Patient education-level affects treatment allocation and prognosis in esophageal- and gastroesophageal junctional cancer in Sweden

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ABSTRACT

Background: Low socioeconomic status and poor education elevate the risk of developing esophageal- and junctional cancer. High education level also increases survival after curative surgery. The present study aimed to investigate associations, if any, between patient education-level and treatment allocation after diagnosis of esophageal- and junctional cancer and its subsequent impact on survival.

Methods: A nation-wide cohort study was undertaken. Data from a Swedish national quality register for esophageal cancer (NREV) was linked to the National Cancer Register, National Patient Register, Prescribed Drug Register, Cause of Death Register and educational data from Statistics Sweden. The effect of education level (low; ≤ 9 years, intermediate; 10–12 years and high > 12 years) on the probability of allocation to curative treatment was analyzed with logistic regression. The Kaplan-Meier-method and Cox proportional hazard models were used to assess the effect of education on survival.

Results: A total of 4112 patients were included. In a multivariate logistic regression model, high education level was associated with greater probability of allocation to curative treatment (adjusted OR: 1.48, 95% CI: 1.08–2.03, p = 0,014) as was adherence to a multidisciplinary treatment-conference (adjusted OR: 3.13, 95% CI: 2.40–4.08, p < 0,001). High education level was associated with improved survival in the patients allocated to curative treatment (HR: 0.82, 95% CI: 0.69–0.99, p = 0,036).

Discussion: In this nation-wide cohort of esophageal- and junctional cancer patients, including data regarding many confounders, high education level was associated with greater probability of being offered curative treatment and improved survival.

1. Introduction

Cancer of the esophagus and gastro-esophageal junction is the eight most common type and the sixth most lethal type of cancer in the world [1]. There are several life-style associated risk factors where low socioeconomic and educational status elevate the risk of developing these cancers [2,3]. Patients with higher education are known to have better survival after curative esophageal cancer surgery [4].

In esophageal- and gastroesophageal junctional cancers, standard curative treatment regime is multimodal with neoadjuvant chemoradiotherapy (CRT) followed by one of the most extensive oncological surgical procedures [5]. In patients declining surgery or not physically fit to undergo surgical treatment, curative CRT can be offered as an

alternative. The above treatment regimes introduce a significant burden on each individual patient's physical and mental capacities [6,7]. Ideally the choice of treatment should be guided by the preoperative tumor staging, the patient's health and stamina and the recommendation of a multidisciplinary conference [8,9]. Such a recommendation is the base for a final treatment decision made after a discussion with the patient.

Equality of healthcare for each individual patient is strived for in many publicly funded health care systems, like in Sweden. Accordingly it is stated in Swedish law that care should be given equally regardless of socioeconomic status. Socioeconomic status is a wide concept constituting many factors where education, in addition to income, marital status, place of residence and occupation, play an important role. Since poor education is associated with decreased survival after surgery for

esophageal cancer, and patients with low socioeconomic status have an increased risk of the disease, it is of essence to explore mechanisms of how education, and other, corresponding factors influence these risks.

National registries have certain strengths in giving population based data. Moreover, Sweden offers many nationwide data bases and by linking the data, through a unique ten digit personal identification number given to all Swedes at birth, it is possible to explore and strengthen epidemiological findings.

On these grounds the present study aimed to investigate the relationship between the patient's educational level and respective treatment allocation after the diagnosis of esophageal- and gastroesophageal junctional cancer and its subsequent impact on survival.

2. Materials and methods

2.1. Study design

This cohort study recruited data from 2006 to 2012 in the Swedish National Register for Esophageal and Gastric Cancer (NREV). All Swedish patients diagnosed with esophageal- and gastroesophageal junctional cancer (ICD10; C15.*, C16.0A, C16.0B and C16.0X) during the study years were included. Data from NREV was linked to the Swedish Cancer Register, National Patient Register, Prescribed Drug Register and the Cause of Death Register. All the above registries are well described, researched and validated [10–14].

All data from the above-mentioned registers was extracted in 2014. The study was approved by the local Ethics board in Stockholm, Dnr 2013/596-31/3.

2.2. Educational level – exposure

Data on education level was extracted from the Education Register, administered by Statistics Sweden [15]. The educational level was divided into three well-defined classes, as advocated by previous studies [16], based on the highest attained number of years of schooling at the time of data extraction. Low education level, ≤9years, corresponds to compulsory primary school. Intermediate education level, 10–12 years corresponds to completed primary school and partly or fully competed secondary school. High education level, > 12 years, corresponds to post-secondary education such as university or other academic studies.

2.3. Treatment allocation – outcome

In Sweden, patients diagnosed with esophageal- or gastroesophageal junctional cancers are reported to the NREV. The accuracy of this register was recently evaluated and was in 91.1% of entries in exact agreement with reabstracted data. The coverage of NREV was, in the same validation study, 95.5% when compared to the Swedish Cancer Register [12]. The intended choice of treatment (treatment allocation), determined at a multidisciplinary treatment conference (MDC) or by the treating physician, is a mandatory variable reported to the register concluding the diagnostic workup. This variable has, in the present register, been determined to be of high validity [12].

2.4. Covariates and confounding factors

A directed acyclic graph (DAG) model [17] was used to identify possible factors governing outcome as well as confounding factors. Covariates included well-established prognostic factors such as age, sex, TNM-stage, histopathology and ASA-class (American Society of Anesthesiologists) as well as possibly influencing comorbidities such as; myocardial infarction (ICD10; J42-44) or chronic obstructive pulmonary disease (COPD)-diagnosis (ICD10; I21-22) within 10 years before cancer diagnose. Other covariates included geographic region and whether or not the patient was presented at a multidisciplinary treatment conference.

2.5. Statistical methods

The effect of education level on the probability of allocation to curative treatment was analyzed with univariate and multivariate logistic regression. In the survival analysis, patients were followed until death, emigration or December 31st 2013, whichever came first. Survival probability was displayed according to the Kaplan- Meier method and Cox proportional hazard models were used to assess the effect of educational level when adjusting for multiple variables. Separate models were fitted for each allocated treatment. Missing data on histology, ASA class, TNM, multidisciplinary conference and educational level were handled by use of the Multivariate Imputation by Chained Equations (MICE) algorithm [18]. Data were in these cases imputed forty times using all variables as predictors in the MICE algorithm. Separate models were fitted to the dataset in each iteration and the results were then pooled using Rubin's rules [19]. A p-value of 0.05 was considered significant. All statistical analyses were performed with the R statistical software package [20].

3. Results

3.1. Patients

In total, 4112 patients were included in the analysis. Patient characteristics as well as missing and imputed, data are summarized in Table 1. Out of all patients, the duration of education was ≤9 years (Low) in 1686 (41.0%), 10–12 years (Intermediate) in 1522 (37.0%) and > 12 years (High) in 638 (15.5%). Data on the duration of education were missing in 266 patients (6.5%). Patients with higher education were slightly younger and geographically concentrated to the capital region and presented with less comorbidity. In all other aspects the characteristics were similar in the three study groups.

3.2. Educational level and treatment allocation

Curative treatment was planned in 1587 patients (38.7%). In the group with low educational level 36.0% were offered curative treatment. For the intermediate and high educational level groups the percentages were 42.6% and 46.4% respectively. In a univariate model both intermediate education, (OR 1.35, 95% CI 1.17–1.55), and high education level, (OR 1.58, 95% CI 1.31–1.90) were associated with increased probability of being offered curative treatment. When applying a multivariate model adjusting for region, sex, age, ASA-class, TNM-stage, histopathology, myocardial infarction, COPD and multidisciplinary conference, the association between high educational level and curative treatment still remained, with an adjusted OR of 1.48 (95% CI 1.08–2.03). The adherence to a multidisciplinary conference for clinical decision-making, emerged as a robust positive predictor of allocation to curative treatment, (adjusted OR 3.13, 95% CI 2.40–4.08) as were also geographical region South and West. Negative predictors for curative treatment allocation in the multivariate model were geographical region Central, positive N- and M-stage- disease, higher ASA-class, squamous histopathology, COPD, and age > 70 years. Corresponding data are presented in Table 2 and graphically in Fig. 1. In an additional multivariate logistic regression model, stratified by sex, age and histological subtype, the association between high education level and allocation to curative treatment remained for men, (adjusted OR 1.47, 95% CI 1.02–2.12), was strengthened in the elderly (> 70y), (adjusted OR 1.61, 95% CI 1.06–2.44) and in patients with adenocarcinoma, (adjusted OR 1.73, 95% CI 1.13–2.64). The multidisciplinary conference as a predictor for curative treatment allocation was confirmed for the three subgroups in the stratified analysis. Supplementary Table 1.