

# BMJ Open Weekday of oesophageal cancer surgery in relation to early postoperative outcomes in a nationwide Swedish cohort study

Jesper Lagergren,<sup>1,2</sup> Fredrik Mattsson,<sup>1</sup> Pernilla Lagergren<sup>3</sup>

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<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, London, UK  
<sup>3</sup>Surgical Care Science, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden

**Correspondence to** Professor Jesper Lagergren; [jesper.lagergren@ki.se](mailto:jesper.lagergren@ki.se)

## ABSTRACT

**Objectives:** Later weekday of surgery for oesophageal cancer seems to increase 5-year mortality, but the mechanisms are unclear. We hypothesised that early postoperative reoperations and mortality might explain this association, since reoperation after oesophagectomy decreases long-term prognosis, and later weekday of elective surgery increases 30-day mortality.

**Design:** This was a population-based cohort study during the study period 1987–2014.

**Setting:** All Swedish hospitals conducting elective surgery for oesophageal cancer in Sweden.

**Participants:** Included were 1748 patients, representing almost all (98%) patients who underwent elective surgery for oesophageal cancer in Sweden during 1987–2010, with follow-up until 2014.

**Primary and secondary outcome measures:** The risk of reoperation or mortality within 30 days of oesophageal cancer surgery was assessed in relation to weekday of surgery by calculating ORs with 95% CIs using multivariable logistic regression. ORs were adjusted for age, comorbidity, tumour stage, histology, neoadjuvant therapy and surgeon volume.

**Results:** Surgery Wednesday to Friday did not increase the risk of reoperation or mortality compared with surgery Monday to Tuesday (OR=0.99, 95% CI 0.75 to 1.31). A decreased point estimate of reoperation (OR=0.88, 95% CI 0.64 to 1.21) was counteracted by an increased point estimate of mortality (OR=1.28, 95% CI 0.83 to 1.99). ORs did not increase from Monday to Friday when each weekday was analysed separately. There was no association between weekday of surgery and reoperation specifically for anastomotic leak, laparotomy or wound infection. Stratification for surgeon volume did not reveal any clear associations between weekday of surgery and risk of 30-day reoperation or mortality.

**Conclusions:** Weekday of oesophageal cancer surgery does not seem to influence the risk of reoperation or mortality within 30 days of surgery, and thus cannot explain the association between weekday of surgery and long-term prognosis.

## INTRODUCTION

In a recent Swedish cohort study, we found increased 5-year all-cause and disease-specific 5-year mortality following surgery for

## Strengths and limitations of this study

- Large and population-based study with high participation rate.
- Accurate assessment of the exposure, outcomes and confounders.
- Complete follow-up.
- Competing events.
- Retrospective data collection.

oesophageal cancer later in the week compared with earlier weekdays, and the association seemed to increase for each weekday.<sup>1</sup> The mechanism explaining these associations remains to be identified. Another study from our group revealed that patients who require reoperation within 30 days of oesophageal cancer surgery are at an increased risk of all-cause and disease-specific 5-year mortality, also after excluding mortality occurring within the initial 3 months of surgery.<sup>2</sup> Moreover, later weekday of surgery for various elective procedures has been shown to increase the risk of severe postoperative complications, including 30-day mortality.<sup>3 4</sup> Therefore, we hypothesised that occurrence of early and severe postoperative complications requiring reoperation or resulting in mortality explains the association between weekday of surgery and long-term prognosis in oesophageal cancer. This hypothesis was tested in a nationwide Swedish cohort study.

## METHODS

### Design

This was a nationwide Swedish population-based cohort study conducted between 1987 and 2010. Earlier versions of this cohort have been published elsewhere.<sup>1 5–7</sup> The study exposure was the day of the week on which the operation was conducted and the study outcome was reoperations or mortality

occurring within 30 days of the oesophagectomy. By including both these outcomes as the main outcome, we avoided errors from competing risks from the fact that those who died within 30 days of surgery could not be recorded with reoperations. The participating patients represented 98% of all patients with oesophageal cancer who underwent surgery in Sweden between 1 January 1987 and 31 December 2010. Eligible patients were identified from national Swedish healthcare registers. Clinical data were extracted from medical records, retrieved through our Swedish network of clinicians, established in the mid-1990s as part of a prospective and nationwide case-control study.<sup>8</sup> Linkages of data from 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 on birth or immigration.<sup>9</sup> The study was approved by the Ethical Review Board in Stockholm, Sweden.

### Registry data

The Swedish Cancer Registry was used to identify all patients in Sweden with oesophageal cancer, represented by the diagnosis codes 150.0, 150.8 or 150.9 according to the seventh version of the International Classification of Diseases. This register records all cancer diagnoses in Sweden since 1958, and has 98% nationwide coverage of oesophageal cancer.<sup>10 11</sup>

The Swedish Patient Registry provided data on oesophagectomy, comorbidities and hospital admittances. This register records all surgical procedures and diagnoses within in-hospital care in Sweden since 1987.<sup>12</sup> The positive predictive value for the recording of oesophageal cancer surgery in this register is 99.6% according to a validation study.<sup>13</sup>

The Swedish Causes of Death Registry provided causes and dates of death. This register is nationwide since 1961 and highly complete.

### Medical records data

The medical records of all participating patients were continuously collected from the operating hospitals, including surgical charts and pathological reviews of the resected specimens. On the basis of this data collection, we assessed weekday of oesophagectomy; comorbidity; tumour stage, location and histology; neoadjuvant therapy; surgery; and annual surgeon volume of oesophagectomies. The reviewers of the medical records were kept blinded from the study outcomes and filled in a predefined protocol. Comorbidity was assessed according to the well-validated Charlson comorbidity index scoring system.<sup>14</sup> Tumour stage was classified according to the TNM classification of the Union Internationale Contre le Cancer (UICC).<sup>15</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>16</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 oesophageal resection with intrathoracic anastomosis. The preferred oesophageal substitute was a pulled-up gastric tube, anastomosed to the proximal oesophago in the thorax or neck. The surgeon volume variable was created on the basis of a previously described algorithm, where the names of the individual surgeons were used to assign the operation to the most experienced surgeon whenever more than one surgeon conducted the procedure.<sup>6</sup>

### Statistical analysis

The weekday variable was analysed in two ways. First, surgery during Monday or Tuesday was compared with surgery during Wednesday to Friday. Second, each of the 5 weekdays was analysed as a separate category with Monday as the reference. Potential differences in reoperation or mortality within 30 days of surgery between exposure groups were analysed using a multivariable logistic regression, providing ORs with 95% CIs adjusted for potential confounding variables. Seven predefined variables were included in the multivariable model: (1) age (continuous variable), (2) sex, (3) comorbidity (Charlson index score 0, 1 or >1), (4) tumour stage (0–I, II or III–IV), (5) tumour histology (adenocarcinoma or squamous cell carcinoma), (6) neoadjuvant treatment (yes or no) and (7) annual surgeon volume of oesophagectomies (<17 or ≥17, median number). Furthermore, we evaluated if the effect of weekday was modified by surgeon volume by including an interaction term in the model. Thereafter, we derived the ORs for weekday variable within each stratum for surgeon volume. To manage limited missing data (2.8%), a complete case analysis was performed. The statistical software SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) was used for data management and statistical analysis.

## RESULTS

### Patients

The 1799 patients who underwent elective surgery for oesophageal cancer during the weekdays Monday to Friday during 1987–2010 represented 98% of all such procedures in Sweden. Of these, 51 (2.8%) were excluded due to missing data in any of the covariates. **Table 1** presents characteristics of the final 1748 study participants, grouped into those with and without reoperation or mortality within 30 days of surgery. There were no major differences in distribution of age, sex, tumour stage, tumour histology or use of neoadjuvant therapy comparing the groups with and without reoperation or mortality within 30 days of surgery, while lower annual surgeon volume was found in the group with poor short-term outcomes.

### Risk of postoperative reoperation or mortality

The total rates of reoperation and mortality were 10.9% (n=191) and 5.3% (n=93), respectively. The comparison

**Table 1** Characteristics of 1748 study patients who underwent surgical resection for oesophageal cancer in Sweden in 1987–2010, with follow-up until 2014

	No death/ reoperation within 30 days of surgery Number (%)	Death/ reoperation within 30 days of surgery Number (%)
Total	1490 (100)	258 (100)
Age (years): mean (SD)	65 (10)	67 (9)
Sex		
Male	1110 (74)	195 (76)
Female	380 (26)	63 (24)
Charlson comorbidity index		
0	870 (58)	145 (56)
1	306 (21)	57 (22)
>1	314 (21)	56 (22)
Tumour stage		
0–I	357 (24)	54 (21)
II	535 (36)	104 (40)
III–IV	598 (40)	100 (39)
Tumour histology		
Adenocarcinoma	675 (45)	93 (36)
Squamous carcinoma	815 (55)	165 (64)
Neoadjuvant therapy		
No	1013 (68)	170 (66)
Yes	477 (32)	88 (34)
Annual surgeon volume		
<17	719 (48)	155 (60)
≥17	771 (52)	103 (40)

of surgery later in the week (Wednesday to Friday) with earlier in the week (Monday to Tuesday) showed no increased risk of death or reoperation within 30 days of surgery (adjusted OR=0.99, 95% CI 0.75 to 1.31; [table 2](#)). When weekday of surgery was categorised into each of the 5 weekdays, the ORs did not increase from Monday to Friday. A slightly decreased point estimate of reoperation (OR 0.88, 95% CI 0.64 to 1.21) following later weekday of surgery was counteracted by an increased point estimate of mortality (OR 1.28, 95% CI 0.83 to 1.99). There was no increased OR of reoperation for anastomotic leak, laparotomy or wound infection associated with later weekday of surgery ([table 2](#)).

The analyses evaluating effect modification by annual surgeon volume did not reveal any statistically significant associations between weekday of surgery and risk of reoperation or mortality within 30 days of surgery for oesophageal cancer ([table 3](#)).

## DISCUSSION

This study provides no evidence of an association between later weekday of surgery for oesophageal cancer and risk of early postoperative reoperation or mortality.

**Table 2** Risk of death or reoperation within 30 days of surgery for oesophageal cancer

Weekday of surgery	Death/reoperation (n=258) OR (95% CI)*	Death (n=93) OR (95% CI)*	Reoperation (n=191) OR (95% CI)*	Reoperation for anastomotic leak (n=34) OR (95% CI)*	Reoperation with laparotomy (n=54) OR (95% CI)*	Reoperation for wound infection (n=98) OR (95% CI)*
Monday to Tuesday	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Wednesday to Friday	0.99 (0.75 to 1.31)	1.28 (0.83 to 1.99)	0.88 (0.64 to 1.21)	0.98 (0.47 to 2.02)	0.75 (0.42 to 1.34)	1.44 (0.75 to 2.79)
Monday	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Tuesday	0.98 (0.69 to 1.38)	0.61 (0.33 to 1.11)	1.00 (0.68 to 1.46)	0.62 (0.26 to 1.46)	0.92 (0.47 to 1.80)	0.96 (0.39 to 2.41)
Wednesday	1.20 (0.81 to 1.78)	1.16 (0.64 to 2.11)	1.05 (0.67 to 1.65)	1.47 (0.62 to 3.49)	0.74 (0.33 to 1.69)	1.33 (0.50 to 3.53)
Thursday	0.86 (0.55 to 1.34)	0.82 (0.42 to 1.61)	0.81 (0.49 to 1.34)	1.15 (0.02 to 1.17)	0.96 (0.42 to 2.20)	1.54 (0.58 to 4.14)
Friday	0.66 (0.34 to 1.29)	1.04 (0.44 to 2.44)	0.54 (0.24 to 1.23)	0.42 (0.05 to 3.37)	NA	1.33 (0.35 to 5.13)

Results presented as OR with 95% CI.

\*Adjusted for age, sex, Charlson comorbidity index, tumour stage, tumour histology, neoadjuvant therapy and surgeon volume. NA, not available.

**Table 3** Risk of death or reoperation within 30 days of surgery for oesophageal cancer, stratified for surgeon volume

Weekday of surgery	Surgeon volume	Death/reoperation (n=258)	Death (n=93)	Reoperation (n=191)	Anastomotic (n=34)	Laparotomy (n=54)	Wound within 30 days (n=38)
		OR (95% CI)*	OR (95% CI)*	OR (95% CI)*	OR (95% CI)*	OR (95% CI)*	OR (95% CI)*
Monday to Tuesday	<17	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Wednesday to Friday	<17	1.02 (0.72 to 1.46)	1.31 (0.78 to 2.20)	0.88 (0.58 to 1.34)	0.64 (0.19 to 2.16)	0.73 (0.36 to 1.48)	1.55 (0.69 to 3.50)
Monday to Tuesday	≥17	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Wednesday to Friday	≥17	0.94 (0.60 to 1.47)	1.22 (0.54 to 2.75)	0.87 (0.54 to 1.42)	1.26 (0.52 to 3.05)	0.79 (0.28 to 2.24)	1.25 (0.40 to 3.87)
Monday	<17	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Tuesday	<17	0.87 (0.54 to 1.39)	0.55 (0.25 to 1.17)	0.90 (0.52 to 1.54)	0.94 (0.23 to 3.84)	1.55 (0.65 to 3.67)	0.53 (0.15 to 1.84)
Wednesday	<17	1.27 (0.78 to 2.05)	1.24 (0.63 to 2.45)	1.11 (0.63 to 1.93)	0.98 (0.22 to 4.47)	1.29 (0.50 to 3.33)	1.26 (0.43 to 3.71)
Thursday	<17	0.74 (0.41 to 1.32)	0.72 (0.31 to 1.63)	0.72 (0.37 to 1.43)	0.43 (0.05 to 3.90)	0.82 (0.24 to 2.75)	1.16 (0.35 to 3.79)
Friday	<17	0.58 (0.25 to 1.33)	0.92 (0.34 to 2.49)	0.32 (0.09 to 1.09)	NA	NA	0.96 (0.19 to 4.86)
Monday	≥17	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Tuesday	≥17	1.12 (0.67 to 1.87)	0.73 (0.27 to 2.00)	1.11 (0.64 to 1.92)	0.50 (0.17 to 1.47)	0.36 (0.11 to 1.20)	2.34 (0.47 to 11.80)
Wednesday	≥17	1.00 (0.50 to 2.02)	0.78 (0.20 to 3.05)	0.89 (0.41 to 1.94)	1.89 (0.66 to 5.39)	NA	1.09 (0.10 to 12.17)
Thursday	≥17	1.06 (0.54 to 2.05)	1.10 (0.35 to 3.49)	0.92 (0.44 to 1.92)	NA	1.14 (0.37 to 3.53)	2.95 (0.48 to 18.16)
Friday	≥17	0.85 (0.28 to 2.59)	1.48 (0.29 to 7.43)	1.03 (0.33 to 3.16)	0.85 (0.10 to 7.18)	NA	2.89 (0.25 to 33.07)

Results presented as OR with 95% CI.

\*Adjusted for age, sex, Charlson comorbidity index, tumour stage, tumour histology, neoadjuvant therapy and surgeon volume.

NA, not available.

The strengths of the present study include the population-based cohort design, accurate assessment of the exposure (weekday of surgery) and outcome (post-operative reoperation or mortality), complete follow-up, adjustment for several potential confounding factors and the large sample size. A weakness is that the long study period might introduce confounding by changes in treatment or patient selection over time. However, it is unlikely that these changes would influence choice of weekday of surgery, which means that these changes would not act as confounders.<sup>17</sup> The results should be generalisable to other western populations of Caucasian origin. A methodological issue is that reoperation and mortality are competing events, since death occurring before any potential later reoperation is not accounted for. Therefore, the combined reoperation/mortality outcome was selected as the main study outcome, while the results regarding the separate reoperation outcomes should be interpreted more cautiously. An observational study can never rule out residual confounding, but the risk of confounding should be counteracted by the fact that we adjusted the risk estimates for the key potential confounding variables. The retrospective collection of data from medical records might introduce bias, but we avoided such error by keeping the researchers collecting and introducing the medical records data without being aware of the study outcome. Finally, the occurrence of the study outcomes was low, which resulted in limited statistical power to detect weak differences, particularly in stratified subgroup analyses.

To the best of our knowledge, there is no previous study addressing weekday of oesophageal cancer surgery in relation to reoperation or short-term mortality. However, large cohort studies evaluating various types of elective surgery have found an increased risk of 30-day mortality associated with a later weekday of surgery.<sup>3, 4</sup> This was not found in this study, which might be due to a more limited statistical power compared with studies addressing many types of surgical procedures. However, it is unlikely that any potentially weakly increased risk of reoperation or short-term mortality would explain the substantially increased long-term mortality associated with later weekdays of oesophageal cancer surgery reported recently.<sup>1</sup> This suggests that the weekday effect on long-term prognosis is due to other reasons than poor short-term outcomes, for example, increased likelihood of tumour recurrence.

Our previous findings of an association between later weekday of surgery and increased risk of long-term mortality and tumour recurrence do not seem to be explained by worse short-term outcomes linked with weekday of surgery.<sup>1</sup> It is possible that the tumour dissection is negatively influenced by surgeon fatigue, while this factor does not influence the short-term outcomes. Another hypothesis is that surgery later in the week is associated with a lower lymph node harvest. However, in a separate paper from the same cohort, we have found no prognostic role of lymph node harvest.<sup>7</sup> A potential

role of non-radical resection in relation to weekday of surgery and long-term survival is another hypothesis worthy of a separate study.

In conclusion, this population-based and nationwide Swedish cohort study found no influence of weekday of oesophageal cancer surgery on risk of reoperations or mortality within 30 days of surgery. Thus, poor short-term outcomes do not seem to contribute to the association between later weekday of oesophageal cancer surgery and increased 5-year mortality.

**Contributors** JL provided substantial contributions to the conception and design, and acquisition and interpretation of the data; drafting of the paper; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. FM provided substantial contributions to the conception and design, and analysis and interpretation of the data; revising the paper critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. PL provided substantial contributions to the conception and design, and acquisition and interpretation of the data; revising the paper critically for important intellectual content; final approval of the version to be published; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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