Gynecologic Oncology **84,** 437–442 (2002)
doi:10.1006/gyno.2001.6550, available online at http://www.idealibrary.com on IDEAL®

Predictors of Lymphatic Failure in Endometrial Cancer[1,2]

Andrea Mariani, M.D.,* Maurice J. Webb, M.D.,† Gary L. Keeney, M.D.,‡ Giacomo Aletti, M.S.,§ and Karl C. Podratz, M.D., Ph.D.†,[3]

†*Section of Gynecologic Surgery and* ‡*Division of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota 55905;* §*Department of Mathematics, University of Milano, Milan, Italy; and* **Department of Obstetrics and Gynecology, Ospedale Sacra Famiglia, Erba (CO), Italy*

Received August 6, 2001

Objective. **The aim of this study was to identify determinants of lymphatic failure in patients with endometrial cancer after definitive primary treatment.**

Methods. **We observed 142 relapses in endometrial cancer patients who had primary surgery at our institution during the decade before 1994. We defined lymphatic failure as a relapse occurring on the pelvic sidewall (PSW), para-aortic area (PAA), or other node-bearing area (i.e., groin, axilla, supraclavicular, mediastinal). Mean follow-up was 72.8 months.**

Results. **We observed 44 instances of lymphatic failure—6 on the PSW only, 16 in the PAA only, 12 concomitantly in the PAA and on the PSW, and 10 confined in other node-bearing areas. By univariate analysis, body mass index ≥30 kg/m^2, para-aortic lymph node biopsy, cervical stromal invasion (CSI), positive adnexa, myometrial invasion >50%, primary tumor diameter >2 cm, positive peritoneal cytology, positive lymph nodes (pelvic and/or para-aortic), radiotherapy, grade 3 tumor, nonendometrioid histology, and lymph–vascular invasion (LVI) significantly ($P \leq 0.05$) correlated with lymphatic failure. However, on Cox regression analysis, only LVI ($P < 0.01$, relative risk [RR] = 4.27), nodal involvement ($P = 0.02$, RR = 3.43), and CSI ($P = 0.049$, RR = 2.26) were independent predictors of lymphatic failure. Moreover, lymph node metastases ($P = 0.01$, RR = 19.82) and CSI ($P = 0.050$, RR = 3.57) independently predicted failure on the PSW, and only lymph node involvement ($P < 0.01$, RR = 10.15) predicted relapse in the PAA.**

Conclusion. **LVI, positive lymph nodes, and CSI were the strongest predictors of lymphatic failure in endometrial cancer (31% of patients with at least one of the above three variables had a failure at 5 years). Patients with none of the above three factors had an extremely low (<1%) risk of lymphatic failure.**

Key Words: **endometrial cancer; lymphatic failure; cervical invasion; lymph nodes; lymph–vascular invasion; lymphatic metastases.**

INTRODUCTION

Endometrial adenocarcinoma is the most common malignancy of the female genital tract in the United States. For 2001, the estimated number of new cases is 38,300, with 6600 cancer deaths [1].

Poor histologic differentiation, deep myometrial invasion, positive peritoneal cytology, lymph node invasion, and age older than 60 years have been described as significant predictors of distant disease [2–4]. We recently reported deep myometrial invasion to be the strongest predictor of hematogenous dissemination [5]. However, to our knowledge, there are no studies describing the determinants of lymphatic failure in endometrial cancer.

Lymphatic failure can be minimized by formal systematic node dissection [6–10] or adjuvant radiotherapy [11, 12] or both [13, 14]. However, the best means of preventing lymphatic failure is still being debated, and prospective randomized trials are needed [15]. For this reason, it is important to identify patients who are at high risk for lymphatic failure and are suitable for enrollment in new prospective studies.

The objective of the present analysis was to identify determinants of lymphatic failure in patients with endometrial cancer after definitive primary treatment.

MATERIALS AND METHODS

From 1984 through 1993, 815 patients with endometrial cancer were managed surgically at the Mayo Clinic (Rochester, MN). We retrieved their records from the database and selected 612 patients with epithelial endometrial cancer who satisfied the following inclusion criteria: (1) treatment included hysterectomy and removal of existing adnexal structures, and (2) no other malignancy was diagnosed within 5 years before or after the diagnosis of endometrial cancer (except for carcinoma *in situ* or skin cancer other than melanoma). In 2 of the 612 study patients, information was lacking for most of the prognostic variables and these 2 patients were therefore not included in the study; thus, the present analysis was conducted on 610 patients.

Staging was determined according to the International Fed-

[1] Supported by the Mayo Cancer Center (P30CA15083) and the Rochester Research Committee, Mayo Foundation.

[2] Presented at the 32nd Annual Meeting of the Society of Gynecologic Oncologists, Nashville, TN, March 3–7, 2001.

[3] To whom reprint requests should be addressed at Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

0090-8258/02 $35.00

eration of Gynecology and Obstetrics surgical staging system [16]. In patients treated before 1988, stage was determined retrospectively on the basis of surgical and pathologic assessment. For histologic classification, we used the World Health Organization classification [17]. We based architectural grading on the degree of glandular differentiation, in accordance with the FIGO guidelines [16]. Lymph–vascular invasion (LVI) was considered present when tumor cells were within, or were attached to, the wall of a capillary-like space. Hyperplasia associated with tumor was diagnosed when an area of hyperplasia was found in the same sample adjacent to the tumor. Primary tumor diameter was macroscopically measured by the pathologist on fresh tissue by a method that has been described elsewhere [18].

All hematoxylin and eosin-stained slides of the tumor were reviewed retrospectively by one of us (G.L.K.) for confirmation of the original diagnosis of adenocarcinoma and determination of FIGO grade, histologic subtype (endometrioid and nonendometrioid), presence of hyperplasia associated with tumor, and LVI.

All surgical procedures were the responsibility of a gynecologic oncologist. Lymphadenectomy was usually performed for patients considered by the surgeon to be at risk for lymph node metastasis, according to the intraoperative frozen section analysis of the histologic grade of the tumor and the depth of myometrial invasion. Para-aortic lymph node dissection was usually performed in the presence of positive pelvic lymph nodes. Postoperative adjuvant radiotherapy consisted of external pelvic and/or para-aortic and/or abdominal irradiation and/or vaginal brachytherapy. On occasion (especially in patients with advanced disease), oral megestrol acetate was prescribed or adjuvant chemotherapy was administered.

When follow-up information regarding survival and recurrence was not sufficiently detailed in the clinical records, death certificates were obtained and letters to patients and family physicians or telephone calls were used to obtain follow-up data.

We defined lymphatic failure as a relapse occurring on the pelvic sidewall (PSW), para-aortic area (PAA), or other node-bearing area (i.e., groin, axilla, supraclavicular, mediastinal) as the primary site of failure. Recurrence in the pelvic nodes was diagnosed when a mass was observed along the pelvic sidewall and that in the para-aortic nodes when a lesion appeared in an area adjacent to the aorta/vena cava.

For statistical purposes, endometrioid, endometrioid with squamous differentiation, and adenosquamous tumors were considered together as endometrioid and compared with nonendometrioid tumors, which included papillary serous, clear cell, and undifferentiated carcinomas. Grade 1 and 2 lesions were combined and compared with grade 3 cases. The choice of 2 cm as a determinant for the analysis of primary tumor diameter was based on our previous experience [18].

Statistical analysis was performed with Fisher's exact test and χ^2 analysis to test for relationships between pairs of categorical variables. The Kaplan–Meier method, log-rank test, and Cox regression analysis were used for time-to-event analyses with the following endpoints: lymphatic recurrence, failure on the PSW, and failure in the PAA. Censoring was considered at the date of last contact or death in case of no failures in the lymph-node-bearing areas. Differences were considered statistically significant at $P \leq 0.05$. SAS System 6.10 statistical software was used for the analysis.

RESULTS

The studied population ($n = 610$) had a mean age (±standard deviation [SD]) of 64.6 ± 10.5 years (range, 22–90 years) and a mean body mass index (BMI) (±SD) of 30.6 ± 8.3 kg/m^2 (range, 16.0–65.5 kg/m^2). Twelve patients (2%) had preoperative therapy: 9 external radiotherapy and 3 chemotherapy. Pelvic lymph node dissection was performed in 367 patients (60%) and para-aortic dissection in 104 (17%) (overall, 374 patients had pelvic and/or para-aortic lymph node dissection). The mean number of nodes harvested was 15.9 pelvic (range 1–55) and 5.9 para-aortic (range 1–43). Adjuvant radiotherapy was administered to 229 patients (38%), hormone therapy to 33 (5%), and adjuvant chemotherapy to 20 (3%), on the basis of adverse prognostic factors.

After a mean follow-up (±SD) of 72.8 ± 41.3 months (range 0–155 months), 142 (23%) tumor recurrences were documented. Information about the site of recurrence was available in 131 cases. There were 44 (34%) lymphatic failures: 6 on the PSW, 16 in the PAA, 12 concomitantly in the PAA and on the PSW, and 10 confined in other node-bearing areas (i.e., scalene, inguinal, mediastinal, axillary). Median time to lymphatic failure was 12 months (range 0–80 months).

By univariate analysis, BMI ≥30 kg/m^2, para-aortic lymph node biopsy, cervical stromal invasion, positive adnexa, deep myometrial invasion, primary tumor diameter >2 cm, positive peritoneal cytology, positive lymph nodes (pelvic and/or para-aortic), adjuvant radiotherapy, grade 3 histology, nonendometrioid histologic subtype, and LVI significantly predicted lymphatic failure ($P \leq 0.05$) (Table 1). All of the above variables were included in a Cox regression model. Only LVI ($P < 0.01$, relative risk [RR] = 4.27, 95% confidence interval [CI] = 1.76–10.30), nodal involvement ($P = 0.02$, RR = 3.43, 95% CI = 1.50–7.79), and cervical stromal invasion ($P = 0.049$, RR = 2.26, 95% CI = 1.10–4.69) were independent predictors of lymphatic failure. We excluded from the analysis 213 patients for whom the information on at least one of the above three independent prognosticators was missing and for whom negative values were reported for the remaining one or two variables. Considering the 259 patients with negative lymph nodes, negative cervical stroma, and no LVI, we observed a rate of lymphatic failure at 5 years of 0.4%, compared with 31% in the subgroup of 138 patients in whom one or more of the above three factors were positive ($P < 0.0001$)

TABLE 1
Prediction of Lymphatic Failure (LF) in Patients with Endometrial Cancer[a]

Characteristics	% 5-year RFS (LF)	*P*	% 5-year RFS (PSW)	*P*	% 5-year RFS (PAA)	*P*
Age, years						
≤65	91	0.3	96	0.27	93	0.13
>65	94		97		97	
Body mass index, kg/m^2						
<30	94	0.03	98	0.08	97	0.03
≥30	90		95		93	
PLNs biopsy						
Yes	91	0.22	96	0.34	95	0.94
No	94		98		95	
PALNs biopsy						
Yes	87	0.05	94	0.17	93	0.45
No	94		97		96	
Cervical stromal invasion						
Yes	56	<0.0001	67	<0.0001	74	<0.0001
No	95		98		96	
Positive adnexa						
Yes	67	<0.0001	85	0.0002	74	<0.0001
No	94		97		96	
Myometrial invasion						
≤50%	97	<0.0001	98	<0.0001	98	<0.0001
>50%	78		90		86	
Primary tumor diameter, cm						
≤2	98	0.0006	99	0.04	98	0.02
>2	90		96		93	
Peritoneal cytology						
Positive	74	<0.0001	90	0.005	84	<0.0001
Negative	95		98		97	
PLNs						
Positive	55	<0.0001	71	<0.0001	69	<0.0001
Negative	97		99		99	
PALNs						
Positive	30	<0.0001	62	<0.0001	55	<0.0001
Negative	96		99		99	
Total LNs						
Positive	52	<0.0001	71	<0.0001	67	<0.0001
Negative	97		99		99	
Associated hyperplasia						
Yes	92	0.33	95	0.88	96	0.18
No	89		96		93	
LVI						
Yes	65	<0.0001	82	<0.0001	78	<0.0001
No	98		99		98	
Histologic subtype						
Endometrioid	94	0.001	97	0.32	96	0.002
Nonendometrioid	78		95		84	
Histologic grade						
1–2	95	<0.0001	98	0.002	97	<0.0001
3	80		91		86	
Adjuvant CT						
Yes	74	0.26	74	0.02	74	0.09
No	93		97		95	
Adjuvant RT						
Yes	87	0.0002	95	0.32	93	0.05
No	96		98		96	

Note. CT, chemotherapy; LNs, lymph nodes; LVI, lymph–vascular invasion; PAA, recurrence in para-aortic area; PALNs, para-aortic lymph nodes; PLNs, pelvic lymph nodes; PSW, pelvic sidewall failure; RFS, recurrence-free survival; RT, radiotherapy.

[a] In 11 patients the site of failure was not available.

TABLE 2
Failure Frequency at Various Lymphatic Sites According to Corresponding Risk Status

Lymphatic site(s)	*n*	Failure rate at 5 years (%)	*P*
All sites			
Low risk[a]	259	0.4	<0.001
High risk[b]	138	31	
Pelvic sidewall			
Low risk[a]	292	0	<0.001
High risk[c]	94	26	
Para-aortic area			
Low risk[a]	308	1	<0.001
High risk[d]	62	33	

[a] Low risk: none of the corresponding high-risk factors.
[b] High risk: lymph–vascular invasion and/or cervical stromal invasion and/or nodal metastases.
[c] Cervical stromal invasion and/or nodal metastases.
[d] Only nodal metastases.

(in 8 patients information about the site of failure was missing) (Table 2, Fig. 1).

Cervical stromal invasion, positive adnexa, deep myometrial invasion, positive peritoneal cytology, positive lymph nodes (pelvic and/or para-aortic), tumor diameter >2 cm, grade 3 tumor, designation for adjuvant chemotherapy, and LVI significantly predicted recurrence on the PSW ($P < 0.05$) (Table 1). However, on the basis of Cox regression analysis, only lymph node metastases ($P = 0.01$, RR = 19.82, 95% CI = 3.48–113.80) and cervical stromal invasion ($P = 0.050$, RR = 3.57, 95% CI = 1.14–11.10) independently predicted failure on the PSW. We excluded 224 patients who had negative cervical stroma but for whom information about lymph node status was missing. In 292 patients without cervical stromal invasion and with negative lymph nodes, the rate of failure on the PSW at 5 years was 0%, compared with 26% in 94 patients in whom one or both factors were positive ($P < 0.0001$) (in 7 patients information about the site of failure was missing) (Table 2, Fig. 2).

BMI ≥30 kg/m^2, cervical stromal invasion, positive adnexa, deep myometrial invasion, primary tumor diameter >2 cm, positive peritoneal cytology, positive lymph nodes (pelvic and/or para-aortic), nonendometrioid histologic subtype, grade 3 tumor, designation for adjuvant radiotherapy, and LVI significantly predicted recurrence in the PAA ($P \leq 0.05$) (Table 1). However, on the basis of Cox regression analysis, only lymph node involvement ($P < 0.01$, RR = 10.15, 95% CI = 3.20–32.34) predicted relapse in the PAA. Excluding 240 patients for whom information about the site of failure or lymph node status was missing, the 5-year para-aortic recurrence rates were 1% in 308 patients with negative lymph nodes and 33% in 62 who had lymph node involvement ($P < 0.0001$) (Table 2, Fig. 3).

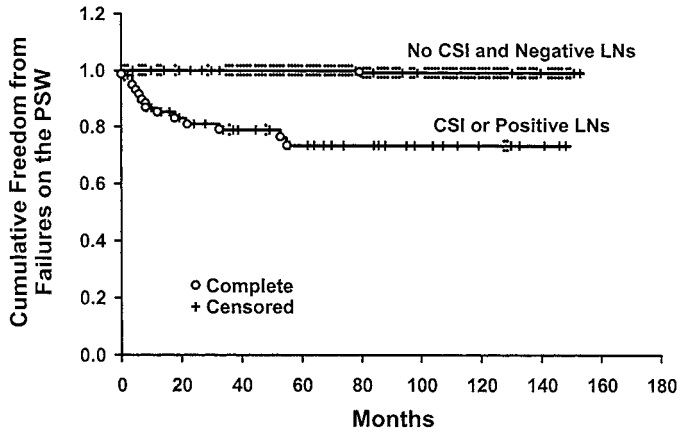

FIG. 2. Predicted freedom from pelvic sidewall (PSW) failure in patients with endometrial cancer, according to lymph node (LNs) status and cervical stromal invasion (CSI) ($P < 0.0001$).

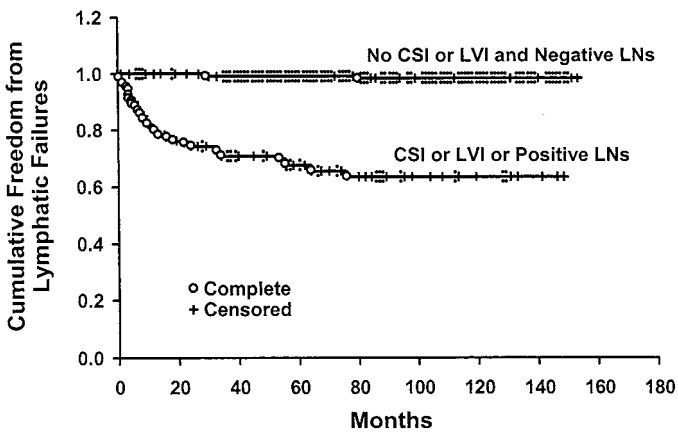

FIG. 1. Predicted freedom from lymphatic failures in patients with endometrial cancer, according to lymph node (LNs) status, cervical stromal invasion (CSI), and lymph–vascular invasion (LVI) ($P < 0.0001$).

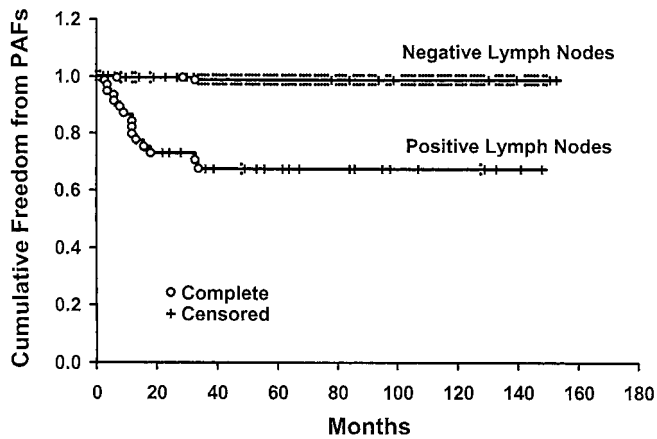

FIG. 3. Predicted freedom from para-aortic failures (PAFs) in patients with endometrial cancer, according to lymph node status ($P < 0.0001$).

Considering only the 44 patients with lymphatic failure, 22 (50%) had an isolated lymphatic failure (ILF), and 22 (50%) had a lymphatic failure associated with recurrence at another site(s) (OLF).

In the analysis of the subgroup of 138 patients at risk for lymph node recurrence (i.e., cervical stromal invasion and/or positive lymph nodes and/or LVI), we observed that age $\leq$65 years, presence of cervical stromal invasion, and positive para-aortic/total lymph nodes significantly ($P < 0.05$) predicted ILFs; BMI $\geq$30 kg/m^2 approached significance ($P = 0.08$). Moreover, stage IV disease, myometrial invasion >50%, and LVI were significant ($P \leq 0.05$) predictors of OLFs. Furthermore, none of 8 patients with tumor diameter $\leq$2 cm and none of 31 patients without LVI had OLF. Therefore, excluding 38 patients without LVI and/or with tumor diameter $\leq$2 cm, we observed that among 72 patients with stage IV tumor or myometrial invasion >50% (in 5 information about the site of failure was missing), 15 (22%) had OLF, whereas among 27 patients with stage I–III disease and myometrial invasion $\leq$50%, only 1 (4%) had OLF (in 1 patient information about the site of failure was missing) ($P = 0.03$).

DISCUSSION

In the present study, we identified characteristics of tumors which can potentially predict lymphatic failure in endometrial cancer (Table 1). We included the type of adjuvant therapy in the regression models in order to identify variables that were independent of postoperative management. Only cervical stromal invasion, LVI, and lymph node involvement were independent predictors of lymphatic failure. In fact, 31% of patients with at least one of the above three variables had lymphatic failure within 5 years of primary surgery, compared with 0.4% of patients when none of these variables was positive (Table 2, Fig. 1). Hence, patients with no cervical stromal invasion, lymph node involvement, or LVI should be stratified or possibly excluded when designing clinical trials that evaluate adjuvant therapies directed at lymph-node-bearing areas. Importantly, the subgroup of patients at risk for lymphatic failure accounts for an estimated 23% of the overall population of endometrial cancer patients.

Focusing on the three variables that independently predicted lymphatic failure, we observed that LVI had previously been demonstrated as a strong predictor of prognosis and distant failure. It is an important prognostic factor even when stratifying patients for lymph node status [19]. LVI is a predictor of both lymphatic and hematogenous dissemination [5]. Cervical stromal invasion is associated with a high prevalence of lymph node metastases in endometrial cancer [20], and positive lymph nodes have been reported to be predictors of lymphatic failure [6, 9, 21]. Interestingly, we observed a 3% lymphatic failure rate at 5 years in patients with negative nodes (Table 1). This observation may be explained by the fact that the true incidence of positive nodes is underestimated because of the limited number of nodes removed [14, 22] and because of the intrinsic limitations of the pathologic analysis of samples [23].

After patients at risk for lymphatic failure have been identified, it is extremely important to design treatment strategies to minimize such recurrences. Radiation therapy can effectively reduce the incidence of regional lymph node recurrence in breast cancer associated with positive lymph nodes and limited node dissection [24]. In our study, the finding that patients who had adjuvant pelvic radiotherapy were at higher risk of lymphatic failure in the para-aortic area but not in the pelvis (Table 1) suggests a possible role of radiotherapy in preventing failure on the pelvic sidewall, as previously described [11–13, 25]. Moreover, the therapeutic role of extended-field irradiation in patients with positive para-aortic nodes has previously been reported [9, 21, 26], but it may be limited in patients with disease of undissected lymph nodes [6]. A possible therapeutic effect of pelvic [7, 14, 27, 28] and para-aortic [6, 9, 26] lymphadenectomy has been suggested, but data to the contrary continue to be cited [29–31].

Treatment of patients with lymphatic recurrence in association with other sites of failure implies the need for systemic adjuvant therapy and/or vaginal brachytherapy and/or abdominal irradiation in addition to definitive therapy to the lymph-node-bearing areas [13, 32]. In the present study, we analyzed separately patients with ILF and those with OLF. Considering only the subgroup of patients at high risk for lymphatic failure (i.e., cervical stromal invasion, positive lymph nodes, or presence of LVI), patients with tumor diameter $\leq$2 cm and those without LVI can probably forego adjuvant therapy to nonlymphatic areas. However, the presence of stage IV disease and/or myometrial invasion >50% are predictors of OLF and identify a subgroup of high-risk patients who should receive definitive treatment of the pelvic and para-aortic areas as well as systemic therapy or abdominal irradiation. Similarly, we previously observed that deep myometrial invasion is the strongest predictor of hematogenous dissemination in corpus cancer [5]. However, neither cervical invasion nor the presence of positive lymph nodes was associated with hematogenous dissemination in our previous study [5], and likewise neither was a predictor of OLF in the present analysis. These observations suggest a different pathogenesis and a possibly altered tumor biology for corpus cancers that metastasize predominantly via the lymphatics as opposed to hematogenously.

CONCLUSION

LVI, node metastasis, and cervical stromal invasion were the strongest predictors of lymphatic failure in endometrial cancer; 31% of patients with at least one of the above three variables had a lymphatic failure within 5 years of primary surgery. Patients with none of the above three factors had an extremely low (<1%) risk of lymphatic recurrence (Table 2). Therefore, patients with at least one risk factor (approximately 23% of patients with endometrial cancer) will be candidates for trials

that test the therapeutic value of systematic lymphadenectomy and adjuvant radiotherapy to the lymph-node-bearing areas. In addition, patients with cervical stromal invasion and/or positive lymph nodes who also have LVI, tumor diameter >2 cm, and myometrial invasion >50% (or patients with stage IV disease) will be optimal candidates for testing the efficacy of concomitant systemic cytotoxic therapy in preventing associated distant failure.

REFERENCES

1. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics, 2001. CA Cancer J Clin 2001;51:15–36.
2. Descamps P, Calais G, Moire C, Bertrand P, Castiel M, Le Floch O, Lansac J, Body G. Predictors of distant recurrence in clinical stage I or II endometrial carcinoma treated by combination surgical and radiation therapy. Gynecol Oncol 1997;64:54–8.
3. Grigsby PW, Perez CA, Kuten A, Simpson JR, Garcia DM, Camel HM, Kao MS, Galakatos AE. Clinical stage I endometrial cancer: prognostic factors for local control and distant metastasis and implications of the new FIGO surgical staging system. Int J Radiat Oncol Biol Phys 1992;22:905–11.
4. Lanciano RM, Corn BW, Schultz DJ, Kramer CA, Rosenblum N, Hogan WM. The justification for a surgical staging system in endometrial carcinoma. Radiother Oncol 1993;28:189–96.
5. Mariani A, Webb MJ, Kenney GL, Calori G, Podratz KC. Hematogenous dissemination in corpus cancer. Gynecol Oncol 2001;80:233–8.
6. Corn BW, Lanciano RM, Greven KM, Schultz DJ, Reisinger SA, Stafford PM, Hanks GE. Endometrial cancer with para-aortic adenopathy: patterns of failure and opportunities for cure. Int J Radiat Oncol Biol Phys 1992; 24:223–7.
7. Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojin F III, Conner W. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. Gynecol Oncol 1995;56:29–33.
8. Larson DM, Broste SK, Krawisz BR. Surgery without radiotherapy for primary treatment of endometrial cancer. Obstet Gynecol 1998;91:355–9.
9. Mariani A, Webb MJ, Galli L, Podratz KC. Potential therapeutic role of para-aortic lymphadenectomy in node-positive endometrial cancer. Gynecol Oncol 2000;76:348–56.
10. Podratz KC, Mariani A, Webb MJ. Staging and therapeutic value of lymphadenectomy in endometrial cancer. Gynecol Oncol 1998;70:163–4.
11. Aalders J, Abeler V, Kolstad P, Onsrud M. Postoperative external irradiation and prognostic parameters in stage I endometrial carcinoma: clinical and histopathologic study of 540 patients. Obstet Gynecol 1980;56:419–27.
12. Creutzberg CL, van Putten WL, Koper PC, Lybeert ML, Jobsen JJ, Warlam-Rodenhuis CC, De Winter KA, Lutgens LC, van den Bergh AC, van de Steen-Banasik E, Beerman H, van Lent M. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet 2000; 355:1404–11.
13. Nelson G, Randall M, Sutton G, Moore D, Hurteau J, Look K. FIGO stage IIIC endometrial carcinoma with metastases confined to pelvic lymph nodes: analysis of treatment outcomes, prognostic variables, and failure patterns following adjuvant radiation therapy. Gynecol Oncol 1999;75: 211–4.
14. Onda T, Yoshikawa H, Mizutani K, Mishima M, Yokota H, Nagano H, Ozaki Y, Murakami A, Ueda K, Taketani Y. Treatment of node-positive endometrial cancer with complete node dissection, chemotherapy and radiation therapy. Br J Cancer 1997;75:1836–41.
15. Randall ME, Spirtos NM, Dvoretsky P. Whole abdominal radiotherapy versus combination chemotherapy with doxorubicin and cisplatin in advanced endometrial carcinoma (phase III): Gynecologic Oncology Group Study No. 122. J Natl Cancer Inst Monogr 1995;19:13–5.
16. Announcements: FIGO stages—1988 revision. Gynecol Oncol 1989;35: 125–6.
17. Scully RE, Bonfiglio TA, Kurman RJ, Silverberg SG, Wilkinson EJ. Histological typing of female genital tract tumours, 2nd ed. Berlin: Springer-Verlag, 1994:13–8.
18. Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am J Obstet Gynecol 2000;182:1506–19.
19. Inoue Y, Obata K, Abe K, Ohmura G, Doh K, Yoshioka T, Hoshiai H, Noda K. The prognostic significance of vascular invasion by endometrial carcinoma. Cancer 1996;78:1447–51.
20. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer 1987;60(Suppl):2035–41.
21. Hicks ML, Piver MS, Puretz JL, Hempling RE, Baker TR, McAuley M, Walsh DL. Survival in patients with paraaortic lymph node metastases from endometrial adenocarcinoma clinically limited to the uterus. Int J Radiat Oncol Biol Phys 1993;26:607–11.
22. Chuang L, Burke TW, Tornos C, Marino BD, Mitchell MF, Tortolero-Luna G, Levenback C, Morris M, Gershenson DM. Staging laparotomy for endometrial carcinoma: assessment of retroperitoneal lymph nodes. Gynecol Oncol 1995;58:189–93.
23. Giradi F, Petru E, Heydarfadai M, Haas J, Winter R. Pelvic lymphadenectomy in the surgical treatment of endometrial cancer. Gynecol Oncol 1993;49:177–80.
24. Galper S, Recht A, Silver B, Bernardo MV, Gelman R, Wong J, Schnitt SJ, Connolly JL, Harris JR. Is radiation alone adequate treatment to the axilla for patients with limited axillary surgery? Implications for treatment after a positive sentinel node biopsy. Int J Radiat Oncol Biol Phys 2000;48:125–32.
25. Schorge JO, Molpus KL, Goodman A, Nikrui N, Fuller AF Jr. The effect of postsurgical therapy on stage III endometrial carcinoma. Gynecol Oncol 1996;63:34–9.
26. Rose PG, Cha SD, Tak WK, Fitzgerald T, Reale F, Hunter RE. Radiation therapy for surgically proven para-aortic node metastasis in endometrial carcinoma. Int J Radiat Oncol Biol Phys 1992;24:229–33.
27. Mohan DS, Samuels MA, Selim MA, Shalodi AD, Ellis RJ, Samuels JR, Yun HJ. Long-term outcomes of therapeutic pelvic lymphadenectomy for stage I endometrial adenocarcinoma. Gynecol Oncol 1998;70:165–71.
28. Trimble EL, Kosary C, Park RC. Lymph node sampling and survival in endometrial cancer. Gynecol Oncol 1998;71:340–3.
29. Belinson JL, Lee KR, Badger GJ, Pretorius RG, Jarrell MA. Clinical stage I adenocarcinoma of the endometrium—analysis of recurrences and the potential benefit of staging lymphadenectomy. Gynecol Oncol 1992;44: 17–23.
30. Faught W, Krepart GV, Lotocki R, Heywood M. Should selective paraaortic lymphadenectomy be part of surgical staging for endometrial cancer? Gynecol Oncol 1994;55:51–5.
31. Kim YB, Niloff JM. Endometrial carcinoma: analysis of recurrence in patients treated with a strategy minimizing lymph node sampling and radiation therapy. Obstet Gynecol 1993;82:175–80.
32. Faught W, Fung MFK, Krepart GV, Lotocki RJ, Heywood MS, Genest P. Microscopic surgical stage IIIc endometrioid adenocarcinoma of the endometrium: implications for bimodal adjuvant therapy. Int J Gynecol Cancer 1998;8:41–5.