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Uterine carcinosarcoma, leiomyosarcoma and endometrial stromal sarcoma
Epidemiological, clinical and prognostic aspects

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ACADEMIC DISSERTATION

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ABSTRACT

Uterine carcinosarcoma (CS), leiomyosarcoma (LMS) and endometrial stromal sarcoma (ESS), which have historically been considered as subtypes of uterine sarcomas (USs), represent only a small proportion of uterine malignancies. However, it has been estimated that USs account for nearly one third of deaths from uterine malignancies (Nordal and Thoresen 1997).

The aims of these studies were to assess clinical behavior, survival, prognostic markers and epidemiological aspects of uterine CS, LMS and ESS. In a retrospective study we analyzed survival and prognostic markers (both clinical and immunohistochemical) in patients treated from 1990 to 2001 at Helsinki University Central Hospital (HUCH). In the epidemiological studies the incidence and occupational risk of uterine LMS and ESS were examined by using the NORDCAN and Nordic Occupational Cancer Study (NOCCA) databases. A cohort of 8606 cases of USs from 13 cancer registries was used to evaluate the risk of a second primary malignancy after the first primary US. This study was coordinated by the International Agency for Research on Cancer (IARC).

The age-adjusted incidence of LMS was about 0.4–0.5 per 100 000 and that of ESS about 0.2 per 100 000 in Iceland, Denmark, Finland and Norway during the study period 1978–2007. Age-specific incidences were highest around menopause for both subtypes of USs. Shoe and leather workers, farmers and teachers showed elevated standardized incidence ratios (SIRs) as regards LMS. However, no occupations were associated with increased SIRs in connection with ESS.

One hundred patients with uterine CS (n = 40), LMS (n = 39) and ESS (n = 21) were treated in our institution during 1990–2001. The 2-, 5-, and 10-year disease-specific survival rates were 64%, 56% and 38% for all subtypes grouped together and 5-year survival rates for each subtype separately were 49% (CS), 57% (LMS) and 65% (ESS). Stage, age, tumor size and delivery status were independently associated with survival when all subtypes were combined. Immunohistochemical (IHC) analysis (n = 65) of ten markers showed that estrogen receptor-α (ER-α) and progesterone receptor (PR) positivity were associated with statistically significantly better disease-specific survival times and p53 positivity with worse disease-specific survival in patients with LMS.

The risk of a second primary cancer after the first primary US was analyzed in a cohort of 8606 cases of USs, in which 499 cancer cases were observed. Women with a primary US had a 26% increased risk (SIR 1.26, 95%CI 1.16–1.38) of developing a second primary cancer. SIRs were elevated as regards cancers of the mouth and pharynx (2.16, 95%CI 1.15–3.69), colorectum (1.60, 95%CI 1.28–1.98), lung (1.73, 95%CI 1.27–2.29), breast (1.25, 95%CI 1.05–1.49), urinary bladder (1.74, 95%CI 1.02–2.79), kidney (2.00, 95%CI 1.24–3.06), thyroid gland (2.74, 95%CI 1.42–4.79), and soft tissue sarcoma (5.23, 95%CI 2.51–9.62). The

risk of breast cancer increased along with increasing age at US diagnosis (p trend=0.040). The risk of kidney cancer increased along with lower age at the time of US diagnosis (p trend = 0.004) and short time since US diagnosis (p trend = 0.018).

In conclusion, the incidences of LMS and ESS showed constant trends in Nordic countries during the study period. Overpresentation of uterine LMS in shoe and leather workers and farmers might be associated with the etiology of LMS and this should be clarified in the future. Our institutional survival rates in cases of uterine CS, LMS and ESS were comparable with or even better than in earlier reports, and stage, age, tumor size, and delivery status of the patient emerged as the main prognosticators. Immunohistochemical expression of ER-α, PR and p53 were associated with survival of patients with LMS. After diagnosis of US there is an elevated risk of a second primary malignancy. Excesses of colorectal and urinary bladder cancers may reflect the effects of earlier treatments of US (radiotherapy and chemotherapy). The elevated risk of mouth and pharynx, lung and urinary bladder cancers after USs might be associated with common etiological factors such as smoking. The excesses of breast cancer in US patients may be related to a shared hormonal etiology.