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Do stage of disease, comorbidity or access to treatment explain socioeconomic differences in survival after ovarian cancer? – A cohort study among Danish women diagnosed 2005–2010

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ABSTRACT

Aims: In order to reduce social inequality in cancer survival, knowledge is needed about where in the cancer trajectory disparities occur, and how social and health-related aspects may interact. We aimed to determine whether socioeconomic factors are related to cancer diagnosis stage, and whether socioeconomic disparities in survival after ovarian cancer can be explained by socioeconomic differences in cancer stage, comorbidity, treatment or lifestyle factors.
Methods: In the Danish Gynaecological Cancer Database we identified 2873 cases of ovarian cancer diagnosed between 2005 and 2010. From this data we retrieved information on prognostic factors, treatment information and lifestyle factors. Age, vital status, comorbidity, education, income and cohabitation status were ascertained from nationwide administrative registers. Associations were analyzed with logistic regression and Cox regression models.
Results: Educational level was weakly associated with cancer stage. Short education, lower income and living without a partner were related to poorer survival after ovarian cancer. Among women with early cancer stage, HR (95% CI) for death was 1.75 (1.20–2.54) in shorter compared to longer educated women. After adjustment for comorbid conditions, cancer stage, tumour histology, operation status and lifestyle factors, socioeconomic differences in survival persisted.
Conclusions: Socioeconomic disparities in survival after ovarian cancer were to some extent, but not fully explained by differences in important prognostic factors, suggesting further investigations into this problem, however implying that socially less advantaged ovarian cancer patients should receive attention during cancer treatment and rehabilitation.

1. Introduction

The prognosis of ovarian cancer is generally poor, with a 5-year survival rate in Denmark of <40%, and socioeconomic differences in survival after ovarian cancer have been suggested [1,2]. In order to plan effective interventions to reduce this survival gap, it is important to determine at what point in the cancer trajectory socioeconomic differences occur and how social and health-related aspects may interact.

One hypothesis is that differences in survival are due to later diagnosis of cancer in women with lower socioeconomic positions [3], presumably because they delay seeking health care or because of delayed referral to specialized care. The symptoms of ovarian cancer are often weak or non-specific, and about 70% of cases are diagnosed in advanced stages [4]. Cancer patients with lower socioeconomic positions also tend to have more comorbid conditions at time of diagnosis [5], a prognostic factor for all-cause mortality among these patients [6,7]. Comorbidity may affect the timing of diagnosis by delaying health care-seeking or,

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conversely, increasing the frequency of health care contacts [7], which may also influence the choice or aggressiveness of cancer treatment [8,9]. Other studies suggest that patients in lower socioeconomic positions receive suboptimal treatment [3,10,11]. Additionally, risk factors such as smoking and overweight may affect the relation between socioeconomic factors and survival [12,13].

Most previous studies in this area focused on disparities by ethnicity or marital status, lacked socioeconomic information at the individual level and had limited data on prognostic factors [3,10,11,14–17]. We used nationwide clinical and administrative registers to retrieve data on important prognostic factors and individual socioeconomic characteristics. Our aim was to determine whether there are socioeconomic differences in cancer stage at diagnosis, and whether any disparities in survival could be explained by socioeconomic differences in cancer stage, comorbidity, access to treatment or lifestyle factors.

2. Material and methods

2.1. Study population

The study population was identified from the Danish Gynaecological Cancer database (DGCD), established in 2005 and covers about 96% of gynaecological cancer cases in Denmark [4]. All data are entered into the database by gynaecologists at hospitals for clinical information and by pathologists. Between 1 January 2005 and 31 December 2010, 3076 cases of ovarian cancer (including tubal and peritoneal cancers) were recorded. By use of the unique Danish ten-digit personal identification number, DGCD data was merged with administrative population-based registers: the Civil Registration System (CRS), the Danish National Patient Register (NPR), the Danish Cancer Registry (DCR), the nationwide Danish Pathology Register (DPR) and registers of Statistics Denmark.

Patients were excluded if no date of registration in DGCD or DCR was available ($n = 14$), if the cancer stage was unspecified ($n = 38$) or missing ($n = 39$); or if information on tumour histology was missing in the DGCD or the DPR and the case was not registered in the DCR ($n = 8$). We also excluded patients who had immigrated to or emigrated from Denmark within 2 years before diagnosis ($n = 10$) as socioeconomic data were not available, or they were lost to follow-up; patients born before 1920 (before which date registers for socioeconomic data were incomplete) ($n = 48$), those under the age of 25 (final income or educational level were considered not established) ($n = 27$) and those with no match on any of three main socioeconomic variables ($n = 19$). This left 2873 women (93%) for the study.

2.2. Cancer characteristics and treatment

The date of registration (date of operation), clinical cancer stage, tumour histology, surgical treatment and treating hospital were obtained from the DGCD. For cases with no registration date in DGCD we searched the DCR in which it is mandatory to register all cancer patients in Denmark, and diagnosis dates were retrieved for further 23 cases. Staging was carried out according to the recommendations of the Fédération Internationale des Gynaecologistes et Obstetristes (FIGO) [18]. *Cancer stage* was divided into early (I–II) and advanced (III–IV) cancer for analysis of stage as the outcome. For cases with missing information on tumour histology, histologic data were searched in the DPR and retrieved for 91 cases [19]. *Tumour histology* was grouped into serous, endometrioid, mucinous and clear cell adenocarcinomas, other types and unknown. Treatment was given according to national clinical guidelines [20]. We had limited treatment information from the DGCD, except whether a patient had undergone exploratory surgery and whether the operation was radical. Chemotherapy treatments were underreported in the DGCD and the NPR [4] and therefore were not included. To apply such information would require additional data from medical records, which we did not collect. For the analyses, a measure of whether the first intention was to operate was constructed, and *operation status* was categorized into: operated (exploratory or radical surgery), not operated and unknown.

2.3. Other health-related factors

To estimate the burden of *comorbidity*, all somatic diagnoses other than ovarian cancer that required hospitalization or outpatient visit since 1977 and 1995, respectively, were retrieved from the NPR [21]. Diagnoses were coded into a modified Danish version of the International Classification of Diseases version 8 (ICD-8) until 1993 and thereafter into ICD-10. The Charlson comorbidity index (CCI) was calculated, covering 19 selected clinical conditions scored by severity [22] and cumulated until 1 year before the cancer diagnosis (Appendix A). Scores were grouped into 0 (none), 1, 2 and ≥ 3 for the analyses.

The American Society of Anesthesiologists (ASA) score and lifestyle factors at the time of diagnosis were obtained from the DGCD. The *ASA score* assesses the patient's physical status before surgery and is categorized into five groups. We used this score as a complement to the CCI score, as a measure of how disease affects health condition. *Smoking* was categorized into 'never smokers', ex-smokers and current smokers and *body mass index* (*BMI*) into normal, underweight, overweight and obese.

2.4. Socioeconomic indicators

Socioeconomic information was retrieved from the CRS and from registers of education and income run by Statistics Denmark, which contain individual data and are updated each year [23–25]. Socioeconomic information was retrieved 2 years before cancer diagnosis to minimize any reverse effect of early disease symptoms on socioeconomic position. Three indicators were selected to cover aspects of social influences on health: knowledge-related assets, material resources and social support [26,27]. Highest attained *level of educational* was categorized into short, medium or higher education, household *disposable income* was divided into quartiles of the national gender-specific disposable household income per person distribution, and *cohabitation status* was defined as living with a partner or not. Details about construction of the socioeconomic measures are found elsewhere [28].

2.5. Survival

Age, emigration status and date of death at the end of November 2011 were obtained from the CRS.

2.6. Statistical analysis

A diagram of hypothesized causal relations was drawn, from which confounders and mediators were identified (Fig. 1). Using logistic regression models, we analyzed associations between each socioeconomic indicator and cancer stage (FIGO III–IV vs. I–II), with adjustment for age and comorbidity. Linearity in the effect of age was assured. We evaluated the stage categorization by repeating the analyses after dividing cancer stage into FIGO II–IV vs. I. Effect modification of each of the three socioeconomic factors by age and comorbidity (CCI categorized in 0, 1, 2 and ≥ 3) was tested for one pair at a time, and no significant interactions were found.