

POSTOPERATIVE RADIATION THERAPY AFTER VAGINAL SURGERY FOR ENDOMETRIAL CANCER

L. PIRTOLI (*), E. CIMINO (*),
G. L. TADDEI (**),
M. COLAFRANCESCHI (**), P. PACINI (***),
S. CIATTO (*), L. CIONINI (*)

(*) Institute of Radiology,
University of Florence (Italy)

(**) Institute of Pathologic Anatomy and His-
tology, University of Florence (Italy)

(***) Department of Radiotherapy, USL 10/D,
Florence (Italy)

SUMMARY

From 1958 to 1978, 88 consecutive patients affected by endometrial cancer were referred to the Radiology Institute of the University of Florence, for radiation therapy after vaginal hysterectomy and bilateral salpingo-oophorectomy. Five and ten-year actuarial survival rates are 71% and 62%.

In the evaluable patients, results are analysed according to: extension of the tumor, as assessed by pathological evaluation (60 pats.), histologic grade of differentiation (44 pats.), and neoplastic infiltration of miometrium (32 pats.). When the tumor is limited to the uterine body, a 5-year actuarial survival is achieved in 89% of the cases; when the cervix or the adnexa and other pelvic structures are involved, this percentage decreases to 62.5% and 37.5%. The prognosis is also affected by the histological grade of differentiation and the depth of miometrial infiltration.

The primary therapeutical approach in operable endometrial cancers usually includes total abdominal hysterectomy and bilateral salpingo-oophorectomy: the laparotomic incision allows a proper visualization of the pelvic organs and a thorough exploration of the iliac and paraortic nodes, that can be excised and subjected to pathologic examination.

Postoperative irradiation can be performed, if pathologic findings (highly undifferentiated tumor, deeply infiltrated miometrium, involvement of cervix, adnexa or other pelvic organs) shows a high risk of relapse. Radiotherapy has been widely proved to reduce the incidence of postoperative relapses (^{1, 2, 3, 4}).

Many patients affected by endometrial cancer are obese, hypertensive, diabetic and old: in these cases vaginal hysterectomy and adnexectomy can be an alternative surgical approach, that is reported to be better tolerated than abdominal surgery (^{5, 6}) and to allow a larger number of patients to be operated (⁵). However, vaginal surgery entails a major disadvantage: useful information on lymph nodes status can be obtained only by indirect means, such as lymphangiography or CT scan. Their diagnostic accuracy is by far lower than that of the laparotomic exploration. Therefore, postoperative irradiation seems advisable for most patients. Up to now, the literature has reported no data on the value of this procedure.

A considerable number of patients affected by endometrial cancer are referred to the Radiology Institute of the University of Florence for radiotherapy, after a vaginal hysterecto-adnexectomy. In this paper we carry out a retrospective analysis of the results achieved in this group of patients, with the aim of giving a contribution to the surgico-radiotherapeutical management of endometrial cancer.

Table 1. — Correspondence between clinical and pathological evaluation of tumor spread in 60 patients.

| Clinical stage | Pathological evaluation | | |
|----------------|-----------------------------------|------------------------------|---------------------------------------------------------|
| | Tumor limited to the uterine body | Tumor extended to the cervix | Tumor extended to the adnexa or other pelvic structures |
| I | 38 | 7 | 11 |
| II | | 1 | 1 |
| III | | | 2 |
| Total | 38 | 8 | 14 |

MATERIAL AND METHODS

88 patients with histologically proven endometrial carcinomas after vaginal hysterectomy and bilateral salpingo-oophorectomy, were consecutively referred to the Radiology Institute of the University of Florence, for radiation therapy, from July 1958 to July 1978.

Their age ranged from 36 to 79, with a maximum incidence (44.5%) in the sixth decade. Hypertension and obesity were present in about 50% of the patients, and diabetes in 15%.

Before surgery, all patients had been submitted to a diagnostic check-up, including general and gynecological evaluation, diagnostic curettage, chest X-ray and IVP; in many cases barium enema, cystoscopy and proctoscopy had also been performed. Clinically, 84 patients presented a tumor limited to the uterine body, 2 showed involvement of the cervix and other 2 of the adnexa. Therefore, according to the International Federation of Gynecology and Obstetrics (FIGO 1971) criteria, 84 patients were retrospectively classified as stage I, 2 as stage II and 2 as stage III.

A reliable pathologic description of the surgical specimen was available for 60 patients and assessed the local extension of the disease. The tumor was limited to the uterine body in 38 cases, extended to the cervix in 8 and to the adnexa or other pelvic structures in 14 cases; the correspondence between the clinical and pathological evaluations of the tumor diffusion is shown in tab. 1.

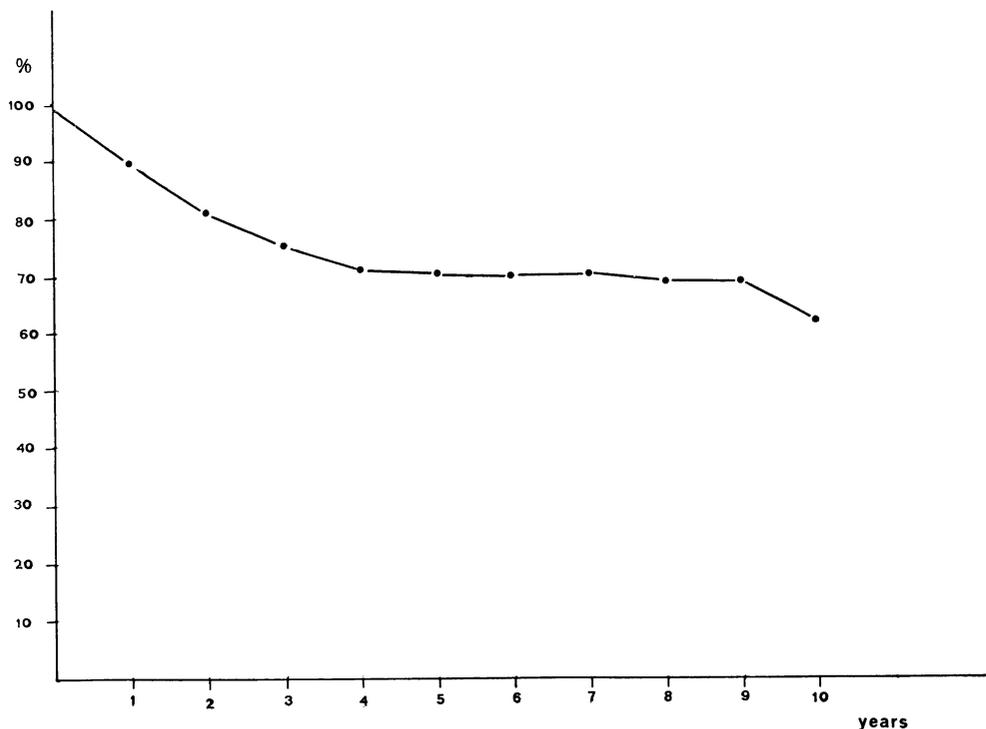


Fig. 1. — Actuarial survival of the overall patients.

Histological samples for a re-evaluation of the histologic degree of differentiation of carcinomas, according to the FIGO (1971) classification, were available in 44 patients; 15 of them showed a high degree of differentiation, 18 a moderate 11 a low degree. In 32 patients miometrial infiltration too was evaluable; it appeared that the tumor was limited to the endometrium in 12 patients, extended to the inner third of the

loaded applicator or a mould device for the after loading technique, with Cesium or Iridium.

The results were evaluated in terms of actuarial survival; the patients' conditions were assessed in December 1980. All patients who died were considered as "dead from the disease". Radiation negative side effects were observed in 54 patients, submitted to an accurate follow-up for at least two years.

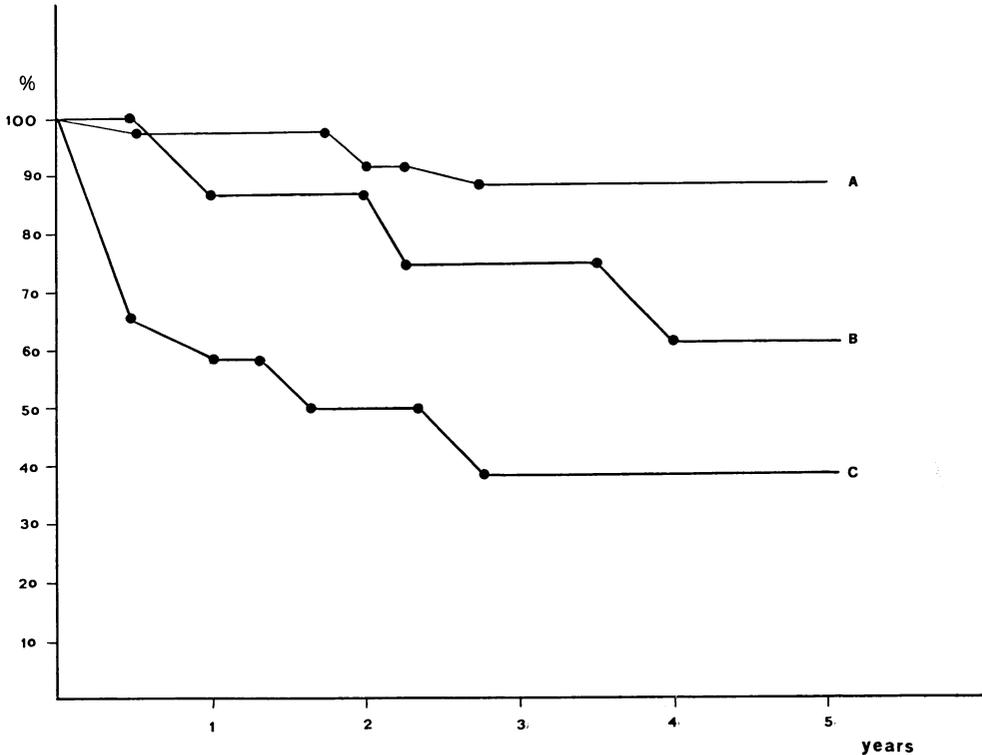


Fig. 2. — 5 years actuarial survival, analyzed according to the pathological evaluation of the extension of the disease: curve A: patients with a tumor limited to the uterine body (38 pats.); curve B: patients with a tumor extended to the cervix (8 pats.); curve C: patients with a tumor extended to the adnexa or other pelvic structures (14 pats.).

miometrium in 11, to the medium third in 10 and to the outer third in 9.

In all patients, irradiation was started within 1 month from surgery; telecobalt or 31 MV X-rays of a betatron were used. The irradiation concerned the whole of the pelvis and the vagina. It was performed through anterior and posterior opposite fields; the midplane absorbed dose was 40-50 Gy over 5 weeks; in 11 patients, as cervical involvement or deep miometrial infiltration had been demonstrated, a vaginal boost of 20 to 30 Gy was also given to the mucosal surface, using a radium

RESULTS

The actuarial survival curve of the 88 patients is shown in fig. 1 probability of surviving is 71% at 5 and 62% at 10 years.

The five-year actuarial survival data were worked out according to the extension of the disease, as evaluated by the pathologic examination of the surgical

samples, the degree of histological differentiation and the miometrial infiltration.

Extension of the disease

The actuarial survival percentages at 5 years are 89% for patients with a tumor limited to the uterine body, 62.5% when

Miometrial infiltration

A 76% five-year actuarial survival percentage is achieved when less than 2/3 of the miometrium are infiltrated. When infiltration extends to the outer third, this percentage decreases to 51% (fig. 4).

No heavy radiation damage was observed, except for one patient, subjected

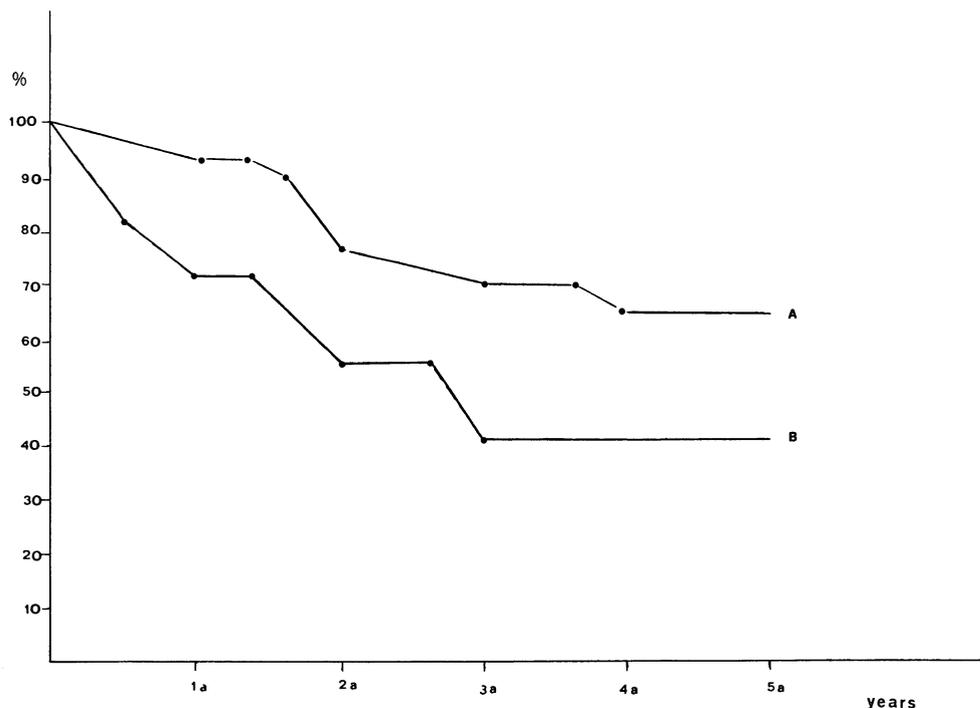


Fig. 3. — 5 years actuarial survival, analyzed according to histological grading: curve A: patients with a tumor with a high or medium grade of differentiation (33 pats.); curve B: patients with a tumor with a low grade of differentiation (11 pats.).

the cervix is involved and 37.5% in patients with adnexal or other pelvic diffusion (fig. 2).

Grade of histologic differentiation

The actuarial survival percentages at 5 years are 65% for patients with highly or moderately differentiated tumors and 41.5% for patients with tumors with a low grade of differentiation (fig. 3).

to external irradiation and vaginal boost, who developed an hemorrhagic proctitis, 4 months after the treatment.

DISCUSSION

Endometrial cancer is the most frequent gynecologic malignancy, and ranks third among female malignant tumors (7). Its therapeutical management is there-

fore of great interest; it has been demonstrated that the best outcome is achieved when the primary treatment includes surgery⁽⁸⁾.

Very good results in operable tumors with the therapeutical means available

gical risk; obesity, whose incidence is 50% or more^(9, 10), can technically interfere with abdominal operations. Vaginal hysterectomy and adnexectomy can be performed in these cases, improving the operability and reducing the risk^(5, 6).

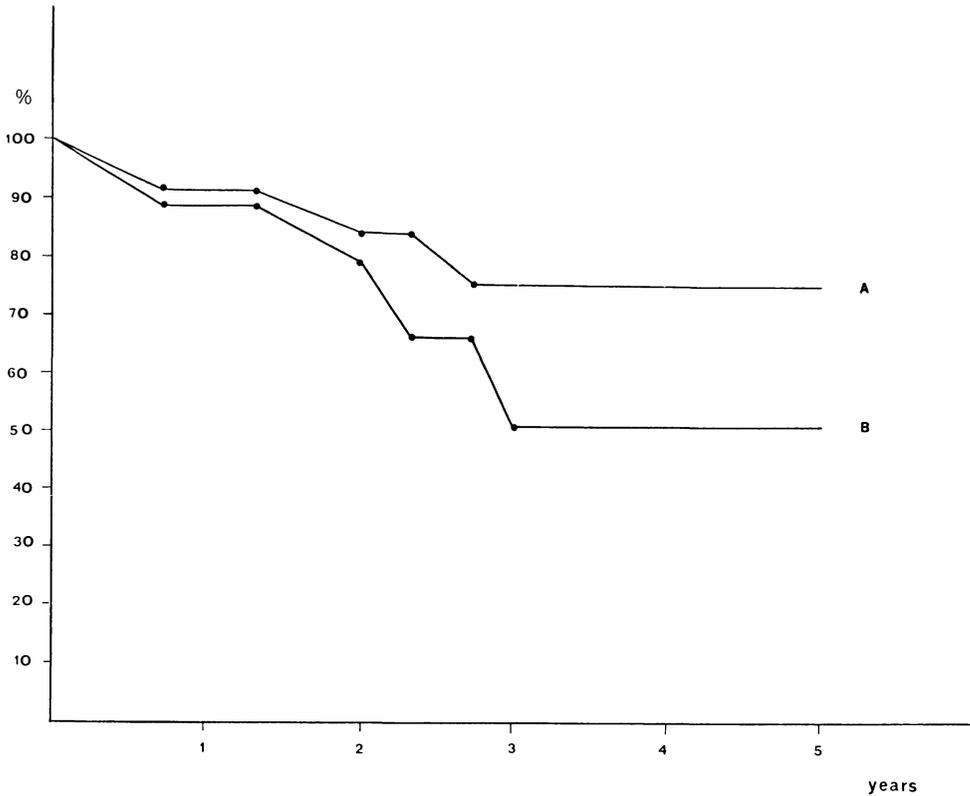


Fig. 4. — 5 years actuarial survivals, analyzed according to myometrial infiltration: curve A: patients with neoplastic infiltration limited to the inner two thirds of myometrium (23 pats.); curve B: patients with neoplastic infiltration extended to the outer two thirds of myometrium (9 pats.).

today, have been reported. It is therefore advisable to select treatments that are effective for the largest possible number of patients, with the lowest possible morbidity.

Late age, hypertension, diabetes, frequently associated with endometrial cancer, can imply an increased anesthesiolo-

The series reported in the literature present a 75-85% survival rate at 5 years, with this kind of surgery only^(5, 6, 11); these series are composed, to some extent, of selected patients. The abdominal surgical approach has in fact been adopted in 10 to 85% of the cases, according to the different reports, on account of fac-

tors like a greatly enlarged uterus, cervical involvement or pathologic features of high malignancy. Radiotherapy has never been systematically associated with vaginal surgery, even if the lack of direct information on the lymph nodes condition made it advisable for most of the patients, unless factors (low grade malignancy, growth limited to endometrium), that have been correlated with a low incidence of nodal metastases, are demonstrated⁽¹²⁾.

The results obtained in our series with the systematic use of radiotherapy after vaginal hysterectomy do not significantly differ from those reported in the literature. However, the pathologic examination of surgical samples, in our patients, revealed involvement of the cervix (13.5% of the evaluable patients), and the adnexa or other pelvic organs (23.5%) in a higher percentage than previously reported by other Authors (respectively 6.5% and 10% in the Frick's and Coll. series)⁽¹³⁾.

The analysis of the present results considering the extension of the disease, revealed that an 89% actuarial survival at 5 years is obtained in patients with a tumor limited to the uterine body. This result is comparable with the corresponding figures of the laparotomy series⁽¹⁴⁾; the results in cases of tumoral diffusion to the cervix (62.5%) and the adnexa or other pelvic structures (37.5%), favourably compare with others, previously published^(14, 15).

Prognostic factors, like the grade of tumor differentiation and myometrial infiltration, confirm, in these series, the importance that had been attached to them by several Authors^(3, 14, 16, 17, 18, 19).

This paper does not aim at advocating vaginal surgery and postoperative irradiation as the elective therapy for endometrial cancers. Therapeutical approaches, including laparotomy, are by far more suitable, from an oncologic point of view.

However, when patients present medical or surgical problems, liable to prevent an abdominal operation, the procedure here reported can be safely and effectively adopted.

REFERENCES

- 1) Graham J.: *The value of preoperative or postoperative treatment by radium for carcinoma of the uterine body*. Surg. Gyn. Obst., 132, 855, 1971.
- 2) Leibel S. A., Wharam M. D.: *Vaginal and paraortic lymph node metastases in carcinoma of the endometrium*. Int. J. Radiat. Oncol. Biol. Phys., 6, 893, 1980.
- 3) Morrow C. P., Di Saia P. J., Townsend D. E.: *Current management of endometrial carcinoma*. Obst. Gyn., 42, 399, 1973.
- 4) Piver M. S., Yazigi R., Blumenson L., Tsukuda Y.: *A prospective trial comparing hysterectomy, hysterectomy plus vaginal radium and uterine radium plus hysterectomy in stage I endometrial carcinoma*. Obst. Gyn., 54, 85, 1979.
- 5) Gasparri F., Buzzoni P., Locatelli F.: *La via vaginale nella terapia chirurgica del carcinoma del corpo dell'utero*. Atti 59° Congr. Soc. It. Ost. Gin., Parma, 1978, 573.
- 6) Pratt J. H., Symmonds R. E., Welch J. S.: *Vaginal hysterectomy for carcinoma of the fundus*. Am. J. Obst. Gyn., 88, 1063, 1964.
- 7) Morrow C. P., Di Saia P. J., Townsend D. E.: *The role of post-operative irradiation in the management of stage I adenocarcinoma of the endometrium*. Am. J. Roentgenol., 127, 325, 1976.
- 8) Joelsson I., Sandri A., Kottmeier H. L.: *Carcinoma of the uterine corpus. A retrospective survey of individualized therapy*. Acta Radiol., Suppl. 334, Stockholm, 1973.
- 9) McCabe J. B., Sagerman R. H.: *Treatment of endometrial cancer in a regional radiation therapy center. Analysis of 379 consecutive patients*. Cancer, 43, 1052, 1979.
- 10) Onsrud M., Kolstad P., Norman T.: *Post-operative external pelvic irradiation in carcinoma of corpus stage I: a controlled clinical trial*. Gyn. Oncol., 4, 222, 1976.
- 11) Van Bouwddijk Bastiaanse M. A.: *Cancer of the body of the uterus*. J. Obst. Gyn. Br. Emp., 59, 611, 1952.
- 12) Creasman W. T., Boronow R. C., Morrow C. P., Di Saia P. J., Blessing J.: *Adenocarcinoma of the endometrium: its metastatic lymph node potential. A preliminary report*. Gyn. Oncol., 4, 239, 1976.

- 13) Frick H. G., Munnel E. W., Richart R. M., Berger A. P., Lawry M. F.: *Carcinoma of the endometrium*. Am. J. Obst. Gyn., 115, 663, 1973.
- 14) Keller D., Kempson R. L., Levine G., McLennan C.: *Management of the patient with early endometrial carcinoma*. Cancer, 33, 1108, 1974.
- 15) Bruckman J. E., Goodman R. L., Murthy A., Marck A.: *Combined irradiation and surgery in the treatment of stage II carcinoma of the endometrium*. Cancer, 42, 1146, 1978.
- 16) Colafranceschi M., Taddei G. L.: *Aspetti istomorfolologici del carcinoma endometriale in riferimento alla prognosi*. Atti 59° Congr. Soc. It. Ost. Gin., Parma, 1978, 845.
- 17) Lewis G. C., Mortel R., Slack N. H.: *Endometrial cancer. Therapeutic decision and the staging process in "early disease"*. Cancer, 39, 959, 1971.
- 18) Ng A. B. P., Reagan J. W.: *Incidence and prognosis of endometrial carcinoma by histologic grade and extent*. Obst. Gyn., 35, 437, 1970.
- 19) Shah C. A., Green T. H. Jr.: *Evaluation of current management of endometrial carcinoma*. Obst. Gyn., 39, 500, 1972.