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Original research article

The effect of lymphadenectomy and radiotherapy on recurrence and survival in endometrial carcinoma. Experience in a population reference centre

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ABSTRACT

Aim: To evaluate the effect of lymphadenectomy and/or radiotherapy on recurrence and survival patterns in endometrial carcinoma (EC) in a radiotherapy reference centre population.
Material and Methods: A retrospective population-based review was conducted on 261 patients with stages I–III EC. Univariate and multivariate analyses were carried out. Both recurrence and survival were analysed according to patient age, FIGO stage, tumour size, myometrial invasion, tumour grade, lymphadenectomy, external beam irradiation (EBI), and brachytherapy (BT).
Results: Median age: 64.8 years. Median follow-up: 151 months. The following treatments were administered: surgery, 97.32%; lymph-node dissection, 54.4%; radiotherapy, 162 patients (62%) (EBI and BT: 64.1%, BT alone: 30.2%, EBI alone: 5.6%).

Twenty-six patients (9.96%) suffered loco-regional recurrence, whilst 27 (10.34%) suffered distant failure. The 5-year overall survival (OS) for all stages was 80.1%. The 5-year disease free survival (DFS) was 92.1% for all patients. The 10-year DFS was 89.9%.

The independent significant prognostic factors for a good outcome identified through the multivariate analysis were: age <75 years ($p = 0.001$); tumour size ≤2 cm ($p = 0.003$); myometrial invasion ≤50% ($p = 0.011$); lymphadenectomy ($p = 0.02$); EBI ($p = 0.001$); and BT ($p = 0.031$).

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Toxicity occurred in 114 of the 162 patients who received radiotherapy (70.5%). The toxicity was mainly acute, and late in only 28.3% ($n = 45$) of cases. The majority experienced G1-2 toxicity, and only 3% of patients experienced G3 late toxicity (5/162).

Conclusions: Our results suggest that age <75 years, tumour size ≤2 cm, myometrial invasion ≤50%, lymphadenectomy, EBI, and BT, are predictors of a good outcome in EC.

1. Background

Endometrial carcinoma (EC) is the third most common cancer diagnosed in women and the most common female genital tract malignancy. The incidence of EC in Catalonia (Spain) is 730 new cases per year. EC represents 6.1% of newly diagnosed cancers in women.[1,2]

Treatment of EC is mainly surgical and consists of a total abdominal hysterectomy and a bilateral salpingo-oophorectomy (TAH & BSO), with or without pelvic lymph node dissection, followed by postoperative radiotherapy (RT) in most cases. Surgical staging requires the expertise of a gynaecological oncologist in a tertiary care centre. The need for lymphadenectomy remains a point of controversy. Some studies have confirmed that lymphadenectomy can be both diagnostic and therapeutic, and that it allows for more adaptable postoperative RT; others have concluded that there is no evidence of any benefit in terms of overall survival (OS).[3–7] However, many studies have confirmed advantages to lymphadenectomy such as: reduced complexity[8]; increased accuracy of magnetic resonance imaging (MRI) in pre-operative staging[9]; and better prognostics.[10,11]

Prospective randomised studies have shown that RT reduces the risk of pelvic relapse but does not improve OS in patients with early EC.[12–14] The Postoperative Radiotherapy Endometrial Cancer (PORTEC-2) study demonstrated that patients with intermediate-risk EC can be safely treated with brachytherapy (BT) alone.[15]

The decision to offer adjuvant pelvic radiation depends on the type of surgery undertaken, as well as the primary tumour risk factors. In intermediate-risk groups, pelvic radiation may be offered if the patient exhibits adverse prognostic factors. The risk of metastatic pelvic nodes increases in high-risk groups, and therefore, pelvic RT is often offered.[16–21]

Despite the fact that postoperative external beam pelvic RT is offered to minimise the risk of recurrence in case of poor prognostic factors, severe late complications have been reported, occurring mainly in the small bowel, in 3–8% of cases treated with external beam pelvic RT.[14–22]

The Radiation Department at the Hospital Universitari de Sant Joan de Reus is the only referral RT centre in Tarragona Province and receives patients from 7 hospitals performing gynaecological cancer surgery.

2. Aim

The aim of this retrospective study was to determine the prognostic factors that contribute to patient outcomes, and to evaluate the roles and impact on survival of lymphadenectomy and/or RT in EC in this RT reference centre population.

3. Materials and methods

A retrospective population-based review was conducted on 261 patients with stages I–III EC (excluding sarcoma cases) that were treated in one Radiation Oncology Institution after referral from seven different gynaecology departments during the period 1997 to 2006.

Information regarding patients, disease, and treatment characteristics were retrospectively collected from the patient records. After surgery, the patients were staged according to the International Federation of Gynaecology and Obstetrics (FIGO-1992). The surgical procedure, pathologic characteristics of the tumour, RT, chemotherapy, and distance travelled by patients from their home to our centre were recorded.

The lymphadenectomy policies varied among the different centres, but in general it was offered to high risk of recurrence patients. Our institution's protocol during the treatment period (1997–2006) indicated an adjuvant postoperative external beam RT to the pelvis without lymphadenectomy for women with disease stage IB grade 2, stage IB grade 3, all grades of stage IC, and all higher stages. Postoperative adjuvant RT consisted of external beam pelvic radiation, vaginal BT, or both. The time between surgery and RT treatment did not exceed 4 weeks.

Clinical, surgical and pathological data were considered when planning 3D conformal radiotherapy planning treatment. The majority of patients were treated with 6 or 18 MV from a Linac ray (66% of patients), or a 60-cobalt machine (33% of patients) using the pelvic four-field technique. The total planned dose was 46–50 Gy at 180–200 cGy per fraction, 5 fractions/week. BT was administered using the Fletcher colpostats technique for low-dose rate (LDR) ^{137}Cs sources from a Selectron, or using a vaginal cylinder applicator in one or three treatments with a high-dose rate (HDR). After external beam irradiation (EBI), the usual BT plan involved 20 Gy for LDR treatments and 3 fractions of 4 Gy for HDR treatments. When only BT was performed, the dose was 60 Gy for LDR treatments and 3 fractions of 7 Gy for HDR treatments. All BT doses were prescribed for 5 mm inside the vaginal surface.

After the completion of the RT, a radiation oncologist routinely monitored women every 3–4 months for 2 years, and every 6 months thereafter.