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# Evaluation of prognostic factors and treatment outcomes in uterine carcinosarcoma

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ABSTRACT

*Objective:* The aims of this study were to determine the prognostic factors, survival outcomes and response to adjuvant therapy in women with uterine carcinosarcoma treated in a single institution.
*Study design:* This is a cohort study of women diagnosed with carcinosarcoma and treated at the Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead, UK. The medical records of all patients diagnosed with carcinosarcoma between January 1960 and July 2002 were reviewed.
*Results:* A total of 93 women were identified during this period. The median age was 67 years. The most common presentation was abnormal vaginal bleeding, occurring in 85%, followed by pelvic mass in 45%, and abdominal pain in 38%. At surgery there was extra-uterine spread in 54% of women. The median follow-up was 33 months (range 4–146 months). Adjuvant therapy was not associated with survival advantage. Recurrence was diagnosed in 55 patients (59%) and the overall 5-year survival for all stages was 33%. On multivariate analysis depth of myometrial invasion, stage and pelvic nodes metastasis were associated with poor survival.
*Conclusion:* The poor outcome for these patients may reflect the aggressive nature of carcinosarcoma and that at the time of presentation more than 50% have extra-uterine disease, which was associated with significant poorer survival. Systemic adjuvant therapy has not been associated with significant improvement in the outcome. More studies are needed to better define the appropriate treatment for this rare cancer.



## 1. Introduction

Carcinosarcomas of the uterus are rare tumours accounting for less than 5% of all uterine malignancies [1,2]. They are characterized by the presence of both epithelial and stromal malignant components. Most patients with carcinosarcomas are postmenopausal at diagnosis, the median age at presentation being 66 years [3,4].

Because they are rare, experience at any single institution is usually limited. Reports on the prognostic factors and treatment outcomes of these tumours are based on small numbers of patients in most studies [5,6]. However, most studies agree on the poor prognosis of uterine carcinosarcomas in comparison to uterine adenocarcinomas [7–9]. Approximately, 35% of carcinosarcomas are not confined to the uterus at diagnosis, and in most reports the median overall survival was about 21 months [10]. There has been no improvement in survival suggested by recent reports [11–14]. The most important prognostic factor is the extent of the tumour at the time of diagnosis, the prognosis being very poor when the tumour has extended beyond the uterus [14]. Many patients with disease clinically confined to the uterus are found to have extra-uterine disease after surgical and pathological evaluation [12]. As with uterine adenocarcinomas, the mainstay of treatment is surgical removal of the tumour [15].

The high rates of both local and distant relapse after surgery suggest a need for effective adjuvant therapies; however, adjuvant chemotherapy or radiotherapy have yet to be shown to be of benefit. In part this is because carcinosarcomas tend to have low sensitivity to radiotherapy and chemotherapy. Retrospective studies and a few phase II studies have reported on the outcome of patients with carcinosarcoma treated with either adjuvant chemo or radiotherapy, but they have not shown clear benefit in terms of improvement in the survival rates [5,13,16–21].

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The aims of this study were to determine the prognostic factors, survival outcomes and response to adjuvant therapy in women with carcinosarcomas treated in a single institution.

## 2. Materials and methods

This is a retrospective cohort study of patients diagnosed with uterine carcinosarcoma and treated at the Northern Gynaecological Oncology Centre in Gateshead, UK. Information of all cases of uterine cancer diagnosed among women resident in the North East & Cumbria region were obtained from the Northern & Yorkshire Cancer Registry & Information Service (NYCRIS) cancer registry and the Northern Cancer Network (NCN) databases.

The medical records of all patients diagnosed with carcinosarcoma and referred to the regional service in Gateshead between January 1960 and July 2002 were reviewed. A total of 93 women were identified during this period. The diagnosis was based on the original histology reviewed and verified by specialist gynaecological pathologists in Gateshead. Immunohistochemistry was performed where appropriate and clinical data were obtained from medical records. Clinical and surgical data included age at the time of diagnosis, menopausal status, and type of surgery performed, residual disease, sites of tumour metastasis, adjuvant therapy if any, recurrence and survival. Pathology data included stage of tumour, evidence of myometrial invasion, depth of myometrial invasion, lymphovascular space invasion, the presence of heterologous elements in the sarcomatous component, and grade of tumour. Patients were staged according to the 1988 International Federation of Gynecology and Obstetrics (FIGO) staging system for endometrial cancer [22]. Staging was based on information obtained from clinical notes, surgical notes and pathology reports. Routine CT scan was not performed, but, in cases where there was extra-uterine spread evident at laparotomy imaging was performed.

Treatment protocols varied over the 42 years of the review with most of the patients having primary surgery. Primary surgery where performed was in the form of total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy plus debulking in cases where there was extra-uterine disease. Pelvic node dissection where performed was by systematic pelvic node dissection. Follow-up was to the last date seen in the outpatient clinics; data were obtained from the hospital case notes, death certificates and then cross checked with the National Health Service (NHS) strategic tracing service database.

### 2.1. Statistical analysis

Statistical analysis was performed using SPSS 11.0 for Windows. Chi Square and Fisher's exact test or Mann–Whitney *U*-test were used when appropriate to determine significance. All tests were two-tailed with a significance of 95% $p < 0.05$.

Observed survival rates were estimated by using the Kaplan–Meier method. The log-rank test was used to assess differences in survival. The survival of patients who underwent surgery was calculated as the difference between date of first surgical procedure and either the date of death or the date of last patient contact for patients who did not die during follow-up.

In multivariate analyses, a Cox proportional hazards model was used to assess the effects for prognostic variables. Factors assessed in survival analysis were, age, stage, menopausal status, depth of myometrial invasion, lymphovascular space invasion (LVSI), extra-uterine spread of tumour, pelvic node, omental and liver metastasis as well as type of adjuvant therapy given and chemotherapeutic regimen used.

## 3. Results

### 3.1. Clinical findings

93 cases of uterine carcinosarcoma were identified during the study period. The median age of our patients was 67 years, range (33–87 years). Ten (11%) women were premenopausal and 83 (89%) postmenopausal. The most common presentation was abnormal vaginal bleeding occurring in 79 of the women (85%), followed by pelvic mass in 42 women (45%), and abdominal pain in 35 women (38%). Unlike uterine carcinoma, the majority of which presents early, only 46% of patients with carcinosarcoma presented as stages I–II while 54% presented with stages III–IV. Pathological review showed that there was no myometrial invasion in 7 patients (8%), all had disease confined to the uterus. Less than 50% myometrial invasion was seen in 30 patients (32%), of these women 27 were in stages I–II and 3 were stage III disease. The tumour invaded more than 50% in 56 patients (60%). Lymphovascular space invasion was present in 46% of women, absent in 30%, and no information was available in 24%. There were 46% heterologous and 48% homologous elements in the sarcomatous component of the tumours. Pelvic node metastasis was detected in 13 out of the 34 women (38%) who had pelvic node dissection. Omental metastasis was detected in 9 out of 18 (50%) women who had omentectomy. Clinical and pathological characteristics are described in Table 1.

Initial surgery was performed in all women; surgery was in the form of hysterectomy and bilateral salpingo-oophorectomy (BSO), with some combination of omentectomy and pelvic lymph node

**Table 1**
Patient characteristics ($n = 93$).

| Variable | Patients | % |
|---|---|---|
| Age (years) | | |
| Median | 67 | |
| Range | 33–87 | |
| Menopausal status | | |
| No | 10 | 11 |
| Yes | 83 | 89 |
| Initial FIGO stage | | |
| I | 35 | 37 |
| II | 8 | 9 |
| III | 28 | 30 |
| IV | 22 | 24 |
| Tumour grade | | |
| G1 | 8 | 9 |
| G2 | 5 | 5 |
| G3 | 75 | 81 |
| Unknown | 5 | 5 |
| Myometrial invasion | | |
| No myometrial invasion | 7 | 7.5 |
| <50% | 30 | 32.3 |
| >50% | 56 | 60.3 |
| LVSI | | |
| Yes | 28 | 46 |
| No | 43 | 30 |
| Unknown | 22 | 24 |
| Heterologous component | 45 | 48 |
| Homologous component | 48 | 52 |
| Cytoreduction | | |
| Complete | 43 | 46 |
| Optimal | 21 | 23 |
| Sub-optimal | 29 | 31 |
| Nodal assessment | 34 | |
| Pelvic node metastases | 19 | 56 |
| Omental assessment | 18 | |
| Omental metastases | 9 | 50 |