Role of pelvic lymphadenectomy in the management of Stage I endometrial cancer: our experience

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Summary

Objectives: To estimate the prognostic value of pelvic-node removal on survival of patients affected by endometrial carcinoma at presurgical FIGO Stage I.

Methods: A retrospective analysis was performed on a total of 111 patients recruited from 1990 to 1996 at the S. Carlo di Nancy Hospital. Thirty-nine (35%) of them underwent a total hysterectomy and bilateral salpingo-oophorectomy with removal of the vaginal cuff (group 1), while 72 (65%) underwent a total hysterectomy combined with pelvic lymphadenectomy (group 2). Prognostic features including tumor grade, depth of myometrial invasion and histologic subtype. Survival rates were calculated with Cox and Kaplan analyses.

Results: Overall survival rate at five years was 91.2%. The survival rate of group 1 and group 2 was 89% and 92.8%, respectively which is not statistically significant. Stage, grade, histotype, age at diagnosis, and presence of positive lymph nodes did not show any significant prognostic value on survival probability.

Conclusions: The survival rate for patients submitted to lymphadenectomy (group 2) was the same of patients who did not undergo this treatment (group 1). Nevertheless, pelvic lymphadenectomy in endometrial carcinoma at presurgical FIGO stage I was worthwhile as it allowed correct staging to be performed. The prediction of nodal disease based only on preoperative investigations (such as TC, NMR) is often inaccurate.

Key words: Endometrial cancer; Lymphadenectomy; Staging; Total abdominal hysterectomy.

Introduction

Endometrial carcinoma is the most common female pelvic malignancy. At the present the incidence is about 150,000 new cases a year all over the world; 37,000 new cases in the USA, and 5,000 new cases in Italy.

It is a typical peri- and postmenopausal tumor and in 75% of all cases at the time of diagnosis the tumor is confined to the uterine corpus (Stage I).

The five-year survival rate is 75% or higher.

Some pathologic factors are associated with an increased risk of recurrence: tumor grade, histologic subtype, depth of myometrial invasion and nodal status.

Positive pelvic lymph nodes occur in about 10% of patients with at presurgical FIGO Stage I endometrial carcinoma.

Morrow *et al.* [1] showed a good prognosis for patients with positive pelvic nodes in the absence of other risk factors while DiSaia *et al.* [2] showed a higher death rate in patients with positive nodes.

The primary treatment of presurgical FIGO Stage I endometrial carcinoma is surgery but the role of pelvic node removal is still debated.

Some authors [3] have hypothesized a therapeutic benefit of lymphadenectomy because occult metastatic emboli can be removed.

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The purpose of this study was to analyze retrospectively the efficacy of pelvic and lumboaortic lymphadenectomy in improving lifetime expectancy.

Patients and methods

A total of 111 patients affected by adenocarcinoma of the endometrium in presurgical FIGO Stage I were recruited from 1990 and 1996.

The median age of the study group was 66 years (range 40-92). Preoperative evaluation, according to FIGO 1971 criteria, was performed by transvaginal sonography, CO2 hysteroscopy with endometrial guided biopsies, magnetic resonance or CT.

Some patients were submitted to a cystoscopy and a rectosigmoidoscopy.

All patients (111) underwent to a total extrafascial hysterectomy (type 1 according to Piver *et al.*, 1974) [4] with bilateral salpingo-oophorectomy with or without pelvic lymphadenectomy.

The mode of surgery and use of lymphadenectomy depended on the personal preference and risk-factor evaluation of the surgeon.

Thirty-nine (35%) patients underwent a total hysterectomy and bilateral salpingo-oophorectomy with removal of the vaginal cuff (group 1), while 72 (65%) underwent a total hysterectomy combined with pelvic lymphadenectomy (group 2).

At the beginning of the procedure, inspection of the omentum and abdominal viscera as well as peritoneal cytology (washing) were always performed. Patients were submitted to postsurgical staging using the FIGO classification and classified into two different groups considering the main prognostic factors such as tumor grade, depth of myometrial invasion, histologic subtype and nodal status.

The Kaplan method and Cox regression analysis were applied to determine survival curves and rate (p-value < 0.05).

All patients have been followed for five years since the surgical treatment.

Results

No statistical differences were found in the distribution of risk factors and prognostic features distributions in the two groups.

No patients presented with suspected lymph-node metastases at preoperative imaging and no patients had preoperative irradiation. Diabetes and metabolic disorders were found in 22 patients.

From the histological analysis performed on the surgical specimens to determine depth of myometrial invasion, nine cases of M0 (9.9%), 76 cases of M1 (61.4%), seven cases of M2 (7.7%), 17 cases of M3 (18.8%) and two cases of M4 (2.2%) were found.

Ninety-three patients (80.1%) had a common endometrioid adenocarcinoma, ten patients (11.1%) had the papillary serous variety and eight patients had (8.8%) endometrioid carcinoma.

Grade 1 tumor accounted for 37 cases (34%), grade 2 for 52 cases (50.8%), grade 3 for 20 cases (13%) and Gx for two cases (2.2%). In eight patients positive washings were found.

According to the literature, positive nodes have beenfound in 4-10% of endometrial carcinoma Stage I: 3% for G1, 9% for G2 and 18% for G3.

We found positive nodes in two cases of G3 (2.2%) of our 111 endometrial carcinoma Stage I and the crude survival rate for patients submitted to pelvic lymphadenectomy was not statistically different between patients who were not submitted to this practice (89% for group I and 92.8% for group II) (p value = 0.3777).

Stepwise Cox regression did not show any significant value in predicting survival of the covariates (staging, grading, age at diagnosis, histotype, positive nodes) used to adjust survival.

Discusion

The removal of regional lymph nodes is one of the most important rules in the surgical management of many cancers.

As regards the importance of pelvic lymphadenectomy in endometrial cancer at presurgical Stage I, many controlled clinical studies are in progress [5], with the purpose of evaluating if this technique could be effective in improving survival and relapse-free survival.

In our study the rate of lymph-node metastatses was 2.2%.

Pelvic lymph nodes involved in endometrial carcinoma metastases are generally the external iliac chain, the internal iliac chain and the obturator chain [6, 7].

In our study the median number of nodes sampled was 29 (range 11-67).

The extent of lymph-node dissection was always adequate and the incidence of nodal metastases was not underdiagnosed.

The role of adjuvant radiotherapy in patients with presurgical Stage I endometrial carcinoma is still controversial. Recently, several authors reported comparable survival rates in patients treated with lymphadenctomy alone [8, 9] while other studies failed to prove the value of adjuvant radiotherapy on survival and protection from recurrences [10, 11].

The low incidence of nodal metastases in our study, as well as in other studies, means that, in the absence of a clearly proven survival benefit, the physical and economical costs of adjuvant radiotherapy must be well weighed. The therapeutic role of lymphadenectomy is still unclear.

Two important studies [6, 12] found a survival advantage associated with this practice as unrecognized microscopic metastases could be present in some nodal samples.

In contrast other studies [13, 14] showed no significant difference between patients who underwent lymph-node sampling and those who did not.

Among these we also add our experience.

Conclusions

It is concluded that pelvic lymphadenectomy is a very useful procedure for prognostic and staging purposes but does not improve survival.

The therapeutic effect reported by some authors [6, 11] could be in large part due to the importance of accurate surgical staging.

Thus lymphadenectomy permits us to define the need for adjuvant radiotherapy and to correctly estimate prognosis. We therefore consider pelvic lymphadenectomy a worthwhile diagnostic procedure because it provides definitive surgical staging. The prediction of nodal disease based only on preoperative and intraoperative investigations is often inaccurate and always insufficient.

In the future, major prospective randomized multicentric studies will give us conclusive data regarding the therapeutic value of lymphadenectomy.

We would like to emphasize that in our Division between 1990 and 1996, 111 of 143 (78%) cases of endometrial carcinoma in Stage I were found, which was possible due to to the extensive and excellent use of hysteroscopy, a very important technique for the early diagnosis of endometrial carcinoma.

References

[1] Morrow C. P., Bundy B. N., Kurman R. J. et al.: "Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study". Gynecol. Oncol., 1991, 40 (1), 55.

- [2] Di Saia P. J., Creasman W. T., Boronow R. C., Blessing J. A.: "Risk factors and recurrence patterns in stage I endometrial cancer". *Am. J. Obstet. Gynecol.*, 1985, *151*, 1009.
- [3] Homesley H. D., Kadar N., Barrett R. J. *et al.*: "Selective pelvic and periaortic lymphadenectomy does not increase morbidity in surgical staging of endometrial carcinoma". *Am. J. Obstet. Gynecol.*, 1992, *167* (5), 1225.
- [4] Piver M., Rutledge F., Smith J.: "Five classes of extended hysterectomy for women with cervical cancer". Obstet. Gynaecol., 1974, 44, 265.
- [5] The LINCE study group (Italy): "Feasibility and complications of systematic lymphadenectomy in endometrial cancer. Preliminary results of a prospective randomized multicentric clinical trial". *Int.* J. Gynecol. Cancer, 1999, 9, (suppl. 1), 4.
- [6] Kilgore L. C., Partridge E. E., Alvarez R. D. et al.: "Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling". Gynecol. Oncol., 1995, 56, 29.
- [7] Orr J. W.: "Surgical staging of endometrial cancer: does the patient benefit?". *Gynecol. Oncol.*, (editorial), 1998, 71, 335.
- [8] Mohan D. S., Samuels M. A., Selim M. A. et al.: "Long-term outcomes of therapeutic pelvic lymphadenectomy for stage I endometrial carcinoma". Gynecol. Oncol., 1998, 70, 165.
- [9] Orr J. W., Holimon J. L., Orr P. F.: "Stage I corpus cancer: is teletherapy necessary?". Am. J. Obstet. Gynecol., 1997, 176, 777.

- [10] Partridge E. E.: "Endometrial cancer, changing concepts in therapy". Surg. Clin. North Am., 1991, 71, 991.
- [11] Wolfson A. H., Slightier S. E., Markoe A. M. *et al.*: "The prognostic significance of surgical staging for carcinoma of the endometriu". *Gynecol. Oncol.*, 1992, 45, 142.
- [12] COSA-NZ-UK: "Endometrial Cancer Study Groups: Pelvic lymphadenectomy in high risk endometrial cancer". *Int. J. Gynecol. Cancer*, 1996, 6, 102.
- [13] Bar-Am A., Ron I. G., Kupermink M. et al.: "The role of routine pelvic lymphnode sampling in patients with stage I endometrial carcinoma: second thoughts". Acta Obstet. Gynecol. Scand., 1998, 77, 347.
- [14] Trimble E. L., Kosary C., Park R. C.: "Lymph node sampling and survival in endometrial cancer". *Gynecol. Oncol.*, 1998, 71, 340.

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