Weekday of cancer surgery in relation to prognosis

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The text is limited to 2700 words (now 2697), with an abstract of maximum 250 words, a maximum of 5 tables and figures (total), and up to 40 references.

Abstract (max 250 words, now 250)

Background: Later weekday of surgery might reduce the prognosis in esophageal cancer. We aimed to assess whether weekday of surgery influences the prognosis following all commonly performed cancer operations.

Methods: This was a nationwide Swedish population-based cohort study in 1997-2014. Weekday of elective surgery for 10 cancer groups was analyzed in relation to disease-specific and all-cause mortality. Multivariable Cox regression provided hazard ratios with 95% confidence intervals (CI), adjusted for the covariates age, sex, co-morbidity, hospital volume, calendar year, and tumor stage.

Results: Later weekday of surgery, i.e., Thursdays and more so Fridays, was followed by increased HRs of mortality for gastrointestinal and gynecological cancers, but not of cancer of the head/neck, lung, thyroid, breast, urinary tract, or prostate. The adjusted hazard ratio for disease-specific mortality comparing surgery on Friday with Monday were 1.57 (95%CI 1.31-1.88) for esophago-gastric cancer, 1.49 (95%CI 1.17-1.88) for liver-pancreatic-biliary cancer, 1.53 (95%CI 1.44-1.63) for colorectal cancer, and 1.23 (95%CI 1.05-1.44) for ovarian/uterine cancer. Excluding mortality during the initial 90 days of surgery made little change, except for making the association with ovarian/uterine cancer non-significant. The all-cause mortality rates were similar to the disease-specific mortality. The associations were similar in analyses stratified for each of the covariates.

Conclusions: This worse prognosis following later weekday of surgery (Thursday-Friday) for cancer of the gastrointestinal tract and possibly also gynecological tract indicates that these operations should be performed during the first part of the working week (Monday-Wednesday), while no such re-scheduling is needed for surgery of other cancer sites.

Introduction (max 2700 words, now 2741)

Cancer is a growing and global public health concern,[1] and surgery is the cornerstone in the curatively intended treatment of most solid carcinomas.[2] Among 15.2 million individuals diagnosed with cancer worldwide in 2015, over 80% underwent surgery.[2] Centralization of certain complex cancer procedures has been shown to improve the prognosis in a few tumors,[3] but otherwise, research examining surgical strategies that might improve cancer prognosis is sparse.[2] We recently found that later weekday of elective surgery for esophageal cancer negatively influences the prognosis.[4] When comparing surgery on a Friday with a Monday, the 5-year disease-specific mortality was 44% increased.[4] A "weekday effect" has been noted for surgery in general with regards to an increased 30-day postoperative mortality,[5,6] but the study on esophageal cancer surgery was the first to investigate weekday of cancer surgery in relation to long-term prognosis.[4] In the present study, we aimed to evaluate whether weekday of surgery also influences the prognosis in other cancer groups. We hypothesized the surgeons' alertness and thus the level of surgical precision and radicality might be negatively influenced by the cumulative workload during the working week, and that this would particularly influence the outcomes following complex and time-consuming cancer surgery. To test this hypothesis, we conducted a nationwide Swedish study examining the associations between weekday of surgery and mortality for groups of cancer where surgical tumor removal is the main treatment.

Methods

Design

This was a population-based nationwide Swedish cohort study conducted during the period January 1, 1997 to December 31, 2014. A detailed pre-defined study protocol was followed. The study exposure was weekday of elective cancer surgery from Monday to Friday. The main and secondary outcomes were disease-specific mortality and all-cause mortality, respectively. Included in the cohort were patients who had undergone resectional surgery for all common cancer sites where surgery is the main curatively intended treatment. The study was approved by the Regional Ethical Review Board in Stockholm (2015/1916-31/1).

Cohort

Selected as cohort members were adult patients (at least 18 years) who had undergone elective surgical resection corresponding in site and time with the primary cancer diagnosis according to the Swedish Cancer Register. Only carcinomas were considered as defined by the histopathological codes in the Cancer Register. We only included cancer sites where at least an average yearly number of 100 operations were conducted in Sweden during the study period. Resectional surgery was defined by the operation codes in the Swedish Classification of Surgical Procedures from 1997 and onwards. These codes were available in the Swedish Patient Register. Eligible cancer sites were combined into 10 cancer groups on the basis of anatomical proximity, shared clinical characteristics (diagnostic procedures, treatment, and prognosis), and surgical sub-specialty performing the operations. These cancer groups were: 1) esophagus/stomach, 2) liver/pancreas/bile ducts, and 3) colon/rectum, and the remaining seven were cancer of the 4) head/neck, 5) lung, 6) thyroid, 7) breast, 8) kidney/ureter/urine bladder, 9) prostate, and 10) ovary/uterus.

Exposure

The study exposure was each weekday of surgery from Monday to Friday. These data were retrieved from the variable 'date of surgery' in the Swedish Patient Register.

Outcomes

The main and secondary study outcomes were overall disease-specific and all-cause mortality, respectively. These outcomes were retrieved from the Swedish Causes of Death Register until 31st December 2014. Disease-specific mortality was defined as a death caused by a tumor diagnosis of the same type as the one operated for. All-cause mortality was defined as the date of any death during the follow-up.

Covariates

Six covariates were considered due to their influence on prognosis: age, sex, comorbidity, annual hospital volume of each procedure, calendar year of surgery, and tumor stage. Data on age and sex were available in all registers. Comorbidities were recorded in the Patient Register and were defined and categorized according to the most updated version of the well-validated Charlson comorbidity index.[7] Data on annual hospital volume and calendar year of surgery were derived from the Patient Register. Tumor stage data were available only from year 2004 in the Cancer Register. The seventh version of the Union for International Cancer Control TNM-classification was used for tumor staging.[8]

Data retrieval prerequisites

The nationwide Swedish registers used for this study originate from a long tradition of well-maintained and complete recording of diseases, surgical procedures, and deaths among Swedish residents. All physicians are obliged by Swedish law to report these data to the Swedish National Board of Health and Welfare, a governmental agency that maintains these registers. The uniform and tax paid Swedish healthcare system facilitates complete and uniform reporting. Accurate linkage of each participant's information between registers was made possible by the unique personal identity number, a system for identification of all Swedish residents, which was recorded by all registers used in the present study.[9] This 10-digit number was assigned to each Swedish resident in 1947 and is thereafter assigned to all new residents upon birth or immigration, and has been validated as a robust tool for research purposes.[10]

Data sources and validity

Data sources were three nationwide Swedish registers:

The Swedish Cancer Register: The cancer diagnoses were retrieved from the Cancer Register, initiated in 1958. The completeness of recording all new cancers in the Cancer Register is 96%,[11] and is even higher in patients who undergo surgery. Data on tumor stage have excellent completeness (98%) and concordance (98%) for resected esophageal cancer.[12]

The Swedish Patient Register: Data on surgery and comorbidity were collected from the Patient Register. This register contains all in-hospital diagnoses and surgical procedures in Sweden since 1987 and all out-patient specialist care since 2001.[13] The exposure variable 'date of surgery' is available since 1997, and has 95% accuracy for esophageal cancer surgery.[14] The codes representing cancer surgery in the Patient Register have shown almost 100% positive predictive values compared to operation charts.[15,16] The diagnoses defining comorbidities have good nationwide coverage for all diagnoses, with positive predictive values ranging between 85% and 95%.[13]

The Swedish Causes of Death Register: Data on dates and causes of deaths were retrieved from the Causes of Death Register, initiated in 1952. This Register has 99% completeness of causes of deaths and 100% completeness of dates of deaths for all deceased Swedish residents.[17]

Statistical analysis

Each weekday of surgery (Monday to Friday) was analyzed in relation to risk of overall mortality, using Monday as the reference category. Each of the 10 cancer groups was analyzed separately. Cox regression was used to calculate crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI). The covariates included in the model (with categorizations) were: 1) age at surgery (continuous variable), 2) sex (male or female), 3) comorbidity (Charlson index 0, 1-2, or ≥3), 4) hospital volume (in quartiles for each cancer group), and 5) calendar year of surgery (1997-2002, 2003- 2008, or 2009-2014). Additionally, tumor stage (I-II or III-IV) was included in a second model as well as in a sensitivity analysis for the period 2004 to 2014 when this variable was available. Finally, stratified analyses were performed for each of the six covariates, which were dichotomized to preserve statistical power as: below and above mean age, male and female sex, Charlson comorbidity index 0 and ≥1, hospital volume quartiles 1-2 and 3-4 of, and calendar year 1997-2005 and 2006-2014. The statistical software SAS version 9.4 (SAS Institute, Cary, NC) was used for data management and statistical analysis.

Results

Patients

Among all 228,927 patients included in the study, 52,589 (23.0%) had surgery on a Monday, 61,045 (26.7%) on Tuesday, 54,140 (23.6%) on Wednesday, 49,833 (21.8%) on Thursday, and 11,320 (4.9%) had their surgery on a Friday. Numbers and characteristics of the study participants per cancer group are presented in Table 1. The mean age was between 62 and 71 years for the studied cancer groups, except for thyroid cancer with a mean age of 52 years. There was a clear male predominance in esophago-gastric cancer, liver-pancreas-bile duct cancer, head-and-neck cancer, and urinary tract cancer, while thyroid cancer was overrepresented in women. Patients with cancer of the thyroid, breast, ovary-uterus, and prostate had less comorbidity than other tumor groups. The number of operations increased during the study period in all cancer groups, except for esophago-gastric cancer (Table 1).

Esophago-gastric cancer

Surgery for esophago-gastric cancer indicated that later weekday in the working week, i.e. on Thursdays and Fridays, was followed by increased HRs of mortality (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 1.57 (95% CI 1.31-1.88). The corresponding HRs were 1.45 (95% CI 0.87-2.39) for esophageal cancer and 1.70 (95% CI 1.38-2.09) for gastric cancer when analyzed separately.

Hepatico-pancreatico-biliary cancer

Surgery for cancer in the liver/pancreas/bile ducts showed increased mortality rates after later weekday of surgery, i.e. Thursdays and Fridays (Table 2). Comparing surgery on Friday with Monday, the adjusted HRs of disease-specific mortality was 1.49 (95% CI 1.17-1.88).

Colorectal cancer

The colorectal cancer mortality was negatively influenced by later weekday of surgery, but only for Fridays (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 1.53 (95% CI 1.44-1.63).

Head-and-neck cancer

Later weekday of surgery did not increase the mortality in head-and-neck cancer (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 0.77 (95% CI 0.56-1.06).

Lung cancer

For lung cancer, the point HRs were increased for surgery on Tuesdays to Fridays compared to Monday, but there was no trend with worse prognosis following later weekday of surgery (Table 2). The adjusted HR assessing disease-specific mortality comparing surgery on Friday with Monday was 1.04 (95% CI 0.82-1.31).

Thyroid cancer

Later weekday of surgery for thyroid cancer did not statistically significantly increase the risk of mortality (Table 2). Comparing surgery on Friday with Monday, the HRs of disease-specific and all-cause mortality were 1.14 (95% CI 0.68-1.91) and 0.85 (95% CI 0.55-1.31), respectively.

Breast cancer

Later weekday of surgery for breast cancer did not increase the mortality (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 0.90 (95% CI 0.83-0.98).

Urinary tract cancer

Later weekday of surgery for cancer of the kidney, ureter, or bladder did not entail increased HRs of mortality (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 0.98 (95% CI 0.79-1.21).

Prostate cancer

For prostate cancer, later weekday of surgery did not increase the mortality (Table 2). Comparing surgery on Friday with Monday, the adjusted HR of disease-specific mortality was 0.92 (95% CI 0.61-1.38).

Gynecological cancer

For cancer of the uterus or ovary, surgery on Fridays entailed moderately increased HRs of mortality (Table 2). Surgery on Friday showed an adjusted HR of disease-specific mortality of 1.23 (95% CI 1.05-1.44) compared to Monday.

Sensitivity analyses

The all-cause mortality rates were generally similar to the disease-specific mortality rates (Table 2). The findings remained stable after excluding the patients who died within 90 days of surgery, except for that the association between weekday of surgery and gynecological cancers became statistically non-significant (Table 3). In analyses of the sub-group of patients with data on tumor stage, adjustment for this variable did not strongly influence the point HRs of disease-specific or all-cause mortality rates (data not shown).

Stratified analyses

The analyses of disease-specific mortality stratified by age, sex, co-morbidity, hospital volume, and calendar year showed occasional limited differences between the categories, but not any clear patterns of deviances from the overall results (Table 4). In a sub-group analysis of patients with tumor stage data, the HRs did not change much with stratification. For example, when comparing surgery on Friday with Monday, the HR for tumor stages I-II and III-IV for cancer of the liver-pancreas-bile ducts were 1.42 (95% CI 0.938-2.16) and 1.38 (0.91-2.080), respectively, and the corresponding HRs for colorectal cancer were 1.30 (95% CI 1.06-1.59) and 1.54 (1.40-1.70).

Discussion

This first study examining weekday of surgery in relation to disease-specific mortality in several cancer groups, provides some evidence that later weekday of elective resectional surgery increases the disease-specific and all-cause mortality for cancer of the gastrointestinal tract (esophago-gastric, liver-pancreas-bile ducts, and colon-rectum) and to a weaker extent also the gynecological tract (uterus-ovary). No such associations were found for cancer surgery of the head-and-neck, lung, thyroid, breast, urinary tract, or prostate.

The nationwide and population-based design with unselected inclusion of patients in Sweden who underwent surgical removal of common cancers during the study period counteracted selection bias, made it possible to compare differences between cancer sites, and provided large sample size. Due to the possibility to follow all patients up through their personal identity numbers, there were no losses to follow-up. Other methodological advantages include the accurate assessment of the exposure (weekday of surgery) and outcome (disease-specific and all-cause mortality). Confounding is a source of error in observational studies in general. However, we could not from the literature identify any factor that would conceivably influence the choice of performing the surgery on any specific weekday, which is needed to define confounding.[18] Nevertheless, the results were adjusted for six prognostic factors, and this adjustment did not change the results much, indicating lack of confounding from these factors. Moreover, there were no clear indications of effect modification of these covariates in the stratified analyses. Many tests increase the risk of chance errors (type I). Therefore, closely located cancer sites with similar characteristics and operated by the same surgical sub-specialty were combined into larger groups. This strategy also secured the statistical precision. It is unlikely that the consistent patterns of the results are due to chance errors.

The study was prompted by the weekday effect on mortality in esophageal cancer.[4] That study included patients who underwent surgery partly during another study period (1987-2010) and where data on tumor stage were available for all patients, while in the present study tumor stage data were only available in a subset of patients. The similar esophageal cancer disease-specific mortality (HR 1.44 in the previous study and 1.45 in the present, comparing surgery on Friday with Monday) supports the finding of a weekday effect on prognosis, and further indicates that tumor stage was not a confounder in this study. The finding that the associations were limited to gastrointestinal and gynecological cancers, and no other studied cancer groups, argues against biases shared for cancer surgery in general, e.g. selection of less healthy patients or patients with worse tumor stages or with semi-acute indications for surgery at the end of the week. Most operations were conducted in the first part of the week, but still 17% to 24% of the operations for cancer groups associated with weekday of surgery were conducted on Thursdays or Fridays.

Disease-specific mortality was chosen as main outcome since it mirrors deaths from tumor recurrence better than all-cause mortality. The hypothesis that tiredness later in the week reduces the surgical accuracy and radicality would entail increased risk of tumor recurrence, particularly for complex and long procedures was supported by the increased disease-specific mortality following later weekday of surgery for gastrointestinal and gynecological cancer. Moreover, the fact that exclusion of the first 90 postoperative days did not change the results argues against a “weekend effect”, i.e., that patients who undergo surgery during the last part of the week get less good healthcare during weekends, which would increase the short-term mortality.[5,6] However, the lack of weekday effect in other complex cancer procedures argues against this hypothesis. A potential explanation for these findings is the typically heavier on-call duties encountered by general surgeons (conducting gastrointestinal cancer surgery) and gynecologists (performing surgery for gynecological cancer). General surgeons usually have responsibility for the many general emergency surgery patients and trauma patients, and gynecologists cover the many obstetrics and general gynecology emergency cases. It might not be ideal to perform complex elective cancer surgery after a week of heavy on-calls and surgery nighttime as well as daytime. The surgery specialties conducting cancer surgery for cancer of the head-and-neck (otolaryngologists), lung (thoracic surgeons), and urinary tract or prostate (urologists) usually have a less heavy on-call burden and less nighttime operations compared to general surgeons and gynecologists. Surgery for cancer of the thyroid and breast is usually conducted by general surgeons, but these procedures are less complex and time-consuming than the other cancer procedures studied. Thus, complex and long-lasting cancer procedures combined with the heavy on-call duties might contribute to the increased disease-specific mortality following later weekday of surgery for gastrointestinal and gynecological cancer.

In conclusion, this nationwide and population-based study of nearly a quarter of a million patients who underwent surgery for commonly performed cancer in Sweden indicates that the prognosis in gastrointestinal and gynecological tract cancer is influenced by weekday of surgery, while no such influence was found for cancer of the head-and-neck, lung, thyroid, breast, urinary tract, or prostate. Re-scheduling of operation days for some specific cancer procedures might improve the outcomes of the surgical treatment.

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Table 1. Characteristics of patients who have undergone surgery for cancer, presented as number and percentages.

Cancer group	Total	Age	Sex		Charlson comorbidity score			Hospital volume (quartiles)				Calendar period		
		Mean (SD)	Male	Female	0	1-2	≥3	I	II	III	IV	1997-2002	2003-2008	2009-2014
Esophago-gastric	6124	68 (11)	4017 (66)	2107 (34)	3642 (59)	2145 (35)	337 (6)	1515 (25)	1559 (25)	1270 (21)	1780 (29)	2115 (35)	1993 (33)	2016 (33)
Liver-pancreas-bile ducts	4073	65 (10)	2095 (51)	1978 (49)	2160 (53)	1681 (41)	232 (6)	1000 (25)	906 (22)	792 (19)	1375 (34)	779 (19)	1143 (28)	2151 (53)
Colorectal	60899	71 (11)	31356 (51)	29543 (49)	36477 (60)	20570 (34)	3852 (6)	14843 (24)	15444 (25)	14074 (23)	16538 (27)	16597 (27)	19603 (32)	24699 (41)
Head-neck	5323	63 (13)	3334 (63)	1989 (37)	3451 (65)	1623 (30)	249 (5)	1068 (20)	1408 (26)	590 (11)	2257 (42)	1232 (23)	1669 (31)	2422 (46)
Lung	2537	65 (9)	1287 (51)	1250 (49)	1379 (54)	1021 (40)	137 (5)	539 (21)	554 (22)	739 (29)	705 (28)	663 (26)	781 (31)	1093 (43)
Thyroid	4691	52 (17)	1284 (27)	3407 (73)	3695 (79)	877 (19)	119 (3)	1128 (24)	1212 (26)	834 (18)	1517 (32)	988 (21)	1281 (27)	2422 (52)
Breast	78824	62 (13)	-	78824 (100)	61311 (78)	15777 (20)	1736 (2)	19065 (24)	19020 (24)	17751 (23)	22988 (29)	22016 (28)	24932 (32)	31876 (40)
Kidney-bladder	9044	66 (11)	5433 (60)	3611 (40)	5475 (61)	3106 (34)	463 (5)	2033 (22)	2241 (25)	2200 (24)	2570 (28)	2410 (27)	2987 (33)	3647 (40)
Prostate	28481	63 (5)	28481 (100)	-	22457 (79)	5778 (20)	246 (1)	6755 (24)	6877 (24)	6441 (23)	8408 (30)	2718 (10)	9955 (35)	15808 (56)
Ovary-uterus	28931	64 (13)	-	28931 (100)	21713 (75)	6547 (23)	671 (2)	6833 (24)	6766 (23)	7440 (26)	7892 (27)	8078 (28)	9505 (33)	11348 (39)

Table 2. Weekday of surgery for cancer in relation to overall disease-specific and all-cause mortality, expressed as hazard ratio (HR) with 95% confidence interval (CI).

Cancer group	Weekday of surgery	Patients	Disease-specific mortality		All-cause mortality	
		Number (%)	Crude HR (95% CI)	Adjusted HR* (95% CI)	Crude HR (95% CI)	Adjusted HR* (95% CI)
Esophago-gastric	Monday	2078 (33)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	1398 (22)	1.04 (0.96-1.14)	1.05 (0.96-1.15)	1.03 (0.95-1.12)	1.05 (0.97-1.14)
	Wednesday	1566 (25)	1.00 (0.92-1.09)	1.00 (0.92-1.09)	1.01 (0.94-1.10)	1.02 (0.94-1.10)
	Thursday	904 (14)	1.13 (1.03-1.25)	1.11 (1.00-1.22)	1.09 (1.00-1.20)	1.07 (0.97-1.17)
	Friday	178 (3)	1.55 (1.29-1.85)	1.57 (1.31-1.88)	1.48 (1.25-1.76)	1.50 (1.26-1.78)
Liver-pancreas-bile ducts	Monday	1331 (31)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	893 (21)	1.01 (0.90-1.13)	1.07 (0.96-1.20)	1.02 (0.91-1.13)	1.08 (0.97-1.20)
	Wednesday	1137 (27)	1.01 (0.91-1.12)	1.01 (0.91-1.12)	1.02 (0.93-1.13)	1.02 (0.93-1.13)
	Thursday	595 (14)	1.20 (1.06-1.35)	1.25 (1.10-1.41)	1.20 (1.07-1.35)	1.25 (1.11-1.40)
	Friday	117 (3)	1.39 (1.10-1.75)	1.49 (1.17-1.88)	1.32 (1.05-1.66)	1.40 (1.11-1.76)
Colorectal	Monday	11642 (18)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	18631 (29)	0.98 (0.94-1.02)	0.96 (0.92-1.00)	0.99 (0.95-1.02)	0.97 (0.94-1.01)
	Wednesday	12509 (20)	1.04 (0.99-1.08)	1.01 (0.96-1.06)	1.04 (1.01-1.08)	1.02 (0.98-1.05)
	Thursday	15053 (23)	1.04 (1.00-1.09)	0.99 (0.95-1.04)	1.07 (1.03-1.10)	1.01 (0.98-1.05)
	Friday	3064 (5)	1.62 (1.52-1.73)	1.53 (1.44-1.63)	1.53 (1.45-1.62)	1.44 (1.37-1.52)
Head-neck	Monday	928 (17)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	1902 (35)	1.19 (1.03-1.39)	1.14 (0.98-1.33)	1.18 (1.04-1.34)	1.15 (1.01-1.31)
	Wednesday	919 (17)	0.97 (0.81-1.16)	0.99 (0.83-1.19)	1.01 (0.87-1.17)	1.03 (0.89-1.19)
	Thursday	1353 (25)	0.95 (0.81-1.12)	0.93 (0.79-1.11)	1.03 (0.91-1.18)	1.02 (0.89-1.18)
	Friday	221 (4)	0.73 (0.53-1.01)	0.77 (0.56-1.06)	0.82 (0.64-1.05)	0.83 (0.65-1.06)
Lung	Monday	609 (23)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	572 (22)	1.19 (1.00-1.42)	1.15 (0.96-1.37)	1.18 (1.01-1.38)	1.15 (0.98-1.35)
	Wednesday	632 (24)	1.32 (1.12-1.56)	1.27 (1.07-1.50)	1.20 (1.03-1.39)	1.17 (1.00-1.36)
	Thursday	480 (18)	1.28 (1.07-1.53)	1.20 (1.00-1.44)	1.19 (1.01-1.40)	1.12 (0.95-1.32)
	Friday	244 (9)	1.09 (0.87-1.37)	1.04 (0.82-1.31)	1.07 (0.87-1.32)	1.03 (0.84-1.27)
Thyroid	Monday	1214 (26)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	1091 (23)	1.16 (0.89-1.51)	1.09 (0.83-1.42)	1.09 (0.89-1.34)	1.00 (0.81-1.23)
	Wednesday	1250 (26)	1.01 (0.77-1.31)	0.99 (0.75-1.29)	1.13 (0.93-1.38)	1.08 (0.89-1.33)
	Thursday	1010 (21)	1.10 (0.84-1.44)	1.13 (0.86-1.49)	0.95 (0.77-1.19)	1.01 (0.81-1.25)
	Friday	126 (3)	1.56 (0.93-2.60)	1.14 (0.68-1.91)	1.19 (0.77-1.84)	0.85 (0.55-1.32)
Breast	Monday	18247 (23)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	18799 (24)	1.01 (0.96-1.07)	0.97 (0.92-1.02)	1.05 (1.01-1.09)	0.99 (0.95-1.03)
	Wednesday	19738 (25)	0.99 (0.94-1.04)	0.95 (0.91-1.01)	1.03 (0.99-1.07)	0.97 (0.94-1.01)
	Thursday	17477 (22)	0.97 (0.92-1.03)	0.94 (0.89-1.00)	1.01 (0.97-1.05)	0.98 (0.94-1.02)
	Friday	4563 (6)	0.93 (0.85-1.01)	0.90 (0.83-0.98)	0.96 (0.90-1.03)	0.94 (0.88-1.01)
Kidney-bladder	Monday	2518 (27)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	2076 (22)	1.04 (0.94-1.15)	1.04 (0.94-1.16)	1.05 (0.96-1.14)	1.05 (0.96-1.14)
	Wednesday	2460 (27)	0.92 (0.83-1.02)	0.91 (0.82-1.01)	0.95 (0.87-1.03)	0.93 (0.86-1.02)
	Thursday	1671 (18)	1.01 (0.91-1.13)	1.00 (0.90-1.11)	1.01 (0.92-1.11)	1.01 (0.92-1.10)
	Friday	319 (3)	0.96 (0.77-1.19)	0.98 (0.79-1.21)	0.90 (0.75-1.08)	0.94 (0.78-1.13)

Prostate	Monday	7775 (27)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	6432 (22)	0.99 (0.80-1.21)	0.98 (0.79-1.20)	1.07 (0.94-1.21)	1.06 (0.93-1.21)
	Wednesday	7573 (26)	0.89 (0.72-1.10)	0.89 (0.72-1.10)	1.00 (0.88-1.14)	1.00 (0.88-1.14)
	Thursday	4861 (17)	0.82 (0.65-1.04)	0.83 (0.65-1.06)	0.95 (0.82-1.09)	0.95 (0.82-1.10)
	Friday	1840 (6)	0.88 (0.59-1.31)	0.92 (0.61-1.38)	0.94 (0.73-1.20)	0.96 (0.75-1.23)
Ovary-uterus	Monday	6247 (21)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Tuesday	9251 (31)	1.00 (0.94-1.07)	1.00 (0.94-1.07)	0.99 (0.94-1.05)	1.01 (0.96-1.07)
	Wednesday	6356 (21)	0.97 (0.90-1.04)	0.98 (0.91-1.05)	0.98 (0.93-1.04)	1.00 (0.94-1.06)
	Thursday	6429 (22)	1.07 (1.00-1.15)	1.05 (0.98-1.13)	1.03 (0.98-1.10)	1.03 (0.97-1.09)
	Friday	648 (2)	1.17 (1.00-1.37)	1.23 (1.05-1.44)	1.08 (0.94-1.24)	1.17 (1.02-1.34)

* Adjusted for age at surgery (continuous variable), sex (male or female), comorbidity (Charlson index 0, 1-2, or ≥3), hospital volume (in quartiles for each cancer group), and calendar year of surgery (1997-2002, 2003- 2008, or 2009-2014).

Table 3. Weekday of surgery for cancer in relation to overall disease-specific mortality, stratified by covariates, expressed as hazard ratio (HR) with 95% confidence interval (CI).

Cancer	Stratified by		Weekday of surgery				
			Monday	**Tuesday**	**Wednesday**	**Thursday**	**Friday**
			HR (95% CI)*	HR (95% CI)*	HR (95% CI)*	HR (95% CI)*	HR (95% CI)*
Esophago-gastric	**Age**	<65	1.00 (reference)	1.02 (0.88-1.18)	0.93 (0.80-1.08)	1.03 (0.86-1.23)	1.30 (0.90-1.86)
		≥65	1.00 (reference)	1.07 (0.96-1.19)	1.03 (0.93-1.14)	1.15 (1.02-1.29)	1.69 (1.37-2.09)
	Sex	Male	1.00 (reference)	1.03 (0.93-1.15)	0.99 (0.89-1.10)	1.08 (0.96-1.22)	1.49 (1.18-1.88)
		Female	1.00 (reference)	1.10 (0.94-1.28)	1.01 (0.88-1.17)	1.15 (0.98-1.36)	1.72 (1.28-2.30)
	Charlson comorbidity	0	1.00 (reference)	1.01 (0.90-1.13)	0.99 (0.89-1.11)	1.10 (0.97-1.25)	1.33 (1.03-1.70)
		≥1	1.00 (reference)	1.12 (0.98-1.28)	1.00 (0.88-1.14)	1.11 (0.95-1.30)	1.97 (1.51-2.56)
	Hospital volume (quartiles)	1+2	1.00 (reference)	1.17 (1.03-1.33)	1.01 (0.90-1.13)	1.17 (1.03-1.34)	1.53 (1.23-1.92)
		3+4	1.00 (reference)	0.97 (0.86-1.09)	1.00 (0.88-1.14)	1.04 (0.90-1.20)	1.73 (1.26-2.38)
	Calendar period	1997-2005	1.00 (reference)	1.03 (0.93-1.15)	0.94 (0.84-1.05)	1.05 (0.93-1.18)	1.77 (1.40-2.24)
		2006-2014	1.00 (reference)	1.06 (0.92-1.22)	1.10 (0.96-1.26)	1.22 (1.04-1.44)	1.37 (1.03-1.83)

Liver-pancreas-bile ducts	**Age**	<65	1.00 (reference)	1.26 (1.06-1.50)	1.13 (0.96-1.33)	1.19 (0.97-1.45)	1.52 (1.01-2.29)
		≥65	1.00 (reference)	0.94 (0.81-1.09)	0.93 (0.81-1.06)	1.29 (1.10-1.51)	1.46 (1.09-1.94)
	Sex	Male	1.00 (reference)	1.00 (0.85-1.17)	1.07 (0.93-1.23)	1.23 (1.03-1.46)	1.26 (0.86-1.84)
		Female	1.00 (reference)	1.15 (0.98-1.35)	0.94 (0.81-1.09)	1.27 (1.07-1.52)	1.67 (1.23-2.25)
	Charlson comorbidity	0	1.00 (reference)	1.08 (0.93-1.25)	0.93 (0.81-1.07)	1.27 (1.08-1.50)	1.57 (1.12-2.18)
		≥1	1.00 (reference)	1.05 (0.88-1.24)	1.11 (0.95-1.29)	1.22 (1.02-1.47)	1.41 (1.01-1.96)
	Hospital volume (quartiles)	1+2	1.00 (reference)	1.15 (0.98-1.34)	0.99 (0.86-1.14)	1.35 (1.13-1.61)	1.98 (1.42-2.75)
		3+4	1.00 (reference)	0.91 (0.78-1.07)	1.00 (0.86-1.17)	1.13 (0.95-1.35)	1.10 (0.79-1.53)
	Calendar period	1997-2005	1.00 (reference)	1.26 (1.06-1.49)	0.95 (0.81-1.11)	1.31 (1.07-1.61)	1.30 (0.84-2.01)
		2006-2014	1.00 (reference)	0.96 (0.83-1.11)	1.07 (0.93-1.22)	1.21 (1.04-1.42)	1.54 (1.16-2.05)
Colon-rectum	**Age**	<65	1.00 (reference)	0.97 (0.89-1.06)	1.06 (0.96-1.17)	0.98 (0.89-1.08)	1.39 (1.21-1.60)
		≥65	1.00 (reference)	0.95 (0.90-0.99)	1.00 (0.95-1.05)	1.00 (0.95-1.05)	1.60 (1.49-1.72)
	Sex	Male	1.00 (reference)	0.94 (0.89-1.00)	0.99 (0.93-1.06)	0.98 (0.92-1.04)	1.57 (1.44-1.71)
		Female	1.00 (reference)	0.97 (0.92-1.04)	1.03 (0.96-1.10)	1.01 (0.94-1.07)	1.50 (1.37-1.64)
	Charlson comorbidity	0	1.00 (reference)	0.98 (0.93-1.03)	1.01 (0.95-1.07)	1.01 (0.95-1.07)	1.52 (1.40-1.65)
		≥1	1.00 (reference)	0.93 (0.87-0.99)	1.02 (0.95-1.09)	0.98 (0.91-1.04)	1.56 (1.41-1.71)
	Hospital volume (quartiles)	1+2	1.00 (reference)	0.89 (0.84-0.94)	0.95 (0.89-1.01)	0.92 (0.87-0.98)	1.39 (1.27-1.52)
		3+4	1.00 (reference)	1.02 (0.96-1.08)	1.07 (1.00-1.14)	1.05 (0.99-1.12)	1.66 (1.52-1.82)
	Calendar period	1997-2005	1.00 (reference)	0.92 (0.87-0.97)	0.98 (0.93-1.04)	0.97 (0.91-1.02)	1.36 (1.25-1.47)
		2006-2014	1.00 (reference)	1.01 (0.94-1.07)	1.04 (0.97-1.12)	1.03 (0.96-1.10)	1.84 (1.67-2.02)
Head-neck	**Age**	<65	1.00 (reference)	1.14 (0.91-1.43)	0.91 (0.69-1.19)	0.80 (0.62-1.04)	0.70 (0.42-1.15)
		≥65	1.00 (reference)	1.15 (0.94-1.42)	1.09 (0.86-1.38)	1.04 (0.84-1.31)	0.86 (0.56-1.30)
	Sex	Male	1.00 (reference)	1.14 (0.94-1.38)	0.99 (0.79-1.24)	0.93 (0.75-1.15)	0.80 (0.53-1.18)
		Female	1.00 (reference)	1.15 (0.88-1.49)	1.00 (0.74-1.35)	0.94 (0.71-1.24)	0.73 (0.43-1.25)
	Charlson comorbidity	0	1.00 (reference)	1.11 (0.91-1.35)	0.89 (0.71-1.12)	0.82 (0.66-1.02)	0.62 (0.40-0.97)
		≥1	1.00 (reference)	1.19 (0.94-1.52)	1.17 (0.88-1.55)	1.12 (0.86-1.45)	1.00 (0.63-1.59)
	Hospital volume (quartiles)	1+2	1.00 (reference)	0.97 (0.78-1.20)	1.01 (0.82-1.25)	0.84 (0.65-1.08)	0.70 (0.45-1.08)
		3+4	1.00 (reference)	1.33 (1.03-1.72)	0.90 (0.65-1.25)	1.04 (0.80-1.36)	0.74 (0.46-1.20)
	Calendar period	1997-2005	1.00 (reference)	1.07 (0.87-1.33)	1.00 (0.78-1.27)	0.89 (0.71-1.11)	0.72 (0.47-1.09)
		2006-2014	1.00 (reference)	1.24 (0.99-1.55)	0.98 (0.75-1.29)	1.01 (0.79-1.29)	0.83 (0.50-1.37)
Lung	**Age**	<65	1.00 (reference)	1.06 (0.82-1.39)	1.14 (0.89-1.47)	1.15 (0.87-1.52)	1.16 (0.83-1.62)

		≥65	1.00 (reference)	1.22 (0.96-1.54)	1.38 (1.10-1.73)	1.23 (0.97-1.56)	0.94 (0.68-1.30)
	Sex	Male	1.00 (reference)	1.02 (0.81-1.29)	1.20 (0.97-1.50)	1.14 (0.91-1.44)	0.96 (0.71-1.31)
		Female	1.00 (reference)	1.34 (1.02-1.75)	1.35 (1.04-1.75)	1.27 (0.95-1.69)	1.14 (0.80-1.63)
	Charlson comorbidity	0	1.00 (reference)	1.10 (0.87-1.39)	1.14 (0.91-1.43)	1.18 (0.94-1.50)	0.90 (0.66-1.23)
		≥1	1.00 (reference)	1.21 (0.93-1.59)	1.43 (1.11-1.83)	1.21 (0.91-1.60)	1.25 (0.89-1.77)
	Hospital volume (quartiles)	1+2	1.00 (reference)	1.03 (0.80-1.33)	1.17 (0.92-1.49)	1.17 (0.91-1.51)	0.91 (0.65-1.29)
		3+4	1.00 (reference)	1.26 (0.99-1.61)	1.36 (1.08-1.71)	1.19 (0.91-1.54)	1.16 (0.85-1.60)
	Calendar period	1997-2005	1.00 (reference)	1.10 (0.87-1.40)	1.21 (0.97-1.51)	1.20 (0.94-1.52)	1.00 (0.74-1.34)
		2006-2014	1.00 (reference)	1.17 (0.89-1.53)	1.30 (1.00-1.69)	1.19 (0.90-1.57)	1.02 (0.69-1.49)
Breast	**Age**	<65	1.00 (reference)	0.97 (0.89-1.04)	0.96 (0.88-1.04)	0.90 (0.83-0.97)	0.88 (0.78-1.00)
		≥65	1.00 (reference)	0.97 (0.90-1.04)	0.96 (0.90-1.04)	0.98 (0.91-1.05)	0.92 (0.81-1.03)
	Charlson comorbidity	0	1.00 (reference)	0.96 (0.90-1.02)	0.94 (0.88-1.00)	0.94 (0.88-1.00)	0.86 (0.77-0.95)
		≥1	1.00 (reference)	0.99 (0.89-1.10)	1.00 (0.91-1.11)	0.96 (0.86-1.07)	1.04 (0.88-1.22)
	Hospital volume (quartiles)	1+2	1.00 (reference)	1.01 (0.94-1.09)	0.98 (0.91-1.06)	0.97 (0.90-1.05)	0.91 (0.81-1.03)
		3+4	1.00 (reference)	0.90 (0.82-0.97)	0.94 (0.87-1.02)	0.91 (0.84-0.99)	0.91 (0.80-1.03)
	Calendar period	1997-2005	1.00 (reference)	0.97 (0.91-1.03)	0.96 (0.90-1.02)	0.94 (0.88-1.00)	0.84 (0.76-0.93)
		2006-2014	1.00 (reference)	0.98 (0.88-1.08)	0.93 (0.85-1.03)	0.95 (0.86-1.05)	1.07 (0.91-1.26)
Prostate	**Age**	<65	1.00 (reference)	1.12 (0.83-1.50)	0.88 (0.64-1.19)	0.89 (0.63-1.25)	0.94 (0.51-1.72)
		≥65	1.00 (reference)	0.84 (0.63-1.13)	0.90 (0.68-1.20)	0.79 (0.57-1.11)	0.90 (0.52-1.55)
	Charlson comorbidity	0	1.00 (reference)	0.98 (0.78-1.25)	0.84 (0.66-1.07)	0.84 (0.64-1.10)	0.82 (0.51-1.32)
		≥1	1.00 (reference)	0.95 (0.62-1.48)	1.05 (0.69-1.62)	0.83 (0.50-1.39)	1.30 (0.61-2.78)
	Hospital volume (quartiles)	1+2	1.00 (reference)	0.98 (0.73-1.32)	0.87 (0.66-1.14)	1.04 (0.74-1.47)	0.75 (0.39-1.44)
		3+4	1.00 (reference)	1.00 (0.74-1.35)	0.91 (0.66-1.26)	0.72 (0.51-1.00)	1.07 (0.63-1.82)
	Calendar period	1997-2005	1.00 (reference)	1.09 (0.85-1.41)	0.90 (0.69-1.17)	0.93 (0.70-1.24)	0.77 (0.43-1.40)
		2006-2014	1.00 (reference)	0.80 (0.55-1.16)	0.90 (0.64-1.26)	0.70 (0.45-1.08)	1.02 (0.59-1.79)
Ovary-uterus	**Age**	<65	1.00 (reference)	1.00 (0.90-1.11)	0.91 (0.81-1.02)	1.07 (0.96-1.19)	1.03 (0.80-1.33)
		≥65	1.00 (reference)	1.00 (0.92-1.09)	1.02 (0.93-1.12)	1.04 (0.95-1.14)	1.36 (1.10-1.67)
	Charlson comorbidity	0	1.00 (reference)	0.98 (0.91-1.05)	0.94 (0.87-1.02)	1.03 (0.95-1.11)	1.25 (1.04-1.50)
		≥1	1.00 (reference)	1.09 (0.96-1.24)	1.09 (0.95-1.25)	1.13 (0.99-1.30)	1.19 (0.87-1.63)
	Hospital volume (quartiles)	1+2	1.00 (reference)	1.04 (0.94-1.14)	1.03 (0.93-1.14)	1.18 (1.06-1.30)	1.42 (1.15-1.76)
		3+4	1.00 (reference)	0.97 (0.89-1.06)	0.93 (0.84-1.03)	0.97 (0.88-1.07)	1.04 (0.82-1.32)

	Calendar period	1997-2005	1.00 (reference)	1.01 (0.92-1.10)	0.99 (0.90-1.08)	1.10 (1.00-1.20)	1.40 (1.15-1.72)
		2006-2014	1.00 (reference)	0.99 (0.90-1.09)	0.97 (0.87-1.08)	0.98 (0.88-1.09)	1.01 (0.78-1.31)
Kidney-bladder	**Age**	<65	1.00 (reference)	1.10 (0.93-1.30)	0.96 (0.81-1.14)	1.06 (0.89-1.26)	0.97 (0.69-1.36)
		≥65	1.00 (reference)	1.01 (0.89-1.15)	0.88 (0.78-1.00)	0.96 (0.84-1.10)	0.99 (0.75-1.30)
	Charlson comorbidity	0	1.00 (reference)	1.02 (0.89-1.16)	0.82 (0.72-0.94)	0.92 (0.80-1.06)	0.82 (0.63-1.09)
		≥1	1.00 (reference)	1.08 (0.91-1.28)	1.06 (0.90-1.25)	1.14 (0.96-1.35)	1.31 (0.93-1.84)
	Hospital volume (quartiles)	1+2	1.00 (reference)	0.98 (0.84-1.14)	0.80 (0.69-0.93)	0.97 (0.82-1.14)	1.10 (0.83-1.46)
		3+4	1.00 (reference)	1.06 (0.92-1.23)	1.02 (0.89-1.18)	1.02 (0.88-1.18)	0.83 (0.60-1.16)
	Calendar period	1997-2005	1.00 (reference)	0.97 (0.85-1.12)	0.93 (0.81-1.06)	0.94 (0.82-1.09)	0.93 (0.70-1.24)
		2006-2014	1.00 (reference)	1.15 (0.99-1.34)	0.87 (0.75-1.02)	1.10 (0.93-1.29)	1.06 (0.77-1.46)
Thyroid	**Age**	<65	1.00 (reference)	1.20 (0.72-1.99)	1.01 (0.60-1.70)	0.61 (0.33-1.12)	1.58 (0.61-4.10)
		≥65	1.00 (reference)	1.06 (0.78-1.45)	0.90 (0.66-1.24)	1.36 (0.99-1.85)	1.05 (0.57-1.95)
	Sex	Male	1.00 (reference)	0.93 (0.63-1.38)	0.77 (0.50-1.19)	0.96 (0.61-1.49)	0.63 (0.27-1.48)
		Female	1.00 (reference)	1.22 (0.85-1.74)	1.16 (0.82-1.63)	1.27 (0.89-1.80)	1.81 (0.94-3.47)
	Charlson comorbidity	0	1.00 (reference)	0.97 (0.69-1.36)	0.99 (0.71-1.38)	1.07 (0.76-1.51)	1.18 (0.60-2.31)
		≥1	1.00 (reference)	1.31 (0.86-2.01)	1.00 (0.64-1.56)	1.23 (0.77-1.96)	1.09 (0.49-2.47)
	Hospital volume (quartiles)	1+2	1.00 (reference)	0.99 (0.69-1.43)	0.76 (0.50-1.15)	1.23 (0.83-1.81)	1.81 (0.96-3.42)
		3+4	1.00 (reference)	1.23 (0.84-1.81)	1.17 (0.82-1.67)	1.06 (0.72-1.56)	0.62 (0.25-1.55)
	Calendar period	1997-2005	1.00 (reference)	0.86 (0.60-1.23)	0.96 (0.67-1.37)	1.06 (0.74-1.51)	0.98 (0.53-1.79)
		2006-2014	1.00 (reference)	1.46 (0.98-2.16)	1.02 (0.68-1.53)	1.22 (0.79-1.87)	1.46 (0.52-4.06)