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Original Paper

Uterine Sarcomas in Norway 1956-1992: Incidence, Survival and Mortality

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A total of 1042 patients diagnosed with uterine sarcoma were reported to The Cancer Registry of Norway from 1956 to 1992. In the present study long-term trends in incidence, survival and mortality were analysed. To evaluate the effect of the introduction of chemotherapy in the treatment of this disease, special attention was paid to the time periods 1971–1975 and 1983–1987. The reporting system is based on pathology reports, clinical records and death certificates. Histological type, diagnostic period, clinical stage and age were included in the study. The analysis of survival was based on 5-year relative survival. Both the incidence and mortality rate of uterine sarcomas in Norway doubled in the time period 1956–1992, mainly due to an increase of carcinosarcomas. The overall annual incidence rate in 1987–1992 was 1.7 per 100 000 females in the population per year, accounting for 9.7% of all uterine corpus malignancies. In 1990–1992, 26% of the mortality due to uterine corpus malignancies was caused by sarcoma. No change in 5-year survival was seen after the introduction of chemotherapy in the treatment of the disease ($P = 0.35$). Stage ($P < 0.001$) and age ($P < 0.001$) were both important prognostic factors. Patients with an endometrial stromal sarcoma ($P < 0.001$) had a more favourable prognosis than those with other histological types. © **1997 Elsevier Science Ltd.**

Key words: uterine sarcomas, incidence, survival, mortality

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INTRODUCTION

POPULATION-BASED ESTIMATES on the incidence of uterine sarcomas vary between 1.55 and 1.95 per 100 000 females per year [1–3]. The frequency has usually been given as either the relative rate of all malignancies of the uterine corpus, all uterine malignancies or all malignant tumours of the female genital tract. It has been estimated that 3–5% of all cancers of the uterine corpus are sarcomas [4–6].

Although little is known about the mortality rate of the uterine sarcomas, the poor prognosis is well established from several clinical series [7–14]. Reports on the prognostic importance of the histopathological type are contradictory [15–18]. The predictive value of the stage and mitotic indices is still under discussion [13, 16, 19, 20]. The better outcome of premenopausal women with uterine leiomyosarcoma is also known from several studies [13, 19, 21].

Radiotherapy was formerly used both pre- and postoperatively. Now, we know that the radiosensitivity of sarcomas is low. Since the late 1970s, a variety of different drugs have been reported as active, measuring an objective response [22–24]. In the mid-1980s, doxorubicin-based regimes were recommended in Norway as adjuvant, regardless of the extension of the initial surgery.

The aim of the present study was to examine long-term trends in incidence, relative survival and mortality rates in women with uterine sarcomas diagnosed in Norway over the 37-year period 1950–1992. Special attention was paid to the periods 1971–1975 and 1983–1987. In the second period chemotherapy was widely recommended. In addition, the prognostic importance of histopathological type, clinical stage and age was evaluated.

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Table 1. Number of patients with uterine sarcomas by histological type in Norway, 1956–1992

Period	LMS	ESS	CS	NOS	Others	Total
1959–1960	59			10	1	70
1961–1965	62			24	10	96
1966–1970	65	7	8	39	5	124
1971–1975	58	18	42	12	7	137
1976–1980	65	30	53	10	5	163
1981–1985	67	17	62	8	3	157
1986–1990	75	39	69	5	2	190
1991–1992	25	13	50	4	13	105
Total	476 (46%)	124 (12%)	284* (27%)	112 (11%)	46†(4%)	1042

*119 heterologous and 165 homologous tumours. †33 sarcoma botryoides, 11 rhabdomysarcoma and 2 angiosarcoma.
LMS, leiomyosarcoma; ESS, endometrial stromal sarcoma; CS, carcinosarcoma; NOS, not otherwise specified.

MATERIALS AND METHODS

Since 1953 the Norwegian Cancer Registry has received information about all cancer patients in the population. The reporting system is based on pathology reports, clinical records and death certificates. Site, histological type, stage of disease at the time of diagnosis, residence and the 11-digit National identity number allocated to every Norwegian resident are reported. This multiple reporting practice provides an accurate and complete set of data for each patient. Registration is based on a modified version of ICD-7. Classification of the tumour is in accordance with the World Health Organization's new classification of histological typing of female genital tract tumours [25].

The following variables were included in the present study: histological type, diagnostic period, clinical stage and age. The three main histological types applied are leiomyosarcoma (LMS), homologous and heterologous carcinosarcoma (CS) and endometrial stromal sarcoma (ESS). The group classified as NOS (not otherwise specified), sarcoma botryoides, rhabdomyosarcoma and angiosarcoma were included in the incidence and mortality rates, but were excluded from the other analyses because of the small number of patients. Clinical staging was performed retrospectively according to The International Federation of Gynecology and Obstetrics System [26]. The time span was divided into 5-year periods. The patients were organised into three age groups, <50 years, 50–69 years and 70+ years.

Methods

Incidence and mortality rates per 100 000 females were computed for every age group. Direct standardisation was used for age adjustment with respect to the European standard population. The analyses of survival was based on five-year relative survival rates. The actuarial method was used for the calculations. Relative survival represents an estimate of the ratio between the proportion of patient survivors and the proportion of survivors in a group of the general population with the same age distribution and birth cohort, but without the disease under study. The Central Bureau of Statistics receives all death certificates in Norway. Records of deaths during the observation periods were matched against the files of patients with uterine sarcomas. The mortality rates are based on those patients with sarcoma as the cause of death. The final date of follow-up was 31 December 1992. The follow-up system is based on the National identity number.

A multivariate analysis was carried out as outlined by Hakulinen and Teukanen [27]. The computations were performed by the statistical package Epicure [28]. The significance of each prognostic variable was tested by a log likelihood ratio test.

RESULTS

Incidence and mortality

A total of 1042 histologically verified uterine sarcomas were reported to The Cancer Registry between 1956 and 1992. The most frequent type was leiomyosarcoma (Table 1). The classification of uterine sarcomas changed during this period and histological types other than leiomyosarcoma were reported for the first time in the period 1966–1970. The overall annual incidence rate of uterine sarcomas was 1.7 per 100 000 females in the population in the last 5-year span (1987–1992) of the study period.

In the time period 1971–1990, leiomyosarcoma cases accounted for 41% of all the uterine sarcomas, carcinosarcoma cases for 35%, endometrial stromal sarcoma cases for 16% and NOS cases for 5.4%. Other sarcomas (sarcoma botryoides, rhabdomyosarcoma and angiosarcoma) accounted for 2.6%.

Of the carcinosarcomas reported, 119 were heterologous and 165 homologous. In the time period 1971–1990 the incidences of both leiomyosarcoma and endometrial stromal sarcoma were highest in the age group 50–64 years, whereas the carcinosarcomas peaked 5–10 years later, as demonstrated in Figure 1. The incidence of heterologous carcino-

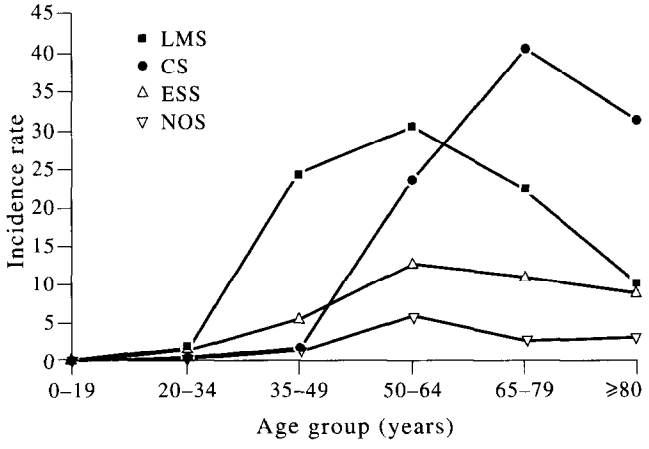

Figure 1. Age-specific incidence rates by histological type in uterine sarcoma (1971–1990).

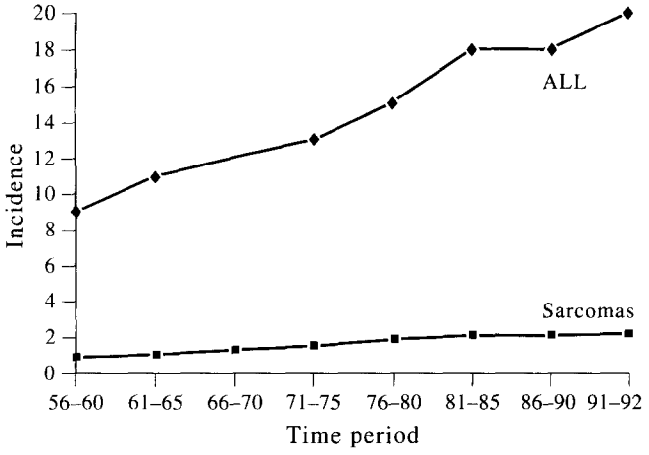

Figure 2. Time trend for incidence rates of all uterine malignancies and uterine sarcomas.

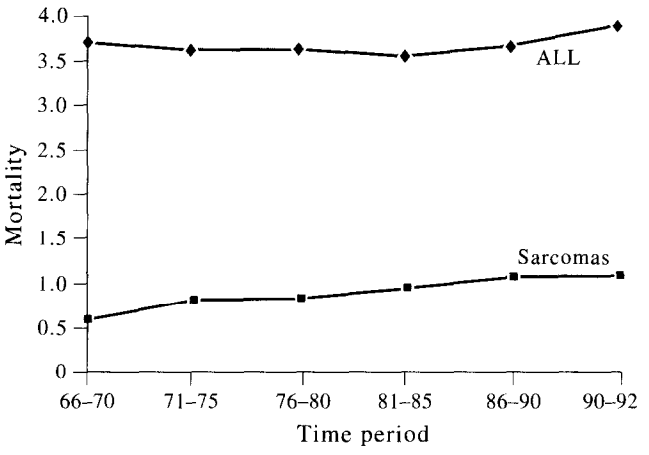

Figure 3. Time trend for mortality rates of all uterine malignancies and uterine sarcomas.

sarcomas increased successively up to the age of 80 years and older. The incidences of both sarcomas and all uterine corpus malignancies increased in the period 1956–1992 (Figure 2). Annually, 40 new cases of uterine sarcomas were reported in the last 5 years of the observed period, accounting for 9.7% of all new diagnoses of uterine corpus cancer. Mortality was recorded from 1966 (Figure 3). In the time period 1966–1992, 507 deaths were caused by uterine sarcoma, 60 in the first 5-year span and 130 in the last 5-year span of the observed period. Although the mortality rate from all uterine corpus malignancies remained unchanged, the contribution from uterine sarcoma has increased. In 1990–1992, 26% of all deaths due to uterine corpus malignancy were caused by sarcomas.

Stage distribution

The clinical stage distribution in all uterine sarcomas by age and time period is given in Table 2. Most cases were classified as stage I; 69% in the first period and 60% in the second. Stage IV was diagnosed in 22% of the patients in both periods. The elderly patients were at a more advanced stage at the time of initial diagnosis. The stage distribution was the same in the two time periods examined.

Survival

The 5-year relative survival rates for all uterine sarcomas related to histology, clinical stage, age at diagnosis and time period are shown in Table 3. For all age groups, the survival rate was similar when the time periods 1971–1975 and 1983–1987 were compared. Younger patients had a much better prognosis than the older. Patients with endometrial stromal sarcoma had a more favourable prognosis than patients with carcinosarcoma or leiomyosarcoma in both periods. Endometrial stromal sarcoma showed a decline in survival from 84% in the first period to 73% in the second.

Survival by stage and histological type were also studied. The five-year survival in leiomyosarcoma ranged from 65% in stage I to 0% in stage IV, in carcinosarcoma from 62% in stage I to 17% in stage IV and in endometrial stromal sarcoma from 85% in stage I to 37% in stage IV (data not shown).

Multivariate analysis

A multivariate analysis of relative survival was performed by fitting a main effect model with all four variables. This gave an acceptable fit; deviance = 24.9 with 28 degrees of freedom. The estimates of regression coefficients are given in Table 4, positive estimates indicate a poorer survival. In a multivariate setting all variables but time period were found to be significant at a 5% level.

DISCUSSION

The data in the present epidemiological study are based on the Norwegian Cancer Registry data from all women diagnosed with uterine sarcoma in Norway during the period 1956–1992. The analysis reflects incidence and survival of uterine sarcomas in the Norwegian female population over a 37-year time period. The mortality rate is

Table 2. Clinical stage distribution by age and time period in patients with uterine sarcomas in Norway

Period	Age (years)	Stage I *n* (%)	II–III *n* (%)	IV *n* (%)	Unknown *n* (%)	Total *n* (%)
1971–1975	0–49	19		6		25 (18)
	50–69	53	5	16	2	76 (55)
	>70	22	6	8		36 (26)
	Total	94 (69)	11 (8)	30 (22)	2 (2)	137 (100)
1983–1987	0–49	30	3	2		35 (20)
	50–69	53	10	18	4	85 (47)
	>70	24	14	20	1	59 (33)
	Total	107 (60)	27 (15)	40 (22)	5 (3)	179 (100)

Table 3. Five-year relative survival rates (%) in patients with uterine sarcomas in Norway, by histology, clinical stage, age and time period

	Time period	
	1971–1975	1983–1987
Histology		
ESS	83.7	73.0
LMS	50.4	45.9
CS	44.0	38.6
Stage		
I	67.4	66.9
II–III	0.0	27.2
IV	15.0	14.4
Age		
0–49	80.9	80.6
50–69	49.8	53.0
>70	22.6	11.8
Total	50.2	48.0

given from 1966 and reflects the last 27 years of the time period.

The incidence of uterine corpus malignancy increased during the study period, but the contribution from sarcomas doubled. In the last 5 years of the time period sarcomas accounted for 9.7% of all new diagnoses of uterine corpus cancer in Norway. This is approximately double the incidence of earlier estimates of uterine sarcomas [1–3]. This finding may partly be explained by the introduction of a new tumour classification in this time period and by changes in criteria of malignancy. However, these changes are not sufficient to explain the total increase in incidence of uterine sarcomas. The increased incidence was mainly due to a rise in the occurrence of carcinosarcomas, as no change was seen in the incidence of leiomyosarcomas. A similar increase in the former has been found by The Swedish Cancer Registry (unpublished data). Several studies [13, 14, 21] have found an over-reporting of uterine leiomyosarcomas, mainly due to overdiagnosis of benign leiomyosarcomas. In the Norwegian Radium Hospital, this was found to be the case in 13% of leiomyosarcomas [14]. In spite of this, the overall annual incidence of uterine sarcomas reported by Harlow and associates [1] from the SEER program of the National Cancer Institute in 1986 and also found in the Swedish Cancer Registry in 1989 was nearly the same as that found in Norway at the end of the study period.

Table 4. Multivariate analysis of relative survival in patients with uterine sarcomas by age, histology, stage and time period

Variable	Estimate of effect	Standard error	*P*-value Log likelihood ratio test of factor
Constant	−3.995	0.685	
Age at diagnosis			
<50	0.000	Referent	
50–69	1.409	0.382	
>70	2.762	0.490	<0.001
Histology			
ESS	0.000	Referent	
LMS	1.332	0.506	
CS	2.056	0.501	<0.001
Stage at diagnosis			
I	0.000	Referent	
II–III	0.609	0.551	
IV	2.000	0.368	<0.001
Time period			
1971–1975	0.000	Referent	
1983–1987	0.275	0.301	0.35

The mortality rates from uterine sarcomas also doubled in the time period studied. The total mortality from uterine corpus malignancy was unchanged in spite of increased incidence of the disease. This could reflect either better diagnostic procedures or better treatment. For women diagnosed with uterine sarcoma, however, the treatment given or the diagnostic procedure failed to improve the survival, which remained unchanged. According to our study, the 5-year survival for patients with uterine sarcomas was unchanged between 1971 and 1975 and between 1983 and 1987, despite the introduction of chemotherapy in the treatment of this disease in the late 1970s. Neither was a decrease in the mortality rate observed. Both the primary surgical treatment and the stage distribution were similar in both periods.

Most recent studies on uterine sarcomas emphasise stage as an important prognostic factor [5, 6, 11, 16]. This is also confirmed in our study. Improvement in diagnostic procedures over time and changes to surgical staging may support this.

Our study also revealed age as an important prognostic factor in uterine sarcoma. This might partly explain the extremely poor outcome for patients with carcinosarcomas, as this group included the oldest patients. The better outcome of younger patients with leiomyosarcoma reported in many studies, and confirmed in the present study, might well be explained by the age factor. In contrast to other authors [5, 16] we found valuable prognostic information in the histopathological classification. The dismal prognosis of the patients with uterine leiomyosarcoma and carcinosarcoma confirms that these tumours are two of the most aggressive neoplasms of the female genital tract.

The difference in age-specific incidence of the different histological types of uterine sarcomas suggests that there is a difference in their aetiology. The age-specific incidence of uterine leiomyosarcoma and endometrial stromal sarcoma closely resembles that of endometrial adenocarcinomas and breast cancer. This suggests hormonal involvement in their aetiology. Prior pelvic irradiation has been associated with heterologous carcinosarcoma [29, 30]. Surgical treatment of a gynaecological malignancy is currently performed more often than in the past. Therefore, the increased incidence of carcinosarcomas could only be partly explained by previous irradiation. The possibility that some environmental factors are involved in the aetiology of carcinosarcoma should be considered.

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