Endometrial cancer: factors affecting survival

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Summary

Purpose: To evaluate the influence in survival of clinical and pathological findings in patients with endometrial cancer.

Methods: In 152 women treated for endometrial cancer from 1982 to 1996, personal, obstetrical and oncological data, histology, grade, myometrial invasion, peritoneal cytology, FIGO stage and treatment were correlated with survival.

Results: Mean age was of 60.3 ± 11.1 years old. Eight patients had a previous history of other neoplasms (seven of them gynecological). The mean clinical complaint was abnormal uterine bleeding. The most common histological type was endometrioid (84.9%), only 51 cases did not show myometrial invasion and 119 women were in Stage I at diagnosis. Peritoneal cytology was negative in 113 patients. Seven patients out of 85 in whom lymphadenectomy was performed showed metastasis. Seventeen of the patients died. The factors influencing survival were age, myometrial invasion and lymph node metastasis.

Conclusion: Lack of myometrial invasion, absence of lymph node metastasis and age younger than 60 years seem to be the most significant predicting factors of survival.

Kew words: Endometrial cancer; Survival.

Introduction

Endometrial cancer is the most frequent gynecological cancer [1-3]. Its incidence in developed countries varies from 45.8 cases per 100,000 women in the USA to 1.7 in Japan. Data from 1985 show an incidence rate among European countries that varies from 11.8 per 100,000 women in Romania to 36.5/100,000 in Hungary [4]. In Spain, data from different registries show an adjusted incidence rate between 10.3 and 20.2 per 100,000 [5]. In the majority of women with this disease, the cancer will be confined to the uterus with excellent survival. Five-year disease-free survival rates for women with Stage I endometrial cancer is nearly of 95%. Nevertheless, up to 25% of women with endometrial cancer will be diagnosed with advanced stage disease (Stages III and IV). These women account for 54% of the deaths due to endometrial cancer.

The objective of this paper was to analyze the cases of endometrial cancer seen at the Obstetrics and Gynecological Department of the *Institut Universitari Dexeus* and to compare outcoming factors between surviving and deceased patients.

Material and Methods

From 1982 to 1996, 152 women were treated in our Department for endometrial cancer. Total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic and paraaortic lymphadenectomy was the most commonly performed procedure. The decision to add additional treatment to surgery depended on the features of the tumor and the spread location. The cases were resolved in a multidisciplinary committee. When one or more possibilities were formulated, options were presented to the patient and the choice was made after patient-physician discussion.

Personal, obstetrical and oncological data, histology, grade, myometrial invasion, peritoneal cytology, FIGO stage, treat-

ment, mortality and survival were analyzed retrospectively. Patients were also compared by vital status.

SPSS 11.0 for Windows® (SPS Inc, Chicago, IL) was used for statistical analysis. Chi-square was used to analyze qualitative variables and the Student's t-test for quantitative variables. Survival was analyzed through the life table method.

Results

Among the 152 studied patients, 23 (15.1%) had been diagnosed in another center with both groups being comparable.

The mean age of the patients was 60.3 years (± 11.1) and the median 60 years. The mean follow-up was 118 months, ranging from four to 237 months. One fourth of the patients were nulliparous and 3.3% had a history of infertility. Eight patients (5.3%) had a history of another tumor (5 breast carcinomas, 2 cervical carcinomas, 1 melanoma), and 40 (26.6%) a first-degree relative with endometrial cancer (Table 1).

The main reason for consultation was abnormal uterine bleeding (n = 100, 65.8%), followed by regular gynecological exam (n = 23, 15.1%), second opinion (n = 23, 15.1%), abdominal pain (n = 4, 2.6%), sterility (n = 1, 0.7%), and others (n = 1, 0.7%).

Histologically, most tumors (84.9%) were endometrioid adenocarcinoma. The most frequent histological grade was grade 2 (49.3%) while 44.7% had myometrial invasion less than a half. In 74.3% of the patients preoperative cytology was negative (Table 2).

One hundred and fifty-one patients underwent surgery and one patient received hormone therapy and intravaginal radiotherapy. In 85 (55.9%) cases pelvic lymph nodes were sampled and in 20 of those paraortic nodes were also sampled. Lymph nodes were positive in seven cases (5 positive pelvic/negative paraortic and 2 positive pelvic and paraortic). Seventy-eight percent of the cases were in Stage I, 9.2% in Stage II and 12.5% in Stage III. None of our patients was in Stage IV.

Table 1. — *Personal and family history.*

Mean age at diagnosis (range)	60.3 ± 11.1 years (29-84)
Mean age at menarche (range)	12.7 ± 1.6 years (8-18)
Mean age at menopause (range)	49.7 ± 4.9 years (35-62)
Mean follow-up (range)	117.8 ± 64.1 months (4-237)
Nulliparous	38 (25.0%)
History of sterility	5 (3.3%)
History of other primary tumors	8 (5.3%)
Endometrial cancer in a 1st degree relative	40 (26.3%)

Table 2. — *FIGO stage and histological type.*

	N	%
Stage		
Ia	46	30.3
Ib	55	36.2
Ic	18	11.8
IIa	8	5.3
IIb	6	3.9
IIIa	15	9.9
IIIb	–	–
IIIc	4	2.6
Histology		
Endometroidoid adenocarcinoma	129	84.9
Papillary serous carcinoma	12	7.9
Adenosquamous carcinoma	6	3.9
Mucinous adenocarcinoma	4	2.6
Clear cell carcinoma	1	0.7
Grade		
1	55	36.2
2	75	49.3
3	19	12.5
Not available	3	2.0
Myometrial invasion		
Absent	51	33.6
A half or less	68	44.7
More than a half	32	21.1
Peritoneal cytology		
Negative	113	74.3
Positive	20	13.2
Not available	19	12.5

Table 3. — *Comparison by vital status.*

	n = 135 Alive	n = 17 Deceased	p
Mean age at diagnosis	59.4 ± 11.0	66.9 ± 9.4	< 0.01
Mean follow-up in months	120.5 ± 62.1	95.8 ± 77.2	N.S.
Mean age at menarche	12.7 ± 1.6	12.7 ± 1.6	N.S.
Mean age at menopause	49.8 ± 4.8	49.1 ± 5.8	N.S.
Nulliparous	24.4%	29.4%	N.S.
History of sterility	3.7%	–	
History of other primary tumors	4.4%	11.8%	N.S.
Endometrial cancer in a 1st degree relative	27.4%	17.6%	N.S.
Stage I	79.3%	70.6%	N.S.
Stage II	9.6%	5.9%	
Stage III	11.1%	23.5%	
Grade			
1	40.2%	11.8%	N.S.
2	47.7%	70.6%	
3	12.1%	17.6%	
Myometrial invasion			
Absent	36.6%	11.8%	< 0.05
A half or less	44.8%	47.1%	
More than a half	18.7%	41.2%	
Peritoneal cytology			
Negative	84.5%	88.2%	N.S.
Positive	15.5%	11.8%	
Treatment			
Hysterectomy + BSO alone	43.3%	11.8%	< 0.05
Hysterectomy + BSO + radiotherapy	46.3%	70.6%	N.S.
Hysterectomy + BSO + chemotherapy	2.2%	11.8%	N.S.
Hysterectomy + BSO + hormone therapy	28.4%	64.7%	< 0.01
Histologically positive lymph nodes	4.1%	30.8%	< 0.01

BSO = Bilateral salpingo-oophorectomy; N.S. = Not significant.

Seventy-four (49%) of 151 operated patients also received radiotherapy, five (3.3%) chemotherapy, and 49 (32.5%) hormone therapy as coadjuvant treatment.

Seventeen patients (11.2%) died. Twelve of the patients who died were in Stage I. Of those, four (33.3%) died in the first five years of follow-up, one (8.3%) at 96 months, and the rest (58.3%) after more than ten years of follow-up. The only patient in Stage II who died survived 96 months after diagnosis. The four patients in Stage III who died survived less than five years.

When comparing surviving patients with those who died, the latter were significantly older and more likely to have myometrial invasion or histologically positive lymph nodes. Although the patients who died were more likely to have a history of another primary tumor and less likely to have a first degree relative with endometrial cancer, the differences were not significant. Surviving patients were more likely to be in Stage I and to have histological grade 1, but the differences were not statistically significant (Table 3).

Overall, 5-year survival was 94.5%. By stage, it is worth noting that all patients in Stage II survived and with better survival than those patients in Stage I. Patients in Stage III have the worst survival. When analyzing survival by histological grade, grade 3 is worse than the other two. Taking into consideration myometrial invasion, survival is very similar when there is no invasion or it affects less than half of the myometrium, and worse when more than half of it is affected. Patients with negative preoperative cytology have a better survival than those with positive cytology. The same applies for patients with negative lymph nodes (Table 4).

Discussion

Five-year survival in our series is higher than is has been reported by FIGO [6] and also by other authors [7-12]. The same is true when survival is analyzed by stage [2, 10, 12, 13]. Some authors [14] indicate that although they represent a low percentage of all endometrial cancers, more than half of the mortality occurs in advanced stages (III and IV). The fact that only 12.5% of our patients were in Stage III and that we had no Stage IV cases could explain our good results. Surprisingly, 5-year survival for Stage II in our series is higher than for Stage I, in contrast with what has been described [2].

The mean age at diagnosis in our series (60.3 years) is also lower than it has been reported by FIGO (62.7 years)

Table 4. — *Survival.*

	12 months	24 months	36 months	48 months	60 months
Overall	98.7%	98.0%	96.6%	94.5%	94.5%
By stage					
Stage I	100%	100%	98.2%	96.4%	96.4%
Stage II	100%	100%	100%	100%	100%
Stage III	89.5%	84.2%	84.2%	78.2%	78.2%
By grade					
Grade 1	98.2%	98.2%	96.3%	96.3%	96.3%
Grade 2	100%	100%	98.6%	95.5%	95.5%
Grade 3	94.7%	89.5%	89.5%	83.7%	83.7%
By myometrial invasion					
Negative	100%	100%	100%	97.9%	97.9%
A half or less	100%	100%	98.5%	96.9%	96.9%
More than a half	93.6%	90.2%	86.7%	82.9%	82.9%
By cytology					
Negative	99.1%	98.2%	96.3%	94.4%	94.4%
Positive	95.0%	95.0%	95.0%	90.0%	90.0%
By lymph nodes					
Negative	98.7%	98.7%	96.1%	94.8%	94.8%
Positive	85.71%	71.4%	71.4%	57.1%	57.1%

[6] or by the Cancer Registration in our country (66.2 years) [3]. Our patients are also younger than what other authors [12] have described. The early age at diagnosis can also explain our good results. Our hospital serves middle- and upper-class patients who come yearly for their routine gynecological exam. This explains why 15% of our cases were diagnosed in a routine check-up and at a younger age.

A family history of endometrial cancer doubles the likelihood of being affected [15]. More that one fourth of our patients had such a history, a percentage that is higher that what other authors have described [16]. Although the difference is not significant, surviving women are less likely to have a history of other primary tumors and more likely to have a family history of endometrial cancer. Since family history is a well-known risk factor, they are more likely to be closely followed and to be diagnosed early. It is also possible that these patients are more sensitized to the potential problem and have regular check-ups more often.

When comparing vital status, the only three variables that are significantly related to bad results are age at diagnosis, myometrial invasion and histologically positive lymph nodes. It is well known that early diagnosis of cancer is a good prognostic factor, and involvement of lymph nodes and myometrial invasion imply a more important dissemination of the disease. However, Montella *et al.* [12], did not find a correlation between myometrial invasion and survival.

Nulliparity does not seem to have a prognostic effect. Hachisuga *et al.* [17] also found that nulliparity did not affect survival in young women (< 50 years of age) or in older women (≥ 50 years of age) with early stages (I and II).

The distribution according to the surgical stage is not statistically different between groups, but patients who do not survive are more likely to belong to Stage III. The same is true for histological grading: surviving patients are more likely to have a well differentiated histological grading.

Conclusions

The preponderance of early stage disease at presentation among endometrial carcinoma accounts for the good prognosis of these disease. Nevertheless, some of them alter the pattern of spread and have a high rate of relapse and an unfavorable outcome. Our results suggest the need to pay special attention to Stage I cases because they represent more than 70% of the deaths.

The lack of myometrial invasion and age younger than 60 years at diagnosis seem to be the two most significant factors predicting good survival. In contrast, node involvement implies a worse prognosis.

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