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Submission of the entire lymph node dissection for histologic examination in gynecologic-oncologic specimens. Clinical and pathologic relevance

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Abstract

Background and aims—Lymph node (LN) status in gynecologic malignancies plays an important role in patient staging, management, and prognosis. Therefore, an adequacy of LN harvest is crucial. The aim of this study is to determine whether the submission of the entire LN dissection for histologic examination will affect patients' outcome or clinical stage. We also evaluated the time required and cost-effectiveness for the laboratory.

Materials and methods—A prospective study of 134 surgical cases from various gynecologic malignancies was conducted. The LN dissection specimen was performed using a conventional manual node dissection method with all the remaining fat being submitted in additional cassettes. One pathologist evaluated (1) the number and status of palpable LNs identified by the conventional method as well as the number of tissue cassettes and (2) the number, size, and status of the non-palpable LNs as well as the number of tissue cassettes.

Results—The palpable LNs ranged from 0 to 36 with average 14.8 LNs per case (Poisson 95% CI: 14.1–15.4). The additional non-palpable LNs ranged from 0 to 16 with an average of 3.1 (Poisson 95% CI: 2.8–3.4). In only one case, a 3-mm non-palpable LN with metastasis was identified; however, it did not affect tumor staging or patient management.

Conclusion—The impact on patient outcome is minimal and it does not prove to be cost and time effective when submitting the entire LN dissection specimen in gynecologic malignancies. However, this method could be justified in selective cases in which the manual node dissection does not reveal an adequate number of LNs.

Keywords

Lymph node dissection; Gynecologic malignancies; Impact; Patients prognosis

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Introduction

Lymph node status is crucial when predicting prognosis in women who undergo surgery for gynecologic malignancies. It is an integral part of the International Federation of Gynecologic Oncology (FIGO) staging system and positive LNs are a major determinant in patient management [1]. Patients with positive LNs most often have a shorter disease-free survival in comparison to those patients who are node negative [2-4]. Consequently, the presence of even one lymph node metastasis may be sufficient to justify adjuvant therapy. Therefore, the recovery of an adequate number of LNs is imperative. Adequate histologic evaluation of nodal status would lead to more accurate tumor staging and allow clinicians to offer patients the best therapeutic options. Retrieval of lymph nodes in gynecologic specimens, as in any oncologic specimens, is usually performed by the manual node dissection method, which is based on visual isolation and palpation of the LNs. Unfortunately, this method allows small LNs to be easily missed. Despite a thorough manual search for lymph nodes, there is still a wide variation in the number harvested. This is mainly due to the size of the LN dissection specimen as well as the skill and patience of the pathologists or pathologist assistants. Another method to increase the number of LNs harvesting is the fat clearance technique, where the specimen is immersed in xylene and alcohol for a long period of time usually overnight, allowing the fat to dissolve [5]. As a result, the LNs become more visible and palpable. However, this method is expensive and time consuming, and it can slow the turn-around time for these specimens. In contrast to colorectal and breast cancer, where numerous studies have been performed in order to determine what an adequate lymph node harvest is, this issue has not thoroughly addressed in gynecologic malignancies [6-9]. However, an increased number of LNs is reassuring for adequacy of the surgical dissection, accurate staging, and an optimal therapeutic decision.

In this study, we implemented the conventional manual node dissection method plus the submission of the entire remaining fat for histologic examination. Our purpose was to investigate whether or not the submission of the remaining fat could provide additional data for the diagnosis, staging, and the management for women with gynecologic malignancies.

Materials and methods

This is a prospective study of 134 cases conducted over a 1-year period (2007–2008) to study the impact when submitting the entire LN dissection for histologic examination on patient staging and outcome. The Department of Gynecologic Oncologic Surgery at Roswell Park Cancer Institute has three very experienced gynecologic-oncologic surgeons (two with 10 years experience and the third with N35 years experience in gynecologic-oncologic surgery). These three surgeons had provided us with LN dissection specimens from lymphadenectomy procedures. The first surgeon provided us with 8/134 (6%) of the specimens, the second 20/134 (15%) of the specimens, and the third with the most experience (>35 years) provided the majority of the specimens 106/134 (80%). These specimens were examined by our pathologist assistants (PAs). Our department has three American Society of Clinical Pathology (ASCP) certified PAs with 3 to 4 years of experience in the cancer center. The PAs performed the conventional manual node dissection, which is based on visual identification and palpation of LNs. The PAs will

diligently search for palpable LNs and subsequently submitted in cassettes labeled “palpable LNs”. The remaining fat was submitted in additional cassettes and labeled “remaining fat/non-palpable LNs”. One pathologist (PMF) re-evaluated the surgical pathology report and the LNs slides for (1) number of “palpable LNs”, (2) number of “non-palpable LNs” in the remaining fat, (3) status of the “palpable LN” and “non-palpable LNs” in the remaining fat, (4) number of initial cassettes of the “palpable LNs”, (5) number of additional cassettes of the “non-palpable LNs” in the remaining fat, and (6) the size of the “non-palpable LNs”. In addition, the primary tumor site and the histopathology diagnosis were recorded.

Statistical analysis

Poisson 95 % confidence intervals were computed for the average number of additional LN detected. The same statistic was performed for the whole sample and for each tumor type. Spearman rank correlation coefficient was used to check for an association between the number of palpable lymph node with presence of metastasis and the maximum size of the lymph node. *P* values of 0.05 or less were considered statistically significant. All analyses were performed with the Stata statistical software package (version 10.1; Stata Corporation, College Station, TX).

Results

The 134 evaluated surgical specimens were examined. They consisted of hysterectomy/radical hysterectomy (for cervical cancer primary) with bilateral salpingo-oophorectomy, lymph node dissection, and omentectomy for malignancies from the following primary sites; six cases were vulvar primary and the diagnosis was squamous cell carcinoma (SCC) ($n=5$) and melanoma ($n=1$). The lymph node groups consisted of left and right pelvic lymph nodes and paraaortic lymph nodes for cervical, endometrial, ovarian, and upper vaginal cancers and inguinal and Cloquet lymph nodes for lower vaginal and vulvar cancers. Five cases were vaginal primary; SCC ($n=3$) and melanoma ($n=2$) with three upper vaginectomy and two lower vaginectomy specimens. Twenty-four cases were cervical primary with SCC ($n=18$), adenocarcinoma (AC) ($n=5$), and sarcoma ($n=1$). Sixty cases were uterine corpus primary with AC ($n=53$), sarcoma ($n=3$), and carcinosarcoma ($n=4$). Thirty-seven were ovarian primary with surface epithelial carcinomas ($n=34$), granulosa cell tumor ($n=1$), and metastatic tumor to the ovaries ($n=2$). Synchronous ovarian and endometrial papillary serous carcinomas were seen in one case. Primary peritoneal papillary serous carcinoma was diagnosed in one case. The details of the tumor histologic subtypes are illustrated in Table 1.

Overall 1632 cassettes and 957 additional lymph node cassettes were submitted. The palpable LNs ranged from 0 to 36 with average 14.8 LNs per case (95% CI: 14.1–15.4). The additional non-palpable LNs ranged from 0 to 16 with an average of 3.1 LNs (95% CI: 2.8–3.4). The size of the additional non-palpable LNs ranged from 1 to 7 mm. The number of metastatic palpable LNs ranged from 0 to 21 with an average 0.6 per case (95% CI: 0.5–0.8). The number of metastatic non-palpable LNs ranged from 0 to 1 with an average 0.0072 positive LNs per case (95% CI: 0.0001–0.0401). However, this case already had 21 positive LNs and the positive LN did not affect staging or the patient’s management. The number of original cassettes ranged from 1 to 35 with an average 11.7 cassettes per case. The number

of additional cassettes from submitting the remaining fat ranged from 1 to 22 per case with an average of 6.9 cassettes per case. The results are summarized in Table 2. There was no significant association between the number of palpable lymph node with presence of metastasis and the maximum size of the lymph nodes (Spearman's $\rho = -0.135$; $P = 0.112$).

For cost-effectiveness analysis, we assumed that the pathologist assistant would most likely take an average of 3 to 4 min to make and submit an additional tissue cassette. Moreover, the cost of each cassette is approximately US \$10. This cost encompasses all stages of processing beginning with the embedding, cutting, and staining. The pathologist will take more time to scan the slide ranging from 30 s (if just adipose tissue is present) to 1 min (if LNs are present). In our study, we have an average of seven additional cassettes per case, equaling to an additional US \$70 per case on average. This does not include the time of the pathologist or pathologist assistant.

Discussion

Contrary to colon and breast cancers, there is little debate on the adequacy of LNs number in gynecologic malignancies. The literature has shown a lack of correlation between the presence of LN metastasis and LN size [10]. A similar conclusion was reached based on our study where no correlation was noted between metastasis and LN size in gynecologic malignancies. Thus, examining even smaller LNs of <3 mm is still very important for proper staging, management, and prognosis and our series is a good example where a 3-mm non-palpable LN was found to be positive for metastasis. However, in this particular case LN positivity did not change the pN status and thus did not influence patient management. In addition, we concluded that by submitting the entire LN dissection specimen (manual node dissection plus submission all the remaining fat), the yield of LNs increased remarkably, reaching 14 LNs in several cases. Because there is no literature evaluating this topic in gynecologic malignancies, we compared studies from colon cancer. In a study by Kim et al. [11], which is somewhat similar to ours, but conducted in colorectal adenocarcinoma cases, the authors concluded that although the submission of the entire mesenteric fat after manual node dissection was useful in pN1 cases with fewer than 12 LNs, this method did not add any additional information in N0 or N+ cases with 12 or more LNs. A similar study was conducted by Brown et al. [12] in colon cancer where the authors concluded that the submission of the entire mesenteric fat was useful within pN1 group where few cases were upstage to pN2, but the submission of LN by conventional manual dissection is sufficient for N0 group. In both studies, the size of LNs was very small averaging 1–2 mm. Similar to these two studies, the size of the majority (86%) of the LNs harvested in our study of cases was small, 3 mm in the additional fatty tissue, and that can usually be very easily missed by the conventional manual node dissection method. However, the submission of the entire LN dissection specimen in gynecologic malignancies is somewhat more feasible than submission of the entire mesenteric fat. This is mainly due to the size of the specimen. Mesenteric fat is much larger than gynecological malignancies LN dissection specimens and therefore requires the submission more cassettes for histologic examination.

Based on our study, we concluded that the submission of the entire LN dissection was not time or cost-effective for the laboratory. The additional cassettes ranged from 1 to 22 with an

average 6.9 cassettes/case and 92 cases (68.5%) had 5 cassettes. We estimated that the submission of each additional cassette will cost an additional US \$10 to the total cost of the case. This will translate to an average US \$70 per case. This amount does not include the time and effort of the pathology assistant submitting these cassettes nor the pathologist time reading the hematoxylin–eosin slides.

We also concluded that the submission of the entire LN dissection does not justify the cost when considering patient care and management. However, this method will continue to be valid if the initial LN yield is not adequate or if the surgeons do not feel that the palpable LNs are reflecting the adequacy of his/her procedure. Finally, our recommendation is that the conventional manual node dissection in gynecologic malignancies is an adequate procedure in daily surgical pathology. The results of submitting the entire LN dissection are minimal and would not affect patient management. In conclusion, based on our study we have implemented a new policy in the gynecologic service in such that LN harvesting will be done using the conventional manual detection and the entire specimen will be submitted in only few circumstances such as (1) the remaining fat small enough to be submitted in 3 cassettes and (2) the yield of palpable LNs harvesting is too small.

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References

- [1]. Cancer Committee Report to the General Assembly of FIGO. Classification and staging of malignant tumor in the female pelvis. *Int J Gynaecol Obstet: The official organ of the International federation of gynaecology and Obstetrics*. 1971; 9:172–9.
- [2]. Wolfson AH, Sightler SE, Markoe AM, et al. The prognostic significance of surgical staging for carcinoma of the endometrium. *Gynecol Oncol*. 1992; 45:142–6. [PubMed: 1592280]
- [3]. Bristow RE, Zahurak ML, Alexander CJ, et al. FIGO stage IIIC endometrial carcinoma: resection of macroscopic nodal disease and other determinants of survival. *Int J Gynecol Cancer*. 2003; 13:664–72. [PubMed: 14675352]
- [4]. Hirahatake K, Hareyama H, Sakuragi N, et al. A clinical and pathologic study on para-aortic lymph node metastasis in endometrial carcinoma. *J Surg Oncol*. 1997; 65:82–7. [PubMed: 9209518]
- [5]. Cawthorn SJ, Gibbs NM, Marks CG. Clearance technique for the detection of lymph nodes in colorectal cancer. *Br J Surg*. 1986; 73:58–60. [PubMed: 3512023]
- [6]. Goldhirsch A, Glick JH, gelber RD, Senn HJ. Meeting highlights: international consensus panel on the treatment of primary breast cancer. *J Natl Cancer Inst*. 1998; 90:1601–8. [PubMed: 9811309]
- [7]. Van der Wal BC, Butzelaar RM, van der Meij S, Boormeester MA. Axillary lymph node ratio and total number of removed lymph nodes: predictors of survival in stage I and stage II breast cancer. *Eur J Surg Oncol*. 2002; 28:481–9. [PubMed: 12217299]
- [8]. Compton CC, Fielding LP, Burgart LJ, et al. Prognostic factors in colorectal cancer: College of American Pathologists consensus statement 1999. *Arch Pathol Lab Med*. 2000; 124:979–94. [PubMed: 10888773]
- [9]. Hammond ME, Fitzgibbons PL, Compton CC, et al. College of American Pathologists Conference XXXV: solid tumor prognostic factors—which, how, and so what? *Arch Pathol Lab Med*. 2000; 124:958–65. [PubMed: 10888771]

- [10]. Kotanagi H, Fukuoka T, Shibata Y, et al. The size of regional lymph nodes does not correlate with the presence or absence of metastasis in lymph nodes in rectal cancer. *J Surg Oncol*. 1993; 54:252–4. [PubMed: 8255087]
- [11]. Kim YM, Suh JH, Cha HJ, et al. Additional lymph node examination from entire submission of residual mesenteric tissue in colorectal cancer specimens may not add clinical and pathologic relevance. *Hum Pathol*. 2007; 38:762–7. [PubMed: 17306331]
- [12]. Brown HG, Luckasevic TM, Medich DS, Celebrezze JP, Jones SM. Efficacy of manual dissection of lymph nodes in colon cancer resections. *Modern Pathol*. 2004; 17:402–6.

Table 1

Detail of tumor origin and histologic subtypes.

Origin	Subtypes										
	SCC	PSC	EAC	CCC	Mucinous K	LMP	MMMT	Sarcoma	GCT	Metastatic K	Melanoma
Vulva	5	0	0	0	0	0	0	0	0	0	1
Vagina	3	0	0	0	0	0	0	0	0	0	2
Cervix	18	0	5	0	0	0	0	1	0	0	0
Corpus	0	5	45	3	0	0	4	3	0	0	0
Ovary	0	12	4	3	4	11	0	0	1	2	0
Ovary and corpus	0	1	0	0	0	0	0	0	0	0	0
Peritoneum	0	1	0	0	0	0	0	0	0	0	0
	134										

SCC = squamous cell carcinoma; PSC = papillary serous carcinoma; EAC = endometrioid adenocarcinoma; mucinous K = mucinous carcinoma; LMP = borderline tumor/low malignant potential; MMMT = mixed malignant müllerian tumor; LMP = low malignant potential; MMMT = mixed malignant müllerian tumor; GCT = granulosa cell tumor; metastatic K = metastatic carcinoma.

Table 2

Summary of the lymph nodes (LNs) and cassettes submitted.

	Number	Size (mm)
Palpable LNs	3–36	4–40
Non-palpable LNs	0–14	1–7
Metastatic palpable LNs	0–21	5–40
Metastatic non-palpable LNs	0–1	3
	Number (cassettes)	
Palpable LNs	1–35	
Non-palpable LNs	1–22	