node Dissection

The utility of MIS technique in pelvic lymph node dissection (PLND) has equally been explored, in terms of yield and outcomes compared to the open technique. In a series of 22 patients who underwent a limited PLND (n=11) and extended PLND (n=11) laparoscopically, Finelli et al [64]. reported a median lymph node yield of 3 and 21 nodes respectively, with the latter adding only about 1.5 hours to the procedure, yield comparable to the open technique. After



a median follow-up of 11 months (range 2–43 months), there was no port site recurrence.

Similarly, Woods et al. [65] demonstrated the comparability of robotic-assisted laparoscopic PLND to the open approach. They reported their experience with 27 patients with a mean total lymph node count of 12.3 (range=7–20) nodes and no intraoperative complications were encountered. In a prospective randomized noninferiority trial comparing robotic (n=21) versus open (n=20) radical cystectomy, with bilateral PLND, Nix et al. evaluated the lymph node (LN) yield as the primary outcome [62]. They reported a mean LN yield of 19 (range 12–30) for the robotic approach and 18 (range 8–30; p=0.515) again indicating the comparability of the MIS to the open approach to PLND.

Urinary Diversion

Following cystectomy, options of urinary diversion include: continent (neobladder or Indiana pouch) and non-continent mechanisms (ileal or colonic conduits; and ureterostomies). When cystectomy and pelvic lymph node dissection is completed, most surgeons will perform urinary diversions extracorporeal [51, 56•, 57, 66]. Several case reports/series have indicated the feasibility of performing intracorporeal urinary diversions [67–69, 70••].

In the older patient population, Gill et al [71]. reported 2 cases of radical cystoprostatectomy and intracorporeal ileal conduit reconstruction in men aged 70 and 78 years. Although the EBL were 1000 and 1200 cc respectively, and the duration of surgery were 10 and 11.5 hours, respectively, there were no intraoperative or postoperative complications encountered and the surgical margins at histological examination were negative.

In a recent series of 9 patients with mean age of 74.1 years, Rehman et al [72]. described their experience with performing ileal-conduit urinary diversion using the da Vinci robotic system without the need for open conversion. The mean operative time for the entire procedure (radical cystectomy, extended PLND, and urinary diversion) was about 6 hours with the urinary diversion aspect accounting for a mean duration of 1.2 hours and a mean EBL of 258 cc (range=200–500). No intraoperative complications were reported, however, one patient experienced postoperative iatrogenic necrosis of the ileal conduit "caused by uncareful retraction of the organ bag and thereby probably injuring the conduit pedicle" necessitating an open revision.

As the MIS technique for intracorporeal urinary diversion is standardized and as surgical expertise improves, it is reasonable to expect that the perioperative and long-term outcomes associated with this procedure will continue to improve. In 2012, Goh et al [73••]. published a step-by-step

technique for robotic, intracorporeal, orthotopic, ileal neobladder, urinary diversion. They described their experience in 24 patients of which 3-month follow-up data was available in 8 patients. The median EBL was 225 mL (range 100–700 mL) and median length of hospital stay was 8 days. Although this study was limited by its small sample size and short-term follow-up, it represents a model for other surgeons in the process of perfecting their technique to follow with the hope that larger cohorts with longer follow-up data will become available in the future.

Conclusions

Minimally invasive urological surgery appears to be a safe and valid option in the management of urological conditions in the elderly. Although most of the published literatures have relatively small sample size, retrospective in nature, and with short follow-up period, the data available demonstrates comparable perioperative, functional and oncological outcomes between minimally invasive and open approach to urological surgery. Furthermore, as techniques are perfected and as the experience of surgeons grow, the outcomes of the MIS approach has the potential of comparing to or outperforming those of open surgery in the elderly patient population. However, prospective and where possible, randomized trials with larger sample size and long term follow up will be needed to demonstrate the safety and efficacy of the MIS approach to urological surgery.

Conflict of Interest Simpa S. Salami declares he has no conflict of interest.

Arvin K. George declares he has no conflict of interest. Soroush Rais-Bahrami declares he has no conflict of interest.

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