Review Article

Anatomical basis of lymph node detection in gynecologic cancers: a review from a surgical perspective

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Abstract: Pelvic and para-aortic lymphadenectomy are associated with increased risk of complications and are responsible for a significant proportion of morbidity and impaired quality of life following surgical management of pelvic malignancies. Sentinel lymph node (SLN) was developed as a trade-off between systematic and no lymphadenectomy to limit morbidity while conserving good oncological staging and outcomes. In this comprehensive review, we aimed to synthetize the anatomical basis of the SLN procedure in patients with pelvic malignancies from a surgical perspective. The reliability of the SLN procedure is based on the knowledge of the dissemination pathways for each type of tumors. The most recent understanding of the uterine lymphatic anatomy defined three consistent channels: an upper paracervical pathway (UPP) with draining medial external and/or obturator lymph nodes; a lower paracervical pathway (LPP) with draining internal iliac and/or presacral lymph nodes and the infundibulo-pelvic pathway (IPP) with a course along the fallopian tube and upper broad ligament via the infundibulo-pelvic ligament to its origin. In patients with endometrial cancer, most SLNs are located on the UPP pathway: obturator and external iliac whereas 80% of the SLNs in patients with cervical cancer are located in the external iliac, interiliac and obturator area. Surgical training is a key step toward improving detection rates and exhaustiveness of SLN research while reducing overall morbidity. This is all the more important that the indications for performing complete lymphadenectomy are becoming increasingly rare.

Keywords: Sentinel lymph node (SLN); cervical cancer; endometrial cancer; vulvar cancer; lymphatic mapping

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Introduction

All recent efforts in gynecological malignancies revolve around reducing induced morbidity whilst conserving—and even improving—good oncological outcomes. The tremendous development of minimally invasive surgery has enabled surgeons to perform radical surgeries while limiting morbidity. However, pelvic and/or para-aortic lymphadenectomy still hold a significant part of induced short and long term morbidity.

The main postoperative complications are lymphoceles in up to 38% of cases and lower limb lymphedemas in 20%

of patients, heavily impairing quality of life (1-3).

In vulvar cancer surgery, inguinofemoral lymphadenectomy is associated with a risk of wound infection or breakdown in 20% to 40% and a risk of chronic lymphedema in 30% to 70% (4-7).

For many years, pelvic and/or para-aortic lymphadenectomy have been performed despite this morbidity because determining lymph node involvement is crucial to evaluate the prognostic and adapt subsequent adjuvant therapies. In endometrial cancer, patients with lymph node involvement (stage IIIC) have their recurrence-free survival rate drops from 87% without node involvement to 71% and 36% in women with pelvic and aortic node involvement, respectively (8). In cervical cancer, lymph node invasion has been added to the latest FIGO classification and is the most important prognostic factor identified so far (9-11).

The price of the surgical morbidity is all the more hard to bear that in most cases, whichever pelvic malignancy is considered, lymph nodes will be free of metastasis (12,13). Thus, most patients will undergo an unnecessary, risky, and morbid procedure with no proven impact on survival. The sentinel lymph node (SLN) biopsy was developed as an appealing solution to solve this issue. It is defined as the very first lymph node or group of nodes that drain the anatomical region or primary tumor (14-16). If the SLN is negative, the rest of the lymph nodes draining the organ could be considered negative. In 1977, the concept of SLN was proposed by Cabanas in the management of patients with penile cancer (16). In 1992, Morton *et al.* (17) applied sentinel node concept successfully in clinical stage I malignant melanoma. After the proof of concept by Giuliano *et al.* (18) in axillary dissection of breast cancer patients, it has been quickly adopted to significantly reduce its morbidity (19-21). Histologic validation of SLN in cervical and endometrial cancer have been published for years now, using several different technics, sometimes combined. In pelvic malignancies, its indications are still evolving, as clinical trials progressively demonstrated its non-inferiority to complete lymphadenectomy, while reducing morbidity. In cervical cancer patients, SLN is currently recommended in patients staged FIGO (Federation International of Gynecology and Obstetrics) IA1 with lymphovascular space invasion (LVSI) until stage IIA1 (22).

In endometrial cancer patients, it should be offered in patients at low or intermediate risk (and could be an option in high risk patients according to NCCN guidelines) (23,24).

In vulvar cancer, it is recommended in patients with tumor T1B <4 cm according to the latest FIGO classification (25).

What is implied in the concept of the SLN procedure is that the lymphatic drainage of the primary site of tumor is fully understood and that no aberrant migration pathway could be responsible of false negative results damaging for the patient. In this aim, the particularity of each cancer type SLN anatomic spread has to be known. In this review, we aimed at synthetizing the anatomical basis of the SLN procedure in patients with pelvic malignancies from a surgical perspective.

Lymphatic drainage of the cervix and the corpus uteri

The lymphatic pathway of the uterus have been extensively described since the early twentieth century as a key step to understand tumors dissemination from primary site (26,27). While the cervix and the endometrium are two parts of the same organ, it seems the patterns of lymphatic spread could differs depending on embryology and mainly according to the injection site within uterus.

Geppert *et al.* (28) described the uterine lymphatic anatomy for endometrial cancer dissemination according to three consistent channels: an upper paracervical pathway (UPP) with draining medial external and/or obturator lymph nodes; a lower paracervical pathway (LPP) with draining internal iliac and/or presacral lymph nodes and the Infundibulo-pelvic pathway (IPP) with a course along the fallopian tube and upper broad ligament via the infundibulo-pelvic ligament to its origin.

Recently, Zuo *et al.* (29) validated this anatomical distribution of the lympatic channels draining endometrial tumors. Furthermore, they showed the influence of the mode of injection on the pathway preferably used to find the SLN with increased detection of para-aortic SLN using fundal injection (LPP).

As for the cervical cancer, a focus has been made to the lymphatic spread through the parametrium. Benedetti-Panici *et al.* (30) investigated the dissemination of cervical tumors through the parametrium with three main trunks: the lateral, the anterior, and the posterior. The lateral trunk runs through the lateral parametrium is the main lymphatic drainage from the uterine cervix. As also described by Girardi *et al.* (31) and by Bonneau *et al.* (32), the lateral parametrium contains many lymph nodes and lymphatic vessels that can be privileged pathway for tumor dissemination.

The posterior lymphatic trunk runs in the sacrouterine

ligament and along the ureter, where lymph nodes and metastases rarely were observed, justifying the rare finding of isolated metastases in the presacral and aortic lymph nodes.

Lymphatic drainage of the vulva

A specificity of vulvar cancer is its dissemination pattern, almost exclusively by local invasion and lymphatic metastasis. Hematogenous metastasis are rare.

The lymphatic drainage was first studied and described on cadavers by Sappey in 1874 but it was not until the studies of Parry-Jones in 1963 (33) and of Iversen and Aas in 1983 (34) that the lymphatic pathways of the vulva was truly understood.

Lymphatic channels of the vulva and distal third of the vagina drain via the labiocrural fold, labia, and mons veneris into the superficial inguinofemoral nodes. These first-line nodes are located medial to the saphenous vein and above the cribriform fascia and are called superficial nodes (about 8–10 in number); Lymphatic flow then proceeds from to the deep groin nodes located beneath the cribriform fascia in the femoral triangle (35-37). The Femoral triangle is bounded superiorly by the inguinal ligament, medially by the medial border of the adductor longus muscle, and laterally by the medial border of the sartorius muscle. The uppermost deep lymph node located under the inguinal (Poupart) ligament is called "the Cloquet" node and leads to the lymphatics around the external iliac vessels. The lymphatic vessels from the vulva do not cross the midline except those coming from the median structures, i.e., the clitoris, urethral meatus and Bartholin glands that have a portion of lymphatic channels that drain directly to pelvic nodes. However, to the best of our knowledge, no isolated metastases of pelvic nodes has been described without inguinal nodes metastases.

The lymphadenectomy in inguinal area being extremely morbid, the extent of the surgical gesture has progressively been modified. An anatomical description of the extent of the inguino-femoral lymphadenectomy was proposed in 2003 by Rouzier *et al*. (6). They showed that medial inguinal and medial femoral lymphadenectomy was associated with the same survival but with a decreased rate of complications such as lymphedema.

We conducted a comprehensive review by searching in PubMed all English-written studies from the first report in each malignancy of the use of the SLN procedure. For cervical cancer, it was the publication by Echt *et al*. (38) in 1999. For endometrial cancer, it was the publication by Burke *et al*. in 1996 (39). For vulvar cancer, it was the publication by Levenback *et al*. in 1994 (40).

The MeSH Terms used were "sentinel lymph node", "lymphatic drainage", "lymphatic mapping", "cervical cancer", "cervix cancer" "cervix neoplasm", "cervical neoplasm", "endometrial cancer", "endometrial neoplasm", "vulvar cancer" "vulvar neoplasm" with the Boolean operator "AND".

The reference list of the possible articles was also reviewed in order to find possible missing articles. We selected article on the basis of their relevance and representativeness. We excluded small size cohorts (less than 10 women included) and studies that did not reported their detection rate. We also excluded studies that did not described precisely the location of the SLN detected.

Topographic distribution of SLNs for patients with endometrial cancer

Table 1 summarizes the SLNs localization in patients reported in the literature. Twenty-seven studies described precisely the location of the SLNs in patients treated for an endometrial cancer. As described by Zuo *et al*. (29), most SLNs are located on the UPP pathway: obturator and external iliac.

When analyzing the distribution of SLN, results must be considered with caution. Indeed, the specificity of SLN detection in patients with endometrial cancer lies within the multiple possibilities for injecting the tracer. If first reports used "direct site" injection of blue dye, endometrial and cervical injections, and the use of Tc99 and fluorescence ICG have been described since then. Eventually, if most surgeries were initially performed by laparotomy, a large majority of recent studies were performed by laparoscopy. All these parameters are of paramount importance since the learning curve might influence not only the ability of the surgeon to detect a potential SLN in usual location but also its ability to explore para-aortic area to look for another sentinel node (66). Indeed, the analysis of *Table 1* shows a great overall number of sentinel nodes located within the para-aortic area. The SENTI-ENDO trial reported by Ballester *et al*. (67) concluded to the efficiency of the SLN to accurately predict lymph node invasion in patients with early stage endometrial cancer.

Topographic distribution of SLNs for patients with cervical cancer

Table 2 summarizes the finding of the review of the

Table 1 SLN locations in patients with endometrial cancer reported in the literature

First author, year	Study size/ number of SLN	Tracer used	Site of injection	External iliac	Inter/ internal iliac	Common iliac	Obturator	Promontory, presacral	Para-aortic	Other
Allameh, 2015 (41)	15/15	BD	Fundus, subserosal	0	6 (40%)	0	8 (53.3%)	0	1 (6.7%)	0
Bats, 2008 (42)	43/86	BD + RT	Cervical	0	71 (82.5%)	9 (10.5%)	0	6 (7%)	0	0
Burke, 1996 (39)	15/31	BD	Triple site, subserosal	13 (39.4%)	0	6 (18.2%)	0	0	12 (36.4%)	0
Delahoye, 2007 (43)	60/180	BD + RT	Hysteroscopy subendometrial	56 (31%)	33 (18%)	30 (17%)	36 (20%)	0	25 (14%)	0
Favero, 2015 (44)	42/100	RT	Hysteroscopy underneath the tumor	35 (26%)	0	8 (4%)	22 (15%)	0	35 (24%)	0
Ferraioli, 2015 (45)	93/30	BD + RT	Cervical	21 (70%)	8 (26.7%)	1 (3.3%)	0	0	0	0
Frumovitz, 2007 (46)	18/13	BD + RT	Fundus, subserosal	3 (23.1%)	0	1 (7.7%)	3 (23.1%)	0	4 (30.8%)	2 (15.4%)
Gien, 2005 (47)	16/13	BD+ RT	Hysteroscopy/ subserosal	7 (53.8%)	0	3 (23.1%)	2 (15.4%)	1 (7.7%)	0	0
How, 2015 (48)	100/288	BD + RT	Submucosal and deep stromal cervical	69 (24%)	57 (19.7%)	–	148 (52%)	0	13 (4.5%)	0
Kadkhodayan, 2014 (49)	24/95	BD + RT	Cervical	19 (20%)	29 (30.5%)	6 (6.4%)	41 (43.2%)	0	0	0
Lopes, 2007 (50)	40/63	BD	Myometrial subserosa	16 (51.6%)	12 (38.7%)	2 (6.5%)	11 (35.5%)	0	22 (71%)	0
López-De la Manzanara Cano, 2014 (51)	50/71	BD + RT	Cervical	33 (46.5%)	3 (4.2%)	13 (18.3%)	17 (23.9%)	0	5 (7.1%)	0
Niikura, 2013 (52)	100/426	BD + RT	Hysteroscopy/ cervical	115 (27.3%)	24 (5.7%)	29 (6.9%)	178 (42.2%)	4 (0.9%)	75 (17.8%)	1 (0.2%)
Paley, 2016 (53)	123/332	ICG	Cervical	167 (49%)	16 (5%)	42 (12%)	72 (21%)	5 (1.5%)	29 (8%)	Parametrial 1 (<1%)
Pandit-Taskar, 2010 (54)	40/78	RT	Cervical	24 (30.8%)	19 (24.4%)	19 (24.4%)	10 (12.8%)	0	5 (6.4%)	Parametrial 1 (1.3%)
Papadia, 2016 (55)	75/NA	ICG	Cervical	32%	0	8%	55%	0	5%	0
Pelosi, 2003 (56)	16/NA	BD + RT	Cervical	0	100%	0	0	0	0	0

Table 1 (*continuned)*

Table 1 (*continued*)

First author, year	Study size/ number of SLN	Tracer used	Site of injection	External iliac	Inter/ internal iliac	Common iliac	Obturator	Promontory, presacral	Para-aortic	Other
Raspagliesi, 2004 (57)	18/45	BD + RT	Hysteroscopy	13 (28.9%)	2 (4.4%)	10 (22.2%)	8 (17.8%)		12 (26.7%)	0
Robova, 2009 (58)	101/133	BD + RT	Subserosal	78 (58.6%)	0	13 (9.8%)	20 (15%)	3 (2.3%)	11 (8.3%)	Parametrium 8 (6%)
Solima, 2012 (59)	80/154	RT	Hysteroscopy	46 (29.9%)	0	27 (17.5%)	48 (31.1%)	0	33 (21.4%)	0
Vidal, 2013 (60)	66/74	BD	Cervical	6 (8.1%)	30 (40.5%)	2 (2.7%)	19 (25.7%)	0	0	Not defined 17 (23%)
Perrone, 2008 (61)	54/29	RT	Cervical and hysteroscopic	25 (92.6%)	0	0	2 (7.4%)	0	2 (7.4%)	0
Rossi, 2013 (62)	385/888	ICG	Cervical	335 (38%)	92 (10%)	68 (8%)	218 (25%)	26 (3%)	139 (15%)	Parametrium 10 (1%)
Shimada, 2018 (63)	57/114	ICG + RT	Cervical	5 (4.4%)	36 (31.6%)	4 (3.5%)	69 (60.5%)	0	0	0
Mendivil, 2018 (64)	87/245	ICG	Cervical	76 (31.0%)	78 (31.8%)	0	45 (18.4%)	29 (11.8%)	17 (6.9%)	0
Ruiz, 2018 (65)	111/429	ICG	Cervical and fundus	70 (16.3%)	121 (28.2%)	23 (5.4%)	50 (11.7%)	14 (3.3%)	151 (35.2%)	0
Zuo, 2019 (29)	115/515	Carbon nanoparticle	Cervical and fundus	229 (44.5%)	106 (20.6%)	49 (9.5%)	116 (22.5%)	0	15 (2.9%)	0

Please note that the figures have been calculated and might not total 100% and/or match the number of total SLNs as it depended of the figures presented in the studies. The percentage refers to the location of lymph nodes. BD, blue dye; RT, radiotracer; ICG, indocyanine green; NA, not available.

literature describing SLNs locations. Forty-three studies described precisely the sentinel node location. Few studies included more than hundred patients with many reports of relatively "small" size cohorts.

As reported by Marnitz (108), removal of SLN in the external iliac, interiliac and obturator area enables evaluation of more than 80% of all SLN. This is in accordance with the lymphatic drainage previously described through the lateral parametrium. Furthermore, they showed that the node location was independent of histology and of tumor stage.

These locations of SLNs are consistent with the locations of metastatic lymph nodes in patients that underwent full lymphadenectomy (109). However, in the different studies reviewed, it is of note that the number of SLNs located within the parametrium is low. Considering the pattern of lymphatic dissemination of cervical tumors, we could expect higher number of lymph nodes located in the parametrium. A possible explanation is that the surgeons failed to biopsy some lymph nodes located in the parametrium as they are deeply located and could be difficult to identify and remove especially if the tracer injection within cervix has been inappropriate. Lymph nodes located within the parametrium are of small size and could have been missed by the surgeons, or described as being part of the obturator fossa.

Topographic distribution of SLNs for patients with vulvar cancer

In most cases, the SLN will be found just below Camper's fascia but its position can sometimes vary within the Femoral triangle. As mentioned by Frumovitz *et al.* (110), patients with clitoral lesions can have short afferent lymph

Table 2 SLN locations in patients with cervical cancer reported in the literature

First author, year	Size of the cohort/ number of SLN	Method of detection	External iliac [NSLN (% tot SLN)]	Inter or internal iliac [NSLN (% tot SLN)]	Common iliac [NSLN (% tot SLN)]	Obturator [NSLN (% tot SLN)]	Parametrium [NSLN (% tot SLN)]	Presacral [NSLN (% tot SLN)]	Paraortic [NSLN (% tot SLN)]	Other [NSLN (% tot SLN)]
Echt, 1999 (38)	13/4	BD	3 (75%)	0	1 (26%)	0	0	0	0	0
O'Boyle, 2000 (68)	20/24	BD	14 (58%)	1 (4%)	4 (17%)	1 (4%)	0	2 (7.9%)	0	2 (7.1%)
Dargent, 2000 (69)	35/63	BD	53 (84.1%)	7 (11.1%)	3 (4.8%)	0	0	0	0	0
Verheijen, 2000 (70)	10/18	RT + BD	8 (44%)	0	3 (17%)	7 (39%)	0	0	0	0
Lantzsch, 2001 (71)	14/26	RT	17 (65.4%)	5 (19.2%)	0	3 (11.5%)	1 (3.8%)	0	0	0
Levenback, 2002 (72)	39/132	RT + BD	32 (24%)	31 (23.5%)	15 (11.3%)	30 (22.7%)	12 (9.1%)	0	12 (9.1%)	0
Rhim, 2002 (73)	26/49	RT + BD	18 (37%)	8 (16%)	2 (4%)	12 (24%)	8 (16%)	0	0	Ing 1 (2%)
Barranger, 2003 (74)	13/21	RT + BD	11 (53%)	6 (28%)	1 (5%)	3 (14%)	0	0	0	0
Buist, 2003 (75)	25 /58	RT + BD	23 (39.7%)	10 (17.2%)	5 (8.6%)	19 (32.8%)	1 (1.7%)	0	0	0
Plante, 2003 (76)	70/135	RT + BD	45 (33%)	34 (25%)	8 (6%)	41 (30%)	3 (2%)	1 (1%)	0	0
Dargent and Enria, 2003 (77)	70/129	BD	21 (16%)	103 (80%)	5 (4%)	0	0	0	0	0
Marchiolè, 2004 (78)	29/29	RT + BD	28 (97%)	1 (3%)	0	0	0	0	0	0
Martínez-Palones, 2004 (79)	25/51	RT + BD	13 (26.2%)	21 (40.9%)	7 (14.7%)	4 (8.2%)	1 (1.6%)	2 (4.9%)	2 (3.2%)	0
Niikura, 2004 (80)	20/46	RT + BD	21 (45.7%)	1 (2.2%)	2 (4.3%)	15 (32.6%)	7 (15.2%)	0	0	0
Li, 2004 (81)	28/123	RT	27 (21.6%)	34 (27.5%)	2 (2.0%)	60 (49.0%)	0	0	0	0
Roca, 2005 (82)	40/99	RT + BD	19 (19%)	49 (49%)	0	0	0	0	0	0
Di Stefano, 2005 (83)	50/86	BD	47 (55%)	0	5 (6%)	33 (38%)	0	0	0	0
Angioli, 2005 (84)	37/NA	RT	NA (48.0%)	0	NA (18.0%)	NA (34.0%)	0	0	0	0

Table 2 (*continuned)*

Table 2 (*continued*)

First author, year	First author, year	Method of detection	External iliac [NSLN (% tot SLN)]	Inter or internal iliac [NSLN (% tot SLN)]	Common iliac [NSLN (% tot SLN)]	Obturator [NSLN (% tot SLN)]	Parametrium [NSLN (% tot SLN)]	Presacral [NSLN (% tot SLN)]	Paraortic [NSLN (% tot SLN)]	Other [NSLN (% tot SLN)]
Silva, 2005 (85)	56/120	RT	53 (44.2%)	10 (8.3%)	8 (6.7%)	47 (39.2%)	1 (0.8%)	0	1 (0.8%)	0
Rob, 2005 (86)	183/462	RT + BD	208 (45%)	0	22 (4.8%)	197 (42.6%)	14 (3%)	21 (4.6%)	0	0
Lin, 2005 (87)	30/121	RT	17 (14%)	39 (32%)	19 (16%)	46 (38%)	0	0	0	0
Gil-Moreno, 2005 (88)	12/21	RT + BD	4 (19%)	12 (57%)	1 (5%)	3 (14%)	0	1 (5%)	0	0
Wydra, 2006 (89)	100/150	RT + BD	70 (46.7%)	4 (2.7%)	8 (5.3%)	52 (34.7%)	16 (10.7%)	0	0	0
Hauspy, 2007 (90)	39/NA	RT + BD	NA (19%)	NA (3.7%)	NA (9.5%)	NA (67.2%)	0	0	NA (0.5%)	0
Kushner, 2007 (91)	20 /64	RT + BD	19 (30%)	12 (19%)	7 (11%)	21 (33%)	0	3 (5%)	2 (3%)	0
Yuan, 2007 (92)	81/192	BD	39 (20.1%)	34 (17.8%)	34 (17.8%)	83 (43.2%)	1 (0.6%)	0	0	Ing. 1 (0.6%)
Seong, 2007 (93)	89/83	BD	49 (59.0%)	9 (10.8%)	1 (1.2%)	24 (28.9%)	0	0	0	0
Lee, 2007 (94)	57/123	RT + BD	64 (51.9%)	3 (2.5%)	12 (10.1%)	25 (20.3%)	3 (2.5%)	0	0	Ing. 3 (2.5%)
Kara, 2008 (95)	32/67	RT + BD	32 (47.8%)	3 (4.4%)	6 (9.0%)	22 (32.8%)	4 (6.0%)	0	3 (4.4%)	0
Fader, 2008 (96)	38/56	RT + BD	31 (55%)	8 (15.0%)	4 (7.5%)	13 (22.5%)	0	0	0	0
Vieira, 2009 (97)	56/NA	RT + BD	NA (57.1%)	NA (9.1%)	NA (14.9%)	NA (17.5%)	NA (0.6%)	0	NA (0.6%)	0
Acharya, 2009 (98)	30 /60	BD	19 (31.7%)	5 (8.3%)	0	30 (50%)	6 (10%)	0	0	0
Fotiou, 2010 (99)	42/103	RT + BD	37 (35.9%)	21 (20.5%)	5 (5.1%)	37 (35.9%)	0	0	3 (2.6%)	0
Ogawa, 2010 (100)	82/157	RT	57 (36.4%)	12 (7.8%)	5 (3.2%)	80 (50.6%)	1 (0.6%)			
Kato, 2011 (101)	50/102	RT	5 (5.3%)	11 (10.5%)	6 (6.3%)	73 (71.6%)	6 (6.3%)	0	0	0
Roy, 2011 (102)	211/NA	RT + BD	0	NA (85.6%)	0	NA (16.7%)	0	0	NA (3.8%)	0
Lécuru, 2011 (103)	139/263	RT + BD	212 (80.6%)		0	0	0	0	0	0

Table 2 (*continued*)

Table 2 (*continued*)

First author, year	Size of the cohort/ number of SLN	Method of detection	External iliac [NSLN (% tot SLN)]	Inter or internal iliac [NSLN (% tot SLN)]	Common iliac [NSLN (% tot SLN)]	Obturator [NSLN (% tot SLN)]	Parametrium [NSLN (% tot SLN)]	Presacral [NSLN (% tot SLN)]	Paraortic [NSLN (% tot SLN)]	Other [NSLN (% tot SLN)]
Díaz-Feijoo, 2011 (104)	22/57	RT + BD	3 (5.7%)	31 (54.7%)	6 (11.3%)	16 (28.3%)	0	0	0	0
Devaja, 2012 (105)	86/NA	RT + BD	NA (48.8%)	NA (35.7%)	NA (14.2%)	NA (30.7%)	NA (1%)	0	0	0
Zhang, 2014 (106)	56/106	BD	30 (28.3%)	26 (24.5%)	3 (2.8%)	42 (39.6%)	0	0	0	Ing. 5 (4.7%)
Kim, 2018 (107)	103/241	ICG	84 (34.9%)	9 (3.7%)	6 (2.5%)	131 (54.4%)	9 (3.7%)	1 (0.4%)	1 (0.4%)	0
Marnitz, 2006 (108)	151/406	RT + BD	20 (4.9%)	32 (7.9%)	20 (5%)	288 (70.9%)	29 (7.1%)	0	17 (4.2%)	0

Please note that the figures have been calculated and might not total 100% and/or match the number of total SLNs as it depended of the figures presented in the studies. BD, blue dye; RT, radiotracer; ICG, indocyanine green; Ing, inguinal; NA, not available; NSLN, number of sentinel lymph nodes; % tot SLN, percentage of total sentinel lymph nodes.

channels with sentinel nodes often located in a very medial location just lateral to the adductor longus muscle (111). In such cases, surgeons could be helped by combining detection technics to effectively reduce the risk of SLN failure (112,113).

Lymph node procedure has become a key step of gynecologic cancers surgical staging. The knowledge of lymphatic anatomical pathways is therefore mandatory for oncogynecologic surgeons. Here we presented lymphatic drainage according to the type of gynecologic cancer. We also reviewed the topographic distribution rate of SLNs in each of these cancers. These data are important since it can help surgeons reduce both their rate of SLN detection failure and their rate of false negative (non-sentinel nodes).

With the generalization of SLN procedure in patients with endometrial cancer, knowing the usual distribution of the sentinel node is of determinant. Persson *et al*. developed a surgical algorithm to maximize the detection of SLNs (114). Surgeons performing endometrial cancer surgery should be trained to limit failure in lymph nodes detection (115). This is all the more important that it can prevent patients with pre-operative intermediate risk (and sometimes even high risk ESMO) from a secondary staging surgery including pelvic and para-aortic lymphadenectomy, much more at risk of short and long term complications and that could delay adjuvant therapies. An interesting point that is insufficiently reported is the number of SLN positive by localization. Zuo *et al*. (29) reported in 2018 a study that aimed to evaluate the detection rate and accuracy of SLN mapping using cervical and fundal injection of carbon nanoparticles in patients with endometrial cancer. They found in the group of patients that had fundal injection that metastatic lymph nodes were located in the right external iliac (2/36), left external iliac (1/30) and right internal iliac (1/11) with no other metastasis especially in the para-aortic area. In the group of patients that benefited of a cervical injection, metastatic lymph nodes were located in the right external iliac (3/81), right common iliac (1/19), left external iliac (1/82), left internal iliac (1/38), left obturator (1/46), right obturator (1/52). Knowing the proportion of metastatic SLN per location could be helpful for surgeons since failure to identify SLN in these specific areas could lead to immediate lymphadenectomy.

In patients with early stage cervical cancer, the morbidity of radical hysterectomy, i.e., with resection of the parametrium is currently being questioned as in selected patients, the risk of parametrial invasion is almost null (116-118). An option discussed by many authors is a two-steps procedure by performing a conization and SLN procedure to elect whether extension to the parametrium is mandatory. If a non-significant proportion of SLNs should be located within the parametrium, surgeons should make sure to identify correctly

those to remove them.

Anatomical basis of SLN for patients with vulvar cancer are less subject to discussion. As previously mentioned, the several surgical amendments that have been developed since the initial description of the surgery contributed to reduce postoperative morbidity in patients undergoing full lymphadenectomy (111). For example, Saphenous vein sparing improves postoperative outcomes in patients following inguino femoral lymphadenectomy (119). While progressive implementation of SLN in vulvar cancer decreased the risk of lower limb lymphedema by 10 fold, factors associated with secondary morbidity are less described (120). As vulvar cancer are rare, such patients should be managed in experienced centers all the more a learning curve is non-negligible in finding the SLN (121). In the setting of vulvar carcinoma, surgeons benefit from the low anatomical variation of this area located within the femoral triangle.

Our study suffers from some limitations. We made the choice to exclude studies that were not precise enough to describe location of the SLN. By doing so, we excluded large scaled studies, including the SENTI ENDO trial that was a major step toward incorporating SLN procedure into daily practice in expert centers. We searched only PubMed and not included other databases, we excluded studies non-English written. Eventually, while some clinicians are currently studying how SLN could be part of ovarian cancer patients management, we voluntarily excluded this malignancy from the review until more solid data is available (122,123).

Conclusions

The understanding of the anatomical basis underlying the research for SLNs is important. In particular, endometrial and cervical cancers do not have the same patterns of dissemination. As so, surgeons should be cautious when performing SLN research, especially in the parametrium area in patients with cervical cancer and in the para-aortic area in patients with endometrial cancer. Surgical training is a key step toward improving detection rates and exhaustiveness of SLN research while reducing overall morbidity.

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