Journal of Robotic Surgery (2022) 16:1111–1115
https://doi.org/10.1007/s11701-021-01321-5

ORIGINAL ARTICLE

Sentinel lymph node biopsy at robotic-assisted hysterectomy for atypical hyperplasia and endometrial cancer

Vanessa El-Achi[1] · Michael Burling[1,2] · Murad Al-Aker[1]

Received: 17 September 2021 / Accepted: 16 October 2021 / Published online: 2 December 2021

Abstract

Lymph node (LN) evaluation in endometrial cancer is controversial. Sentinel lymph node biopsy (SLNB) allows for an accurate nodal assessment while minimising the risks of a full pelvic lymph node dissection (PLND). The aims of this study are to examine the characteristics and peri-operative outcomes of women with atypical hyperplasia (AH) or endometrial cancer undergoing robotic-assisted hysterectomy (RAH) ± SLNB or PLND; to examine the utilisation, feasibility and role of SLNB and compare their peri-operative outcomes. Retrospective cohort study from December 2018 to February 2021 of women who underwent RAH ± LN assessment for endometrial cancer or AH. 115 women underwent RAH. 59% had SLNB, 29% had no LN assessment, and 12% had PLND. The final diagnosis was mostly early stage low-grade disease; Stage 1A—50%, Grade 1 endometrioid adenocarcinoma (EAC)—56%. The detection rate was 90%. There was a statistically significant trend towards performing SLNB over time (*P* value 0.004). There was a statistically shorter length of stay, less estimated blood loss, and shorter surgical duration in the SLNB cohort, compared to the no LN assessment cohort (*P* values 0.02, 0.01, and 0.03, respectively). There was statistically significant less estimated blood loss and surgical duration in the SLNB compared to the PLND cohort (*P* values 0.03 and 0.001, respectively). SLNB at RAH was utilised and feasible. It was safe with a low complication rate and had advantages compared to PLND cohort. SLNB should be considered in suitable selected women undergoing surgery for endometrial cancer or AH.

Keywords Endometrial cancer · Atypical hyperplasia · Sentinel lymph node biopsy · Robotic-assisted surgery · Hysterectomy

Introduction

Lymph node (LN) evaluation in endometrial cancer is controversial [1]. The data regarding its use are limited and practice varies between surgeons [2]. However, the status of the LNs is potentially crucial information as part of surgical staging. It provides both prognostic information and guides adjuvant therapy [3].

Atypical hyperplasia (AH), or previously referred to as complex hyperplasia with atypia, is a pre-malignant condition, and 30–40% of women have a concurrent diagnosis of endometrial cancer [3]. Given the high frequency of endometrial cancer in this population, there is rationale to consider LN assessment in these women, as well. However, there is no consensus on the role of LN assessment in this population [1, 4, 5].

A full pelvic lymph node dissection (PLND) has the potential for significant morbidity and has not been shown to have a survival benefit in early stage disease [6, 7]. Hence, the role of a sentinel lymph node biopsy (SLNB) bridges the gap between "all" or "nothing" approach [2, 3, 8]. SLNB aims to reduce the number of nodes removed for staging, by targeting those most likely to contain metastasis while still maintaining the ability to find microscopic nodal disease [9]. This allows for assessment of LN status to guide staging and adjuvant treatment. SLNB offers an efficient alternative to selecting patients to be surgically staged based on risk

✉ Vanessa El-Achi
vanessa.elachi@nsw.health.gov.au

Michael Burling
Michael.Burling@health.nsw.gov.au

Murad Al-Aker
Murad.AlAker@health.nsw.gov.au

1 Gynaecology Oncology Department, Liverpool Hospital, Sydney, NSW, Australia

2 Westmead Hospital, Sydney, NSW, Australia

factor-based models [10, 11]. SLNB minimises the risks of a full PLND—including reduction in operative time, peri-operative complications, length of hospital stay, costs, and impact on QOL such as lymphoedema [12–15]. Furthermore, the accuracy of an SLNB is supported by three prospective trials, demonstrating high sensitivity and negative predictive value, and low false-negative rate [8, 16, 17].

In addition, many surgeons have embraced robotic-assisted surgery for endometrial cancer [2]. It has advantages to laparoscopy including superior 3D vision, improved range of motion, and comfortable ergonomics. It has also been shown to increase the number of LNs dissected, and reduce the length of stay and estimated blood loss [18].

Therefore, we aimed to examine the characteristics and peri-operative outcomes of women with AH or endometrial cancer undergoing robotic-assisted hysterectomy. We also aimed to examine the utilisation, feasibility, and role of SLNB, and compare the peri-operative outcomes of women undergoing SLNB versus no LN assessment versus PLND.

Methods

We performed a retrospective cohort study at a single tertiary centre in Sydney. Ethics approval was obtained (2021/ETH01079 and 2021/STE02091). We included all women who underwent a robotic-assisted hysterectomy (RAH) ± adnexal procedure for either AH or endometrial cancer. Two consultant surgeons experienced in robotic-assisted surgery using the DaVinci XI (Intuitive Surgery, Sunnyvale, CA, USA) performed all the robotic surgeries, using the multi-port system, with Gynaeoncology fellows and/or registrars assisting. Each case was reviewed in collaboration at the Gynaeoncology unit multidisciplinary team meeting. In the AH cohort, the decision to perform a SLNB was made prior to surgery based on the consensus at the Gynaeoncology unit multidisciplinary team meeting after the pre-operative histopathology was examined by a dedicated Gynaeoncology pathologist. SLNB was recommended in women with AH who were post-menopausal and therefore considered to be at higher risk for endometrial cancer.

To perform a SLNB, indocyanine green (ICG) fluorescent tracer was injected into the cervix at the beginning of the case following general anaesthesia. The standard technique of using an ICG dose of 0.5 mg/mL was created by diluting the stock solution into sterile water. This was injected into the cervix superficial (1–3 mm) and deep (1–2 cm) at 3 o'clock and 9 o'clock of the ectocervix [3, 13]. After entry to the peritoneal cavity, fluorescence imaging was used to visualise the ICG tracer in the lymphatics. Mapped LNs were then excised, as well as any other suspicious bulky nodes. If there was no mapping to a hemi-pelvis in women with a pre-operative diagnosis of endometrial cancer, then a side-specific LND was performed [3]. If there was no mapping in women with a pre-operative diagnosis of AH, an LND was not performed unless visual assessment of the specimen suggested gross invasion of greater than 50% of the myometrium. Intra-operative frozen sections were not used.

The study period was from December 2018 to February 2021. Patients were excluded if they had diagnoses other than AH or endometrial cancer. Women were also excluded if they were planned for single-site robotic surgery, laparoscopic surgery, or laparotomy approach. LN assessment was classed as either no LN sampling, SLNB, or PLND with intention to treat analysis.

Patients were identified from a prospectively maintained gynaecology oncology database. Data were collected from the Oncology and general medical electronic records, including age, BMI, indication for surgery (pre-operative diagnosis), final pathological diagnosis, type of surgery performed, length of hospital stay, operation duration, estimated surgical blood loss, and adverse events (including mortality within 30 days, conversion to laparotomy, return to theatre, urological injury, and readmissions or representations to the emergency department). Surgical duration was recorded from the time of skin incision to the completion of closure of wounds. For the SLNB cohort, detection rate was defined as the proportion of cases with any successful SLN mapping. Bilaterality was defined as the proportion of cases in which SLNs were identified intra-operatively. Empty packages were defined as samples that did not yield an LN on pathological analysis.

Comparisons were analysed using *t* test for normally distributed continuous data and Chi-square test for categorical data. Yates correction and Fisher's exact tests were used as required. *P* value of <0.05 was considered significant.

Results

115 women had RAH with or without LN assessment. Mean age was 61.9 ± 10.3 years and mean BMI 34.3 ± 10 0.5 kg/m^2. 45% were born in Australia. 59% had SLNB, 29% had no LN assessment, and 12% had PLND (Table 1). 41.9% of

Table 1 Number of patients undergoing each type of lymph node assessment

Type of LN assessment	Number of patients
No LN sampling	33 (28.7%)*
SLNB	68 (59.1%)
PLND	14 (12.2%)

*Of these, 16 (48.5%) patients had a pre-operative diagnosis of hyperplasia; 16 (48.5%) had a pre-operative diagnosis of G1 EAC. 1 (3.0%) patient had other diagnosis

Table 2 Pre-operative and post-operative diagnosis of patients who underwent an SLNB

Pre-op diagnosis ($n=68$)		Number of patients
CH with atypia		13 (19.1%)
EAC	Grade 1	37 (54.4%)
	Grade 2	12 (17.6%)
	Grade 3	3 (4.4%)
Other—carcinosarcoma, serous adenocarcinoma, clear cell		3 (4.4%)
Post-op diagnosis ($n=68$)		**Number of patients**
CH with atypia		8 (11.8%)
EAC	Total	53 (77.9%)
	Stage 1A	34 (50%)
	Stage 1B	16 (23.5%)
	Stage 2	2 (2.9%)
	Stage 3	1 (1.5%)
	Grade 1	38 (55.9%)
	Grade 2	12 (17.6%)
	Grade 3	3 (4.4%)
Other—carcinosarcoma, serous adenocarcinoma, clear cell, stromal sarcoma, serous papillary carcinoma		7 (10.3%)

Table 3 Effectiveness of the SLNB technique

SLNB cohort ($n=68$)	Total (%)
Detection rate	61 (89.7%)
Bilaterality	57 (83.8%)
Empty packages	9/116 (7.8%)

women with a pre-operative indication of AH had a final diagnosis of cancer. 35.7% of the PLND cohort had positive LNs.

76.4% of women in the SLNB cohort had a pre-operative diagnosis of endometrioid adenocarcinoma (EAC), mostly Grade 1 (54.4%) (Table 2). The final diagnosis was mostly early stage low-grade disease (Stage 1A—50%, Grade 1 EAC—56%) (Table 2). The detection rate for SLNB was 90% (Table 3). The rate of bilaterality was 83.8% and empty packages were found in 7.8% (Table 3). There was a statistically significant trend towards performing SLNB over time (47% December 2018–December 2019 versus 75% January 2020–February 2021, P value 0.004).

On comparison of the SLNB and no LN sampling cohort, there was no difference in age and peri-operative complications (Table 4). However, there was a statistically lower BMI, shorter length of stay, less estimated blood loss, and shorter surgical duration in the SLNB cohort, compared to the no LN assessment cohort (P values 0.02, 0.01 and 0.03 respectively) (Table 4).

On comparison of the SLNB and PLND cohorts (Table 5), there was no difference in age, BMI, length of stay, or complications. However, there was statistically significant less estimated blood loss and surgical duration in the SLNB compared to the PLND cohort (P values 0.03 and 0.001, respectively).

Table 4 Demographics and peri-operative outcomes SLNB versus no LN cohorts

Demographics and peri-operative outcome	SLNB ($n=68$)	No LN sampling ($n=33$)	P value
Age	61.6 ± 10.6	61.8 ± 9.8	0.93
BMI	36.1 ± 9.7 ($n=62$)	44.4 ± 10.6 ($n=26$)	0.0002*
Length of stay (days)	1.5 ± 0.5	2.9 ± 5.0	0.02*
EBL (mL)	53.2 ± 41.7	169.6 ± 362.5	0.01*
Surgery duration (mins)	132.3 ± 29.6	151.9 ± 63.9	0.03*
Conversion to laparotomy	0 (0%)	2 (6.1%)	0.10
Return to theatre	0 (0%)	1 (3.0%)	0.33
Ureteric injury	0 (0%)	0 (0%)	1.0
Readmissions or representations to hospital	3 (4.4%)	2 (6.1%)	0.66
Mortality	0 (0%)	0 (0%)	1.0

Table 5 Demographics and peri-operative outcomes SLNB versus PLND cohorts

Demographics and peri-operative outcome	SLNB (n=68)	PLND (n=14)	P value
Age	61.6 ± 10.6	63.3 ± 11.0	0.59
BMI	36.1 ± 9.7 (n=62)	35.9 ± 9.9 (n=14)	0.78
Length of stay (days)	1.5 ± 0.5	1.4 ± 0.5	0.50
EBL (mL)	53.2 ± 41.7	219.8 ± 657.2	0.03*
Surgery duration (mins)	132.3 ± 29.6	170.9 ± 69.9	0.001*
Conversion to laparotomy	0 (0%)	1 (7.1%)	0.17
Return to theatre	0 (0%)	0 (0%)	1.0
Ureteric injury	0 (0%)	0 (0%)	1.0
Readmissions or representations to hospital	3 (4.4%)	3 (21.4%)	0.059
Mortality	0 (0%)	1 (7.1%)	0.17

Discussion

In this study, SLNBs were utilised and feasible using robotic-assisted technology for women undergoing surgery for AH or endometrial cancer. There was a total of 115 patients in our cohort, 59% of which had an SLNB, and there was a statistically significant trend towards an increased utilisation of SLNB over time. This trend towards performing an SLNB is consistent with the changing paradigm in surgical staging for these patients [17].

There was a high detection rate of 90%, comparative to the previous studies [2, 13]. Our bilaterality rate was also moderate at 84%; there is a wide range in bilaterality rates in the previous studies, likely a reflection of the learning curve of different surgeons and centres [13, 16, 17]. Since most of our patients had a pre-operative indication of grade 1 EAC and final diagnosis of early stage low-grade endometrial cancer, it is a suitable approach to surgical staging in this cohort, comparative to previous studies [2, 3, 17].

The no LN sampling cohort had a longer length of stay, higher EBL, and longer surgery duration (Table 4). This is likely a reflection of selection bias; that is, women who did not have LN assessment were more likely to have a higher BMI (P value 0.0002), and hence a higher surgical risk. This may explain why the no LN assessment group had a longer length of stay [19], higher EBL [20], and longer surgical duration [19, 21]. Although not examined in this study, it is likely that these women also had more comorbidities or illnesses, which meant that they were a higher surgical risk and deemed not suitable for longer, more complicated surgery, and these risk factors may have also influenced their peri-operative outcomes.

In the cohort of AH, 42% had a final diagnosis of endometrial cancer, which supports the role of performing an SLNB in these women. This rate of findings cancer in the final pathology in this cohort is consistent with the previous trials [4, 5]. Most of the patients in this cohort that were diagnosed with cancer were diagnosed with Stage 1A Grade 1 disease and no women had positive nodes; hence, there is an argument that SLNB is potentially overtreating these women and an argument for selecting only high-risk women for an SLNB [4, 5]. For example, the previous studies have identified that those patients at greater risk of endometrial cancer on final pathology had a pre-operative diagnosis of AH where cancer could not be excluded, and hence that SLN mapping could be a valuable staging procedure in these patients [4]. Furthermore, they identified that an elevated pre-operative CA 125 was associated with the risk of LN metastasis on final pathology. No patients in our study had positive nodes from the AH cohort, which may be due to a small sample size. In the study by Touhami et al. [4], they included 120 patients with atypical hyperplasia, of which 3.3% had positive LN metastasis. This supports a role for performing an SLNB in high-risk women with a pre-operative diagnosis of AH.

We also demonstrated that SLNB using robotic-assisted technology was safe, consistent with previous findings [16, 17]. We had a low complication rate, which was comparable to the cohort which had no LN sampling performed and previous studies [17]. It also had advantages to a full PLND included statistically significantly less EBL and surgical time [13, 14, 16].

Some of the strengths of this study include that it was conducted at a large tertiary centre and the pathology was reviewed by a dedicated Gynaeoncology pathologist. Some limitations of this study include that is in a single-centre study, it is retrospective, subject to selection bias and confounding, we did not assess long-term outcomes (such as cancer recurrence, survival, and lymphoedema) and we were unable to calculate the sensitivity, specificity, and false-negative rate based on the available data. Future directions could include larger prospective studies, studies that examine the learning curve of surgeons and trainees, long-term outcomes (such as lymphoedema and cancer recurrence), a comparison of robotic and laparoscopic SLNB, and an assessment of patient and surgeon attitudes.

Conclusion

In conclusion, SLNB at RAH was utilised and feasible with a statistically significant trend towards increased utilisation over time and high detection rate. SLNB at RAH was safe with a low complication rate comparable to No LN sampling cohort and had advantages compared to PLND cohort. SLNB should be considered in suitable selected women undergoing surgery for endometrial cancer or AH.

Acknowledgements Not applicable.

Author contributions VE-A contributed to intellectual planning of the project, data collection, intellectual analysis of the data, and writing of the manuscript. MA-A and MB contributed to intellectual planning and revision of the paper.

Funding No funding was obtained to conduct this research.

Availability of data and materials All relevant data are available.

Code availability Not applicable.

Declarations

Conflict of interest The authors, Dr Vanessa El-Achi, Dr Michael Burling, and Dr Murad Al-Aker declare that they have no conflict of interest.

Ethics approval This research project was approved by the local institution ethics committees: South Western Sydney Local Health District (2021/ETH01079 and 2021/STE02091).

References

1. Rossi EC, Tanner E (2021) Controversies in sentinel lymph node biopsy for gynecologic malignancies. J Minim Invasive Gynecol 28(3):409–417
2. Mereu L, Pellegrini A, Carline R, Terreno E, Prasciolu C, Tateo S (2018) Feasibility of sentinel lymph node fluorescence detection during robotic laparoendoscopic single-site surgery in early endometrial cancer: a prospective case series. Gynecol Surg 15(14)
3. NCCN NCCN (2020) Uterine Neoplasms 1:108
4. Touhami O, Grégoire J, Renaud MC, Sebastianelli A, Grondin K, Plante M (2018) The utility of sentinel lymph node mapping in the management of endometrial atypical hyperplasia. Gynecol Oncol 148(3):485–490
5. Whyte JS, Gurney EP, Curtin JP, Blank SV (2010) Lymph node dissection in the surgical management of atypical endometrial hyperplasia. Am J Obstet Gynecol 202(2):176.e1–4
6. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G et al (2008) Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 100(23):1707–1716
7. Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK (2009) Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 373(9658):125–136
8. Cusimano MC, Vicus D, Pulman K, Maganti M, Bernardini MQ, Bouchard-Fortier G et al (2021) Assessment of sentinel lymph node biopsy vs lymphadenectomy for intermediate- and high-grade endometrial cancer staging. JAMA Surg 156(2):157–164
9. Abu-Rustum NR (2014) Sentinel lymph node mapping for endometrial cancer: a modern approach to surgical staging. J Natl Compr Canc Netw 12(2):288–297
10. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J et al (2015) ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up. Radiother Oncol 117(3):559–581
11. Papadia A, Gasparri ML, Siegenthaler F, Imboden S, Mohr S, Mueller MD (2017) FIGO stage IIIC endometrial cancer identification among patients with complex atypical hyperplasia, grade 1 and 2 endometrioid endometrial cancer: laparoscopic indocyanine green sentinel lymph node mapping versus frozen section of the uterus, why get around the problem? J Cancer Res Clin Oncol 143(3):491–497
12. Suidan RS, Sun CC, Cantor SB, Mariani A, Soliman PT, Westin SN et al (2018) Three lymphadenectomy strategies in low-risk endometrial carcinoma: a cost-effectiveness analysis. Obstet Gynecol 132(1):52–58
13. Rossi EC, Ivanova A, Boggess JF (2012) Robotically assisted fluorescence-guided lymph node mapping with ICG for gynecologic malignancies: a feasibility study. Gynecol Oncol 124(1):78–82
14. Geppert B, Lönnerfors C, Bollino M, Persson J (2018) Sentinel lymph node biopsy in endometrial cancer-feasibility, safety and lymphatic complications. Gynecol Oncol 148(3):491–498
15. Helgers RJA, Winkens B, Slangen BFM, Werner HMJ (2020) Lymphedema and post-operative complications after sentinel lymph node biopsy versus lymphadenectomy in endometrial carcinomas-a systematic review and meta-analysis. J Clin Med 10(1)
16. Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, Hanna RK et al (2017) A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. Lancet Oncol 18(3):384–392
17. Persson J, Salehi S, Bollino M, Lönnerfors C, Falconer H, Geppert B (2019) Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. Eur J Cancer 116:77–85
18. Boggess JF, Gehrig PA, Cantrell L, Shafer A, Ridgway M, Skinner EN et al (2008) A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: robotic assistance, laparoscopy, laparotomy. Am J Obstet Gynecol 199(4):360.e1–9
19. McMahon MD, Scott DM, Saks E, Tower A, Raker CA, Matteson KA (2014) Impact of obesity on outcomes of hysterectomy. J Minim Invasive Gynecol 21(2):259–265
20. Harmanli O, Esin S, Knee A, Jones K, Ayaz R, Tunitsky E (2013) Effect of obesity on perioperative outcomes of laparoscopic hysterectomy. J Reprod Med 58(11–12):497–503
21. Mikhail E, Miladinovic B, Velanovich V, Finan MA, Hart S, Imudia AN (2015) Association between obesity and the trends of routes of hysterectomy performed for benign indications. Obstet Gynecol 125(4):912–918