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Review article

Paucity of data evaluating patient centred outcomes following sentinel lymph node dissection in endometrial cancer: A systematic review

Helena M. Obermair [a], Montana O'Hara [b], Andreas Obermair [c,d], Monika Janda [b,*]

[a] Department of Obstetrics and Gynaecology, Royal North Shore Hospital, Sydney, New South Wales, Australia
[b] Centre of Health Services Research, Faculty of Medicine, The University of Queensland, Brisbane, Queensland, Australia
[c] Queensland Centre for Gynaecological Cancer, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia
[d] Centre for Clinical Research, University of Queensland, Brisbane, Queensland, Australia

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ABSTRACT

Sentinel lymph node dissection (SLND) is presently used by the majority of gynaecologic oncologists for surgical staging of endometrial cancer. SLND assimilated into routine surgical practice because it increases precision of surgical staging and may reduce morbidity compared to a full, systematic LND. Previous research focussed on the accuracy of SLND. Patient centred outcomes have never been conclusively demonstrated. The objective of this systematic review was to evaluate patient centred outcomes of SLND for endometrial cancer patients. Literature published in the last five years (January 2015 to April 2020) was retrieved from PubMed, EMBASE, and Cochrane library, across five domains: (1) perioperative outcomes; (2) adjuvant treatment; (3) patient-reported outcomes (PROs); (4) lymphedema, and (5) cost. Covidence software ascertained a standardised and monitored review process. We identified 21 eligible studies. Included studies were highly heterogeneous, with widely varying outcome measures and reporting. SLND was associated with shorter operating times and lower estimated blood loss compared to systematic LND, but intra-operative and post-operative complications were not conclusively different. There was either no impact, or a trend towards less adjuvant treatment used in patients with SLND compared to systematic LND. SLND had lower prevalence rates of lymphedema compared to systematic LND, although this was shown only in three retrospective studies. Costs of surgical staging were lowest for no node sampling, followed by SLND, then LND. PROs were unable to be compared because of a lack of studies. The quality of evidence on patient-centred outcomes associated with SLND for surgical staging of endometrial cancer is poor, particularly in PROs, lymphedema and cost. The available studies were vulnerable to bias and confounding.

Registration of Systematic Review: PROSPERO (CRD42020180339)

1. Introduction

Endometrial cancer is the fifth most common cancer diagnosed in women in developed countries. Globally, it has an incidence of 382,069 new cases per year (Bray et al., 2018) and in the United States endometrial cancer is the most commonly diagnosed gynaecological cancer, with 65,620 new cases estimated to be diagnosed in 2020 (American Cancer Society, 2020).

Practice management guidelines for endometrial cancer recommend removal of the primary tumour (total hysterectomy, bilateral salpingo oophorectomy) (Casarin et al., 2019; Colombo et al., 2016; Kunos et al., 2017) and also prescribe surgical staging to determine the extent of the disease, which is achieved through removal and histopathological assessment of lymph nodes (Shepherd, 1989; Mikuta, 1993). Surgical staging was introduced to gynaecological oncology practices based on the results of observational, clinicopathologic studies (Boronow et al., 1984; Creasman et al., 1987) but not prospective, randomized trials comparing systematic lymph node dissection (LND) versus no LND. Consequently, the International Federation of Gynaecologists and Obstetricians (FIGO) adopted a surgical staging system in 1988 (Amant et al., 2018).

Sentinel lymph node dissection (SLND) evolved from systematic LND using advanced intraoperative imaging technology and has assimilated into routine surgical practice (Casarin et al., 2019; Burke et al., 1996;

* Corresponding author at: Centre for Health Services Research, Faculty of Medicine, The University of Queensland, Building 33, Princess Alexandra Hospital Campus, Woolloongabba, QLD 4102, Australia.
E-mail address: m.janda@uq.edu.au (M. Janda).

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Holloway et al., 2016). Presumed benefits of SLND are that it increases the precision of surgical staging because technology highlights fewer positive nodes for surgical removal thus sparing removal of normal, negative nodes (Holloway et al., 2016; Rossi, 2019). Therefore, it may reduce the morbidity associated with a full LND because fewer nodes are removed (Accorsi et al., 2020) while still obtaining accurate information on lymph node status, which generates information on the patients' risk of relapse. High level evidence suggests SLND is accurate to replace systematic LND in endometrial cancer, identifying at least one sentinel node in 86% of patients (Rossi et al., 2017). Its sensitivity to detect node positive disease is 97.2% and its negative predictive value is 99.6%. Previous research (Holloway et al., 2017; Bodurtha Smith et al., 2017) has focussed on the surgical technique (Frumovitz et al., 2018), the selection of tracer used and accuracy of SLND.

The effect of SLND on key patient outcomes has not been conclusively shown. Therefore, the objective of this systematic review was to evaluate patient centred outcomes of SLND for endometrial cancer patients including perioperative outcomes, adjuvant treatments received, patient reported outcomes (PROs), and lymphedema.

2. Methods

2.1. Search strategy

The checklist of the Preferred Reporting Items for Systematic Review and Meta Analyses (PRISMA) guided our systematic review. Literature published in the last five years (January 2015 to April 2020) was retrieved searching the electronic databases PubMed, EMBASE, and the Cochrane library.

The overarching research topic of patient centred outcomes of SLND for the treatment of endometrial cancer was divided into five searches. Each of these searches was then summarised in narrative form, resulting in five subsections, or 'chapters' within the review. This method was selected as it allowed the authors to capture literature across five important domains including (1) perioperative outcomes (2) adjuvant treatment (3) patient reported outcomes (4) lymphedema outcomes, and (5) cost. The division of the review into five sections allowed for a comprehensive and clearly categorised delineation of articles that contributed to each areas of interest.

The search terms used for all five searches included: (sentinel node biopsy OR sentinel lymph node OR sentinel lymph node biopsy) AND (endometrial cancer OR endometrial carcinoma OR endometrial neoplasms OR endometrium carcinoma OR "cancer of the endometrium"). Additional search terms were then added for each of the five searches, for example: AND (Patient Reported Outcome Measures OR Quality of Life). The search strategy was tailored to multiple databases including MedLine and Embase. A complete list of search terms is provided in the Supplementary material.

2.2. Study eligibility

Only original works, published in English language in peer reviewed journals were included. Studies were required to report on adult women (18 years and above) who had undergone SLND for the treatment of endometrial cancer. Studies were included if they reported on at least one of the five topics of interest. We excluded studies with fewer than 10 patients, as well as articles not available in English and studies on animals. Reviews, commentaries, editorials, letters, protocol papers, conference proceedings, guidelines, and clinical trial registrations were also excluded.

2.3. Study selection

Two reviewers (MO, HO) used the software program Covidence (Covidence, 2020) to screen the titles and abstracts of papers identified through the literature search under the guidance of a third reviewer (MJ). Disagreements were resolved through discussion between the two reviewers, and consultation with other review authors (MJ, AO) to make a final decision. The full text of all potentially relevant articles was obtained and screened against the predefined selection criteria. The reference lists of these articles were checked for additional relevant papers.

2.4. Data extraction

All records were stored in Endnote. Data extracted included author, year, country of study, study design, patient population and sample size, time period, intervention, outcome measure(s), summary of reported findings, and items for quality assessment. Two reviewers (MO, HO) tabulated study characteristics for each of the final studies in Excel and this data was then audited by other members of the review team (MJ, AO).

2.5. Quality assessment

Two researchers (MO, HO) assessed the quality of studies included in the final review using the appropriate appraisal tool for each included study's design. The quality assessment was then audited by a member of the review team (MJ) to settle any disagreements detected. The quality of observational studies were assessed using the Newcastle Ottawa Scale, available for cohort, case control, and cross sectional studies. The Newcastle Ottawa Scale consists of a 9 item checklist to evaluate the quality of non randomised studies to be used in a systematic review (Wells et al., 2019). The quality of cost effectiveness studies were assessed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement. A CHEERS score was calculated for each included study, with one point allocated per item and a maximum of 24 points (Husereau et al., 2013).

3. Results

3.1. Characteristics of the included studies

A total of 1807 citations were identified from the original search, with 500 remaining after removal of duplicates. Following title and abstract screening, 46 potentially relevant studies were identified and the full text copies were obtained for comparison against the full selection criteria. The reference lists of these articles were checked for relevant papers and an additional 9 articles were added for full text review, resulting in a total of 55 papers. Of these, 34 were excluded as they did not meet at least one of the inclusion criteria. Reasons for exclusion included studies with <10 patients (n = 2), unrelated outcome measure (n = 10), unrelated intervention (n = 14), unrelated patient population (n = 1), unrelated study design (n = 1), and articles where participants studied had >50% overlap with another included study (n = 6). Therefore, a total of 21 unique studies were included in the final review. A PRISMA flow diagram outlining the process of selecting studies is presented in Fig. 1.

Of the 21 studies, five studies were prospective observational (Mereu et al., 2018, 2020; Buda et al., 2016; Hagen et al., 2016; Geppert et al., 2018), one was using a historical control (Liu et al., 2017), eleven were retrospective observational studies (Accorsi et al., 2020; Casarin et al., 2020; Stewart et al., 2020; Leitao et al., 2020; Uccella et al., 2018; Moukarzel et al., 2017; St Clair et al., 2016; Goebel et al., 2020; Peiretti et al., 2019; Buda et al., 2017; Imboden et al., 2019), three were retrospective database reviews, (Wright et al., 2017; Polan et al., 2019; Gomez-Hidalgo et al., 2018) and one used a decision analysis model (Suidan et al., 2018). There were no prospective randomized trials.

Of the 21 studies, five compared SLND to systematic LND (Geppert et al., 2018; Liu et al., 2017; Stewart et al., 2020; Buda et al., 2017; Suidan et al., 2018), and seven studies compared SLND to no node sampling and systematic LND (Accorsi et al., 2020; Casarin et al., 2020;

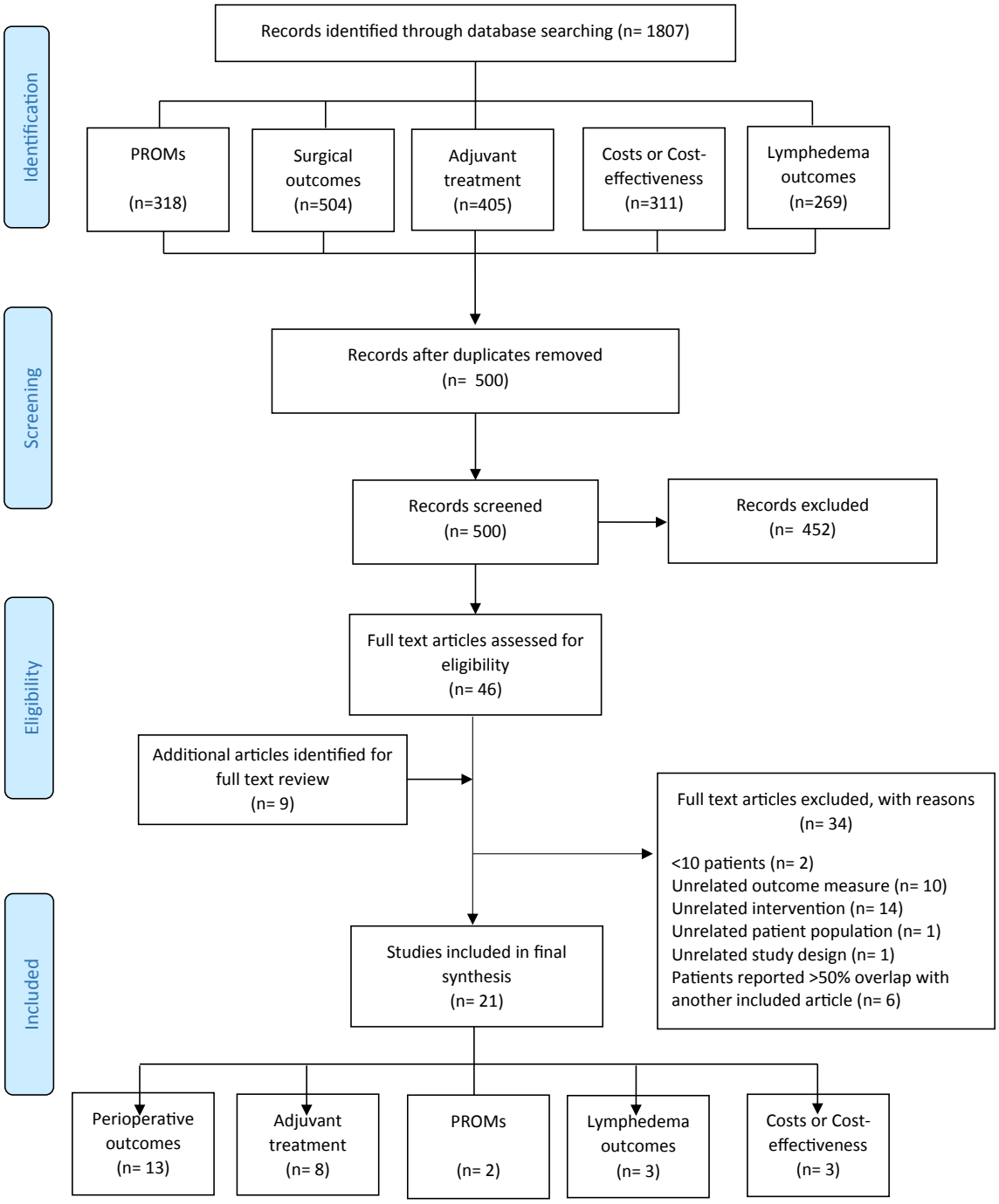

Fig. 1. PRISMA flow diagram of included studies.

Leitao et al., 2020; Imboden et al., 2019; Wright et al., 2017; Polan et al., 2019; Gomez-Hidalgo et al., 2018). Four studies compared SLND between different surgical techniques; between single site versus multiport (Mereu et al., 2020; Moukarzel et al., 2017), mini laparoscopy versus standard laparoscopy (Uccella et al., 2018) and different tracers (Buda et al., 2016). Five studies had no comparison groups (Mereu et al., 2018; Hagen et al., 2016; St Clair et al., 2016; Goebel et al., 2020; Peiretti et al., 2019).

3.2. Quality assessment

The mean quality score of nonrandomised studies was 6.8 (range 4–9). Of these, the mean quality score of the cohort studies was 6.9, and only one cross sectional study (Mereu et al., 2020) was included with a total quality score of 5. Two studies (Wright et al., 2017; Suidan et al., 2018) were evaluated using the CHEERS Statement and received scores of 16/24 and 18/24 respectively.

3.3. Characteristics of the included patients

Participant demographics and clinical characteristics are detailed in Supplementary Table 1 and included patient age, body mass index (BMI), American Society of Anesthesiologists Classification (ASA) score, postoperative histological cell type (endometrioid versus other), final FIGO stage (I, II, III, or IV), and FIGO grade (1, 2, or 3). Data on histopathology, stage and grade were assumed to be postoperative data

unless reported otherwise.

Of the 21 included publications, 18 reported mean or median patient age. The mean/median age of women ranged from 53 years (Moukarzel et al., 2017) to 79.5 years (Geppert et al., 2018). BMI was reported in 16 studies with the mean/median BMI of women ranging from 23 kg per m^2 (Mereu et al., 2018) to 35.2 (Casarin et al., 2020). Four studies reported ASA scores. One study (Peiretti et al., 2019) reported a median ASA score of 2, while another (Casarin et al., 2020) reported ASA scores of ≥3 (n = 63). The remaining two studies reported median ASA scores of 2 (range 1–3). Final histology was reported in 12 studies. Histologic types included 3060 endometrioid cancers and 712 other cancer types (including: non-endometrioid, endometrial atypical hyperplasia, endometrial intraepithelial neoplasia, serous, clear cell, carcinosarcoma and mucinous). Fifteen studies reported FIGO stage, most frequently stage I (n = 4028) and least frequently stage IV (n = 8). Ten studies reported cancer grade (median = 1; range 1–3).

3.4. Perioperative outcomes

Thirteen studies reported operating time, estimated blood loss (EBL), length of stay (LOS), procedure related morbidity and conversion rates (Table 1). These studies included a total of 5922 patients, with 1164 patients receiving SLND. Of the 13 studies, four were prospective (Mereu et al., 2018, 2020; Hagen et al., 2016; Geppert et al., 2018), two included retrospective and prospective cohorts (Liu et al., 2017; Imboden et al., 2019) and seven were retrospective studies (Accorsi et al., 2020; Casarin et al., 2020; Stewart et al., 2020; Uccella et al., 2018; Moukarzel et al., 2017; Peiretti et al., 2019; Polan et al., 2019). There was considerable heterogeneity within the group of publications with regards to inclusion and exclusion criteria for histopathology, stage, grade and surgical management, and some studies also included patients with complex atypical hyperplasia (n = 3). All 13 studies reported using a SLND protocol, with the most common being the National Comprehensive Cancer Network SLND algorithm (n = 3). Seven studies compared SLND to either no node assessment or varying extents of systematic LND, and three studies reported on SLND when they compared other factors e.g. single site vs multiport, differing port size. Three studies reported only on cohorts having SLND, with no comparisons.

Operating time was reported in all 13 included studies. Median or mean operating time ranged from 118.5 mins (Hagen et al., 2016) to 235 mins (Geppert et al., 2018) in the SLND groups. In studies comparing SLND to systematic LND (n = 7) (Accorsi et al., 2020; Imboden et al., 2019; Polan et al., 2019; Geppert et al., 2018; Liu et al., 2017; Casarin et al., 2020; Stewart et al., 2020), all reported a lower mean/median operating time in SLND and five (Accorsi et al., 2020; Casarin et al., 2020; Stewart et al., 2020; Imboden et al., 2019; Polan et al., 2019) demonstrated a statistically significant difference. In studies that compared SLND to no node dissection (n = 4), two demonstrated longer operating time in the SLND group (Accorsi et al., 2020; Polan et al., 2019), one demonstrated the same operating time between the groups (Imboden et al., 2019), and one found a longer operating time in the group with no node dissection (Casarin et al., 2020).

Estimated blood loss was reported in eleven studies, with some reporting mean or median, and one study reporting the proportion of patients with less than 100 mL estimated blood loss (Mereu et al., 2020). Estimated blood loss (mean or median) ranged from 20 mL (Accorsi et al., 2020) to 160 mL (Peiretti et al., 2019) in SLND groups. In studies comparing SLND with systematic LND (n = 6) (Accorsi et al., 2020; Imboden et al., 2019; Geppert et al., 2018; Liu et al., 2017; Casarin et al., 2020; Stewart et al., 2020), all but one (Geppert et al., 2018) reported a lower mean/median blood loss with SLND compared to systematic LND, and four (Accorsi et al., 2020; Liu et al., 2017; Casarin et al., 2020; Imboden et al., 2019) demonstrated a statistically significant reduction. Of studies (n = 3) (Accorsi et al., 2020; Casarin et al., 2020; Imboden et al., 2019) comparing estimated blood loss with SLND to no node dissection, one found higher blood loss with SLND (Imboden et al., 2019), one found no difference between the two groups (Casarin et al., 2020), and one found higher blood loss with no node dissection (Accorsi et al., 2020).

Postoperative length of stay was reported in nine of the 13 studies. Three compared length of stay between SLND and systematic LND (Liu et al., 2017; Casarin et al., 2020; Polan et al., 2019), and two studies compared length of stay between SLND and no node dissection. (Casarin et al., 2020; Polan et al., 2019) Postoperative length of stay was reported differently in each of these studies; one reported mean hours of length of stay (Liu et al., 2017), one reported percentages discharged on the same day as surgery, after one day and after more than one day (Polan et al., 2019) and one reported the proportion of patients staying for more than 2 days (Casarin et al., 2020).

Seven of the 13 studies reported intraoperative complications and all 13 studies reported on postoperative complications. Of studies comparing intraoperative complications in patients undergoing SLND compared to systematic LND (n = 4) (Accorsi et al., 2020; Casarin et al., 2020; Stewart et al., 2020; Imboden et al., 2019), three studies reported lower rates of intraoperative complications in SLND groups (Accorsi et al., 2020; Casarin et al., 2020; Imboden et al., 2019) (with only one reaching statistical significance (Accorsi et al., 2020), and one study reported a higher rate of intraoperative complications in the SLND group (not statistically significant) (Stewart et al., 2020). Of studies that compared SLND to no node dissection (n = 3), two found that the SLND groups had lower intraoperative complications (Casarin et al., 2020; Imboden et al., 2019), and one found that the SLND group had a higher rate of intraoperative complications compared to no node dissection (Accorsi et al., 2020).

Of studies (n = 7) that compared SLND to systematic LND (Accorsi et al., 2020; Imboden et al., 2019; Polan et al., 2019; Geppert et al., 2018; Liu et al., 2017; Casarin et al., 2020; Stewart et al., 2020), five (Accorsi et al., 2020; Liu et al., 2017; Casarin et al., 2020; Imboden et al., 2019; Polan et al., 2019) reported lower rates of postoperative complications with SLND, and three of these reached statistical significance (Accorsi et al., 2020; Liu et al., 2017; Polan et al., 2019). One study demonstrated a higher rate of postoperative complications in the SLND group which was not statistically significant (Stewart et al., 2020). A comparison of postoperative complications reported in Geppert et al. (2018) was unable to be determined due to reporting of multiple risk groups. Of studies (n = 4) that compared SLND to no node dissection, two found that postoperative complications were higher in the SLND group (Imboden et al., 2019; Polan et al., 2019), while 2 reported higher complications in the group with no node dissection (Accorsi et al., 2020; Casarin et al., 2020).

Five of the 13 studies reported on conversion rates, which ranged between 0.0% (Accorsi et al., 2020) and 43% (Geppert et al., 2018), with no consistent relationship between conversion rate and approach to lymph node sampling reported across the studies (Accorsi et al., 2020; Geppert et al., 2018; Casarin et al., 2020; Stewart et al., 2020). Similarly, of studies comparing conversion rates between SLND compared to no node dissection (n = 2), one found higher conversion rates in SLND (Casarin et al., 2020), and one found higher conversion rates in the group with no node dissection (Accorsi et al., 2020).

3.5. Adjuvant treatment

Overall, eight studies reported the rate of patients who received adjuvant treatment (Table 2). These studies included 56,796 patients, of which 2478 had a SLND. Four studies were retrospective observational (St Clair et al., 2016; Goebel et al., 2020; Buda et al., 2017; Imboden et al., 2019); two reported prospective cohorts (Hagen et al., 2016; Geppert et al., 2018); one compared data from a prospective cohort with historical controls (Liu et al., 2017); and one was a retrospective database review (Gomez-Hidalgo et al., 2018). There was significant heterogeneity in patient cohorts, which are described in Supplementary

Table 1
SLN and perioperative patient outcomes.

Author (year)	Study size: total number of patients (SLND group)	Operative time (mins)	Estimated intraoperative blood loss (mL)	Length of stay	Intraoperative Complications	Postoperative Complications	Conversion Rates
Comparison of SLND vs Systematic LND or No node dissection							
Liu et al. (2017)	381 (166)	SLND: mean 135.8 (SD 37.2) Systematic LND: mean 144.6 (SD 48.0) P = 0.053	SLND: mean 57.3 cm^3 (SD 58.0) Systematic LND: mean 79.0 cm^3 (SD 70.0) P = 0.0014	Mean hours of stay SLND: 9.94 (SD 8.4) Systematic LND: 9.9 (SD 13.5) P = 0.97	–	SLND: 8/153 (5.2%) Systematic LND: 10/77 (13%) P = 0.04	–
Geppert et al. (2018)	278 (79)	Low risk SLND: median 135 (range 97–212) High risk SLND: median 157.5 (range 89–272) High risk systematic pelvic LND: median 186 (129–347) High risk systematic infra-mesenteric LND: median 212 (145–277) High risk systematic infra-renal LND: median 226 (154–440)	Low risk SLND: median 50 (range 0–500) High risk SLND: median 100 (range-10–500) High risk systematic pelvic LND: median 50 (0–200) High risk systematic infra-mesenteric LND: median 100 (10–300) High risk systematic infra-renal LND: median 100 (10–700)	–	–	Low risk SLND: 7/53 (13.2%) High risk SLND: 8/26 (30.8%) High risk systematic pelvic LND: 6/14 (43%) High risk systematic infra-mesenteric LND: 4/10 (40%) High risk systematic infra-renal LND: 16/85 (18.8%)	Low risk SLND: 0/53 (0%) High risk SLND: 2/26 (7.7%) High risk systematic pelvic LND: 0/14 (0%) High risk systematic infra-mesenteric LND: 1/10 (10%) High risk systematic infra-renal LND: 2/85 (2.4%)
Imboden et al. (2019)	729 (118)	No LND: median 140 (range 50–540) SLND: median 140 (range 80–480) Systematic LND: median 244 (range 110–510) P = 0.000	No LND: mean 75 (range 10–700) SLND: mean 84 (range 10–400) Systematic LND: mean 240 (range 50–1000) P = 0.000	–	No LND: 4/103 (3.9%) SLND: 0/118 (0.0%) Systematic LND: 3/58 (5.2%) P = 0.063	No LND: 8/103 (7.8%) SLND: 10/118 (8.5%) Systematic LND: 11/58 (19.0%) P = 0.134	–
Polan et al. (2019)	3282 (144)	No LND: Median 141 (IQR 110–183) SLND: Median 166 (IQR 138–209) Systematic LND: Median 171 (IQR 133–211) P = <0.001	–	Same day discharge % No LND: 8.3% SLND: 5.6% Systematic LND: 11.9%	–	Major complication composite No LND: 41/2049 (2.0%) SLND: 3/144 (2.1%) Systematic LND: 39/1089 (3.6%) P = 0.03	–
Accorsi et al. (2020)	250 (61)	No LND: median 135 (50–270) SLND: median 152 (60–300) Systematic LND: median 370 (80–600) SLND + systematic LND: median 240 (125–400) P = <0.001	No LND: median 35 mL (0–500) SLND: median 20 mL (0–500) Systematic LND: median 100 mL (0–2300) SLND + systematic LND: median 45 mL (0–500) P = <0.001	–	No LND: 0/54 (0.0%) SLND: 1/61 (1.6%) Systematic LND: 9/89 (10.1%) SLND + systematic LND: 6/46 (13.0%) P = 0.005	No LND: 8/54 (14.8%) SLND: 7/61 (11.5%) Systematic LND: 34/89 (38.2%) SLND + systematic LND: 9/46 (19.6%) P = <0.001	No LND: 1/54 (1.9%) SLND: 0/61 (0.0%) Systematic LND: 2/89 (2.2%) SLND + systematic LND: 0/46 (0.0%)
Casarin et al. (2020)	621 (188)	No LND: mean 155.1 (SD 55.5) SLND: mean 136.6 (SD 42) Systematic LND: mean 225.3 (SD 71.4) P LND vs SLND = <0.01 P SLND vs no LND = 0.002	No LND: median 50 (IQR 50–100) SLND: median 50 (IQR 50–100) Systematic LND: median 100 (IQR 60–200) P LND vs SLND = <0.001 P SLND vs no LND = 0.26	Length of stay >= 2 days No LND: 18.3% SLND: 8.0% Systematic LND: 23.2% P LND vs SLND = <0.001 P SLND vs no LND 0.006	No LND: 4/235 (1.7%) SLND: 1/188 (0.5%) Systematic LND: 4/198 (2.0%) P SLND vs no LND = 0.30 P LND vs SLND = 0.23	ASC Grade >=2 No LND: 13/235 (5.5%) SLND: 9/188 (4.8%) Systematic LND: 15/198 (7.6%) P LND vs SLND = 0.26 P SLND vs no LND = 0.73	No LND: 0/235 (0.0%) SLND: 1/188 (0.5%) Systematic LND: 2/198 (1.0%) P SLND vs no LND = 0.42 P LND vs SLND = 0.60
Stewart et al. (2020)	203 (130)	SLND: Median 171 (range 96–416) Systematic LND: Median 210 (range 92–366) P = 0.007	SLND: Median 75 (range 10–1500) Systematic LND: Median 100 (range 20–2630) P = 0.081	–	SLND: 3/130 (2.3% Systematic LND: 1/71 (1.4%) P = 1.00	SLND: 4/130 (3.1%) Systematic LND: 1/71 (1.4%) P = 0.30	SLND: 9/130 (7.4%) Systematic LND: 4/71 (6.3%) P = 1.00
Comparison of other surgical techniques							
Uccella et al. (2018)	38 (38)	3 mm port: median 120 (range 90–180)	3 mm port: median 50 (range 0–150)	3 mm port: 2 days (range 1–3)	3 mm port = 0/15 (0.0%)	3 mm port = 0/15 (0.0%)	–

(*continued on next page*)

Table 1 (*continued*)

Author (year)	Study size: total number of patients (SLND group)	Operative time (mins)	Estimated intraoperative blood loss (mL)	Length of stay	Intraoperative Complications	Postoperative Complications	Conversion Rates
		5 mm port: median 135 (range 100–220)	5 mm port: median 50 (range 0–200)	5 mm port: 2 days (range 1–5)	5 mm port = 1/23 (4.3%)	5 mm port = 3/23 (13%)	
Moukarzel et al. (2017)	27 (27)	Single site: median 175 (range 150–230) Multiport: median 184 (range 118–262)	Single site: median 50 (range 10–100) Multiport: median 50 (range 10–500)	Single site: 100% discharged within 23 h Multiport: 100% discharged within 23 h	Single site = 0/14 (0.0%) Multiport = 0/13 (0.0%)	Single site = 0/14 (0.0%) Multiport = 0/13 (0.0%)	Single site = 0/14 (0.0%) Multiport = 0/13 (0.0%)
Mereu et al. (2020)	76 (76)	Single site: mean 148.7 (SD 18.7) Multiport: mean 158.2 (SD 47.6) P = 0.247	Single site: 96% <100 mL Multiport: 84.3% <100 mL P = 0.112	Single site: mean 2.1 days (SD 0.6) Multiport: mean 3.1 days (SD 1.6) P = <0.0001	3/76 (3.9%) of all cases	Grade 2 complications = 4/76 (5.2%) of all cases	–
Publications without comparison groups							
Hagen et al. (2016)	108 (108)	Median 118.5 (range 50–223)	Median 50 mL (Range 10–300)	Two thirds of patients had post-operative length of stay of 1 day	–	5/108 (4.6%)	–
Mereu et al. (2018)	15 (15)	Mean 155 (range 112–175)	–	All patients discharged within 48 h of surgery	1/15 (6.67%)	–	–
Buda et al. (2017)	14 (14)	Median 157.5 (range 70–240)	Median 160 mL (range 50–600)	Median 3 days (range 1–6)	–	0/14 (0.0%)	–

Abbreviations: CAH = complex atypical hyperplasia.
Note: the study design, SLN protocol and comparison groups for each study are detailed in Supplementary Table 1.

Table 1. Three of the eight studies compared SLN to systematic LND, two compared SLN to no node sampling and systematic LND, and three reported no comparison group.

Three of five studies comparing SLND to systematic LND reported that fewer patients who had a SLND received adjuvant treatment compared to systematic LND (Geppert et al., 2018; Buda et al., 2017; Imboden et al., 2019), whereas two studies showed no difference in rates of adjuvant treatment received between the groups (Liu et al., 2017; Gomez-Hidalgo et al., 2018). Geppert et al. (2018) specifically reported that high risk tumour factors were a larger determinant of receiving adjuvant treatment than the lymph node dissection method. Goebel et al. (2020) stated that isolated tumour cells in the sentinel node did not influence adjuvant treatment recommendations in their institution, as other risk factors indicated the need for adjuvant treatment.

3.6. Patient Reported Outcomes (PROs)

Two of 21 identified studies described PROs (Mereu et al., 2020; Buda et al., 2016). Neither of these publications compared SLND to systematic LND or no LND. Buda et al. (Buda et al., 2016) described PROs as a secondary outcome when comparing two tracer protocols; preoperative Tc99m nanocolloid (on the day before surgery) plus intraoperative blue dye (from 2010 to 2014), compared to intraoperative ICG or blue dye SLND (from 2014 onwards). In this study, the European Organisation for Research and Treatment of Cancer (EORTC) IN-PATSAT32 questionnaire was used to assess patients' satisfaction with the care received by doctors, nurses and the hospital. This study included both patients with clinical stage 1 endometrial (n = 106) and stage IA2 to 1B1 cervical (n = 37) cancer. The authors found higher patient satisfaction and perception of higher quality of care in intraoperative ICG/blue dye compared to the Tc99m radiocolloid group, possibly due to the need for hospital admission on the day prior to surgery, patient discomfort due to preoperative injection of radiocolloid, imaging performed 3 h after the injection and exposure to radiation through preoperative imaging.

Mereu et al. (2020) conducted a prospective multicentre case control study comparing 51 patients who had robotic multiport TLHBSO and SLND versus 25 robotic single site surgery for low risk endometrial cancer or complex atypical hyperplasia from 2017 to 2019. The authors assessed PROs using the EORTC questionnaire QLW-C30 up to 12 months post surgery. This study reported better physical function in the single site compared to the multiport group (97.1 vs 91.6, p = 0.007) at 6 and 12 months postoperatively, but no statistically significant differences in emotional, cognitive or social functioning or fatigue. The authors described less pain in the multiport versus the single port group (98.6 vs 94.4, p = 0.029) at 6 months postoperatively. There were no statistically significant differences in body image and cosmetic results between the two approaches.

3.7. Lymphedema

Of 21 included studies, three publications reported lower limb lymphedema (LLL) outcomes (Accorsi et al., 2020; Geppert et al., 2018; Leitao et al., 2020). All three studies compared SLND to systematic LND and found SLND had lower incidence or point prevalence of lymphedema compared to systematic LND.

Leitao et al. (2020) reported point prevalence of self reported lymphedema from a retrospective cross sectional study, comparing endometrial cancer patients who had a SLND (n = 180) versus systematic LND (n = 352), versus hysterectomy without a lymph node dissection (n = 67). Self reported LLL prevalence was 49 of 180 (27%) after SLND, 144 of 352 (41%) after systematic LND (OR 1.85, p = 0.002), even after adjusting for radiation therapy and BMI. The prevalence of LLL was 27 of 67 (40.3%) after hysterectomy alone.

Geppert et al. (2018) conducted a prospective, non randomised single centre cohort study between 2014 and 2016, comparing incidence of lymphedema, lymphocele and chylous ascites formation in 188 patients with endometrial cancer. Patients with high risk preoperative features (non-endometrioid cell type, FIGO Grade 3, non-diploid flow cytometry, myometrial invasion deeper than 50%, cervical invasion) received a systematic LND whereas patients with low risk features had a SLND. At a follow up of 12 months, the incidence of grade 1 LLL was significantly lower after SLND compared to systematic LND (1/76 patients, 1.3% vs 15/83 patients, 18.1%, p = 0.0003).

Table 2
SLN and adjuvant treatment.

Study	Study size: total number of patients (number in SLN group)	SLN protocol	Comparison group	Adjuvant Treatment
Comparison of SLND vs Systematic LND				
Liu et al. (2017)	381 (166)	National Comprehensive Cancer Network SLND algorithm (SLND, frozen section if failed mapping + systematic pelvic LND on side where SLN not identified)	Systematic pelvic with selective para-aortic LND if high risk on frozen section	Adjuvant treatment (SLND): 67/166 (40.3%) Adjuvant treatment (systematic LND): 85/215 (39.5%)
Buda et al. (2017)	802 (145)	Memorial Sloan Kettering Cancer Centre algorithm (systematic LND if failed mapping, surgeon discretion para-aortic LND)	Frozen section + systematic pelvic LND if high grade features +/- para-aortic LND if positive pelvic nodes at frozen section	Adjuvant treatment (SLND): 35/145 (24.1%) Adjuvant treatment (systematic LND): 272/657 (41.4%) P = <0.0001 Types of treatments similar between the two groups
Gomez-Hidalgo et al. (2018)	54,039 (863)	SLND identified on National Cancer Database	Systematic LND; no nodal assessment	Radiation treatment (no node dissection): 1694/13657 (12.4%) Radiation treatment (SLND): 524/1929 (27.2%) Radiation treatment (systematic LND): 9733/38453 (25.3%) P = <0.001 For stage I tumours, no difference in radiation treatment between SLND and systematic LND (aRR = 0.92, 95% CI 0.82–1.05)
Geppert et al. (2018)	188 (79)	SLND. Systematic LND if failed mapping and high risk	Systematic pelvic + para aortic LND if high risk endometrial cancer	Adjuvant treatment in low risk with SLND: 2/53 (3.8%) Adjuvant treatment in high risk with SLND: 9/26 (34.6%) Adjuvant treatment in high risk with systematic pelvic + infra-renal para-aortic LND: 49/85 (57.6%) Adjuvant treatment in high risk with systematic infra-mesenteric para-aortic and pelvic LND: 5/10 (50%) Adjuvant treatment in high risk with systematic pelvic LND: 10/14 (71.4%)
Imboden et al. (2019)	279 (118)	SLND, systematic pelvic/para aortic lymph node dissection based on risk factors at frozen section	No lymph node dissection; Systematic pelvic +/-para aortic lymph node dissection	Overall, adjuvant treatment given in 16.7% of patients* Adjuvant treatment more frequent in systematic LND group than SLND. No difference in adjuvant treatment between SLND group to no node dissection group.
Publications without comparison groups				
St Clair et al. (2016)	844 (844)	Memorial Sloan Kettering Cancer Centre algorithm (systematic LND if failed mapping, surgeon discretion para-aortic LND)	No comparison	Adjuvant treatment including chemotherapy in 87% of patients with positive nodes by isolated tumour cells and 81% of patients with positive nodes by micrometastasis
Hagen et al. (2016)	108 (108)	Memorial Sloan Kettering Cancer Centre algorithm (systematic LND if failed mapping, surgeon discretion para-aortic LND)	No comparison	37/108 (34%) received postoperative chemotherapy
Goebel et al. (2020)	155 (155)	National Comprehensive Cancer Network SLND algorithm (SLND, frozen section if failed mapping + systematic pelvic LND on side where SLN not identified)	No comparison	Isolated tumour cells: 20/23 (87.0%) received chemotherapy postoperatively Micrometastasis: 17/21 (81.0%) received chemotherapy Adjuvant treatment initiated due to high risk uterine factors or advanced stage disease; ITCs did not change adjuvant treatment management.

* Raw numbers unavailable.

Accorsi et al. (2020) performed a retrospective cohort study of endometrial cancer patients treated surgically at a single institution in Brazil. Patients were categorised into one of four groups; hysterectomy only (n = 54), hysterectomy with SLND (n = 61), hysterectomy with systematic pelvic +/− para aortic LND (n = 89) and hysterectomy with SLND and systematic LND (n = 46). LLL was found only in patients who had systematic pelvic +/− para aortic LND (10.1%), compared to 0% in all other groups (p = 0.01). There was no difference in rates of LLL when comparing SLND and no node dissection (0% vs 0%).

3.8. Cost

Three of 21 studies described cost outcomes for SLND. Two studies (Wright et al., 2017; Suidan et al., 2018) compared SLND to systematic LND, finding that SLND attracted lower costs than systematic LND. Additionally, Wright et al. (Wright et al., 2017) also compared SLND to no lymph node assessment, finding that no nodal assessment had lower costs than both SLND and systematic LND.

Suidan et al. (2018) used a decision analysis model to compare the cost utility (taking into account cost, survival and quality of life) in low risk endometrial cancer patients between minimally invasive hysterectomy, bilateral salpingo oophorectomy with systematic LND, selective LND (based on intraoperative frozen section criteria) and SLND. Of the three strategies, SLND attracted the lowest cost ($16401 compared to $18041 for systematic LND and $17036 for selective LND, respectively). Systematic LND attracted the highest cost due to the surgeon, pathology and lymphedema treatment costs associated. SLND had slightly higher pathology fees, but less operating time and lymphedema treatment.

Wright et al. (2017) performed a retrospective analysis of 23,362 patients who underwent hysterectomy for endometrial cancer in the United States from 2011 to 2015. They examined billing and charge codes, finding that 9327 patients (32.8%) did not undergo lymph node assessment, 17,669 (62.3%) underwent systematic LND and 1366 (4.8%) underwent SLND, with SLND becoming more frequent over time, and more common during robotic hysterectomy. Mean cost for patients with no nodal assessment was $8877, compared to $9550 for SLND and $10259 for systematic LND, respectively.

Stewart et al. (2020) analysed the hospital financial costs (e.g. operative time, use of intraoperative frozen section, hospital charges) for 203 patients (71 in 2012, 130 in 2017) with clinical Stage I endometrial cancer pre and post implementation of a SLND algorithm at a single institution in the United States. Compared to pre implementation, the authors found a decrease in median hospital charges by 2.73% ($p = 0.96$). Within these charges, pharmacy charges decreased by 80.36% ($p < 0.01$), whereas post anaesthesia care charges increased by 40.95% ($p < 0.01$), as did pathology charges (by 63.38%, $p < 0.01$).

4. Discussion

This review summarises relevant and meaningful clinical and patient centred outcomes from 21 studies of SLND for endometrial cancer. Amongst the available literature sources, there were no publications reporting the outcomes of randomised clinical trials comparing SLND versus other methods of node sampling or no node sampling, and 14 of the 21 studies were retrospective. 12 of 21 studies compared SLND to systematic LND and very limited data was available for comparisons between SLND and no node sampling.

A central finding of this review is that literature on patient centred outcomes of SLND compared to other node sampling techniques in endometrial cancer is sparse in all areas, and particularly limited for PROs, lymphedema and cost outcomes. The reported data is prone to bias and confounding. There was minimal stratification for low risk/high risk endometrial cancer, which was a major confounding factor for many of the included studies (Holloway et al., 2017; Reneé Franklin and Tanner, 2018). Furthermore, allocation to certain lymph node sampling strategies was often based on uterine risk factors (e.g. high risk patients allocated to systematic LND, low risk patients to SLND), which was another source of potential bias. There was limited comparison of SLND compared to no node sampling, which made it difficult to draw conclusions. There was a large variety of outcomes reported between studies, and a large variation in reporting measures used; for example, for length of stay postoperatively, some studies reported this in days, some in hours, and some reported proportions of patients staying for longer than a certain period of time. This indicates that future research into patient centred outcomes in endometrial cancer should standardise outcomes reporting to make high quality outcome reviews and meta analyses feasible (Luckett and King, 2010; Cormier et al., 2015).

There was a consistent finding of lower operating time for SLND than systematic LND, and lower estimated blood loss in SLND compared to LND. The length of stay, intraoperative and postoperative complications and conversion rates were unable to be conclusively compared between groups. The widely varying study protocols used made extraction of comparable data and drawing conclusions difficult. These differences in SLND protocol, patient populations, and approach to surgery may all contribute to the lack of consistency, for example, postoperative complications for women with no node dissection ranged from 2.0% (Polan et al., 2019) to 14.7% (Accorsi et al., 2020); while for SLND these ranged from 2.1% (Polan et al., 2019) to 30.8% (Geppert et al., 2018).

Eight studies reported adjuvant therapy in patients following SLND. In five studies comparing SLND to systematic LND, patients who underwent SLND received lower or equal adjuvant therapy compared to patients undergoing systematic LND. There was insufficient data to draw conclusions about SLND versus no node sampling. High risk tumour factors were a larger determinant of receiving adjuvant treatment than the lymph node dissection method (Geppert et al., 2018). There were wide differences in SLND protocol, patient populations, and approach to surgery, which contributed to widely ranging outcomes reported, for example, the proportion of patients who received adjuvant treatment ranged widely from 20% (Imboden et al., 2019) to 40% (Liu et al., 2017).

There were only two studies that investigated PROs following SLND, and neither of these publications compared SLND to systematic LND or no LND. Therefore, we are unable to form conclusions about the impact of SLND on PROs. Those studies available seemed to indicate a reduction in lymphedema with SLND compared to systematic LND, but findings were less clear comparing SLND with no node dissection, with one study reporting the perhaps unexpected finding of higher lymphedema prevalence in patients with no node dissection (40%) than those with SLND (27%) (Leitao et al., 2020). However, with only three studies reporting on lymphedema as an outcome, the uncertainties on drawing robust conclusions must be regarded as considerable.

SLND is still a relatively novel procedure in endometrial cancer and the majority of studies to date have focussed on the accuracy of SLND compared to systematic lymph node dissection. Based on the scarce PROs evidence summarised by this review, it is important that future studies, such as those comparing surgery with or without SLND (such as NCT04073706) integrate PROs assessment as part of the clinical trial protocol. If these studies show equivalent oncological outcomes, the PROs data will be important to decide which treatment should become standard clinical care in the future.

Although there were only three studies devoted to the costs of SLND, these provided support for the notion that SLND may be more cost effective than a systematic LND, but is likely more expensive than no lymph node dissection. These studies had to rely on modelled or routine service data, due to the absence of data from prospective comparative studies. Any future planned randomised controlled trials should integrate a cost effectiveness assessment.

4.1. Strengths & limitations

This review summarises the literature available for patient centred outcomes for SLND in endometrial cancer over the past five years since SLND has accelerated in many countries of the world. To the best of our knowledge, this is the first review to highlight these aspects of patient care. Rigorous search criteria and exclusion criteria were applied, and the use of Covidence allowed for a standardised and monitored approach to inclusion and exclusion of studies. However, this review is limited by the low number of studies available, and by the lack of standardised reporting limiting the ability to perform a meta analysis for any outcomes. Non-English studies, and studies with <10 patients were excluded. The analysis of results was not weighted by study quality or study size.

5. Conclusion

In this systematic review of 21 studies reporting on patient centred outcomes of SLND, we describe potentially favourable patient intra and postoperative outcomes of SLND compared to systematic LND, although limited by the substantial lack of high quality studies comparing the two methods. Results were even less conclusive when comparing SLND to no node dissection due to the limited literature available, which may be reflective of systematic LND being the standard of care in many countries during the study analysis period. As more research calls into question the value of systematic LND, it may become increasingly necessary to compare SLND, as the new standard of care, to no node dissection given the findings of this review.

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CRediT authorship contribution statement

Helena M. Obermair: Writing - original draft, Writing - review & editing. **Montana O'Hara:** Writing - original draft, Visualization. **Andreas Obermair:** Conceptualization, Supervision, Writing - review & editing. **Monika Janda:** Conceptualization, Supervision, Writing - review & editing.

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Appendix A. Supplementary material

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References

Bray, F., Ferlay, J., Soerjomataram, I., et al., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 68 (6), 394–424.

American Cancer Society, 2020. Key Statistics for Endometrial Cancer American Cancer Society: American Cancer Society [cited 2020 August 2nd]. Available from: https://www.cancer.org/cancer/endometrial-cancer/about/key-statistics.html#:~:text=The%20average%20age%20of%20women,cancer%20in%20the%20US%20today.

Casarin, J., Multinu, F., Abu-Rustum, N., et al., 2019. Factors influencing the adoption of the sentinel lymph node technique for endometrial cancer staging: an international survey of gynecologic oncologists. Int. J. Gynecol. Cancer 29 (1), 60–67.

Colombo, N, Creutzberg, C, Amant F, et al., 2016. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up. Int. J. Gynecol. Cancer 26(1), 2–30.

Kunos, et al., 2017. Corpus: epithelial tumours. In: Berchuck, C., Yashar, D. (Eds.), Principles and Practice of Gynecologic Oncology, 7th ed. Wolters Kluwer, p. 522f.

Shepherd, J.H., 1989. Revised FIGO staging for gynaecological cancer. Br. J. Obstet. Gynaecol. 96 (8), 889–892.

Mikuta, J.J., 1993. International federation of gynecology and obstetrics staging of endometrial cancer 1988. Cancer 71 (4 S), 1460–1463.

Boronow, R.C., Morrow, C.P., Creasman, W.T., et al., 1984. Surgical staging in endometrial cancer: clinical-pathologic findings of a prospective study. Obstet. Gynecol. 63 (6), 825–832.

Creasman, W.T., Morrow, C.P., Bundy, B.N., et al., 1987. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer 60 (8 Suppl), 2035–2041.

Amant, F., Mirza, M.R., Koskas, M., et al., 2018. Cancer of the corpus uteri. Int. J. Gynaecol. Obstet. 143, 37–50.

Burke, T.W., Levenback, C., Tornos, C., et al., 1996. Intraabdominal lymphatic mapping to direct selective pelvic and paraaortic lymphadenectomy in women with high-risk endometrial cancer: results of a pilot study. Gynecol. Oncol. 62 (2), 169–173.

Holloway, R.W., Gupta, S., Stavitzski, N.M., et al., 2016. Sentinel lymph node mapping with staging lymphadenectomy for patients with endometrial cancer increases the detection of metastasis. Gynecol. Oncol. 141 (2), 206–210.

Rossi, E.C., 2019. Current state of sentinel lymph nodes for women with endometrial cancer. IJGC 29 (3), 613–621.

Accorsi, G.S., Paiva, L.L., Schmidt, R., et al., 2020. Sentinel lymph node mapping vs systematic lymphadenectomy for endometrial cancer: surgical morbidity and lymphatic complications. J. Minim. Invasive Gynecol. 27(4), 938–945.e2.

Rossi, E.C., Kowalski, L.D., Scalici, J., 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.

Holloway, R.W., Abu-Rustum, N.R., Backes, F.J., et al., 2017. Sentinel lymph node mapping and staging in endometrial cancer: A Society of Gynecologic Oncology literature review with consensus recommendations. Gynecol. Oncol. 146 (2), 405–415.

Bodurtha Smith, A.J., Fader, A.N., Tanner, E.J., 2017. Sentinel lymph node assessment in endometrial cancer: a systematic review and meta-analysis. Am. J. Obstet. Gynecol. 216(5), 459–476.e10.

Frumovitz, M., Plante, M., Lee, P.S., et al., 2018. Near-infrared fluorescence for detection of sentinel lymph nodes in women with cervical and uterine cancers (FILM): a randomised, phase 3, multicentre, non-inferiority trial. Lancet Oncol. 19 (10), 1394–1403.

Covidence, 2020. Covidence: About. Melbourne, VIC2020 [cited 2020 20 July]. Available from: https://www.covidence.org/reviewers.

Wells, G.A., Shea, B., O'Connell, D., et al., 2019. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses Ottawa, Ontario: The Ottawa Hospital [cited 2020 16 July]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Husereau, D., Drummond, M., Petrou, S., et al., 2013. Consolidated health economic evaluation reporting standards (CHEERS) statement. Eur. J. Health Econ. 14 (3), 367–372.

Mereu, L., Pellegrini, A., Carlin, R., et al., 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 (1).

Mereu, L., Berlanda, V., Surico, D., et al., 2020. Evaluation of quality of life, body image and surgical outcomes of robotic total laparoscopic hysterectomy and sentinel lymph node mapping in low-risk endometrial cancer patients – A Robotic Gyne Club study. Acta Obstet. Gynecol. Scand.

Buda, A., Elisei, F., Palazzi, S., et al., 2016. Quality of care for cervical and endometrial cancer patients: the impact of different techniques of sentinel lymph node mapping on patient satisfaction. Ann. Surg. Oncol. 23 (9), 2975–2981.

Hagen, B., Valla, M., Aune, G., et al., 2016. Indocyanine green fluorescence imaging of lymph nodes during robotic-assisted laparoscopic operation for endometrial cancer. A prospective validation study using a sentinel lymph node surgical algorithm. Gynecol. Oncol. 143 (3), 479–483.

Geppert, B., Lönnerfors, C., Bollino, M., et al., 2018. Sentinel lymph node biopsy in endometrial cancer—Feasibility, safety and lymphatic complications. Gynecol. Oncol. 148 (3), 491–498.

Liu, C.Y., Elias, K.M., Howitt, B.E., et al., 2017. Sentinel lymph node mapping reduces practice pattern variations in surgical staging for endometrial adenocarcinoma: A before and after study. Gynecol. Oncol. 145 (2), 248–255.

Casarin, J., Multinu, F., Tortorella, L., et al., 2020. Sentinel lymph node biopsy for robotic-assisted endometrial cancer staging: Further improvement of perioperative outcomes. Int. J. Gynecol. Cancer 30 (1), 41–47.

Stewart, K.I., Eska, J.S., Harrison, R.F., et al., 2020. Implementation of a sentinel lymph node mapping algorithm for endometrial cancer: Surgical outcomes and hospital charges. IJGC 30 (3), 352–357.

Leitao Jr., M.M., Zhou, Q.C., Gomez-Hidalgo, N.R., et al., 2020. Patient-reported outcomes after surgery for endometrial carcinoma: Prevalence of lower-extremity lymphedema after sentinel lymph node mapping versus lymphadenectomy. Gynecol. Oncol. 156 (1), 147–153.

Uccella, S., Buda, A., Morosi, C., et al., 2018. Minilaparoscopy vs standard laparoscopy for sentinel node dissection: a pilot study. J Minim Invasive Gynecol. 25(3), 461–466.e1.

Moukarzel, L.A., Sinno, A.K., Fader, A.N., et al., 2017. Comparing single-site and multiport robotic hysterectomy with sentinel lymph node mapping for endometrial cancer: surgical outcomes and cost analysis. J. Minim. Invasive Gynecol. 24 (6), 977–983.

St Clair, C.M., Eriksson, A.G., Ducie, J.A., et al., 2016. Low-volume lymph node metastasis discovered during sentinel lymph node mapping for endometrial carcinoma. Ann. Surg. Oncol. 23 (5), 1653–1659.

Goebel, E.A., St Laurent, J.D., Nucci, M.R., et al., 2020. Retrospective detection of isolated tumor cells by immunohistochemistry in sentinel lymph node biopsy performed for endometrial carcinoma: is there clinical significance? Int. J. Gynecol. Cancer 30 (3), 291–298.

Peiretti, M., Candotti, G., Buda, A., et al., 2019. Feasibility of hand-assisted laparoscopic sentinel node biopsy in open endometrial cancer surgery. Minim. Invasive Ther. Allied Technol. 1–5.

Buda, A., Di Martino, G., Restaino, S., et al., 2017. The impact on survival of two different staging strategies in apparent early stage endometrial cancer comparing sentinel lymph nodes mapping algorithm and selective lymphadenectomy: An Italian retrospective analysis of two reference centers. Gynecol. Oncol. 147 (3), 528–534.

Imboden, S., Mereu, L., Siegenthaler, F., et al., 2019. Oncological safety and perioperative morbidity in low-risk endometrial cancer with sentinel lymph-node dissection. Eur. J. Surg. Oncol. 45 (9), 1638–1643.

Wright, J.D., Cham, S., Chen, L., et al., 2017 Utilization of sentinel lymph node biopsy for uterine cancer. AJOG 216(6), 594.e1–.e13.

Polan, R.M., Rossi, E.C., Barber, E.L., 2019. Extent of lymphadenectomy and postoperative major complications among women with endometrial cancer treated with minimally invasive surgery. Am. J. Obstet. Gynecol. 220(3), 263.e1–.e8.

Gomez-Hidalgo, N.R., Chen, L., Hou, J.Y., et al., 2018. Trends in sentinel lymph node mapping and adjuvant therapy in endometrial carcinoma. Cancer Invest. 36 (3), 190–198.

Suidan, R.S., Sun, C.C., Cantor, S.B., et al., 2018. Three lymphadenectomy strategies in low-risk endometrial carcinoma: a cost-effectiveness analysis. Obstet. Gynecol. Surv. 73 (11), 634–635.

Reneé Franklin, C., Tanner 3rd., E.J., 2018. Where are we going with sentinel lymph node mapping in gynecologic cancers? Curr. Oncol. Rep. 20 (12), 96.

Luckett, T., King, M.T., 2010. Choosing patient-reported outcome measures for cancer clinical research–practical principles and an algorithm to assist non-specialist researchers. Eur. J. Cancer 46 (18), 3149–3157.

Cormier, B., Rozenholc, A.T., Gotlieb, W., et al., 2015. Sentinel lymph node procedure in endometrial cancer: A systematic review and proposal for standardization of future research. Gynecol. Oncol. 138 (2), 478–485.