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Incidence of uterine leiomyosarcoma and endometrial stromal sarcoma in Nordic countries: Results from NORDCAN and NOCCA databases

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ABSTRACT

Objectives and study design: Uterine sarcomas are an uncommon and heterogeneous group of malignancies. Their etiology is mainly unknown. Here, we analyzed trends in incidence and occupational variation in risk of uterine leiomyosarcomas (LMS) and endometrial stromal sarcomas (ESS) in the Nordic countries aided by NORDCAN and NOCCA (Nordic Occupational Cancer) databases.
Main outcome measures: Incidence rates per 100,000 and Standardized incidences rates (SIR) obtained from NORDCAN and NOCCA databases.
Results: The incidence rates were about 0.3 per 100,000 for ESS and about 0.4 per 100,000 for LMS in Denmark, Finland, Iceland, and Norway. During the study-period (1978–2007), the incidence rates in each country were quite similar and constant. The age-specific incidence of LMS showed a peak around menopause. Significantly increased risk for LMS occurred in shoe and leather workers, farmers and teachers, whereas significantly low risk was detected with packers in the NOCCA data from Finland, Norway, and Sweden. For ESS no occupations showed either increased or decreased incidences.
Conclusions: The incidence trends of LMS and ESS in our study were constant in four Nordic countries over time. The elevated risk for LMS with women exposed to leather work and animal dust indicates further exploration.

1. Introduction

Uterine sarcomas (US) are aggressive and rare gynecologic malignancies of largely unknown etiology. Traditionally, the main histological classifications of US have been carcinosarcoma, leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and undifferentiated endometrial sarcoma [1]. Some studies define carcinosarcomas as poorly differentiated metaplastic carcinomas [2]. Depending upon the histological classification used, USs represent about 3–9% of malignant uterine tumors and 1% of all gynecologic malignancies [1,3,4].

Possible etiological factors for USs include a history of pelvic radiation, obesity, long use of estrogens as hormone replacement therapy or tamoxifen, and use of oral contraceptives [5–8]. US incidence also varies between races; the age-adjusted incidence for blacks has been reported at twice that of whites and more than twice that of women of other races [8,9]. The prognosis of US patients is quite poor; overall 5-year survival ranges from 17% to 53% [3,4,10,11]. For ESS, the prognosis is better than for other USs.

The total population of the five Nordic countries is about 25 million inhabitants: Denmark 5.5 million, Finland 5.4 million, Iceland 0.3 million, Norway 4.8 million and Sweden 9.3 million [12]. Each Nordic country has a well-established primary health care system, including secondary and tertiary hospital services, and a nationwide population-based cancer registration system [13,14]. Cancer registration methods are quite similar in the Nordic countries [15], and notification of incident cancer cases is mandatory by law. There are more than 130,000 incident cancer cases and nearly 60,000 cancer deaths in the Nordic countries every year. Cancers of the female reproductive organs constitute more than 12% of all incident female cancer cases [16].

Abbreviations: US, uterine sarcoma; LMS, leiomyosarcoma; ESS, endometrial stromal sarcoma; NOCCA, Nordic Occupational Cancer Study; SIR, standardized incidence ratio.

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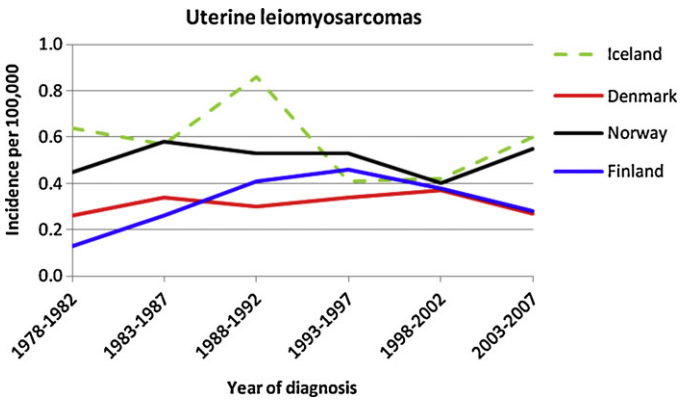

Fig. 1. Incidence of uterine leiomyosarcoma in the Nordic countries, by 5-year period, adjusted for age to the World Standard Population. Tabulation based on NORDCAN data [14].

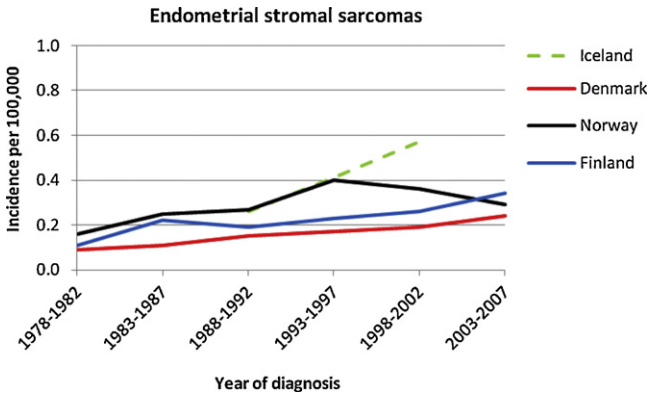

Fig. 2. Incidence of endometrial stromal sarcoma in the Nordic countries, by 5-year period, adjusted for age to the World Standard Population. Tabulation based on NORDCAN data [14].

Only a few epidemiologic studies on possible etiological factors for US have been published so far, and to our knowledge, there are no published studies on potential occupational risks factors. Our aim is to describe trends in the incidence of US and the occupational variation in the incidence for US in the Nordic countries, making use of large Nordic databases.

2. Materials and methods

Based on NORDCAN database (www.ancr.nu; [14]) which includes detailed information on cancer incidence, mortality and prevalence in each of the Nordic countries, the incidences of USs were calculated for five-year periods from 1978–1982 to 2003–2007 and for five-year age-groups. Information was available only for uterine LMSs (ICD-10 C54.21) and ESSs (ICD-10 C54.22). Incidence rates for the US categories could not be calculated for Sweden because of restrictions in the coding systems used over the years.

The Nordic Occupational Cancer Study (NOCCA) cohort comprised 6.4 million women (1.7 million from Finland, 1.3 million from Norway, and 3.4 million from Sweden) aged 30-64 years, as identified in population censuses in 1960, 1970, 1980 or 1990 [13]. The follow-up periods of cancer incidence were 1971–2005 in Finland, 1961–2003 in Norway and 1993–2005 in Sweden. Altogether, 171 million women-years of follow-up were accumulated. Standardized incidence ratios (SIR) of LMS and ESS by country and occupational category were computed. SIR is the ratio of observed (Obs) and expected (Exp) number of cancer cases. The expected numbers were based on the cancer incidence rates of entire national female populations in each country. For SIRs, exact 95% confidence intervals (95% CI) were calculated assuming a Poisson distribution of the observed cancer cases.

The information about occupation for each person was provided though free text in self-administered questionnaires, then centrally coded and computerized in censuses of each country. For NOCCA data, occupations have reclassified into 53 categories and one group of economically inactive persons. The group of economically inactive persons includes housewives, early pensioners, students and persons on social support [13].

3. Results

The incidence of LMS was quite stable over the years in all countries (Fig. 1). The rates in Iceland and Norway were about 0.5 per 100,000, i.e. slightly higher than in Denmark and Finland. The rates for ESS were about 0.2 per 100,000, however with some suggestion of an increase over time (Fig. 2). The incidence of LMS was highest in age groups of 45–59 years (Fig. 3). The incidence rates of ESS were constant from the age group of 45–49 years and above.

During the follow-up period of the NOCCA study, 1163 LMS and 508 ESS cases were detected in Finland, Norway and Sweden. The occupational groups with significantly increased SIRs of LMS were shoe and leather workers (SIR 2.59, 95% CI 1.12–5.11), farmers (SIR 1.62, 95% CI 1.18–2.17) and teachers (SIR 1.38, 95% CI 1.07–1.76) (Table 1). The SIR for domestic assistants was 0.64 (95% CI 0.41–0.96). For ESS, no occupations with elevated SIRs occurred (Table 2). There were no cases of ESS among packers, although the expected number of cases was 5.8.

4. Discussion

Our study shows quite constant incidence trends of ESS and LMS over the 30 years studied in four Nordic countries. The incidences of both LMS and ESS increased up to the age groups around menopause, but decreased after the age of 60 in LMS. The occupations with a significantly elevated incidence of LMS were shoe and leather workers, farmers and teachers.

In a recent study, the use of estradiol-progestin menopausal hormone replacement therapy for 5 years or longer was associated with a twofold risk for USs [17]. The use of menopausal hormone therapy increased from the late 1970s until the late 1990s in all Nordic countries, while there was a marked decrease

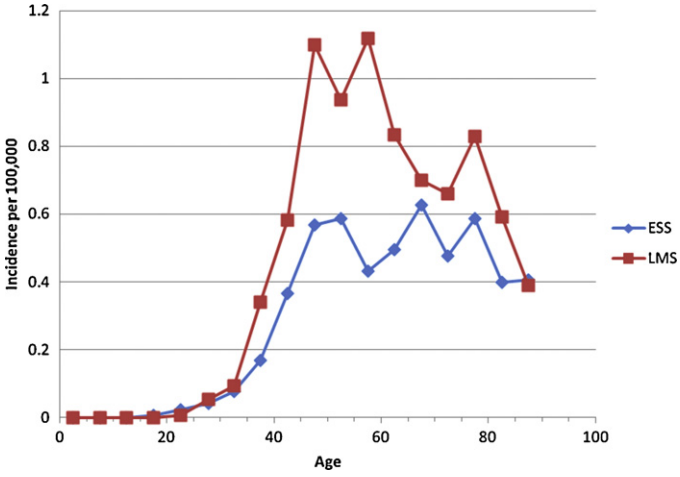

Fig. 3. Age-specific incidence rates of uterine endometrial stromal sarcoma (ESS) and leiomyosarcoma (LMS) in Denmark, Finland, Iceland and Norway from 1978 to 2007. Tabulation based on NORDCAN data [14].