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Mortality after surgery in Europe: a 7 day cohort study

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Summary

Background Clinical outcomes after major surgery are poorly described at the national level. Evidence of heterogeneity between hospitals and health-care systems suggests potential to improve care for patients but this potential remains unconfirmed. The European Surgical Outcomes Study was an international study designed to assess outcomes after non-cardiac surgery in Europe.

Methods We did this 7 day cohort study between April 4 and April 11, 2011. We collected data describing consecutive patients aged 16 years and older undergoing inpatient non-cardiac surgery in 498 hospitals across 28 European nations. Patients were followed up for a maximum of 60 days. The primary endpoint was in-hospital mortality. Secondary outcome measures were duration of hospital stay and admission to critical care. We used χ² and Fisher’s exact tests to compare categorical variables and the t test or the Mann-Whitney test to compare continuous variables. Significance was set at p<0·05. We constructed multilevel logistic regression models to adjust for the differences in mortality rates between countries.

Findings We included 46 539 patients, of whom 1855 (4%) died before hospital discharge. 3599 (8%) patients were admitted to critical care after surgery with a median length of stay of 1·2 days (IQR 0·9–3·6). 1358 (73%) patients who died were not admitted to critical care at any stage after surgery. Crude mortality rates varied widely between countries (from 1·2% [95% CI 0·0–3·0] for Iceland to 21·5% [16·9–26·2] for Latvia). After adjustment for confounding variables, important differences remained between countries when compared with the UK, the country with the largest dataset (OR range from 0·44 [95% CI 0·19–1·05; p=0·06] for Finland to 6·92 [2·37–20·27; p=0·0004] for Poland).

Interpretation The mortality rate for patients undergoing inpatient non-cardiac surgery was higher than anticipated. Variations in mortality between countries suggest the need for national and international strategies to improve care for this group of patients.

Funding European Society of Intensive Care Medicine, European Society of Anaesthesiology.

Introduction More than 230 million major surgical procedures are undertaken worldwide each year.1 For most patients, risks of surgery are low and yet evidence increasingly suggests that complications after surgery are an important cause of death.2–4 About 10% of patients undergoing surgery in the UK are at high risk of complications, accounting for 80% of postoperative deaths.2–4 If this rate is applicable worldwide, up to 25 million patients undergo high-risk surgical procedures each year, of whom 3 million do not survive until hospital discharge. Patients who develop complications but survive to leave hospital often have reduced functional independence and long-term survival.5–8

Despite obvious differences in procedure-related and patient-related mortality risks, most surgical patients use one care pathway, sharing standard facilities for pre-anaesthetic recovery, and hospital wards. This approach is adequate for most patients but might not meet the needs of the small number of patients at high risk of complications and death. In the USA, evidence of variations in postoperative mortality within health-care systems suggest the potential to implement measures that improve patient outcomes.9 Low rates of admission to critical care for patients at high risk of complications undergoing non-cardiac surgery are of particular concern,10–12 and might be affected by international differences in the provision of critical care.13,14 With high volumes of surgery undertaken, even a low rate of avoidable harm will be associated with many preventable deaths.

International comparative data might provide important insights into delivery of health care for surgical patients. However, little or no data are available describing provision of care or outcomes for unselected surgical patients. The objective of the European Surgical Outcomes Study (EuSOS) was to describe mortality rates and patterns of critical care resource use for patients undergoing non-cardiac surgery across several European nations.

Methods

Study design and participants We did this European cohort study between 0900 h (local time) on April 4, 2011, and 0859 h on April 11, 2011. All adult patients (older than 16 years) admitted to participating centres for elective or non-elective inpatient surgery commencing during the 7 day cohort period were...
eligible for inclusion. Patients undergoing planned day-case surgery, cardiac surgery, neurosurgery, radiological, or obstetric procedures were excluded because these patients receive care within separate, dedicated pathways. Participating hospitals (appendix pp 11–68) were a voluntary convenience sample, identified through membership of the European Society of Intensive Care Medicine and the European Society of Anaesthesiology and by direct approach from national study coordinators. Ethics requirements differed by country. In Denmark, centres were exempt from ethics approval because this study was deemed to be a clinical audit. In all other nations formal ethics approval was applied for and given. In Finland alone we were required to obtain written informed consent from individual patients.

Procedures
Local investigators were supported by national coordinators and via a website that provided key documentation, including the protocol and guidance on study procedures. We obtained data describing perioperative care facilities once for each hospital at the beginning of the study. We collected data describing consecutive patients with paper case record forms, which we made anonymous before entering the information onto a secure internet-based electronic case record form (OpenClinica, Boston, MA, USA). We completed an operating theatre case report form for each eligible patient who we then followed up until hospital discharge for data describing hospital stay, admission to critical care, and in-hospital mortality. We completed a critical care case record form to capture data describing the first admission to critical care for any individual patient at any time during the follow-up period. Example case record forms are available from the study website.

We selected patient-level variables on the basis that they were objective, routinely collected for clinical reasons, could be transcribed with a high level of accuracy, and would be relevant to a risk adjustment model in most patients. We censored critical care and hospital discharge data at 60 days after surgery. We assessed data for completeness and then checked for plausibility and consistency with prospectively defined ranges.12 The primary endpoint was in-hospital mortality. Secondary outcome measures were duration of hospital stay and admission to critical care.

Statistical analysis
Our aim was to recruit as many participating hospitals as possible and to recruit every eligible patient in those hospitals. We anticipated that a minimum sample size of 20 000 patients would enable a precise estimate of mortality. This sample size was also expected to provide a sufficient number of events (>200) for construction of a robust logistic regression model for mortality.

We used SPSS (version 19.0) for data analysis. Categorical variables are presented as number (%) and continuous variables as mean (SD) when normally distributed or median (IQR) when not. We used χ² and Fishers exact tests to compare categorical variables and the t test or the Mann-Whitney U test to compare continuous variables. Significance was set at p<0·05. We constructed several binary logistic regression models to identify factors independently associated with hospital mortality and to adjust for differences in confounding factors between countries. These included a one-level model and a hierarchical two-level generalised linear mixed model, with patients being at the first level and hospital at the second. Factors were entered into the model based on their univariate relation to outcome (p<0·05). All factors were biologically plausible with a sound scientific rationale and a low rate of missing data. The results of the model are reported as adjusted odds ratios (OR) with 95% CI. We assessed the models through sensitivity analyses with three random (disjoint) subsamples of countries and a fourth sample removing all patients from the largest country in the dataset (the UK). We explored all possible interacting factors and examined how they might have affected the final results.

This study is registered with ClinicalTrials.gov, number NCT01203605.

Role of the funding source
The study was funded by the European Society of Intensive Care Medicine and the European Society of Anaesthesiology who appointed an independent steering committee (appendix p 11), who were responsible for study design, conduct, and data analysis. Members of the steering committee had full access to the study data and were solely responsible for interpretation of the data, drafting and critical revision of the report, and the decision to submit for publication.

Figure 1: Study profile
(A) All patients. (B) Patients admitted to critical care. CRF=case report form.
Results
We collected data describing patients undergoing in-patient surgery in 498 hospitals across 28 European nations. Median number of operating theatres in each hospital was 15 (IQR 10–22) and median number of critical care beds was 19 (9–40). Data were returned for 46 985 cases of which 446 were removed having been identified as duplicates or having missing critical care or mortality data, leaving 46 539 for analysis (figure 1). A median number of 83 (39–125) patients were included per hospital and 1045 (455–1732) per country. 281 (56%) hospitals were affiliated to a university, recruiting 31 113 patients (68% of total, appendix p 2).

Table 1 shows baseline data for all patients. Overall crude mortality was 4·0% and the median duration of hospital stay was 3·0 days (IQR 1·0–7·0). Prevalence of comorbid disease, grade of surgery, crude mortality rates, duration of hospital stay, and number of critical care admissions differed substantially between countries (table 2, appendix p 2). Median stay in critical care was 1·2 days (0·9–3·6). 1358 patients who died were not admitted to critical care at any stage after surgery (73% of all deaths). 506 patients (14%) admitted to critical care died before hospital discharge, of whom 218 (43%) died after the first admission to critical care was complete.

We explored variables associated with hospital mortality in a univariate analysis, the findings of which were much the same as for a sensitivity analysis of different subsets of the database (table 1, appendix pp 3–4). We then constructed several binary logistic regression models to adjust for baseline differences that might explain the unadjusted OR for individual countries (table 2). We developed both single-level and multilevel models (appendix pp 5–8) with variables that were significant in the univariate analysis. The point estimates for the OR did not differ greatly between the one-level and two-level models, but the hierarchical model consistently provided a more conservative estimate of country effects across the sensitivity tests (appendix p 9).

We constructed a further model including all significant interacting factors (appendix p 10). Since this increased model complexity did not substantially change the country-level estimates, we report results of the more parsimonious two-level model without interactions (figure 3). Factors that were independently associated with mortality and that we therefore used to adjust for baseline confounders were: country where surgery was done, urgency of surgery, grade of surgery, surgical procedure category, age, American Society of Anesthesiologists (ASA) score, metastatic disease, and cirrhosis (appendix pp 7–8). We entered ASA score rather than the Lee Revised Cardiac Index because, although the two were highly correlated, less data describing ASA score were missing.

Table 1: Description of cohort

<table>
<thead>
<tr>
<th>Description of cohort</th>
<th>All patients (n=46 539)</th>
<th>Died in hospital (n=1864)</th>
<th>Survived to hospital discharge (n=44 657)</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56·7 (18·5) 61·0 (18·7) 56·6 (18·5)</td>
<td>1·01 (1·01–1·02)</td>
<td>0·0001</td>
<td>Man</td>
<td>22 607 968 21·629</td>
</tr>
<tr>
<td>Present smoker</td>
<td>9·872 363 9·503</td>
<td>0·90 (0·80–1·01)</td>
<td>0·07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASA score</td>
<td>11 642 362 11 280</td>
<td>Reference</td>
<td>...</td>
<td>2 21 582 633 20·944</td>
<td>0·94 (0·83–1·07)</td>
</tr>
<tr>
<td>Grade of surgery</td>
<td>Minor 12 041 431 11 608</td>
<td>Reference</td>
<td>...</td>
<td>Intermediate 22 231 741 21 483</td>
<td>0·93 (0·82–1·05)</td>
</tr>
<tr>
<td>Urgency of surgery</td>
<td>Elective 35 049 1129 33 968</td>
<td>Reference</td>
<td>...</td>
<td>Urgent 8 923 483 8 436</td>
<td>1·71 (1·52–1·91)</td>
</tr>
<tr>
<td>Surgical specialty</td>
<td>Orthopaedics 12 214 468 11 744</td>
<td>1·02 (0·84–1·24)</td>
<td>0·85</td>
<td>Breast 1 500 43 1456</td>
<td>0·76 (0·53–1·07)</td>
</tr>
<tr>
<td>Kidney</td>
<td>3 792 115 3 857</td>
<td>0·76 (0·59–0·99)</td>
<td>0·04</td>
<td>Vascular 2376 140 2233</td>
<td>1·61 (1·26–2·05)</td>
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<tr>
<td>Urology</td>
<td>2228 155 2071</td>
<td>1·88 (1·48–2·39)</td>
<td>0·001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical specialty</td>
<td>Upper gastrointestinal 4972 284 4683</td>
<td>1·54 (1·25–1·91)</td>
<td>0·0001</td>
<td>Lower gastrointestinal 2247 113 2134</td>
<td>1·35 (1·04–1·74)</td>
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<tr>
<td>Plastic or cutaneous</td>
<td>2432 73 2356</td>
<td>0·79 (0·59–1·06)</td>
<td>0·12</td>
<td>Urology 4881 144 4737</td>
<td>0·78 (0·61–0·99)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>5640 174 5466</td>
<td>0·82 (0·65–1·03)</td>
<td>0·09</td>
<td>Kidney 463 9 454</td>
<td>0·51 (0·26–1·01)</td>
</tr>
<tr>
<td>Other</td>
<td>3463 132 3329</td>
<td>Reference</td>
<td>...</td>
<td>Head and neck 5640 174 5466</td>
<td>0·82 (0·65–1·03)</td>
</tr>
<tr>
<td>Laparoscopic surgery</td>
<td>5510 160 5350</td>
<td>0·69 (0·59–0·82)</td>
<td>&lt;0·0001</td>
<td>Circnh</td>
<td>498 65 433</td>
</tr>
<tr>
<td>Comorbid disorder</td>
<td>Congestive heart failure 2154 166 1985</td>
<td>2·10 (1·78–2·48)</td>
<td>&lt;0·0001</td>
<td>COPD 5162 244 4912</td>
<td>1·21 (1·05–2·48)</td>
</tr>
<tr>
<td>Coronary artery disease 6274 387 5881</td>
<td>1·73 (1·54–1·94)</td>
<td>&lt;0·0001</td>
<td>Diabetes (taking insulin) 2081 135 1939</td>
<td>1·73 (1·44–2·07)</td>
<td>&lt;0·0001</td>
</tr>
<tr>
<td>Diabetes (not taking insulin) 3495 147 3348</td>
<td>1·05 (0·88–1·24)</td>
<td>0·61</td>
<td>Metastatic cancer 2173 155 2017</td>
<td>1·91 (1·61–2·27)</td>
<td>&lt;0·0001</td>
</tr>
</tbody>
</table>
| Stroke                | 2006 120 1884 | 1·57 (1·30–1·90) | <0·0001 | Data are mean (SD) or n unless otherwise specified. Odds ratios were constructed for in-hospital mortality with univariate binary logistic regression analysis. ASA=American Society of Anesthesiologists. COPD=chronic obstructive pulmonary disease.
With the UK study population as the reference category, we identified higher unexplained rates of mortality in Poland, Romania, Latvia, and Ireland (table 2, figure 3).

**Discussion**

This international prospective study has provided data for a population of more than 46,000 unselected patients undergoing inpatient surgery from 28 European countries. 4% of included patients died before hospital discharge, which was a higher mortality rate than expected. 4% of included patients died before hospital discharge, which was a higher mortality rate than expected. We identified substantial differences in crude and risk adjusted mortality rates between countries. When compared with the UK, the recorded mortality rates for Poland, Latvia, Romania, and Ireland were higher even after adjustment for all identified confounding variables. This pattern could relate to cultural, demographic, socioeconomic, and political differences between nations, which might affect population health and health-care outcomes.

A major strength of our study was the large number of consecutive unselected patients enrolled in a multicentre and multinational setting. A vigorous approach to follow-up for missing and incomplete data provided a high-quality dataset for analysis. The dataset allowed us to explore probable prognostic factors and to adjust crude mortality rates to describe differences in outcomes between countries. Our analysis identified several factors associated with increased mortality. These findings suggest that surgery-related and patient-related factors interact to increase mortality risk. Only two comorbid disease categories were identified as independent variables. This finding probably arose because the ASA score was designed to describe the severity of coexisting medical disease.

Evidence suggests that critical-care-based cardiorespiratory interventions can improve outcomes among high-risk surgical patients. However, in our study, only 5% of patients underwent a planned admission to critical care with a median stay of about 1 day. Unplanned admissions to critical care were associated with higher mortality rates than were planned admissions. Remarkably, most patients who died (73%) were not admitted to critical care at any...
Despite the large sample size, our study might not be truly representative of current practice across Europe because only a small proportion of European hospitals took part. Although in some countries the patient sample was large enough to show national practice, the high proportion of patients enrolled in university hospitals in other countries suggests a degree of selection bias. In particular, our data might not show the true surgical...
mortality rates for unselected populations of surgical patients. We identified seven large national studies describing mortality rates for the population of interest, three of which involved prospective data collection. No studies were identified that provided international comparative data. The last search was done on June 15, 2012.

Interpretation
As far as we are aware, this was the first large prospective international epidemiological study of unselected non-cardiac surgical patients and as such it provides a new perspective on mortality after surgery. A few national reports describe mortality rates of 1·3% to 2·0%. In our study, the overall crude mortality rate of 4% was higher than anticipated. We identified important variations in risk-adjusted mortality rates between nations, and critical care resources did not seem to be allocated to patients at greatest risk of death. Our findings raise important public health concerns about the provision of care for patients undergoing surgery in Europe.

Panel: Research in context
Systematic review
We searched Medline for original research from the past 10 years describing mortality rates in large unselected national and international populations of patients undergoing non-cardiac surgery. We used the search terms "surgery", "mortality", and "complications" and widened our search to include retrospective analyses of health-care registries and prospective epidemiological studies. Publications were screened by title and then by abstract for relevance to the objectives of our study. Additionally, co-investigators in various European nations searched for publicly available registry analyses reporting mortality rates for unselected populations of surgical patients. We identified seven large national studies describing mortality rates for the population of interest, three of which involved prospective data collection. No studies were identified that provided international comparative data. The last search was done on June 15, 2012.

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models for the final analysis because our aim had been to construct a parsimonious model that practising clinicians would easily understand.

As far as we are aware, this was the first large, prospective, international assessment of surgical outcomes (panel). In some countries, data are available that describe survival after specific procedures such as vascular, joint replacement, or bowel cancer surgery. However, these audits are poorly representative of overall national surgical populations because high-risk patients are under-represented. The few previous estimates suggest an overall mortality for unselected inpatient surgery of between 1% and 2%, but these values are representative of only a few health-care systems. In a previous study of national registry data from the Netherlands, 30 day mortality was reported as 1·85%, which is much the same as the crude hospital mortality of 2% for this country in the EuSOS study. In the UK, a prospective investigation with a very similar methods to EuSOS identified a postoperative critical care admission rate of 6·7%, which is much the same as to the value of 6% for EuSOS in the UK. However, 30 day mortality was 1·6% compared with 3·6% for 60 day in-hospital mortality for UK patients in EuSOS. Reports from nations outside Europe describe 30 day mortality rates from 1·3% to 2·0%.

Previous investigators have described the differences in provision of health services across Europe, in particular numbers of critical care beds. The reported seven-times greater provision of critical care beds for Germany than for the UK is likely to affect rates of admission to critical care and postoperative outcomes. This finding is in keeping with our present data that show a greater rate of admission to critical care after surgery in Germany than in the UK. Other studies have shown that fewer than a third of high-risk non-cardiac surgical patients are admitted to critical care after surgery in the UK despite high mortality rates, which is consistent with the results of our study; across Europe 73% of surgical patients who died were never admitted to critical care. This situation contrasts with perioperative care for cardiac surgical patients who by definition have severe comorbid disease and undergo major body cavity surgery followed by routine admission to critical care with mortality rates of less than 2%. Several reasons could explain why outcomes for cardiac and non-cardiac surgical patients differ but the quality of perioperative care is likely to be among the most important. The health-care community increasingly recognises the importance of the entire perioperative care pathway including preoperative assessment, optimisation of coexisting medical disease, integrated care pathways relevant to the surgical procedure, WHO surgical checklists, advanced haemodynamic monitoring during surgery, early admission to critical care, acute pain management and critical-care outreach services, and hospital discharge planning together with the
primary care physician. Routine audit and reporting of data for clinical outcomes has also proved a highly effective instrument for improvement of the quality of perioperative care.

Our findings suggest both the need and potential to implement measures to improve postoperative outcomes. In addition to further research in this discipline, the root causes of this problem could be better understood through increased use of high-quality registries designed to capture robust data describing quality of care and clinical outcomes for surgical patients. This step would require increased funding for this specific area of health services research. The high mortality rate after surgery might be modified by changes in the organisation of care.

Contributors
All authors were involved in the design and conduct of the study. Data collection and collation was done by the members of the EuSOS study group. AR, RM, and PB did the data analysis with input from RP. The report was drafted by RP and AR and revised following critical review by all authors.

Conflicts of interest
We declare that we have no conflicts of interest.

Acknowledgments
This study was funded by the European Society of Intensive Care Medicine and the European Society of Anaesthesiology. RP is a National Institute for Health Research (UK) Clinician Scientist.

References