



**Karolinska  
Institutet**

This is an author produced version of a paper accepted by **Annals of Surgery**. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

**Weekday of esophageal cancer surgery and its relation to prognosis**

**Lagergren, Jesper; Mattsson Fredrik; Lagergren, Pernilla.**

Access to the published version may require subscription.  
Published with permission from: **Lippincott, William & Wilkins**

**Title: Weekday of esophageal cancer surgery and its relation to prognosis**

**Running head:** Weekday of esophageal cancer surgery

**Authors:** Jesper Lagergren, MD, PhD,<sup>1,2</sup> Fredrik Mattsson, BSc,<sup>1</sup> and Pernilla Lagergren, PhD.<sup>3</sup>

**Affiliations:** <sup>1</sup> Upper Gastrointestinal Surgery, Department of Molecular medicine and Surgery, Karolinska Institutet, Stockholm, Sweden.

<sup>2</sup> Section of Gastrointestinal Cancer, Division of Cancer Studies, King's College London, United Kingdom.

<sup>3</sup> Surgical Care Science, Department of Molecular medicine and Surgery, Karolinska Institutet, Stockholm, Sweden.

**Research Support:** The study was funded by the Swedish Research Council and the Swedish Cancer Society. The fund givers had no role in the manuscript.

**Corresponding author:** Professor Jesper Lagergren. Address: Department of Molecular medicine and Surgery, Karolinska Institutet. NS 67, 2<sup>nd</sup> Floor, 171 76 Stockholm, Sweden. Telephone: +46 (0)8-5177 6012. Fax: +46 (0)8-517 76280. E-mail: [jesper.lagergren@ki.se](mailto:jesper.lagergren@ki.se).

**Keywords:** Esophageal neoplasm; mortality; tumor recurrence; day of week; timing of surgery.

**Word count:** 2678.

### **Mini-Abstract:**

In this nationwide Swedish study, later weekday of esophageal cancer surgery entailed increased long-term mortality, particularly for earlier tumor stages. The increase in 5-year mortality for each later weekday was 7% for all tumor stages, 24% for stages 0-I, 13% for stage II, but was not increased for stages III-IV.

## **Abstract**

**Objective:** To assess whether weekday of surgery influences long-term survival in esophageal cancer.

**Summary Background Data:** Increased 30-day mortality rates have been reported in patients undergoing elective surgery later compared to earlier in the week.

**Methods:** This population-based cohort study included 98% of all esophageal cancer patients who underwent elective surgery in Sweden in 1987-2010, with follow-up until 2014. The association between weekday of surgery and 5-year all-cause and disease-specific mortality was analyzed using a multivariable Cox proportional hazards model, providing hazard ratios (HRs) with 95% confidence intervals (CIs), adjusted for age, co-morbidity, tumor stage, histology, neoadjuvant therapy, and surgeon volume.

**Results:** Among 1,748 included patients, surgery conducted Wednesday-Friday entailed 13% increased all-cause 5-year mortality compared to surgery Monday-Tuesday (HR=1.13, 95% CI 1.01-1.26). The corresponding association was strong for early tumor stages (0-I) (HR=1.59, 95% CI 1.17-2.16), moderate for intermediate tumor stage (II) (HR=1.28, 95% CI 1.07-1.53), and absent in advanced tumor stages (III-IV) (HR=0.93, 95%CI 0.79-1.09). The increase in 5-year mortality for each later weekday (discrete variable) was 7% for all tumor stages (HR=1.07, 95% CI 1.02-1.12), 24% for early tumor stages (HR=1.24, 95% CI 1.09-1.41), 13% for intermediate stage (HR=1.13, 95% CI 1.05-1.22), while no increase was found for advanced stages (HR=0.98, 95% CI 0.92-1.05). The disease-specific 5-year mortality was similar to the all-cause mortality.

**Conclusions:** The increased 5-year mortality of potentially curable esophageal cancer following surgery later in the week suggests that this surgery is better performed earlier in the week.

## **Introduction**

Curatively intended surgery for esophageal cancer (esophagectomy) is one of the most extensive standard surgical procedures carried out.<sup>1-3</sup> Oncologic therapy is typically used prior to esophagectomy.<sup>4-6</sup> Both short-term and long-term survival following esophagectomy is strongly dependent on the experience of the surgeon.<sup>7-11</sup> These findings have prompted centralization of esophagectomy to dedicated high-volume centers.<sup>6, 12, 13</sup> However, the overall 5-year postoperative survival is only approximately 30%, and strongly dependent on the tumor stage at the time of surgery, with >70% 5-year survival in early stages (0-I), approximately 30% in intermediate stage (II), and <10% in advanced stages (III-IV).<sup>14, 15</sup> Thus, it is important to identify other modifiable factors that can improve the postoperative prognosis. Two large cohort studies found increased 30-day mortality rates in patients who underwent elective surgery later compared to earlier in the week.<sup>16, 17</sup> These studies included a variety of surgical procedures and assessed short-term mortality only, and the suggested mechanism was a “weekend effect”, where postoperative complications might be less well handled during weekends. We hypothesized that any prognostic effect of the weekday of surgery would be stronger for a more extensive surgical procedure such as esophagectomy, and that the long-term prognosis would be reduced due to an increased occurrence of tumor recurrence. The surgeon and the surgical team might be more focused earlier in the working week when completing demanding and time-consuming esophagectomies compared to later in the week, which in turn could influence the prognosis. There are, to the best of our knowledge, no studies that have addressed the potential influence of weekday of surgery for cancer in relation to long-term survival. Therefore, we conducted a study with the aim to test whether esophageal cancer surgery conducted during earlier weekdays is followed by a better prognosis than surgery conducted later in the week.

## **Methods**

### ***Design***

This nationwide Swedish population-based cohort study tested whether weekday of surgery influences the 5-year all-cause or disease-specific mortality following elective esophagectomy for esophageal cancer. The included patients represented 98% of all esophageal cancer patients in Sweden who underwent surgery during the period January 1, 1987 through December 31, 2010, and were followed up until November 13, 2014. Earlier versions of this cohort have been described elsewhere.<sup>10, 14</sup> All patients in Sweden with a diagnosis of esophageal cancer (identified in the Swedish Cancer Registry) who underwent esophagectomy (retrieved in the Swedish Patient Registry) were eligible. Detailed clinical data were extracted from medical records, retrieved through our Swedish network of clinicians established in the mid-1990s as part of another nationwide study.<sup>18</sup> The study exposure was the day of the week on which elective esophagectomy for esophageal cancer was conducted, between Monday and Friday, as retrieved from the Swedish Patient Register. The study outcomes, 5-year all-cause mortality and 5-year disease-specific mortality, were collected from the Swedish Causes of Death Registry. The 5-year cut-off for mortality assessment was used because the vast majority of esophageal cancer patients who die within 5 years of surgery have tumor recurrence as the cause of death, and deaths occurring later than 5 years beyond surgery are rarely due to tumor recurrence, as reflected by mortality rates that are similar to the corresponding background population.<sup>19</sup> The linkages of individuals between registers and the identification of their medical records were enabled by the personal identity number, an individual 10-digit identifier assigned to each Swedish resident upon birth or immigration.<sup>20</sup> The study was approved by the Ethical Review Board in Stockholm, Sweden.

### ***Data from national registers***

*The Swedish Cancer Registry* records all cancer diagnoses in Sweden since 1958, and was used to identify patients (with age and sex) with esophageal cancer, represented by the diagnosis codes 150.0, 150.8, or 150.9 according to the 7<sup>th</sup> version of the International Classification of Diseases. This register has 98% nationwide coverage of all esophageal cancer cases.<sup>21, 22</sup>

*The Swedish Patient Registry* records all surgical procedures and diagnoses with dates and hospitals within in-hospital care in Sweden since 1987.<sup>23</sup> Data on esophagectomy, weekday of esophagectomy, co-morbidities, and hospital admittances were collected from this register. This register has an excellent (99.6%) positive predictive value for the recording of esophageal cancer surgery.<sup>24</sup>

*The Swedish Causes of Death Registry* provided dates of death until November 13, 2014, which were used to assess all-cause mortality. Information on the causes of death was available until December 31, 2013, which was used to assess disease-specific mortality, as defined by a recorded esophageal cancer recurrence in the register.

### ***Data from medical records***

A comprehensive data collection of medical records, including surgical charts and pathological reviews, was conducted to retrieve all relevant clinical data, including co-morbidity, tumor stage, tumor location, tumor histology, neoadjuvant therapy, surgery, and annual surgeon volume of esophagectomies. The reviewers of the medical records, who were kept blinded from the study outcomes, filled in a predefined protocol to include the required clinical data in an objective manner. The assessment of the initial reviewer was validated by two other reviewers, which showed >90% exact concordance of variables subject to interpretation difficulties, e.g. tumor stage.<sup>14</sup> Co-morbidity was assessed according to the well

validated Charlson co-morbidity index scoring system.<sup>25</sup> Tumor stage, location and histology were assessed from the pathology reports of the resected tumor specimens. Tumor stage was classified according to the TNM classification of the Union Internationale Contre le Cancer (UICC).<sup>26</sup> Neoadjuvant therapy was infrequently used in Sweden during the study period, which was due to the limited support of such treatment until recently.<sup>4, 11, 27</sup> When used, the neoadjuvant therapy of choice was a combination of chemotherapy and radiotherapy. The dominating (95%) surgical procedure throughout the study period was open transthoracic esophageal resection with intra-thoracic anastomosis. The preferred esophageal substitute was a pulled-up gastric tube, anastomosed to the proximal esophagus in the thorax or neck. The surgeon volume variable was created based on a previously described algorithm, where **first, the primary surgeon's chronological number of surgeries was calculated for each year over the study period. Thereafter, the surgeon with the highest chronological number of surgeries at index operation was considered responsible for the surgery. Annual surgeon volume was then calculated as the number of times the surgeon had been responsible for a surgery during the index year, whereas cumulative surgeon volume was calculated as the chronological number of operations the surgeon had been responsible for at the time of the index surgery during the inclusion period.**<sup>10</sup>

### ***Statistical analysis***

The weekday variable was analyzed in three ways. First, early weekdays of surgery (Monday-Tuesday) were compared with late weekdays (Wednesday-Friday). Second, each of the 5 weekdays was analyzed as separate categories. Third, weekday of surgery was analyzed as a discrete variable to evaluate linear trend with the following coding: Monday=1, Tuesday=2, Wednesday=3, Thursday=4, and Friday=5. Potential differences in mortality between exposure groups were analyzed using a multivariable Cox-proportional hazards model,



providing hazard ratios (HRs) with 95% confidence intervals (CIs) adjusted for potential confounding factors. Six pre-defined covariates were included in the multivariable model because of their known prognostic influence in combination with a possibility that they might influence weekday of surgery. These covariates and their categorizations were: 1) age (continuous variable), 2) co-morbidity (Charlson index score 0, 1, or  $\geq 2$ ), 3) tumor stage (0-I, II, or III-IV), 4) tumor histology (adenocarcinoma or squamous cell carcinoma), 5) neoadjuvant treatment (yes or no), and 6) **cumulated** surgeon volume of esophagectomies (in 4 equal sized groups;  $<7$ , 7-16, 17-46, or  $>46$ ). We also conducted analyses stratified for the six covariates using the same categorization as presented above. To manage missing data, a complete case analysis was performed. Since the study period was long, we added an analysis restricted to the more recent calendar period (2000-2010). Follow-up ended at date of death or end of study period, whichever occurred first. To evaluate the proportional hazards assumption, the correlation was calculated between Schoenfeld residuals for the covariates and the ranking of individual treatment failure times, and the assumption was met. The statistical software SAS 9.4 (SAS Institute, Cary, NC) was used for the data management and statistical analysis.

## **Results**

### ***Patients***

Among 1,799 patients who underwent elective surgery for esophageal cancer in 1987-2010, representing 98% of all such procedures in Sweden, 51 (2.8%) were excluded due to missing data in any of the covariates. Characteristics of the final 1,748 study participants, grouped into early (Monday or Tuesday) and later (Wednesday-Friday) weekdays of surgery are presented in Table 1. There were no major differences in distribution of age, sex, co-morbidity scores, tumor stage, or neoadjuvant therapy between the groups. Adenocarcinoma histology, higher surgeon volume, and more recent calendar period were overrepresented in the Monday-Tuesday group. The 90-day mortality was 10% in the Monday-Tuesday surgery group and 14% in the Wednesday-Friday group. The absolute 5-year all-cause mortality and the 5-year disease-specific mortality were lower when the surgery was conducted on Monday-Tuesday compared to Wednesday-Friday (Table 1).

### ***Weekday of surgery and risk of mortality***

The comparison of surgery later in the week (Wednesday-Friday) with earlier in the week (Monday-Tuesday) showed an increased all-cause and disease-specific 5-year mortality (adjusted HR=1.13, 95% CI 1.01-1.26 and HR=1.15, 95% CI 1.02-1.29, respectively) (Table 2 and Figure 1). When weekday of surgery was categorized into each of the 5 weekdays, the point HRs increased from Wednesday through Thursday to Friday. Compared to surgery on a Monday, surgery on a Friday entailed 46% and 44% increased all-cause and disease-specific mortality (HR=1.46, 95% CI 1.15-1.85 and HR=1.44, 95% CI 1.13-1.84), respectively. There was an average of 7% increased all-cause and disease-specific 5-year mortality for each weekday of surgery when weekday was analyzed as a discrete variable (HR=1.07, 95%CI 1.02-1.12 for both outcomes) (Table 2).

In an analysis restricted to surgery conducted during a more recent calendar period (2000-2010), the risk estimates lost precision, but the point HRs were at least as high as those of the total study population (data not shown). When comparing surgery conducted on Fridays with Mondays, the HR was 1.90 (95% CI 0.92-3.92) for surgery during the calendar period 2000-2010.

### ***Weekday of surgery and risk of mortality stratified for six covariates***

Table 3 presents the results comparing the 5-year mortality in relation to early (Monday-Tuesday) and late (Wednesday-Friday) weekdays stratified for each of the six covariates included in the multivariable model. The point HRs of 5-year mortality were higher among patients of older age, with a Charlson comorbidity score of 1, with early tumor stages, squamous cell carcinoma histology, neoadjuvant therapy, and those who had surgery by higher volume surgeons. The clearest finding was the differences between tumor stages. The HRs representing all-cause mortality were greatly increased for early tumor stages (0-I) (adjusted HR=1.59, 95% CI 1.17-2.16), and moderately increased for intermediate tumor stage (II) (HR=1.28, 95% CI 1.07-1.53), while no association remained in advanced tumor stages (III-IV) (Table 3). The difference in association between tumor stages was further evaluated in an analysis for each weekday of surgery and an analysis using weekday of surgery as a discrete variable. These analyses revealed dose-response patterns between later weekday of surgery and 5-year mortality in tumor stage 0-I, and to a more moderate level also in tumor stage II, while no such pattern was seen for tumor stages III-IV (Table 4). When comparing surgery on a Friday with surgery on a Monday, the HR of 5-year all-cause mortality was 2.69 (95% CI 1.27-5.71) in tumor stage 0-I, 1.78 (95% CI 1.22-2.59) in stage II, and 1.16 (95% CI 0.83-1.60) in stage III-IV. The HRs for weekday of surgery as a discrete variable showed an average 24% increase in risk of all-cause mortality for each weekday of

surgery for tumor stage 0-I (HR=1.24, 95% CI 1.09-1.41), 13% increase for stage II (HR=1.13, 95% CI 1.05-1.22) for, and no increase for tumor stage III-IV (HR=0.98, 95% CI 0.92-1.05). The HRs assessing all-cause and disease-specific 5-year mortality were similar (Tables 2-4). In an analysis excluding the initial 90 days of surgery the associations between weekday of surgery and all-cause and disease-specific 5-year mortality remained virtually unchanged (data not shown).

## **Discussion**

This study indicates that esophageal cancer surgery performed later in the week is associated with increased all-cause and disease-specific 5-year mortality. The risk estimates were evident for earlier tumor stages, but not for advanced tumor stages.

It is not feasible to address the relation between the five weekdays of surgery for esophageal cancer and risk of mortality with a randomized clinical trial, which left us with an observational design. The three main concerns with a cohort design, which was used in the present study, are typically selection bias, misclassification, confounding, and loss to follow-up. However, these concerns were accounted for. First, selection bias was counteracted by the population-based design with inclusion of virtually all patients in Sweden who underwent surgery for esophageal cancer. Second, the assessment of the study exposure (weekday of surgery) and outcome (mortality) was accurate. Third, although residual confounding can never be ruled out, potential confounding by all main prognostic factors was carefully adjusted for in the analyses. Fourth, there was no loss to follow-up by virtue of the nationwide complete population registers available in Sweden in combination with the personal identity numbers. Chance is another potential methodological concern, but to enable good precision we included all eligible patients in Sweden since 1987 (when the Swedish Patient Registry became nationwide) which provided robust risk estimates, for all except for some of the sub-analyses. This long study period might, on the other hand, introduce confounding by changes in the treatment of esophageal cancer over time, particularly introduction of preoperative oncologic therapy and centralization of surgery. However, it is unlikely that these changes would influence choice of weekday of surgery. Moreover, all risk estimates were adjusted for both neoadjuvant therapy and surgeon volume of esophagectomies. Additionally, the analyses stratified for calendar periods showed no difference in association between weekday of

surgery and mortality. Finally, all esophagectomies done in Sweden are performed in public hospitals where the individual surgeon cannot choose the day of scheduled surgery.

Therefore, factors like the age or experience of the surgeon would not influence the choice of operation day in this study. This is in contrast to many other countries where the individual surgeon together with his patient can decide what day of the week to operate on.

To the best of our knowledge, this is the first study addressing the role of weekday of cancer surgery in relation to long-term survival. Previous research has identified earlier weekday of surgery as beneficial in the short term (30 days) following elective surgery for various disorders.<sup>16, 17</sup> Some research has also revealed that surgical procedures conducted during weekends carry higher 30-day mortality compared to surgery performed during weekdays.<sup>28</sup> However, long-term effects were not addressed and the hypothesis of previous studies has been that the health care services are of lower quality during weekends. The hypothesis of the present study was instead that the surgical precision might to some extent deteriorate later in the week due to the workload of the surgeons and the surgical team. The fact that surgery for esophageal cancer is among the most challenging surgical procedures carried out could contribute to the findings. The results of the present study indicate that the outcomes following esophageal cancer surgery might be influenced by the alertness of the surgeon. Esophageal cancer surgery typically requires several hours (the average operation duration for esophagectomy in Sweden is 6½ hours) of focused work by the surgeon. It might be argued that the surgeon is likely to be well-rested earlier in the working week compared to later in the week and therefore will find it easier to focus on exhausting and demanding surgery. This in turn might result in more precise surgery, followed by a lower risk of later tumor recurrence. This hypothesis gains support from the findings of stronger associations in high-volume surgeons and in earlier tumor stages. High-volume surgeons might conduct several

esophagectomies each week, which is exhaustive. This also indicates that the on-going centralization of services might enhance the weekday effects seen in the present study. In earlier tumor stages surgery plays a more crucial role for the chance of long-term survival, while the lack of association in advanced tumor stages might be due to the low chance of cure (<10% 5-year survival).<sup>14, 15</sup>

The findings of this study need confirmation in other studies. If proven true, these results argue in favor of a change of the scheduling of esophageal cancer surgery to the first part of the week, while less time-consuming and tiring surgery might be scheduled for later in the week. Although this study focused on surgery for esophageal cancer, it is fully possible that the results might be generalizable to other challenging surgical cancer procedures, e.g. surgery for cancer of pancreas, bile ducts and liver.

In conclusion, this large and population-based cohort study with adjustment for prognostic factors and complete follow-up indicates that esophageal cancer surgery for more readily surgically curable tumor stages (0-II) is followed by a better all-cause and disease-specific 5-year survival if conducted earlier during the week compared to later. Thus, changes in the scheduling of esophageal cancer surgery might improve the prognosis in patients operated on for esophageal cancer.

**Acknowledgments:** The study was funded by the Swedish Research Council and the Swedish Cancer Society. These study sponsors had no role in the design of the study; the collection, analysis, or interpretation of the data; the writing of the manuscript; or the decision to submit the manuscript for publication.

## References

1. Allum WH, Blazeby JM, Griffin SM, et al. Guidelines for the management of oesophageal and gastric cancer. *Gut* 2011; 60(11):1449-72.
2. Lagarde SM, Vrouenraets BC, Stassen LP, et al. Evidence-based surgical treatment of esophageal cancer: overview of high-quality studies. *Ann Thorac Surg* 2010; 89(4):1319-26.
3. Wu PC, Posner MC. The role of surgery in the management of oesophageal cancer. *Lancet Oncol* 2003; 4(8):481-8.
4. Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. *Lancet Oncol* 2011; 12(7):681-92.
5. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med* 2012; 366(22):2074-84.
6. Lagergren J, Lagergren P. Oesophageal cancer. *BMJ* 2010; 341:c6280.
7. Birkmeyer JD, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. *N Engl J Med* 2003; 349(22):2117-27.
8. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. *N Engl J Med* 2009; 361(14):1368-75.
9. Finks JF, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery. *N Engl J Med* 2011; 364(22):2128-37.
10. Derogar M, Sadr-Azodi O, Johar A, et al. Hospital and surgeon volume in relation to survival after esophageal cancer surgery in a population-based study. *J Clin Oncol* 2013; 31(5):551-7.
11. Rustgi AK, El-Serag HB. Esophageal carcinoma. *N Engl J Med* 2014; 371(26):2499-509.
12. Groene O, Chadwick G, Riley S, et al. Re-organisation of oesophago-gastric cancer services in England and Wales: a follow-up assessment of progress and remaining challenges. *BMC Res Notes* 2014; 7:24.
13. Dikken JL, van Sandick JW, Allum WH, et al. Differences in outcomes of oesophageal and gastric cancer surgery across Europe. *Br J Surg* 2013; 100(1):83-94.
14. Rouvelas I, Zeng W, Lindblad M, et al. Survival after surgery for oesophageal cancer: a population-based study. *Lancet Oncol* 2005; 6(11):864-70.
15. Rutegard M, Charonis K, Lu Y, et al. Population-based esophageal cancer survival after resection without neoadjuvant therapy: an update. *Surgery* 2012; 152(5):903-10.
16. Zare MM, Itani KM, Schifftner TL, et al. Mortality after nonemergent major surgery performed on Friday versus Monday through Wednesday. *Ann Surg* 2007; 246(5):866-74.
17. Aylin P, Alexandrescu R, Jen MH, et al. Day of week of procedure and 30 day mortality for elective surgery: retrospective analysis of hospital episode statistics. *Bmj* 2013; 346:f2424.
18. Lagergren J, Bergstrom R, Lindgren A, et al. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999; 340(11):825-31.
19. Lagergren J, Mattson F. Diverging trends in recent population-based survival rates in oesophageal and gastric cancer. *PLoS One* 2012; 7(7):e41352.
20. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, et al. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *Eur J Epidemiol* 2009; 24(11):659-67.
21. Barlow L, Westergren K, Holmberg L, et al. The completeness of the Swedish Cancer Register: a sample survey for year 1998. *Acta Oncol* 2009; 48(1):27-33.
22. Lindblad M, Ye W, Lindgren A, et al. Disparities in the classification of esophageal and cardia adenocarcinomas and their influence on reported incidence rates. *Ann Surg* 2006; 243(4):479-85.
23. Ludvigsson JF, Andersson E, Ekblom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011; 11:450.
24. Lagergren K, Derogar M. Validation of oesophageal cancer surgery data in the Swedish Patient Registry. *Acta Oncol* 2012; 51(1):65-8.



25. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5):373-83.
26. Sobin LH, Gospodarowicz MK, C. W. UICC TNM Classification of Malignant Tumours, 7th Edition: Wiley-Blackwell, 2009.
27. Pennathur A, Gibson MK, Jobe BA, et al. Oesophageal carcinoma. *Lancet* 2013; 381(9864):400-12.
28. Mclsaac DI, Bryson GL, van Walraven C. Elective, major noncardiac surgery on the weekend: a population-based cohort study of 30-day mortality. *Med Care* 2014; 52(6):557-64.

**Table 1.** Characteristics of 1748 study patients who underwent surgical resection for esophageal cancer in Sweden in 1987-2010.

| Characteristic                                   |                         | Weekday of surgery |                  |
|--|-------------------------|--------------------|------------------|
|  |                         | Monday-Tuesday     | Wednesday-Friday |
|  |                         | Number (%)         | Number (%)       |
| <b>Total</b>                                     |                         | 1083 (100)         | 665 (100)        |
| <b>Age (in years):</b> Mean (standard deviation) |                         | 65 (9)             | 66 (10)          |
| <b>Sex</b>                                       | Men                     | 818 (76)           | 487 (73)         |
|  | Women                   | 265 (24)           | 178 (27)         |
| <b>Charlson co-morbidity index</b>               | 0                       | 608 (56)           | 407 (61)         |
|  | 1                       | 238 (22)           | 125 (19)         |
|  | >1                      | 237 (22)           | 133 (20)         |
| <b>Tumor stage</b>                               | 0-I                     | 292 (27)           | 119 (18)         |
|  | II                      | 368 (34)           | 271 (41)         |
|  | III-IV                  | 423 (39)           | 275 (41)         |
| <b>Tumor histology</b>                           | Adenocarcinoma          | 513 (47)           | 255 (38)         |
|  | Squamous cell carcinoma | 570 (53)           | 410 (62)         |
| <b>Neoadjuvant therapy</b>                       | No                      | 738 (68)           | 445 (67)         |
|  | Yes                     | 345 (32)           | 220 (33)         |
| <b>Surgeon volume</b>                            | <7                      | 263 (24)           | 219 (33)         |
|  | 7-16                    | 229 (21)           | 163 (25)         |
|  | 17-46                   | 289 (27)           | 155 (23)         |
|  | >46                     | 302 (28)           | 128 (19)         |
| <b>Calendar period</b>                           | 1987-1999               | 513 (47)           | 420 (63)         |
|  | 2000-2010               | 570 (53)           | 245 (37)         |
| <b>90-day all-cause mortality</b>                | No                      | 973 (90)           | 576 (87)         |
|  | Yes                     | 110 (10)           | 89 (13)          |
| <b>5-year all-cause mortality</b>                | No                      | 314 (29)           | 135 (20)         |
|  | Yes                     | 769 (71)           | 530 (80)         |
| <b>5-year disease-specific mortality</b>         | No                      | 387 (36)           | 169 (25)         |
|  | Yes                     | 696 (64)           | 496 (75)         |

**Table 2.** Weekday of surgery for esophageal cancer conducted in 1987-2010 in Sweden in relation to 5-year all-cause and disease-specific mortality, presented as hazard ratios (HR) with 95% confidence intervals (CI).

| <b>Weekday</b>          | <b>Number (%)</b> | <b>5-year all-cause mortality HR (95% CI)*</b> | <b>5-year disease-specific mortality HR (95% CI)*</b> |
|-------------------------|-------------------|--|---|
| <b>Monday-Tuesday</b>   | 1083 (62)         | 1 (reference)                                  | 1 (reference)   |
| <b>Wednesday-Friday</b> | 665 (38)          | 1.13 (1.01-1.26)                               | 1.15 (1.02-1.29)                                      |
| <b>Monday</b>           | 498 (28)          | 1 (reference)                                  | 1 (reference)   |
| <b>Tuesday</b>          | 585 (33)          | 1.03 (0.89-1.18)                               | 0.99 (0.85-1.15)                                      |
| <b>Wednesday</b>        | 305 (17)          | 1.07 (0.91-1.27)                               | 1.07 (0.90-1.27)                                      |
| <b>Thursday</b>         | 261 (15)          | 1.12 (0.94-1.34)                               | 1.13 (0.94-1.35)                                      |
| <b>Friday</b>           | 99 (6)            | 1.46 (1.15-1.85)                               | 1.44 (1.13-1.84)                                      |
| <b>Monday-Friday†</b>   | 1748 (100)        | 1.07 (1.02-1.12)                               | 1.07 (1.02-1.12)                                      |

\* Adjusted for age, comorbidity, tumor stage, tumor histology, neoadjuvant treatment, and surgeon volume.

† Discrete variable to evaluate linear trend.

**Table 3.** All-cause and disease-specific 5-year mortality depending on weekday of surgery for esophageal cancer conducted in 1987-2010 in Sweden, stratified by six covariates, presented as hazard ratios (HR) with 95% confidence intervals (CI).

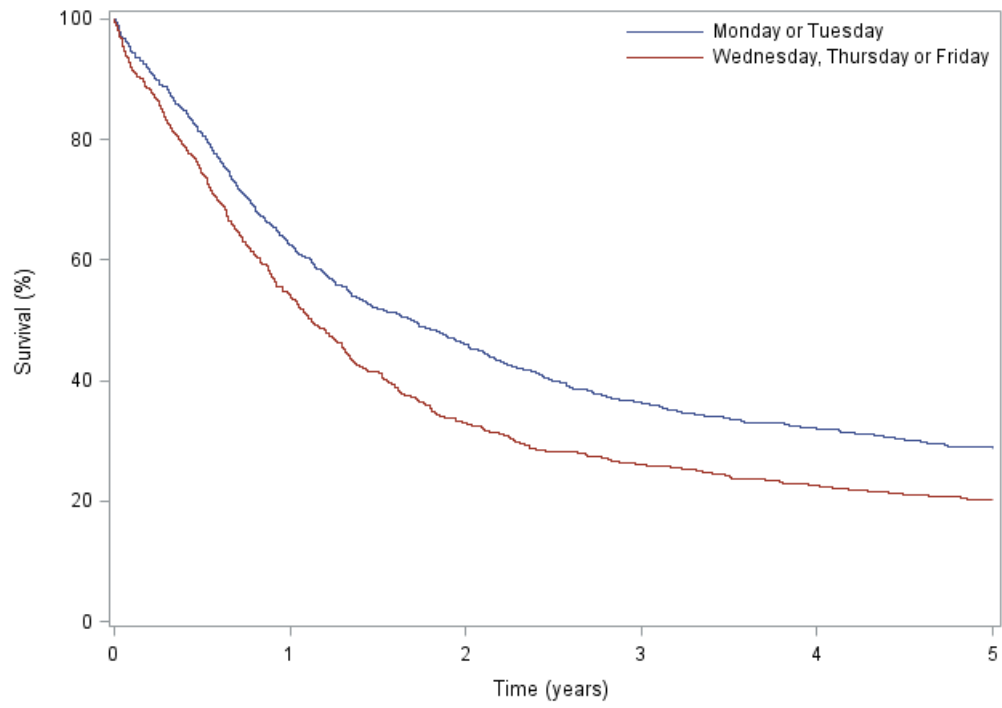
| Covariate                         | 5-year all-cause mortality |                |                  |                  |
|-----------------------------------|----------------------------|----------------|------------------|------------------|
|                                   | Number (%)                 | Monday-Tuesday | Wednesday-Friday |                  |
|                                   |                            | Reference      | HR (95% CI)*     |                  |
| Age (median, years)               | <66                        | 892 (51)       | 1                | 1.07 (0.91-1.25) |
|                                   | ≥66                        | 856 (49)       | 1                | 1.19 (1.02-1.39) |
| Co-morbidity score                | 0                          | 1015 (58)      | 1                | 1.12 (0.97-1.30) |
|                                   | 1                          | 363 (21)       | 1                | 1.25 (0.97-1.60) |
|                                   | >1                         | 370 (21)       | 1                | 1.04 (0.82-1.33) |
| Tumor stage                       | 0-I                        | 411 (24)       | 1                | 1.59 (1.17-2.16) |
|                                   | II                         | 639 (37)       | 1                | 1.28 (1.07-1.53) |
|                                   | III+ IV                    | 698 (40)       | 1                | 0.93 (0.79-1.09) |
| Tumor histology                   | Adenocarcinoma             | 768 (44)       | 1                | 1.03 (0.86-1.23) |
|                                   | Squamous                   | 980 (56)       | 1                | 1.20 (1.04-1.38) |
| Neoadjuvant therapy               | No                         | 1183 (68)      | 1                | 1.08 (0.94-1.24) |
|                                   | Yes                        | 565 (32)       | 1                | 1.24 (1.02-1.52) |
| Surgeon volume                    | <7                         | 482 (28)       | 1                | 1.12 (0.92-1.37) |
|                                   | 7-16                       | 392 (22)       | 1                | 0.99 (0.78-1.24) |
|                                   | 17-46                      | 444 (25)       | 1                | 1.26 (1.00-1.57) |
|                                   | >46                        | 430 (25)       | 1                | 1.16 (0.91-1.49) |
| 5-year disease-specific mortality |                            |                |                  |                  |
| Age (median, years)               | <66                        | 892 (51)       | 1                | 1.06 (0.89-1.25) |
|                                   | ≥66                        | 856 (49)       | 1                | 1.24 (1.05-1.46) |
| Co-morbidity score                | 0                          | 1015 (58)      | 1                | 1.14 (0.98-1.32) |
|                                   | 1                          | 363 (21)       | 1                | 1.30 (1.00-1.69) |
|                                   | ≥2                         | 370 (21)       | 1                | 1.04 (0.80-1.35) |
| Tumor stage                       | 0-I                        | 411 (24)       | 1                | 1.58 (1.12-2.22) |
|                                   | II                         | 639 (37)       | 1                | 1.37 (1.14-1.66) |
|                                   | III-IV                     | 698 (40)       | 1                | 0.93 (0.79-1.09) |
| Tumor histology                   | Adenocarcinoma             | 768 (44)       | 1                | 1.04 (0.86-1.25) |
|                                   | Squamous                   | 980 (56)       | 1                | 1.22 (1.05-1.42) |
| Neoadjuvant therapy               | No                         | 1183 (68)      | 1                | 1.11 (0.97-1.28) |
|                                   | Yes                        | 565 (32)       | 1                | 1.23 (1.00-1.51) |
| Surgeon volume                    | <7                         | 482 (28)       | 1                | 1.14 (0.93-1.40) |
|                                   | 7-16                       | 392 (22)       | 1                | 0.99 (0.78-1.27) |
|                                   | 17-46                      | 444 (25)       | 1                | 1.28 (1.01-1.62) |
|                                   | >46                        | 430 (25)       | 1                | 1.19 (0.92-1.54) |

\* Adjusted for age, comorbidity, tumor stage, tumor histology, neoadjuvant treatment, and surgeon volume.

**Table 4.** All-cause and disease-specific 5-year mortality depending on weekday of surgery for esophageal cancer conducted in 1987-2010 in Sweden, stratified by tumor stage, presented as hazard ratios (HR) with 95% confidence intervals (CI).

| <b>5-year all-cause mortality</b>        |                   |                  |                     |
|--|-------------------|------------------|---------------------|
| <b>Tumor stage</b>                       | <b>Number (%)</b> | <b>Weekday</b>   | <b>HR (95% CI)*</b> |
| <b>0-I</b>                               | 130 (32)          | Monday           | 1 (reference)       |
|  | 162 (39)          | Tuesday          | 1.07 (0.74-1.54)    |
|  | 60 (15)           | Wednesday        | 1.47 (0.93-2.31)    |
|  | 49 (12)           | Thursday         | 1.70 (1.05-2.74)    |
|  | 10 (2)            | Friday           | 2.69 (1.27-5.71)    |
| <b>II</b>                                | 157 (25)          | Monday           | 1 (reference)       |
|  | 211 (33)          | Tuesday          | 1.24 (0.97-1.59)    |
|  | 115 (18)          | Wednesday        | 1.35 (1.02-1.79)    |
|  | 114 (18)          | Thursday         | 1.46 (1.10-1.92)    |
|  | 42 (7)            | Friday           | 1.78 (1.22-2.59)    |
| <b>III-IV</b>                            | 211 (30)          | Monday           | 1 (reference)       |
|  | 212 (30)          | Tuesday          | 0.90 (0.74-1.10)    |
|  | 130 (19)          | Wednesday        | 0.84 (0.67-1.06)    |
|  | 98 (14)           | Thursday         | 0.83 (0.64-1.07)    |
|  | 47 (7)            | Friday           | 1.16 (0.83-1.60)    |
| <b>0-I</b>                               | 411 (24)          | Monday to        | 1.24 (1.09-1.41)    |
| <b>II</b>                                | 639 (37)          | Friday, discrete | 1.13 (1.05-1.22)    |
| <b>III-IV</b>                            | 698 (40)          | variable         | 0.98 (0.92-1.05)    |
| <b>5-year disease-specific mortality</b> |                   |                  |                     |
|  |                   |                  | <b>HR (95% CI)*</b> |
| <b>0-I</b>                               | 130 (32)          | Monday           | 1 (reference)       |
|  | 162 (39)          | Tuesday          | 1.11 (0.73-1.67)    |
|  | 60 (15)           | Wednesday        | 1.43 (0.85-2.41)    |
|  | 49 (12)           | Thursday         | 1.82 (1.07-3.08)    |
|  | 10 (2)            | Friday           | 2.57 (1.08-6.11)    |
| <b>II</b>                                | 157 (25)          | Monday           | 1 (reference)       |
|  | 211 (33)          | Tuesday          | 1.18 (0.91-1.53)    |
|  | 115 (18)          | Wednesday        | 1.41 (1.05-1.88)    |
|  | 114 (18)          | Thursday         | 1.51 (1.13-2.02)    |
|  | 42 (7)            | Friday           | 1.86 (1.26-2.73)    |
| <b>III-IV</b>                            | 211 (30)          | Monday           | 1 (reference)       |
|  | 212 (30)          | Tuesday          | 0.87 (0.71-1.08)    |
|  | 130 (19)          | Wednesday        | 0.83 (0.65-1.06)    |
|  | 98 (14)           | Thursday         | 0.82 (0.63-1.06)    |
|  | 47 (7)            | Friday           | 1.11 (0.80-1.56)    |
| <b>0-I</b>                               | 411 (24)          | Monday to        | 1.25 (1.07-1.44)    |
| <b>II</b>                                | 639 (37)          | Friday, discrete | 1.16 (1.07-1.25)    |
| <b>III-IV</b>                            | 698 (40)          | variable         | 0.98 (0.91-1.04)    |

\* Adjusted for age, comorbidity, tumor stage, tumor histology, neoadjuvant treatment, and surgeon volume.



**Figure 1.** Kaplan-Meier survival curves following surgery for esophageal cancer conducted on Monday-Tuesday compared to Wednesday-Friday. The surgery was performed in 1748 patients in Sweden during 1987 and 2010.