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SHORT REPORT

Completeness of colon and rectal cancer staging in the Danish Cancer Registry, 2004–2009

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Objective: To explore the completeness of tumor, node, metastasis (TNM) staging for colon and rectal cancer in the Danish Cancer Registry.

Material and methods: From the Danish Cancer Registry, we retrieved data on TNM stage, year of diagnosis, sex, and age for 15,976 and 8292 patients, respectively, with first diagnoses of colon or rectal cancer during the 2004–2009 period. From the Danish National Patient Register, we retrieved data on comorbidity (computed as Charlson Comorbidity Index scores). We calculated the completeness of TNM staging overall, by each stage component, and according to a stage algorithm allowing some missing stage components. Analyses were stratified by sex, age, year of diagnosis, and Charlson Comorbidity Index score.

Results: For colon and rectal cancer, overall TNM completeness was 67.8% (95% confidence interval [CI]: 67.0%–68.5%) and 68.1% (95% CI: 67.0%–69.1%), respectively. For both cancers, completeness decreased with increasing age and level of comorbidity, whereas differences between the sexes were minor. Over the study period, TNM completeness for colon cancer decreased from 71.3% (95% CI: 69.5%–73.0%) to 64.8% (95% CI: 63.0%–66.6%), whereas the completeness for rectal cancer remained stable over time. When using the stage algorithm, the completeness rose markedly, to 81.1% for colon cancer and 79.0% for rectal cancer.

Conclusion: One-third of colon and rectal cancer cases in the Danish Cancer Registry had missing TNM stage information, which varied with age and level of comorbidity. Cancer cases with unknown staging warrant serious consideration of the methodological implications in future epidemiological studies monitoring cancer incidence and outcomes.

Keywords: colorectal neoplasm, neoplasm staging, TNM, registries, epidemiology, cancer

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and the fourth most common cause of cancer-related death.[1] Tumor stage is a key determinant of CRC prognosis and provides guidance to the optimal planning of treatment. Furthermore, the stage is important for monitoring trends in CRC incidence and mortality across populations. The tumor, node, metastasis (TNM) stage classification is based on the anatomic extent of the tumor, including the tumor size (T), the number of lymph nodes involved (N), and the presence of metastases (M).[2]

Since 1943, all incident cancers in Denmark have been recorded in the Danish Cancer Registry (DCR).[3,4] Reporting to the DCR has been mandatory since 1987, and ascertainment of cancer cases in the registry is virtually complete.[3–5] TNM staging has been recorded for cancer cases since 2004.[4] However, no studies have hitherto examined the completeness of TNM staging in the DCR. Some studies have suggested that factors such as age, race, sex, marital status, income, and residence influence the

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proportion of unstaged cancers.[6–8] Given that information on TNM might not be missing at random, unstaged CRCs could bias results of studies monitoring cancer incidence and outcomes. We therefore aimed to evaluate the completeness of CRC staging in the DCR according to the TNM classification – overall, and by sex, age, year of diagnosis, and level of comorbidity.

Methods

We performed this study in Denmark, within a population of 5.4 million inhabitants. The Danish National Health Service provides free medical care by general practitioners and hospitals. All health-related services are registered with a unique ten-digit personal identifier – the CPR number – assigned since 1968 to each resident.[9] This number allows unambiguous individual-level data linkage between Danish registers.

Ascertaining patients with CRC

We used the DCR to identify patients with a primary diagnosis of CRC between January 1, 2004 and December 31, 2009. During this period, the DCR recorded cancer diagnoses according to the International Classification of Disease, 10th revision (ICD-10).[3,4] Colon and rectal cancer cases were identified by the ICD-10 codes C18 and C19–20, respectively. From the DCR, we also obtained information on CPR number, date of diagnosis, age, sex, and TNM stage at diagnosis.

Comorbidity data

The Danish National Patient Register contains data on all nonpsychiatric discharges from hospitals in Denmark since 1977 and all outpatient visits since 1995.[10] Information includes CPR number, date of contact/discharge, and diagnoses according to ICD-10 since 1994. From the Danish National Patient Register, we obtained information on preexisting comorbidity 10 years prior to the date of CRC diagnosis using a modified version of the Charlson Comorbidity Index (CCI). The CCI is based on disease categories that are each weighted according to the adjusted risk of one-year mortality.[11,12] Excluding CRC from the index, we defined the level of comorbidity as low (CCI score = 0), medium (CCI score = 1–2), and high (CCI score ≥ 3).

Statistical analysis

We calculated the completeness of TNM stage registration and the corresponding 95% confidence intervals (CIs), both overall and for each component individually (ie, T, N, and M). The completeness was defined as the number of individuals with no missing factors (ie, T1–4, N0–3, and M0–1) divided by the total number of patients. We stratified completeness by sex, age (0–39 years, 40–59 years, 60–79 years, and ≥ 80 years), year of colon or rectal cancer diagnosis, and CCI score.

Complete information on T, N, and M is necessary to derive a definite TNM stage in the DCR. For additional categorization of colon or rectal cancers into localized, regional, distant, or unknown stages, we designed an algorithm, allowing certain missing stage components, under the assumption that the remaining information was sufficient to provide a meaningful categorization (eg, cancers assigned T4, Nx, M1 in the DCR were categorized as "distant"; see Appendix 1). The algorithm was based on knowledge of tumor growth and clinical coding practice In addition, we restricted the analysis to histologic verified CRC cases.

Analyses were performed using SAS (v 9.2; SAS Institute, Inc, Cary, NC).

Results

Colon cancer

A total of 15,976 patients were diagnosed with colon cancer during the 2004–2009 period (Table 1). Females accounted for 51.5% of the colon cancer cases, with a median age at diagnosis of 74 years. The median age for men was 72 years. Overall TNM completeness was 67.8% (95% CI: 67.0%–68.5%) (Table 1). Examining each stage component, the overall registration proportion was slightly higher for M (83.5% [95% CI: 82.9%–84.0%]) than for T (80.3% [95% CI: 79.7%–80.9%]) and N (76.4% [95% CI: 75.8%–77.1%]) (Table 2). We found that 93.3% of the colon cancer cases were histologically verified. Restricting to this proportion, overall TNM was 70.8% (95% CI: 70.1%–71.5%).Differences in TNM completeness between the sexes were minor, with males exhibiting a slightly higher completeness than females. Completeness of the TNM staging decreased with (1) increasing age, from 68.5% (95% CI: 61.2%–75.1%) in patients <40 years to 57.0% (95% CI: 55.5%–58.5%) in patients ≥ 80 years; (2) year of diagnosis, from 71.3% (95% CI: 69.5%–73.0%) in 2004 to 64.8% (95% CI: 63.0%–66.6%) in 2009; and (3) level of comorbidity, from 70.8% (95% CI: 69.9%–71.7%) in patients with lowest comorbidity (CCI score = 0) to 57.2% (95% CI: 54.8%–59.5%) among those with high level of comorbidity (CCI score ≥ 3) (Table 1). Using the algorithm for stage classification (Appendix 1), we found that 5473 (34.3%) of the colon cancers were localized, whereas regional and distant cases accounted for 3463 (21.7%) and 4022 (25.2%), respectively. A total of 3018 (18.9%) colon cancers were not classifiable according to the algorithm (data not shown).

Table 1 TNM completeness for colon and rectal cancer; overall and by sex, age, year, and comorbidity

	Colon Cancer				Rectal cancer			
	Total	TNM completeness			Total	TNM completeness		
	No.	No.	%	(95% CI)	No.	No.	%	(95% CI)
Overall	15,976	10,824	67.8	(67.0–68.5)	8292	5643	68.1	(67.0–69.1)
Sex								
Female	8233	5534	67.2	(66.2–68.2)	3341	2180	65.3	(63.6–66.9)
Male	7743	5290	68.3	(67.3–69.4)	4951	3463	70.0	(68.7–71.2)
Age								
≤39 years	168	115	68.5	(61.2–75.1)	63	65	78.3	(68.6–86.1)
40–59 years	2327	1737	74.6	(72.9–76.4)	1667	1266	75.9	(73.9–78.0)
60–79 years	9262	6568	70.9	(70.0–71.8)	4926	3517	71.4	(70.1–72.7)
≥ 80 years	4219	2404	57.0	(55.5–58.5)	1616	795	49.2	(46.8–51.6)
Year of diagnosis								
2004	2555	1822	71.3	(69.5–73.0)	1339	930	69.5	(67.0–71.9)
2005	2615	1782	68.1	(66.3–69.9)	1284	858	66.8	(64.2–69.4)
2006	2704	1885	69.7	(68.0–71.4)	1417	962	67.9	(65.4–70.3)
2007	2656	1802	67.9	(66.1–69.6)	1371	950	69.3	(66.8–71.7)
2008	2706	1757	64.9	(63.1–66.7)	1442	938	65.1	(62.6–67.5)
2009	2740	1776	64.8	(63.0–66.6)	1439	1005	69.8	(67.4–72.2)
Comorbidity[a]								
Low	9617	6806	70.8	(69.9–71.7)	5464	3903	71.4	(70.2–72.6)
Medium	4706	3073	65.3	(63.9–66.7)	2192	1409	64.3	(62.3–66.3)
High	1653	945	57.2	(54.8–59.5)	636	331	52.0	(48.2–55.9)

Notes: [a]Level of comorbidity according to the Charlson comorbidity index (CCI) score; Low (CCI score = 0), Medium (CCI score = 1–2), High (CCI score ≥ 3).
Abbreviations: CI, confidence interval; TNM, tumor, node, metastasis.

Table 2 T, N, and M completeness for colon cancer; overall and by sex, age, year, and comorbidity

	Total	T completeness			N completeness			M completeness		
	No.	No.	%	(95% CI)	No.	%	(95% CI)	No.	%	(95% CI)
Overall	15,976	12,831	80.3	(79.7–80.9)	12,212	76.4	(75.8–77.1)	13,334	83.5	(82.9–84.0)
Sex										
Female	8233	6611	80.3	(79.4–81.2)	6257	76.0	(75.1–76.9)	6802	82.6	(81.8–83.4)
Male	7743	6220	80.3	(79.4–81.2)	5955	76.9	(76.0–77.8)	6532	84.4	(83.5–85.2)
Age (in years)										
≤39	168	134	79.8	(73.2–85.3)	128	76.2	(69.3–82.2)	141	83.9	(77.8–88.9)
40–59	2327	1966	84.5	(83.0–85.9)	1914	82.3	(80.7–83.8)	2081	89.4	(88.1–90.6)
60–79	9262	7655	82.7	(81.9–83.4)	7324	79.1	(78.2–79.9)	7950	85.8	(85.1–86.5)
≥ 80	4219	3076	72.9	(71.6–74.2)	2846	67.5	(66.0–68.9)	3162	75.0	(73.6–76.2)
Year of diagnosis										
2004	2555	2205	86.3	(84.9–87.6)	2082	81.5	(80.0–83.0)	2141	83.8	(82.3–85.2)
2005	2615	2191	83.8	(82.3–85.2)	2074	79.3	(77.7–80.8)	2141	81.9	(80.4–83.3)
2006	2704	2223	82.2	(80.7–83.6)	2132	78.9	(77.3–80.4)	2242	82.9	(81.5–84.3)
2007	2656	2104	79.2	(77.6–80.7)	2016	75.9	(74.3–77.5)	2225	83.8	(82.3–85.1)
2008	2706	2048	75.7	(74.0–77.3)	1960	72.4	(70.7–74.1)	2265	83.7	(82.3–85.1)
2009	2740	2060	75.2	(73.5–76.8)	1948	71.1	(69.4–72.8)	2320	84.7	(83.3–86.0)
Comorbidity[a]										
Low	9617	7965	82.8	(82.1–83.6)	7589	78.9	(78.1–79.7)	8242	85.7	(85.0–86.4)
Medium	4706	3690	78.4	(77.2–79.6)	3511	74.6	(73.4–75.8)	3822	81.2	(80.1–82.3)
High	1653	1176	71.1	(68.9–73.3)	1112	67.3	(65.0–69.5)	1270	76.8	(74.8–78.8)

Notes: [a]Level of comorbidity according to the Charlson comorbidity index (CCI) score; Low (CCI score = 0), Medium (CCI score = 1–2), High (CCI score ≥ 3).
Abbreviations: CI, confidence interval; T, tumour; N, node; M, metastasis.

Rectal cancer

Of the 8,292 rectal cancer patients diagnosed during the study period (Table 1), 40.3% were female with a median age at diagnosis of 71 years. Median age for men was 69 years. Overall, TNM was complete for 68.1% (95% CI: 67.0%–69.1%) of the rectal cancer cases. M was the most complete stage component (84.8% [95% CI: 84.0%–85.6%]), T completeness was close to that of M (84.0% [95% CI: 83.2%–84.8%]), but N completeness was considerably lower (72.9% [95% CI: 72.0%–73.9%]) (Table 3). Restricting to

the 95.3% of the rectum cancer cases that were histologically verified left the overall TNM completeness nearly unchanged (69.6% [95% CI: 70.8%–71.5%]). TNM completeness was slightly higher in males compared with females and decreased with increasing age, from 78.3% (95% CI: 68.6%–86.1%) in patients <40 years to 49.2% (95% CI: 46.8%–51.6%) in patients ≥ 80 years. Also, TNM completeness declined with comorbidity level, from 71.4% (95% CI: 70.2%–72.6%) in patients with lowest comorbidity to 52.0% (95% CI: 48.2%–55.9%) in patients with a high comorbidity level. TNM completeness did not vary by year of diagnosis (Table 1). According to our stage algorithm, 2569 (31.0%) rectal cancers were localized, 2350 (28.3%) were regional, and 1633 (19.7%) were distant. For a total of 1740 (21.0%) rectal cancer cases, the TNM stage could not be assessed based on the available information (data not shown).

Discussion

To our knowledge, this nationwide population-based study is the first to evaluate the completeness of TNM registration of CRC in the DCR. Although the ascertaining of cancer diagnoses in the DCR is virtually complete,[3–5] we found that approximately one-third of CRC patients had missing data on TNM classification. In particular, completeness declined with increasing age and level of comorbidity. Using a clinically based stage algorithm, we showed that the proportion of staged cases rose markedly.

The completeness of CRC staging in the US Surveillance, Epidemiology, and End Results, or SEER, database appears to be higher than what we observed in the DCR. Worthington et al reported that only 5.1% of colon and 7.8% of rectal cancers were unstaged during the 1991–2002 period.[8] However, the SEER summary stage is computed using an algorithm that allows staging with one or two missing stage components. Although we also designed a stage algorithm that allowed some missing stage information, it might differ from the SEER template. Thus, the completenesses of TNM staging in the US and Danish registers is probably not directly comparable.

We found that TNM completeness varied substantially by age and level of comorbidity, which is in accordance with previous US studies.[6–8,13,14] In a study examining the proportion of unstaged disease at 18 cancer sites, Merill et al reported a steep increase with age.[6] Likewise, marital status, race, sex, and prognosis of the cancers influenced staging. Koroukian et al reported that patients with more comprehensive needs for care (as measured by dependence of home health care and nursing home care) were two to five times as likely to be unstaged, compared with patients with fewer needs.[13]

TNM completeness for colon cancer in the DCR decreased slightly during the study period, whereas rectal cancer staging remained stable over time. In contrast, a number of studies have reported a decrease in the proportion of patients with unstaged CRCs over recent years.[6–8] In

Table 3 T, N, and M completeness for rectal cancer; overall and by sex, age, year, and comorbidity

	Total	T completeness			N completeness			M completeness		
	No.	No.	%	(95% CI)	No.	%	(95% CI)	No.	%	(95% CI)
Overall	8292	6964	84.0	(83.2–84.8)	6048	72.9	(72.0–73.9)	7032	84.8	(84.0–85.6)
Sex										
Female	3341	2739	82.0	(80.7–83.3)	2354	70.5	(68.9–72.0)	2762	82.7	(81.4–83.9)
Male	4951	4225	85.3	(84.3–86.3)	3694	74.6	(73.4–75.8)	4270	86.3	(85.3–87.2)
Age (in years)										
≤39	83	73	88.0	(79.7–93.6)	69	83.1	(74.0–90.0)	76	91.6	(84.2–96.2)
40–59	1667	1483	89.0	(87.4–90.4)	1338	80.3	(78.3–82.1)	1515	90.9	(89.4–92.2)
60–79	4926	4285	87.0	(86.0–87.9)	3765	76.4	(75.2–77.6)	4275	86.8	(85.8–87.7)
≥ 80	1616	1123	69.5	(67.2–71.7)	876	54.2	(51.8–56.6)	1166	72.2	(69.9–74.3)
Year of diagnosis										
2004	1339	1167	87.2	(85.3–88.9)	998	74.5	(72.2–76.8)	1121	83.7	(81.7–85.6)
2005	1284	1081	84.2	(82.1–86.1)	926	72.1	(69.6–74.5)	1086	84.6	(82.5–86.5)
2006	1417	1201	84.8	(82.8–86.6)	1035	73.0	(70.7–75.3)	1221	86.2	(84.3–87.9)
2007	1371	1158	84.5	(82.5–86.3)	1014	74.0	(71.6–76.2)	1173	85.6	(83.6–87.3)
2008	1442	1156	80.2	(78.1–82.2)	1007	69.8	(67.4–72.2)	1205	83.6	(81.6–85.4)
2009	1439	1201	83.5	(81.5–85.3)	1068	74.2	(71.9–76.4)	1226	85.2	(83.3–87.0)
Comorbidity[a]										
Low	5464	4711	86.2	(85.3–87.1)	4163	76.2	(75.1–77.3)	4749	86.9	(86.0–87.8)
Medium	2192	1793	81.8	(80.1–83.4)	1512	69.0	(67.0–70.9)	1806	82.4	(80.8–83.9)
High	636	460	72.3	(68.8–75.7)	373	58.7	(54.8–62.4)	477	75.0	(71.5–78.3)

Notes: [a]Level of comorbidity according to the Charlson comorbidity index score (CCI); Low (CCI score = 0), Medium (CCI score = 1–2), High (CCI score ≥ 3).
Abbreviations: CI, confidence interval; T, tumour; N, node; M, metastasis.

2004, the DCR computerized and automated the registration of incident cancer cases, facilitating fast notifications from clinicians. A potential negative consequence is that the cancer cases might be reported before the clinical workup has been finalized. However, considering the number of initiatives aiming to improve cancer control, including the implementation of Danish National Cancer Plans in 2000 and 2005,[15,16] and the establishment of a comprehensive CRC database by the Danish Colorectal Cancer Group in 2001,[19] one would have expected improvements in the registration of TNM stage over the study period.

A main strength of this study is its population-based design within the setting of a uniform tax-supported health care system, largely eliminating selection bias. Our study population was identified from updated nationwide registers. Although coding errors on CRC diagnoses and comorbidities cannot be ruled out, data from the DCR and the Danish National Patient Register have been found very complete and highly valid.[3,5,12]

Our study also had limitations. The completeness and accuracy of CRC diagnoses in the automated version of DCR (from 2004 on) have not been specifically validated. Moreover, we had no information on the underlying reasons for the missing information on TNM stages in the DCR, although plausible explanations include incomplete reporting and genuine difficulties on the part of the clinician or pathologist in determining the stage of the particular cancer case. For example, patients who initially received oncological therapy might not have been registered with complete details on TNM. We found that the most vulnerable patients were least likely to undergo staging, suggesting cessation of diagnostic procedures, including lymph node status, if fragility did not allow further treatment. We also observed that approximately 6% of CRC diagnoses were not histologically verified. However, although it might be expected that the majority of non-histologically verified cases pertained to patients with high comorbidity, restriction of the study population to histologically verified CRC cases yielded results quite similar to those presented.

The DCR is a valuable source for cancer research and statistics. Despite the high level of completeness of the diagnoses in this registry, we found that one-third of CRC patients had missing TNM-stage information, although the proportion of unstaged cases declined markedly with our use of a clinically based stage algorithm. However, completeness varied differentially with age and level of comorbidity, indicating that TNM data are not missing at random. This finding warrants serious consideration of the methodological implications in future epidemiological studies on cancer incidence and survival.

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Disclosure

The authors report no conflicts of interest in this work.

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Appendix 1

Appendix 1 Algorithm for colorectal cancer (CRC) staging according to the TNM classification

Tumor stage	TNM[a]
Localized	T1–4,x N0 M0
	T1–2 N0 Mx
	T1 Nx M0,x
Regional	T1–4,x N1–2 M0
Distant	T1–4,x N0–2,x M1
Unknown[b]	T2–4,x Nx M0,x
	T3–4,x N0 Mx
	T1–4,x N1–2 Mx

Notes: [a]In all, 466 CRC cases were assigned N3 (categorized as N2 in the algorithm); [b]Thirty CRC cases were assigned T0, Ta, or Tis (categorized as unknown stage in the algorithm).
Abbreviation: TNM, tumor, node, metastasis.