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The population-based incidence and mortality of biliary tract cancer in Sweden

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ABSTRACT

Background: The incidence trends of biliary tract cancer need to be established. This study investigated the incidence and mortality of biliary tract cancer in Sweden in 1970–2010.

Methods: Sex-specific biliary tract cancer incidence and mortality rates were evaluated using data from the Swedish Cancer Register, Patient Register and Causes of Death Register. Case registration was separate for each register. Gallbladder cancer and cancers of the extra–hepatic bile ducts were analyzed separately. Standardized incidence rates were calculated and joinpoint regression was used to calculate annual percent changes (APC) with 95% Confidence Intervals (CIs).

Results: The incidence of non-gallbladder extra–hepatic cancers assessed from the Cancer Register decreased in men and women from the mid 1980′s (APC: -4.0, 95% CI -5.3 – -2.7 and APC -6.3, 95% CI -7.7 – -4.8, respectively), whereas the mortality of non-gallbladder extra–hepatic cancers rather increased until 1990 (APC: 2.1, 95% CI 1.4–2.8 and APC 2.7, 95% CI 1.3–4.1, in men and women respectively). Notably, the mortality rate was greater than the incidence rate as assessed from the Cancer Register from the early 1990′s and onwards. The incidence of non-gallbladder extra–hepatic cancers derived from the Patient Register also increased over time. Gallbladder cancer incidence and mortality rates generally decreased. However, incidence rates assessed from the Patient Register decreased to a lesser extent.

Conclusions: The incidence of gallbladder cancer seems to have decreased over the past decades in Sweden. The incidence trends for extra–hepatic tumors other than gallbladder cancer may however be obscured by under-reporting.

1. Introduction

Biliary tract cancer are rather uncommon cancers characterized by a poor prognosis, and most patients have advanced disease stage at presentation. [1] The incidence of biliary tract cancer, including cancers of the gallbladder, the extra–hepatic bile ducts and Ampulla, is a matter of debate. Some studies have reported a decreasing trend of gallbladder cancer, over the past 25 years [2,3]. The reasons for this are unclear but an increased use of cholecystectomy for symptomatic gallstone disease as the reason for this has been put forth [4]. However, stable [5,6], or increasing [7] trends have been observed in United Kingdom and China, respectively. For extra–hepatic bile duct cancers, the literature is inconsistent in both size and direction of incidence trends [3,8]. Changes in coding standards and an inability to account for differences in tumor locations have clouded the picture [9]. Moreover, recent literature has emphasized the importance of distinguishing between extra–hepatic and intra–hepatic cancer, due to differences in tumor biology and cancer epidemiology [3].

The validity of cancer incidence estimates based on cancer registers depends on the quality and completeness of the registers. Misclassification of cancers may bias the results in unknown directions and lack of completeness will underestimate the true cancer incidence. A recent study from our group suggested a substantial under-reporting of biliary tract cancer to the Swedish Cancer Register, which increased in more recent time periods. [10] Thus, incidence estimates of biliary tract cancer based on data from the cancer registers only might underestimate the true estimate of this cancer.

Because of the poor prognosis of biliary tract cancer, mortality trends could be used as proxies for incidence trends. In fact, in patients with an advanced biliary tract cancer, death certificates might provide

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the only source of cancer diagnosis. [10] Although there cannot be a direct translation of mortality rate for biliary tract cancer to an absolute measure of cancer incidence, mortality trends could provide additional information to estimate the true incidence and trend of biliary tract cancer.

This study was conducted to estimate the population-based incidence and mortality of biliary tract cancer in Sweden and evaluate the trends over time based on data from three nationwide registers.

2. Methods

2.1. Design

The incidence and trends of biliary tract cancer between 1970 and 2010 in Sweden were investigated using data from three national health data registers: the Cancer Register, the Patient Register and the Causes of Death Register. The National Board of Health and Welfare maintains these three registers, but data collection in each register is independent of one another. The Regional Ethical Review Board in Stockholm approved the study.

2.2. Data sources

The Swedish Cancer Register collects information on newly diagnosed cancers in Sweden. The register was established in 1958 and is of 96% overall completeness. [11] however, a potential underreporting of biliary tract cancer has been reported [10]. Diagnoses are coded according to the 7th version of the International Classification of Diseases (ICD-7) and the most recent version of ICD-code (For time period 1969 – 1986: ICD-8; For time period 1987-1996: ICD-9; For time period 1997-and onwards ICD-10). The foundation of the diagnosis is reported and may be based on a) radiology; b) histopathology following biopsy; c) histopathology following autopsy; d) cytology; e) autopsy without histopathological confirmation; f) surgery without histopathological confirmation; g) laboratory findings; or h) clinical evaluation. [12]

The Swedish Patient Register contains data derived from hospital discharge notes and has complete national coverage from 1987 onwards. [13] Medical data such as diagnoses and surgical procedures are recorded in addition to data about the individual patient and the hospital. Diagnoses are coded according the 9th and 10th version of the ICD after 1987 and 1997, respectively. The accuracy of the diagnoses has been reported to be 85–95 %. [14]

The Swedish Causes of Death Register collects information about deaths in Sweden and is based on data from death certificates. Information of the cause of death and any underlying causes of death is available and diagnoses are coded according to the most recent version of the ICD-code. The register is of high over-all quality and was 99.2% complete in 2008. [15]

The Register of the Total Population provided the annual Swedish population by age and sex between 1970 and 2010 for the incidence calculations. [16]

2.3. Data collection

Incident biliary tract cancer cases between 1970 and 2010 were collected from the Cancer Register and the Patient Register. Furthermore, all reported deaths due to biliary tract cancer from the same time period were extracted from the Causes of Death Register. Cases of biliary tract cancer were identified using the ICD system in all three registers. The diagnosis codes 155.2–155.3, 156.11–156.21, 156B-156C and C24.0-C24.1 denoted non-gallbladder cancers of the extra–hepatic bile ducts and the Ampulla in the ICD-7, ICD-8, ICD-9 and ICD-10, respectively. The corresponding codes for cancer of gallbladder cancer were 155.1, 156.01, 156 A and C23.9 for gallbladder cancer. Cancers without clear origin and/or extensive growth were omitted.

2.4. Statistical analyses

Annual sex-specific and age-adjusted incidence rates per 100,000 individuals of biliary tract cancer between 1970 and 2010 were calculated. For the Patient Register, however, only incidence rates from 1990 and onwards are presented due to incomplete nationwide coverage prior to 1987. The first three years of follow-up in the Patient Register were discarded to avoid an over-estimation of new cancer cases due to prevalent cases. To account for differences in tumor biology, gallbladder cancer was analyzed separately from other extra–hepatic bile duct cancers. The age distribution for each year was used in the denominator. The Swedish population in 2010 was used as reference for standardization purposes. Furthermore, the results for the Cancer Register were stratified on foundation of the diagnosis according to the categories a–h presented above. However, categories e–h (see above) were combined into one group in this study.

Log-linear joinpoint regression was used to evaluate trends over time. The results are presented as annual percent change (APC) with 95% confidence intervals (CI).

Calculations were performed using the statistical software STATA 13 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP.) and SEER*Stat (Surveillance Research Program, National Cancer Institute SEER*Stat software [seer.cancer.gov/seerstat] version 4.3.1.0).

3. Results

3.1. Patients

Between 1970 and 2010, a total of 21,350 and 24,769 biliary tract cancer cases were identified in the Cancer Register and the Causes of Death Register respectively, whereas 16,505 cases were identified in the Patient Register between 1987 and 2010 (Table 1). However, 2593 gallbladder cancers were diagnosed prior to 1990. Gallbladder cancer was the most common biliary tract cancer all three registers. A small

Table 1
Characteristics and distribution of biliary tract cancer cases registered in the Swedish Cancer Register, the Swedish Patient Regsiter and the Swedish Cause of Death Register between 1970 and 2010.

	Cancer Register (%)	Patient Register (%)[α]	Cause of Death Register (%)
Total	21,350 (100)	17,357 (100)	24,769 (100)
Gallbladder cancer	14,181 (66)	7717 (45)	13,963 (56)
Cancer of the extra-hepatic bile ducts	7,196 (34)	10,824 (62)	10,962 (44)
Sex			
Male	6,950 (33)	6403 (37)	7983 (32)
Female	14,400 (67)	10,954 (63)	16,786 (68)
Age			
0-49	762 (3)	675 (4)	666 (3)
50-54	755 (3)	624 (4)	684 (3)
55-59	1,388 (6)	1075 (6)	1263 (5)
60-64	2,162 (10)	1636 (9)	2094 (8)
65.69	3,016 (13)	2241 (13)	3108 (13)
70-74	3,870 (17)	2741 (16)	4125 (17)
75-79	4,204 (19)	3177 (18)	4698 (19)
80 +	6143 (28)	5188 (30)	8131 (33)
Time period			
1970-1974	2,804 (13)	.	2,399 (10)
1975-1979	3,268 (15)	.	2,886 (12)
1980-1984	3,577 (17)	.	3,476 (14)
1985-1989	3,374 (16)	2593 (15)[β]	3597 (15)
1990-1994	2,677 (13)	3494 (20)	3288 (13)
1995-1999	1,999 (9)	3426 (20)	3054 (12)
2000-2004	1,719 (8)	3495 (20)	2870 (12)
2005-2010	1,932 (9)	4349 (25)	3199 (13)

[α]1987-2010.
[β]1987-1989.

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