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Review

Robotic Pelvic Lymphadenectomy in Gynecological and Urological Malignancies

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Abstract

Objectives: Pelvic lymphadenectomy is a crucial step in the management of different pelvic cancers for both prognostic and/or therapeutic goals. Robotic surgeries offered numerous benefits over open and/or laparoscopic surgeries such as better visualization, shorter hospital stay, less pain and better cosmoses. The aim of this narrative review is to evaluate the value and outcomes of robotic pelvic lymph node dissection (PLND). **Mechanism**: The PubMed database was searched using the following keywords "Robotic" AND "pelvic lymph node dissection" to identify all the relevant articles concerned with the role and outcomes of robotic PLND. We included only English articles published between 2010 and 2022. Data from the retrieved articles were then used to formulate this review that highlight the introduction, the outcomes of robotic pelvic lymph node dissection (PLND), and the mapping of sentinel lymph node (SLN) in cervical, endometrial, prostate, and bladder cancers. **Findings in Brief**: PLND is an integral part of gynecological and urological oncology for its role in tumor staging and planning of further treatment plan. Furthermore, it may play an important therapeutic role in bladder cancer. Robotic approach to PLND is safe and efficient and can be potentially used for cervical, endometrial, prostate, and bladder cancers. **Conclusions**: Robotic PLND could be an alternative to open and laparoscopic approaches as it may decrease the associated morbidities without compromising the quality of Lymph node dissection (LND).

Keywords: pelvic lymph node dissection; robotic surgery; bladder cancer; cervical cancer; endometrial cancer; prostate cancer

1. Introduction

The core concept of surgical oncology is the radicalness, which includes the resection of the primary tumor, the surrounding tissues, and loco-regional lymph nodes [1]. Loco-regional (20.5%) and distant (12.9%) lymph nodes (LN) represent the most common sites of metastasis, which justify the inclusion of lymph node dissection as an important step in the surgical management of different solid tumors [2]. Pelvic malignancies are not exception, where pelvic lymph node dissection (PLND) is considered an integral part of the management of several pelvic malignancies for prognostic and/or therapeutic purposes including cervical cancer [3], endometrial carcinoma [4], bladder cancer [5], and prostate cancer [6]. Despite the significance of PLND in pelvic oncological surgeries, it may be associated with increased morbidity and cost. Therefore, surgeons are obliged to weigh the potential benefits of PLND against its inherent drawbacks [7].

The advent of robotic technology to the surgical field offered several advantages to both surgeons and patients in the form of three-dimensional vision, 10× magnification, tremor filtration, endo-wrist instruments, shorter learning curve compared to laparoscopic approaches, better cosmetic outcomes, shorter hospital stay, less estimated blood loss, and less post-operative pain [8–10]. Thus, these technical advantages may theoretically enhance the outcomes of PLND especially in the narrow pelvic region [11]. In these settings, this narrative review aims at exploring the value and outcomes of robotic PLND.

2. Methodology

The PubMed database was searched using the following keywords "Robotic" AND "pelvic lymph node dissection" to identify all the relevant articles concerned with the role and outcomes of robotic PLND. Several search filters were applied to limit the search to only English articles published between 2010 and 2022. Data from the retrieved articles were then used for the formalization of the current narrative review.

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3. Cervical Cancer

3.1 Introduction

Cervical cancer is the fourth most commonly diagnosed female cancer accounting for approximately 6.5% and 7.7% of all newly diagnosed female cancers and cancer specific-mortality in 2020, respectively [12]. Radical hysterectomy is the standard treatment option for early-stage cervical cancer (stage IA1-IB2), which was performed in an open approach for more than 100 years until minimally invasive approaches (laparoscopic and robotic-assisted laparoscopic) were adopted in the field of gynecological oncology [13]. However, it should be noted that the rate of minimally invasive radical hysterectomy has dramatically decreased over the last four years [14], following the publication of a phase three randomized controlled trial (RCTs) reporting that minimally invasive approaches to radical hysterectomy may be associated with worse disease-free survival (86.0% *vs* 96.5%) and overall survival (93.8% *vs* 99%) compared to open approaches [15]. Yet, it is worth mentioning that this trial was not devoid of limitations and concerns (mainly related to the difference in surgeon's experience, centers' volume, and only 15.6% of the patients undergone robotic-assisted approach) that might have affected the outcomes and thus minimally invasive approaches should not be completely abended [13]. Furthermore, a retrospective analysis of patients undergoing robotic-assisted laparoscopic radical hysterectomy (RALRH) for early-stage cervical cancer in Spain showed that centers with higher surgical volume, more participation in clinical trials, greater use of magnetic resonance imaging (MRI) for diagnosis, favorable learning curve, and higher use of sentinel lymph node biopsies usually report lower rates of recurrences and better oncological outcomes, highlighting the impact of surgical practice on the oncological outcomes of RALRH [16].

Radical trachelectomy is another option for the management of selected patients with small early-stage cervical carcinoma (<2 cm) wishing to preserve fertility. It consists of the resection of the cervix, upper vagina, and parametrium [17]. An international retrospective analysis of 646 patients undergoing radical trachelectomy (358 patients undergone open approach, and 288 patients undergone minimally invasive approach), reported comparable 4.5 years disease-free survival (94.3% *vs* 91.5%, p = 0.37) and overall survival (99.2% *vs* 99%, p = 0.49) among open and minimally invasive approaches, respectively [18].

Pelvic Lymph node metastasis is not rare in patients with early-stage cervical cancer, where it may range from 2% in patients with stage IA2 tumors to 14–36% in patients with stage IB tumors; while, para-aortic lymph node metastasis is less common (2–5% in patients with stage IB tumors) [19]. Thus, regardless the chosen treatment option (radical hysterectomy or radical trachelectomy), bilateral PLND remains an important step in the management plan of early-stage cervical cancer as the lymph node status is the most crucial prognostic factor and plays an essential role in guiding adjuvant protocols [20].

3.2 Robotic PLND in Cervical Cancer

Generally, minimally invasive approaches appear to be an attractive alternative to open pelvic lymphadenectomy with comparable surgical and oncological outcomes [21,22]. Despite the controversy regarding the value of nodal yield on the survival of patients with negative lymph nodes, a more extensive lymph node dissection theoretically improves the pathological accuracy of lymph node status as a greater number of retrieved lymph nodes potentially increase the chance of detecting and resecting micrometastasis [3]. Thus, the number of retrieved pelvic lymph nodes remains a surrogate marker of the extent and quality of surgery [23]. Table 1 (Ref. [15,18,24–38]) shows a summary of nodal yield in the included studies about different approaches to radical hysterectomy. Considering comparative trials, the majority of authors reported a comparable nodal yield among different surgical approaches (16–36 for robotic, 14–27 for laparoscopic, 17–25 for open) [21,26–37,39]. On the contrary, some studies demonstrated a significantly higher nodal yield for the open approach [36,37], while others supported the superiority of minimally invasive approaches [22,38].

Noteworthy, the minimally invasive approaches offer several advantages in the form of less estimated blood loss (50–317.5 mL for robotic [18,30,37,38], 50–325 mL for laparoscopic [31,33], and 200–2000 mL for open approach [18,27]) and shorter hospital stay [18,27,32,36–39]. However, minimally invasive approaches are usually associated with longer operative times [18,27,28,37,39].

3.3 Sentinel Lymph Node Mapping (SLN) in Cervical Cancer

The concept of SLNs was initially described by Gould *et al*. [40], in 1960 for patients with parotid carcinoma, subsequently this concept was introduced to different types of solid malignancies. Generally, SLN may provide the missing balance between the value of PLND and the associated lymphatic complications [41]. SLN mapping is based on the concept that a negative first lymph node group receiving lymphatic drainage from a primary tumor indicates a theoretically negative lymph nodes in the remainder of that basin [42]. In patients with cervical cancer, SLN may be used as an alternative to lymphadenectomy only in patients with early-stage cervical carcinoma and tumors <2 cm due to its low sensitivity and detection rates [43]. However, this recommendation was based mainly on studies that typically use radiocolloid tracer (^{99}Technetium (^{99}Tm)) either alone or in combination with blue dye [44]. Indocyanine Green (ICG) is another dye introduced for the use in cervical carcinoma few years ago. Several authors studied the value of ICG during RALRH reporting a SLN detection rate ranging from 86% to 100% and a rate of bilateral mapping ranging

Table 1. Summary of included studies about the comparison of nodal yield, operative times, blood loss, and hospitalization in patients undergoing different approaches to radical hysterectomy for cervical cancer.

Article	Approach	Patients	Nodal yield	Operative time (min)	Blood loss (mL)	Hospital stay (days)
Salvo *et al.* [18]	Open-RT	358	17	171	200	6
	MIS-RT	288	18	262	50	2
Gao *et al.* [24]	RSS-RH	32	21.37	223.56	217.25	7.5
	LESS-RH	35	20.71	248.61	294.74	7.17
Ding *et al.* [28]	2D-LRH	54	21.7	151.6	233.5	10.4
	3D-LRH	85	23	111.8	211.6	10.7
	RALRH	100	22.4	171.6	317.5	10.9
Ramirez *et al.* [15]	Open-RH	312	21	NA	NA	5
	MIS-RH	319	20	NA	NA	3
Pellegrino *et al.* [29]	RALRH	34	35.58	227.64	67.88	2.58
	LRH	18	24.23	242.87	203.33	3.27
Nie *et al.* [30]	RALRH	100	22.39	171.64	317.5	10.41
	LRH	833	22.51	192.1	322.51	11.5
Wallin *et al.* [36]	Open-RH	155	28.9	197	596	6.3
	RALRH	149	22.7	206	80.9	2.4
Diver *et al.* [38]	MIS-RH	101	19.4	NA	50	1.9
	Open-RH	282	16	NA	500	4.9
Li *et al.* [31]	3D-LRH	24	18.08	222	325	15.54
	RALRH	37	16.05	215.84	309.73	15.57
Corrado *et al.* [32]	Open-RH	43	25	290	480	8
	LRH	41	20	220	250	6
	RALRH	41	23	180	150	4
Corrado *et al.* [33]	Mini-LRH	30	17.5	180	50	2
	RALRH	30	20	185	60	3
Yim *et al.* [34]	RALRH	60	18	200.5	100	11
	LRH	42	19.9	215.6	145	10
Vizza *et al.* [35]	LRH	25	21	188	220	6
	RALRH	25	23	190	160	4
Tinelli *et al.* [25]	LRH	76	27.1	255	95	4
	RALRH	23	24.7	323	157	3
Sert *et al.* [37]	RALRH	35	19.5	263.8	82.8	3.8
	LRH	7	15.4	364.2	164.2	8.4
	Open-RH	26	26.1	163.4	595	9.2
Schreuder *et al.* [27]	RALRH	13	29	434	300	4
	Open-RH	14	26	225	2000	9
Nam *et al.* [26]	RALRH	32	20.2	218.8	220.9	11.6
	Open-RH	32	24.2	209.9	531.5	16.9

MIS, minimally invasive surgery; RH, radical hysterectomy; NA, not available; RT, radical trachelectomy; RSS, robotic single site surgery; LESS, laparoendoscopic single site surgery; LRH, laparoscopic radical hysterectomy; RALRH, robotic-assisted laparoscopic radical hysterectomy; 2D, two-dimensional; 3D, three-dimensional.

from 55% to 98.5% [41,42,45,46]. Similarly, Luhrs *et al.* [41] indicated that ICG was associated with higher SLN detection rates compared to ^{99}Tm. Furthermore, the authors reported that combining ICG with ^{99}Tm did not improve the bilateral detection rates of SLNs [41]. On the same hand, Kim *et al.* [46], demonstrated that the sensitivity, specificity, negative predictive value (NPV), false negative rates (FNR), and accuracy, are generally affected by the tumor size supporting the previous recommendations, where they were 71.43%, 100%, 28.57%, 93.98%, and 94.76% when all tumor sizes (ranging from 0.1–8 cm) were considered, while they improved to 100%, 100%, 0%, 100%, and 100% when only patients with primary tumor <2 cm in size and no lymphadenopathy on imaging were considered. Yet, further studies are required to support the use of ICG guided SLNs as an alternative to lymphadenectomy in patients with cervical cancer.

4. Endometrial Cancer

4.1 Introduction

Endometrial cancer (ECa) is the fifth most commonly diagnosed malignancy in women. Unlike other solid tumors, ECa is showing an increasing incidence and mortality in developed and high-income countries [47]. Surgery remains the cornerstone management for patients with ECa. It includes the radical resection of cervix, uterus, fallopian tubes, and ovaries. Lymph node dissection (LND) is a fundamental part of this surgery as it may provide staging information and guide adjuvant therapy [48]. The decision and extent of LND in patients with ECa is still a matter of debate and is dependable on the preoperative findings (tumor grade, size, site, and myometrial invasion) together with the surgeon's evaluation of all the peritoneal surfaces, pelvic and para-aortic lymph nodes because the lymphatic drainage of the uterus is not limited to the pelvic lymph nodes but it may have a direct lymphatic communication between the fundus of the uterus and the aortic lymph node chains [49]. Generally, this surgery can be performed either through an open, laparoscopic, or robotic approaches. Studies about the minimally invasive approaches (laparoscopic and robotic) in the management of early and advanced ECa supported the advantages of these approaches over laparotomy as regards blood loss, recovery, and hospital stay without compromising the complication rates and oncological outcomes [48]. However, similar to cervical cancer, some concerns were raised regarding the long-term oncological outcomes (recurrence-free survival, overall survival, and disease-specific survival) of robotic surgery compared to laparoscopic surgery [50]. Yet, the robotic approach is still an interesting option for the surgical treatment of patients with ECa.

As previously mentioned, the lymphatic drainage of the uterus includes both pelvic and para-aortic lymph nodes rendering lymph node metastasis in ECa patients a challenging situation as it greatly affects patients' 5-years survival (94% for patients with negative lymph nodes, 75% for patients with positive pelvic nodes, and 38% for patients with positive para-aortic nodes) [51]. Pelvic lymph node metastasis ranges from 3.8–15.2%, 7.3–17.1%, and 6.9–35.3% in low-grade, intermediate-grade, and high-grade tumors, respectively. Similarly, aortic lymph node metastasis ranges from 0.8–9.4%, 5.3–20.5%, 0–25% in low-grade, intermediate-grade, and high-grade tumors, respectively [52]. Overall, the risk of paraaortic lymph node metastasis is 50% in case of positive pelvic lymph nodes, while isolated positive aortic lymph nodes are reported in only 2–3% of patients [49]. Tumor size is another predictor of lymph node metastasis in those patients; however, the cutoff size is controversial in the literature ranging from 2–5 cm. A recent systematic review and meta-analysis of 40 articles identified 2 cm as the ideal cutoff size for prediction of lymph node metastasis (odds ratio (OR) = 4.11, 95% confidence interval (CI) 3.36–4.66, $p < 0.001$).

4.2 Robotic PLND in Endometrial Cancer

Several studies assessed the value of robotic surgery during lymphadenectomy in ECa patients [53,54]. Generally, compared to open and laparoscopic approaches, robotic surgery was associated with a comparable nodal yield (10.5–13 for open and 11–13 for robotic) [53–56], even in obese patients (pelvic nodes 18 *vs* 14, aortic nodes 9 *vs* 3) [53]. On the contrary, Backes *et al.* [57] reported that robotic approach may be associated with significantly lower pelvic nodal yield compared to laparotomy (15 *vs* 18, $p = 0.007$), while the aortic nodal yield was not statistically different. Interestingly, minimally invasive surgeries were associated with higher rates of pelvic lymphadenectomy compared to open surgery [55,57].

Robotic single site docking is a feasible option in patients undergoing robotic hysterectomy and lymphadenectomy (pelvic and/or para-aortic) for surgical staging of ECa with few reported complications including early postoperative complications (8%), lower limb lymphedema (14%), and pelvic lymphocysts (8%) [51,56,58]. Noteworthy, retrospective cohorts showed that patients with intermediate- or high-risk ECa should undergo combined pelvic and para-aortic lymphadenectomy as it is associated with better survival outcomes compared to pelvic lymphadenectomy only [59]. Table 2 (Ref. [53–57]) show a summary of included studies about different approaches to the management of endometrial cancer.

4.3 Sentinel Lymph Node Mapping in Endometrial Cancer

Sentinel lymph node biopsy is proposed as an alternative to lymphadenectomy in ECa. In this setting, a dye with/without a radiotracer is injected into the cervical (most common) or uterine stroma, subsequently, it will be accumulated in the corresponding lymph nodes to aid the recognition of SLNs using the robotic or laparoscopic camera [60]. In ECa, bilateral pelvic mapping is an integral part of the procedure of SLN to decrease the rate of pelvic lymphadenectomies without omitting the mapping of one side of the pelvis [61]. Initially, SLN in ECa was performed using a combination of ^{99}Tm and a visible dye (such as Isosulfan blue dye) [62]; however, this practice was replaced by the use of ICG as it is superior to blue dye in detecting SLNs (64% *vs* 83%, $p < 0.0001$) [63].

The Fluorescence Imaging for Robotic Endometrial Sentinel lymph node biopsy (FIRES) trial is a prospective, multicenter, cohort study that aims to assess the value of ICG-SLN biopsy as an alternative to lymphadenectomy in 385 patients undergoing robotic surgery for stage I ECa. The authors reported that ICG-SLN biopsy can safely replace lymphadenectomy with a sensitivity of 97.2% and a NPV of 99.6%. Cusimano *et al.* [64], supported the same finding in 156 high-grade ECa patients undergoing minimally invasive surgery (laparoscopic or robotic) showing a detection of 97.4% per patient, 87.5% per hemipelvis, and 77.6% bilaterally. In this prospective cohort of patients,

Table 2. Summary of included studies about the comparison of nodal yield, operative times, blood loss, and hospitalization in patients undergoing different approaches to radical hysterectomy for endometrial cancer.

Article	Approach	Patients	Nodal yield	Operative time (min)	Blood loss (mL)	Hospital stay (days)
Bernardini *et al.* [53]	Open-RH	41	14	165	300	4
	RALRH	45	18	270	200	2
Eklind *et al.* [54]	RALRH	40	13	127	76	1.8
	Open-RH	48	13	179	317	4.8
Pulman *et al.* [55]	Open-RH	69	14	210	300	4
	LRH	44	17	240	150	1
	RALRH	63	18	240	150	1
Corrado *et al.* [56]	RSS-RH	125	13	122	50	2
Backes *et al.* [57]	Open-RH	93	18	NA	300	4
	RALRH	89	15	NA	75	1

RH, Radical Hysterectomy; NA, not available; RSS, robotic single site surgery; LRH, laparoscopic radical hysterectomy; RALRH, Robotic-assisted Laparoscopic Radical Hysterectomy.

ICG-SLN biopsy showed a sensitivity of 96.3%, FNR of 3.7%, and a NPV of 99.2% [64]. Similar to SLNs in cervical cancer, the combination of ICG with ^{99}Tm was not superior to ICG alone in the detection of SLN [61]. A recent systematic review and meta-analysis of 14 studies accounting for 2117 patients were in line with the pervious findings showing an overall and bilateral ICG-SLN detection rates of 95.6% and 76.5%, respectively. Furthermore, the authors showed a pooled NPV of 100% for patients with grade I & II ECa and 99.2% for patients with grade I, II, & III ECa [60]. Several other meta-analyses supported these findings [65–67]; however, their results should be interpreted with caution as the quality of these studies are doubtful [68].

5. Prostate Cancer

5.1 Introduction

According to the GLOBCAN study 2020, prostate cancer (PCa) is the second most common male malignancy worldwide with an incidence and mortality of 14.1% and 6.8%, respectively [12]. Nerve sparing radical prostatectomy (RP) is considered the current standard of care for patients with clinically localized prostate cancer and life expectancy of >10 years [8,69]. Considering, the relatively significant incidence of lymph node metastasis (5–10%) in patients with PCa [70], the combination of PLND with RP is indicated in patients with risk of nodal metastasis $\geq$5% on validated nomograms [69]. Yet, the oncological value of PLND in the setting of RP remains one of the most controversial topics in the urological literature but its diagnostic and prognostic role should not be neglected [71].

The extent of LND is another point of debate, where the literature describes several templates extending from minimal or limited LND (including only the obturator fossa), standard dissection (obturator fossa and external iliac LNs), to extended dissection (extends to the common iliac up to the crossing of the ureter) [70]. Generally, the European Association of Urology (EAU) guidelines recommends the extended template of PLND [69].

Currently, the robotic approach to RP is the most commonly used approach for treating patients with PCa rendering robotic-assisted laparoscopic radical prostatectomy (RALP) the most commonly performed robotic procedure worldwide [10]. This may be attributed to the technical advantages of robotic surgery over laparoscopic and open surgeries [72]. Furthermore, there is some evidence that RALP may provide superior outcomes as regards the oncological and functional domains [73–76]. In this setting, robotic PLND as a part of RP is common in the urological discipline [70].

5.2 Robotic PLND in Prostate Cancer

Over the last two decades, there was a decrease in the rate and indications of PLND during RP even among patients with intermediate and high risk PCa. Some surgeons related this finding to the wide adoption of the robotic approach to RP as surgeons wanted to avoid longer operative times, which may subsequently increase the risk of complications and the operative costs [7,77]. Interestingly, Gandaglia *et al.* [77] used the Surveillance, Epidemiology, and End Results Program (SEER) database to assess the impact of robotic surgery on PLND during RP between October 2008 and December 2009, showing that patients undergoing open RP were more likely to undergo PLND compared to RALP (71.2% *vs* 48.6%, $p < 0.001$). This finding was consistent after stratifying the patients according to PCa risk [77]. On the contrary, a more recent study (including patients undergoing RP between 2004–2013) showed significant increase in the rate of PLND from 58.9% to 72.1%. Furthermore, this finding persists when patients were stratified according to the surgical approach (from 57.1% to 67.9%, 67.8% to 73.9%, and 77.6% to 81.3%, for robotic, laparoscopic, and open approaches, respectively). Yet, the rate of PLND during open and laparoscopic approaches was higher compared to robotic approach [78].

LN yield in PCa patients is an important predictor of lymph node positivity and surrogate marker of the quality of LND [79]. Two systematic reviews reported that the lymph node yield during robotic PLND ranges from 3.3 to 24 based on the template of dissection [7,80]. Results from RCTs showed that that the nodal yield is comparable among robotic and laparoscopic approaches [81], while it was higher for RALP compared to open RP [82]. Noteworthy, these studies were not designed to compare the nodal yield among different approaches [81,82].

5.3 Sentinel Lymph Node Mapping in Prostate Cancer

SLN biopsy in patients undergoing RALP aims to provide the balance between the potential value of PLND and its associated morbidities through identifying the patients who might benefit from PLND [83]. However, it is still considered an experimental procedure because of the complex lymphatic drainage of the prostate and the heterogeneous results of SLN biopsy in the medical literature [70]. Currently, ICG is the most commonly used dye for the SLN biopsy in PCa patients.

Hence, PCa is a multifocal neoplasm, it is not clearly known which lesion will metastasize or which one is the index lesion [84]. In this setting, the site of injection of the dye might have an impact on the outcomes of SLN biopsy. A recent RCT showed that ultrasound guided, transrectal, intratumoral injection of ICG-Technetium 99 m was associated with significantly higher percentage of positive SLNs compared to intraprostatic injection in the peripheral zone of the prostate [85].

Considering the outcomes of SLN biopsy, a systematic review and meta-analysis of 21 studies accounting for 2509 patients undergoing SLN biopsy through either transrectal or transperineal injection of tracers in the peripheral zone of the prostate or the whole prostate during RP (open, robotic, or laparoscopic), reported a pooled non-diagnostic ratio, sensitivity, specificity, positive predictive value (PPV), and NPV of 4.1%, 95.2%, 100%, 100%, and 98%, respectively [86]. Noteworthy, this meta-analysis included studies using different types of tracers [86]. In this setting, a more recent systematic review and meta-analysis assessed only the performance of ICG-SLN biopsy in patients undergoing RP concluded that the diagnostic performance of this procedure is relatively low (sensitivity = 0.75, and specificity = 0.66) rendering it a suboptimal alternative to PLND [87]. However, the combination of prostate specific membrane antigen positron emission tomography and computed tomography (PSMA PET/CT) and SLN biopsy is capable of improving the detection rate of positive lymph nodes by 26% [88]. Generally, a consensus meeting in Germany considered that extended PLND remains the standard of care for lymph node staging, while SLN biopsy can be considered in conjunction with PLND in intermediate- and high-risk PCa patients [89].

6. Bladder Cancer

6.1 Introduction

Bladder cancer (BCa) is one of the most common urological neoplasms [12]. Approximately, 75% of bladder cancers are confined to the mucosa without invasion of the detrusor muscle. The treatment those patients with non-muscle invasive BCa consists of complete endoscopic resection of the mass followed by intravesical chemo- or immune-therapy [90]. Unfortunately, the remaining 25% are muscle invasive BCa, which is a more aggressive form of the disease that requires a more radical intervention in the form of radical cystectomy (RC) with bilateral PLND [70]. Generally, the extent of LND in patients with BCa is debatable as the lymphatic drainage of the bladder is complex as it mainly includes the obturator, external and internal iliac, and presacral lymph nodes. However, it may also extend to the common iliac, paraaortic, interaortocaval, and paracaval LNs [91]. Unlike PCa, the advantage of PLND in patients with BCa is not limited to its prognostic value but it extends to include also a survival benefit [92]. In this setting, an extended PLND template is recommended as a standard template may underestimate the presence of LN metastasis by 11% [93], and is generally associated with significantly higher all-cause and cancer-specific mortalities [94]. In these settings, PLND is considered an integral part of the treatment of patients with BCa.

Robotic approach to RC started to gain popularity among urologists due to the high complexity of open approach with its associated morbidity and mortality together with the steep learning curve of pure laparoscopic RC [95]. Despite the lack of high-level evidence, robotic assisted laparoscopic radical cystectomy (RARC) continues to expand at the expenses of open and laparoscopic approaches. Noteworthy, results from RCTs comparing RARC to open and laparoscopic approaches showed that RARC is associated with significantly longer operative times, lower estimated blood loss, lower postoperative pain and shorter hospitalization. Yet, there was no significance difference as regards the post-operative complication rates and the oncological outcomes. It should be mentioned that most of the RCTs comparing the robotic approach to other approaches was limited to patients undergoing RARC with extracorporeal urinary diversion, which may limit the benefits of minimally invasive surgery [96]. In this setting, the most recent RCT comparing open radical cystectomy to RARC with intracorporeal urinary diversion showed significantly higher rates of perioperative blood transfusion in patients undergoing open RC (41% *vs* 22%, p = 0.047) [97].

6.2 Robotic PLND in Bladder Cancer

Theoretically, minimally invasive approaches to RC are associated with better quality of LND in the form of higher Lymph node yield and lower density compared to open approach because minimally invasive approaches allow enbloc resection of lymphatic tissue with a 10× magnified view of the surgical field [98,99]. A recent analysis of 1425 BCa patients from the Italian Radical Cystectomy Registry showed that robotic and laparoscopic approaches were associated with higher rates of PLND compared to open approach (97.1%, 93.5%, and 85.6%, respectively, $p < 0.001$). Furthermore, the authors reported that the rate of limited template of PLND was comparable among the three approaches, while RARC was associated with 2-folds higher rates of using extended PLND template compared to the other approaches [100]. Similar to the previously discussed tumors, LNs yield is an important indicator of the quality of LND and it may have an impact on the patients' survival [101]. In this setting, an analysis of 16,505 muscle invasive BCa patients undergoing RC with PLND reported that the oncological outcomes (in patients not receiving neoadjuvant chemotherapy) were significantly superior in patients who had adequate LND ($\geq$10 nodes) compared to those with inadequate LND ($<$10 nodes) [102].

Some authors demonstrated that RARC may be associated with higher LN yield compared to other approaches (16–20 nodes *vs* 11–14 nodes based on the extent of dissection, respectively) [103,104]. However, when considering the results from RCTs, the lymph node yield in patients undergoing RARC seems to be comparable to open and laparoscopic approaches [97,105–108].

LN density was proposed as an alternative to LN yield in the assessment of the quality of LND as LN yield is related to several factors that may affect its assessment including the method of submission (enbloc or separate packets), the surgeon's experience and technique, and the pathologists' experience [70]. Lymph node density refers to the number of positive LNs to the total number of nodes retrieved. A density of $>$20% is associated with a 10% reduction of survival. However, there is still no consensus on the ideal way of assessment of the quality of PLND [109].

6.3 Sentinel Lymph Node Mapping in Bladder Cancer

The concept of SLN biopsy in patients with BCa is less commonly utilized as it is still experimental [110]. In this setting, Schaafsma *et al*. [111] injected ICG bound to human serum albumin (an experimental material not available in market) cystoscopically around the bladder tumor after bladder distention demonstrating the feasibility of this technique in identifying of SLNs in BCa patients. In line with this study, Rietbergen *et al.* [112] demonstrated the feasibility of ICG-^{99m}Tc-nanocolloid injected one day before surgery in identifying SLN in 63% of patients. Furthermore, the authors demonstrated that preoperative imaging in the form of lymphoscintigraphy and SPECT/CT was capable of identifying 83% of patients who showed any SN on intra-operative guidance, thus highlighting the value of preoperative imaging in patients undergoing SLN-biopsy [112]. Despite being a promising tool for intraoperative guidance, SLN biopsy in BCa patients requires further assessment and no recommendations can be built based on the currently available evidence [110].

7. Conclusions

PLND is an integral part of gynecological and urological oncology for its role in tumor staging and planning of further treatment plan. Furthermore, it may play an important therapeutic role in bladder cancer. Robotic approach to PLND seems to be an interesting alternative to open and laparoscopic approaches as it may decrease the associated morbidities without compromising the quality of LND (nodal yield). SLN-biopsy can be applied during minimally invasive surgery to improve the quality of LND, while reducing the associated morbidity.

Abbreviations

BCa, Bladder cancer; ECa, Endometrial cancer; EAU, European Association of Urology; FNR, False negative rate; ICG, Indocyanine green; LND, Lymph node dissection; LN, Lymph nodes; MRI, Magnetic resonance imaging; NPV, Negative predictive value; PCa, Prostate cancer; PPV, Positive predictive value; PSMA PET/CT, Prostate specific membrane antigen positron emission tomography and computed tomography; PLND, Pelvic lymph node dissection; RP, Radical prostatectomy; RALP, Robotic-assisted laparoscopic radical prostatectomy; RCTs, Randomized controlled trials; RALRH, Robotic-assisted laparoscopic radical hysterectomy; RC, Radical cystectomy; RARC, Robotic-assisted laparoscopic radical cystectomy; SLN, Sentinel lymph node; SPECT/CT, single-photon emission computerized tomography and computed Tomography; ^{99}Tm, ^{99}Technetium.

Author Contributions

Conceptualization—AEis, MCS, GG, AZ, BR, SM, AHE; Methodology—GH, IE, AEls, AM, MAE; Database Search & Data Extraction—GH, IE, SP, AEls, AZ, ME, MR; Original Drafting—AEis, MCS, SP, MR, MAE, GG; Article Writing—ME, AEis, AM, MR; Review & Supervision—MAE, ME, AHE, SM, BR. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. Giorgia Gaia is serving as one of the Guest editors of this journal. We declare that Giorgia Gaia had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Ugo Indraccolo.

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