

Distinguished expert series

by Peter Bószé

The use of lymphadenectomy in clinical stage I endometrial adenocarcinoma at a large community hospital

C. A. Strittmatter, M.D.; M. Steven Piver, M.D., LLD (h.c.)

Department of Obstetrics and Gynecology, Sisters of Charity Hospital, Buffalo, NY (USA)

Summary

Purpose and materials and methods: Because of the inaccuracies in clinical staging of endometrial cancer, the International Federation of Gynecology and Obstetrics (FIGO) in 1988 changed the staging of endometrial cancer to surgical staging consisting of intraoperative findings and histologic evaluation of the specimen. A decade later, 1998, the United States Society of Gynecologic Oncologists published Practice Guidelines for the surgical staging of endometrial cancer. The purpose of this study was to review the use of lymph node sampling and peritoneal washings in 100 consecutive cases of clinical stage I endometrial cancer and compare these results to the Practice Guidelines of the Society of Gynecologic Oncologists.

Results: The vast majority of patients (86%) had peritoneal washings and frozen section (69%) of the uterus. However, only slightly more than half (52%) had palpitation of the pelvic and/or para-aortic lymph nodes. Most encouraging and consistent with the Society of Gynecologic Oncologists' Guidelines is that 87% of the patients with histologically more aggressive cancers (grade III or deep myometrial invasion), had lymph node sampling as did 90.5% with more aggressive histologic subtypes.

Conclusion: Notwithstanding these results, there is still the need in the 21st century for more uniform guidelines for the surgical staging of endometrial cancer.

Key words: Endometrial cancer; Staging; Lymph nodes.

With endometrial cancer being the fourth most common cancer in females in the United States after breast, lung, and colon cancer, with an estimated 38,300 cases in 2001, the majority of these cases will be initially surgically managed in community hospitals [1]. Because of the inaccuracies in clinical staging of endometrial cancer, which primarily consisted of physical examination and chest X-ray findings, the International Federation of Gynecology and Obstetrics changed the staging of endometrial cancer in 1988 to surgical staging consisting of intraoperative findings and histologic evaluation of the specimen [2].

Although it was not until 1988 that surgical staging of endometrial cancer was proposed, the 1970 report of Ng and Regan of stage I endometrial adenocarcinoma operated on at Case Western Reserve primarily by total abdominal hysterectomy and bilateral salpingo-oophorectomy from 1948-1968 clearly suggested that there were prognostically different subgroups of clinical stage I endometrial carcinoma [3]. The five-year survival of their grade I cancers was 85.7% as compared to only 40.5% for the grade III tumors. Also, the five-year survival for the patients with tumors invading the myometrium less than 50% was 72.3%, but only 27.3% for tumors invading greater than 50%. The reason for this disparity in survival of what appeared to be a clinically localized malignancy became somewhat clearer by the 1970 report of Lewis et al in which the authors performed pelvic lymphadenectomy in addition to total abdominal hysterectomy and bilateral salpingo-oophorectomy in FIGO stage I endometrial cancer cases [4]. There was a 5.5% incidence of pelvic lymph node metastasis for grade I tumors but this increased to 26.0% for grade III or poorly differentiated malignancies. Similarly, for patients with no invasion or only very superficial myometrial invasion, there were no cases of pelvic lymph node metastasis as compared to 36.2% for those with deep myometrial invasion.

However, it was the 1976 seminal report by Creasman *et al.* that truly explained the varying survival rates reported by Ng and Regan and which eventually led to surgical staging of endometrial cancer [5]. The authors reported not only on the incidence of pelvic lymph node metastasis from stage I endometrial cancers, but also on the incidence of para-aortic lymph node metastasis. Only 3.1% and 1.5%, respectively, of grade

I tumors were associated with pelvic lymph node and aortic lymph node metastasis as compared to 36.0% and 28.0% of grade III tumors. Moreover, for patients with very superficial myometrial invasion (less than one-third), 11.5% and 9.8% respectively had pelvic and aortic lymph node metastasis as compared to 43.0% and 21.0% for very deep myometrial invasion (outer one-third).

Subsequently, it became evident that in addition to intraoperative findings, histologic grade and myometrial invasion, that certain histologic variants, clear cell, uterine papillary serous, adenosquamous, and mucinous carcinomas, had a much worse prognosis than the more common endometrioid adenocarcinoma. Therefore, as we start the 21st century, it is clear that there are important histologic subtypes, histologic grade and amount of myometrial invasion that portend a good or poor prognosis in clinically localized endometrial cancer. What is not clear is what is the appropriate surgical management of stage I endometrial cancer. This is of special concern to the private practice gynecologist who will be the first to diagnose many of these patients by way of endometrial sampling for abnormal uterine bleeding. Is endometrial cancer a condition that can be treated by the primary obstetrician/gynecologist with simple hysterectomy and bilateral salpingo-oophorectomy or is this a malignancy that needs to be routinely surgically staged? And if so, what does surgical staging consist of, and in what cases should it be done?

In 1998, the Society of Gynecologic Oncologists published *Practice Guidelines of Endometrial Cancer* with the caveat "the information in the Society of Gynecologic Oncologists' Clinical Practice Guidelines should not be viewed as a body of rigid rules. The guidelines are general and are intended to be adapted to many different situations, taking into account the needs and resources particular to the locality, the institution or the type of practice... The purpose of these guidelines will be served if they provide a fundamental basis on which local norms may be built" [6].

The staging procedure described in the guidelines is as follows:

"The abdomen is opened with a vertical, lower abdominal incision, and peritoneal washings are taken of the pelvis and abdomen. Careful exploration is then carried out looking and feeling for evidence of omental, liver, peritoneal, cul-de-sac and adnexal metastases. The aortic and pelvic areas are palpated for nodal metastases. An extrafascial, total hysterectomy with bilateral salpingo-oophorectomy is then performed.

The uterus is opened off the field to determine the extent of the growth. If the depth of invasion is not grossly evident, it may be determined by frozen-section analysis. Though an integral part of the FIGO staging system for endometrial carcinoma, the indications for lymph node sampling must always be evaluated in light of the risk to the patient and the likelihood of their involvement based on operative findings. The node-bearing retroperitoneum should first be evaluated with the peritoneum opened to identify enlarged or suspicious lymph nodes. If these are positive on frozen section, node dissection may be unnecessary unless clinically positive nodes can be excised with minimal risk to the patient.

Indications for aortic node sampling include: (1) suspicious aortic or common iliac nodes; (2) grossly positive adnexa; (3) grossly positive pelvic nodes; (4) any grade carcinoma with outer-half myometrial invasion; and (5) clear cell, papillary serous, or carcinosarcoma histologic subtypes.

Indications for pelvic node dissection include: (1) suspicious pelvic nodes; (2) aortic node sampling not feasible; (3) cases in which the nodal findings would be the basis for deciding whether the patient would receive postoperative radiation therapy".

Given the change in FIGO staging from clinical to surgical in 1988, and the suggested 1998 *Practice Guidelines of the Society of Gynecologic Oncology*, the purpose of this study was to retrospectively review the recent use of lymph node sampling and peritoneal washings in 100 consecutive cases of clinical stage I endometrial cancer at a large community hospital.

Materials and Methods

One hundred consecutive cases of clinical stage I adenocarcinoma of the endometrium were retrospectively reviewed. Starting from June 2000 and working backwards, all inpatient charts with an ICD-9 code 182.0 (malignant neoplasm corpus uteri) or 182.8 (malignant neoplasm body uterus NEC) were requested. We included those patients who prior to surgery were believed to have stage I endometrial cancer and were treated surgically with total abdominal hysterectomy and bilateral salpingo-oophorectomy. We excluded those patients who were felt to be advanced stage prior to admission, those with sarcomas, and those treated with prior radiation or chemotherapy. The entire chart was reviewed with focus on the discharge summary, the data form for cancer staging, the admission history and physical, the written and dictated operative reports and the final pathology report. We recorded each patient's medical record number, age, height, weight, whether the patient had a preoperative office endometrial biopsy and/or D&C (although the exact results of this endometrial sampling (i.e. grade, histology) were rarely documented in the in-patient chart), tumor grade, depth of myometrial invasion and histology of the cancer,

along with the results of frozen section, peritoneal washings, and lymph node sampling. The total number of lymph nodes found by the pathologist in the pelvic and para-aortic specimens was noted for comparison. The final FIGO stage as recorded in the data form for cancer staging was also collected. We then tabulated the data looking to compare the surgical pathologic risk factors that could possibly be used by the gynecologist to determine whether a lymph node sampling procedure should be performed and whether or not this was actually done and under what circumstances.

Results

Table 1. — Characteristics of 100 consecutive cases of clinical stage I endometrial cancer at a community hospital

Characteristics	%
<i>Preoperative Diagnosis</i>	
Endometrial Biopsy	63
Dilation & Curettage	27
Both EMB* + D&C	8
Neither EMB or D&C	2
<i>Grade</i>	
1	48
2	32
3	20
<i>Depth of Invasion</i>	
Confined to Endometrium	14
Less than 50% Invasion	66
Greater than 50% Invasion	20
<i>Histology</i>	
Endometrioid	79
Mucinous	5
Adenosquamous	1
Papillary Serous	8
Mixed	7

*EMB - endometrial biopsy.

The clinical characteristics are shown in Table I. Two percent of the patients had neither a D&C nor an endometrial biopsy prior to surgery. Eighty percent were grade I or II and 80% were confined to the endometrium or had less than 50% myometrial invasion. Endometrioid adenocarcinoma accounted for 79% of the cases.

As shown in Table 2, the vast majority of patients (86%) had peritoneal washings performed as suggested by the Society of Gynecologic Oncologists Practice Guidelines, and 69% had frozen section performed on the uterus. However, in only 52% of the cases were the lymph nodes palpated, and in 52% and 50%, respectively, were the pelvic and/or aortic lymph nodes sampled. Of the 52 patients who had pelvic lymph nodes sampled, the mean number of lymph nodes removed was 8.04 (± 4.04) with a maximum number of 24 and minimum number of 2. Similarly, of the 50 patients who had para-aortic lymph nodes sampled, the mean number of lymph nodes removed was 3.40 (± 2.60) with a maximum of 10 and a minimum of 0 (no lymph nodes seen histologically).

Of the 80 patients with grade I or II tumors, 47.5% (38) and 70% (14) of those with grade III tumors had pelvic lymph nodes sampled. Similarly, 45% (36) of the patients with grade I or grade II tumors had para-aortic lymph nodes sampled as did 70% (14) of those with grade III tumors (Table 3).

Table 2. — Peritoneal washings, frozen sections, lymph node palpation and lymph node sampling (N=100)

Surgical Procedures	Yes	No
Peritoneal washings	86	12
Frozen section	69	31
Lymph node palpation	52	48
Pelvic lymph node sampling	52	48
Para-aortic lymph node sampling	50	50

Table 3. — Pelvic and para-aortic lymph node sampling vs grade, myometrial invasion and histology

	Pelvic lymph node sampling		Para-aortic lymph node sampling	
	Yes	No	Yes	No
<i>Grade</i>				
1	23	25	20	28
2	15	17	16	16
3	14	6	14	6
<i>Myometrial</i>				
0%	7	7	7	7
< 50%	31	35	25	41
> 50%	14	6	18	2
<i>Histology</i>				
Endometrioid	36	43	34	44
Mucinous	3	2	3	2
Adenosquamous	1	0	1	0
Papillary serous	6	2	7	1
Mixed	6	1	4	3
Totals	52	48	50	50

Of the 14 cases confined to the endometrium, seven (50%) had pelvic and/or para-aortic sampling. Of the 32 patients with grade III tumors or deep myometrial invasion, both associated histologically with a significantly higher percentage of lymph node metastasis, 87.5% had lymph nodes sampled. Also, of the 21 patients with more aggressive histologic subtypes (mucinous, adenosquamous, uterine papillary serous), 90.5% had lymph nodes sampled. All six patients with clinically positive lymph nodes had lymph nodes sampled (Table 4).

Although not the focus of this study, of those patients who had pelvic and/or para-aortic lymph node sampling, the association with grade, myometrial invasion, and histologic subtype is shown in Table 5. Nine (17.3%) of the 52 patients who had

Table 4. — Lymph node sampling vs histopathologic and clinical findings

Characteristics	Lymph Node Sampling	
	Yes	No
Grade 1 or 2 and <50%		
Myometrial Invasion (n=68)	29 (42.6%)	39 (57.4%)
Grade 3 or >50%		
Myometrial Invasion (n=32)	28 (87.5%)	4 (12.5%)
Endometrioid Adenocarcinoma (n=79)	38 (48%)	41 (52%)
Other Histologies (n=21)	19 (90.5%)	2 (9.5%)
Clinically Positive Nodes (n=6)	6 (100%)	0 (0%)

Table 5. — Surgical pathologic findings in patients who underwent pelvic and/or para-aortic lymph node sampling

Surgical Pathologic Findings	Pelvic lymph node sampling n=52		Para-aortic lymph node sampling n=50	
	Positive n=9	Negative n=43	Positive n=6	Negative n=44
Grade				
1	3	20	2	18
2	3	12	3	13
3	3	11	1	13
Depth of invasion				
Endometrium	0	7	0	7
<50% invasion	3	28	0	25
>50% invasion	6	8	6	12
Histology				
Endometrioid	3	33	3	32
Mucinous	2	1	1	2
Adenosquamous	1	0	1	1
Papillary serous	0	6	0	7
Mixed	3	3	1	3

pelvic lymph nodes sampled had metastasis and 12 (20%) of the 50 patients who had para-aortic lymph nodes sampled had metastasis. Only two patients had malignant peritoneal washings.

Discussion

Although this study was a retrospective assessment of surgical staging performed by many gynecologists with or without gynecologic oncology assistance, in clinical stage I endometrial cancer, certain points seem clear relative to the Society of Gynecologic Oncologists Practice Guidelines for endometrial cancer. The vast majority of patients (86%) had peritoneal washings and frozen section (69%) of the uterus. However, only slightly more than half (52%) had palpation of the pelvic and/or para-aortic lymph nodes. Accuracy of palpation of retroperitoneal nodes has been questioned by Girardi et al because 37% of lymph node metastases in their cases of endometrial cancer measured less than or equal to 2 mm, clearly not detectable by the most experienced surgeon [7]. Most encouraging and consistent with the Society of Gynecologic Oncologists Guidelines is that 87.5% of the patients with histologically more aggressive cancers, grade III or deep myometrial invasion in this series had lymph node sampling as did 90.5% with the more aggressive histologic subtypes.

It has now been over 25 years since the important report by the Gynecologic Oncology Group on pelvic and para-aortic lymph node metastasis in clinical stage I endometrial cancer [5]. However, notwithstanding the Society of Gynecologic Oncologists Practice Guidelines on lymph node sampling and endometrial cancer, which are "intended to be adapted to many situations, taking into account the needs and resources particular to the locality", given the rising health care costs as well as the need to deliver the very best health care, it is still far from settled which patients should have lymph node evaluation as part of surgical staging of endometrial cancer and whether this should be lymph node biopsy, pelvic lymphadenectomy, para-aortic lymphadenectomy and whether results of lymph node removal will determine the need for postoperative radiation.

References

- [1] Greenlee R. T., Hill-Harmon B., Murray T., Thun M.: "Cancer Statistics 2001". *CA*, 2001, 51, 15.
- [2] FIGO Stages 1888 Revision: *Gynecologic Oncology*, 1989, 35, 125.
- [3] Ng A., Reagan J. W.: "Incidence and prognosis of endometrial carcinoma by histologic grade and extent". *Obstet. & Gynecol.*, 1970, 35, 437.
- [4] Lewis B. V., Stallworthy J. A., Cowdel R.: "Adenocarcinoma of the body of the uterus". *J. Obstet. Gynaecol. of the Brit. Commonwealth*, 1970, 77, 343.
- [5] Creasman W. T., Boronow R. C., Morrow C. P., DiSaia P. J., Blessing J.: "Adenocarcinoma of the endometrium: Its metastatic lymph node potential. Preliminary report". *Gynecol Oncol.*, 1976, 4, 239.
- [6] Practice guidelines: "Uterine corpus-endometrial cancer". *Oncology*, 1998, 12, 122.
- [7] Girardi F., Petru E., Heydarfadaei M., Haas J., Winter R.: "Pelvic lymphadenectomy in the surgical treatment of endometrial cancer". *Gynecol. Oncol.*, 1993, 49, 177.

Address reprint requests to:
M. STEVEN PIVER, M.D., LLD (hc)
Senior Gynecologic Oncologist
Sisters of Charity Hospital
2157 Main St.
Buffalo, NY 14214