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Minimal versus Definitive Surgery in Managing Peptic Ulcer Bleeding: A Population-Based Cohort Study

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Key Words
Peptic ulcer bleeding · Minimal surgery · Definitive surgery · Survival

Abstract
Objective: To compare radical surgery with a minimal approach for peptic ulcer bleeding in relation to survival. Design: A Swedish nationwide population-based cohort study from 1987–2008 compared survival after minimal surgery and definitive surgery. The cohort was also stratified into calendar year before and after the year 2000 for subgroup analyses. Data were collected from the Swedish Patient Register. The two surgical groups were matched based on the propensity score to mimic a randomized trial design. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox regression models adjusted for potential confounders. Results: 4,163 patients were included. There were no differences in survival in patients who underwent definitive surgical procedures compared to those who underwent minimal surgery for a bleeding peptic ulcer during the full study period. Using minimal surgery group as the reference, the HRs for death in the definitive surgery group within 30 days, 90 days, 1 year, and 5 years were 0.87 (95% CI 0.72–1.05), 0.93 (0.80–1.09), 1.00 (95% CI 0.87–1.14), and 1.05 (95% CI 0.95–1.16), respectively. The corresponding HRs during the calendar period after the year 2000 were 1.05 (95% CI 0.65–1.69), 1.18 (95% CI 0.81–1.73), 1.17 (0.84–1.62), and 1.27 (95% CI 0.99–1.63), respectively. Conclusion: This study found no worse overall survival after minimal surgery compared to more extensive surgery for refractory peptic ulcer bleeding, and indicated better long-term survival in the minimal surgery group during the more recent study period. A minimal approach is probably sufficient in most cases.
other comorbidities [3, 4], making surgery more hazardous. Although the need for surgery for peptic ulcers has declined [5], it still plays an important role when other modalities fail. Traditionally, resection of parts of the stomach and duodenum has been the gold standard method for peptic ulcer surgery, and vagotomy has been performed for the purpose of postoperative acid reduction [6]. With the introduction of effective anti-secretory drugs and eradication therapy of Helicobacter pylori, the need for resection or vagotomy for treatment of the underlying ulcer disease has decreased [5]. The primary goal for surgery has instead become to obtain hemostasis in emergency situations, while causing as little trauma as possible. Medical treatment is then used to cure the ulcer disease. Therefore, simply underrunning a duodenal ulcer or a small excision of a gastric ulcer, has become increasingly common [7], although not all agree with this minimal surgery strategy [8, 9]. The role of different surgical strategies in an era when endoscopic therapy, H. pylori eradication, medical therapy and endovascular embolization is available is not well enough studied to provide evidence in this matter. There is no broad consensus on which surgical strategy is better. Younger surgeons are not experienced in elective ulcer surgery, which may be a problem when performing emergency gastric resection or vagotomy, or placement of ligatures of major arteries. Using the Swedish Patient Register, we conducted a nationwide cohort study to compare less extensive surgery with more radical surgery for peptic ulcer bleeding in relation to survival.

Methods

Study Design

A Swedish nationwide population-based cohort study was conducted during the period 1987 through 2008. Less extensive surgery, labeled ‘minimal surgery’, was compared with more radical surgery, labeled ‘definitive surgery’, for bleeding peptic ulcer in relation to survival. All patients who underwent surgery for peptic ulcer bleeding from 1987 were identified from the Swedish Patient Register. This register also provided data on comorbidities. The personal identity number, a 10-digit identifier assigned to all Swedish residents, was used for linkages of all individuals in the study cohort to the Swedish Register of the Total Population and the Causes of Death Register, to ascertain the outcome mortality and other end points (defined below). The study was approved by the Regional Ethical Review Board in Stockholm, Sweden.

Data Sources

The Swedish Patient Register was used to identify patients who had undergone surgery for peptic ulcer disease, and to retrieve information about the type of surgery conducted as well as comorbidities. The register contains complete nationwide data of in-hospital care in Sweden since 1987. Diagnosis codes at discharge, codes of surgical procedures and hospitalization dates can be obtained. Validation studies have shown that 85–95% of all diagnoses are valid [10], and codes representing upper gastrointestinal surgery have been shown to have up to 99.6% positive predictive value [11]. The diagnoses are coded according to the International Classification of Diseases (ICD) versions 9 and 10. The Patient Register also contains complete data of outpatient care and day surgery in Sweden since 2001, including both private and public caregivers.

The Register of the Total Population was used to ascertain dates of mortality and emigration. This register provides complete information on updated dates of birth, death and migration in Sweden with a maximum of 14 days’ delay.

Identification of Peptic Ulcer Bleeding

Diagnosis codes representing peptic ulcer bleeding according to the ICD-9 (1987–1996) and 10 (1997–2009) versions were used to identify the cohort members by the ICD-9 codes 531A, 531E, 532A, 532E, 533A, or 533E, and the ICD-10 codes K250, K254, K260, K264, K270, or K274. Patients who were diagnosed with a gastric cancer at the time of diagnosis of peptic ulcer bleeding were excluded.

Identification of Surgical Method

Surgical procedures were defined using codes from the classification of surgical procedures by the Nordic Medico-Statistical Committee (NOMESCO, Swedish version, 1997), and retrieved from the Patient Register. The codes for the surgical procedures in this study were:

(1) Minimal surgery: Underrunning of the ulcer through a gastrotomy or duodenotomy with or without ligation of major artery or local excision of the ulcer. These procedures were defined by the ICD-9 codes 4400, 4403, 4460, 4461, or 4466 and the ICD-10 codes JDA60, JDA63, JDH00, JDH070, or JDW96.

(2) Definitive surgery: Resection of a part of the stomach or duodenum, with or without vagotomy. These procedures were defined by the ICD-9 resection codes 4420, 4411, 4412, 4422, 4413, 4414, 4415, 4416, 4417, 4418, 4419, 4424, 4425, 4426, 4429, 4430, 4432, 4434, 4435, 4462, 4404, 4485, or 4488 and ICD-9 vagotomy codes 4471, 4472, 4473, 4474, 4475, 4476, or 4477 and the ICD-10 vagotomy codes JDG00 or JDG10. In one subanalysis, the vagotomies were excluded.

Identification of Diagnostic Endoscopy and Endoscopic Interventions

Data on diagnostic and interventional endoscopy were retrieved from the Patient Register, using codes for surgical procedures by the Nordic Medico-Statistical Committee (NOMESCO, Swedish version, 1997). ICD-9: 4487, 4483, 9003, 9004, 9021 and 4480. ICD-10: JDA42, JDA52, JDW98, DJ003, DJ012, UJD02 and UJD05.

Comorbidity

Comorbidity was defined as having one or more of the following diagnoses as a recorded ICD code in the present or in any former hospitalizations, or as an outpatient: chronic heart failure (ICD-9: 428 and ICD-10: I50.0–I50.9), ischemic heart disease (in-
including angina pectoris, myocardial infarction, ICD-9: 410–414 and ICD-10: I20.0–I25.9, stroke (ICD-9: 434, 438 and ICD-10: I63.0–I63.9), diabetes (ICD-9: 249–250 and ICD-10: E10.0–E14.9), chronic liver insufficiency or cirrhosis (ICD-9: 571 and ICD-10: K71.7, K74.3–K74.6, K72.0–K72.9, or K70.2–K70.9), chronic renal insufficiency (ICD-9: 585 and ICD-10: I20.0, I31.1, I13.2, N18.2–N18.9, or N19.9), any malignancy (ICD-9: 140–249 and ICD-10: C00.0–C09.9), and chronic obstructive lung disease (ICD-9: 490–496 and ICD-10: J42.9, J43.0–J43.9, or J44.0–J44.9).

Data on history of ulcer disease before index bleeding hospitalization (categorized as yes or no) were obtained from the Patient Register. It was defined as any recorded ulcer diagnosis since the start of the registers. An ulcer diagnosis recorded within 30 days before the index bleeding date was considered to be part of the same episode and thus not a former ulcer history.

**Hospital Volume**

Hospitals were grouped in quartiles based on their annual volume of the surgical procedures defined above. Hospitals in the lowest quartile were considered ‘low-volume centers’, hospitals between the 25th and the 75th percentiles were considered ‘medium-volume centers’, and hospitals within the highest annual volume quartile were considered ‘high-volume centers’.

**Statistical Analysis**

Cox proportional hazard regression models were used to compare the relative risk of death between the two comparison groups, presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Minimal surgery was used as the reference category. Outcomes of the study were death within 30 days, 90 days, 1 year, or 5 years after discharge from the hospital. Other end points included hospitalization for the second emergency surgery for peptic ulcer bleeding, emigration, or the end of the study period (December 31, 2008), whichever occurred first. A basic statistical model included adjustment for sex and age (categorized into four groups: <60, 60–69, 70–79, or ≥80 years). A full multivariable model further adjusted for comorbidity (0, 1, 2, or >2 predefined comorbidities), hospital volume (low, medium, or high), endoscopic intervention (no or yes), ulcer history (no or yes), and calendar period (in 5-year intervals: 1987–1991, 1992–1996, 1997–2001, 2002–2006, or 2007–2008).

In addition, a propensity score-matched analysis was conducted to mimic a randomized clinical trial design. The propensity score was defined as the predicted probability of treatment derived from the logistic regression model. Pairs were formed using one individual from each treatment group with similar values of the propensity score. Matching based on the propensity score makes the distribution of observed baseline covariates similar between the comparison groups. All statistical analyses were conducted using the SAS 9.2 software (the Statistical Analysis System, SAS Institute, Cary, N.C., USA).

**Results**

**Study Participants**

In total, 4,163 patients who underwent surgery for peptic ulcer were included in the final study cohort. Among these, 2,132 patients (51.2%) underwent minimal surgery, and 2,031 patients (48.8%) underwent definitive surgery. Basic characteristics of the study participants are shown in table 1. The male:female ratio among all study participants was 1.5:1, and this ratio was slightly higher in the definitive surgery group. The minimal surgery group contained more patients of older age and with comorbidity. Of all patients who underwent surgical treatment, 1,860 (44.7%) had a gastric ulcer, 2,092 (50.3%) had a duodenal ulcer, 37 (0.9%) had both a gastric and duodenal ulcer, and 174 (4.2%) had peptic ulcers without a specified sublocation.

**Mortality after Surgery for Ulcer Bleeding**

**Total Study Period (1987–2008)**

The total number of deaths within 30 days, 90 days, 1 year and 5 years was 565 (13.6%), 798 (19.2%), 1,077 (25.9%), and 1,933 (46.4%), respectively. Using minimal surgery as reference, the fully adjusted HR for death within 30 days was 0.87 (95% CI 0.72–1.05) in the definitive surgery group. The corresponding HRs for death within 90 days, 1 year, and 5 years were 0.93 (0.80–1.09), 0.99 (95% CI 0.86–1.14), and 1.08 (95% CI 0.97–1.19), respectively.

Based on the propensity score-matched analysis, the HR for death within 30 days in the definitive surgery group was 1.01 (95% CI 0.82–1.24) compared to the minimal surgery group. The corresponding HRs for death within 90 days, 1 year, and 5 years were 1.04 (95% CI 0.87–1.23), 1.10 (95% CI 0.99–1.28), and 1.08 (95% CI 0.97–1.21), respectively (table 2).

**Early Study Period (1987–1999)**

Before 2000, using minimal surgery as a reference, the fully adjusted HR for death within 30 days was 0.84 (95% CI 0.70–1.02) in the definitive surgery group, while the HR for death within 90 days was 0.90 (95% CI 0.77–1.06); the HR for death within 1 year was 0.98 (95% CI 0.85–1.13), and the HR for death within 5 years was 1.03 (0.93–1.15; table 3). Using the propensity score model, the HR for death within 30 days was 0.96 (95% CI 0.77–1.21). For 90 days, 1 year and 5 years, the HRs for death were 0.98 (95% CI 0.81–1.17), 1.06 (95% CI 0.91–1.24), and 1.05 (95% CI 0.93–1.18), respectively.

**Late Study Period (2000–2008)**

From the year 2000 onwards, the fully adjusted HR for death within 30 days was 1.05 (95% CI 0.65–1.69), the HR for death within 90 days was 1.18 (95% CI 0.81–1.73), the
HR for death within 1 year was 1.17 (0.84–1.62), and the HR for death within 5 years was 1.27 (95% CI 0.99–1.63).

Using the propensity score model, the HR for death within 30 days was 1.59 (95% CI 0.81–3.12). For 90 days, 1 year and 5 years, the HRs for death were 1.69 (95% CI 0.98–2.92), 1.56 (95% CI 0.99–2.48), and 1.39 (95% CI 0.99–1.94), respectively.

Discussion

This study indicates no major differences in overall survival in patients who undergo definitive surgical procedures for peptic ulcer bleeding compared to those who undergo minimal surgery, after adjusting for clinically relevant factors. The results for the more recent
The study period (from the year 2000 onwards) showed better survival point risk estimates in the minimal surgery group, but there were no statistically significant differences.

The main strengths of this study include the population-based design, the large sample size, and the completeness of the follow-up. The adopted registers contained valid data and were complete, which guarantees robust identification of exposures and outcomes with minimal missing data or loss to follow-up. There are also several limitations. Compared to the cohort study design, a randomized clinical trial might be superior to assess the influence of confounding factors, but randomization is virtually infeasible due to the small sample size and

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**Table 2.** Risk of all-cause mortality after surgery for peptic ulcer bleeding, expressed as HR with 95% CI

|                     | 30-day mortality | 90-day mortality | 1-year mortality | 5-year mortality |
|---------------------|------------------|------------------|------------------|------------------|
|                     | HR   | 95% CI | HR   | 95% CI | HR   | 95% CI | HR   | 95% CI |
| Model 1<sup>a</sup> |       |        |       |        |       |        |       |        |
| Minimal surgery     | 1 (reference)   | 1 (reference)   | 1 (reference)   | 1 (reference)   |
| Resection/vagotomy  | 0.80 | 0.68–0.95 | 0.85 | 0.74–0.98 | 0.87 | 0.77–0.98 | 0.92 | 0.84–1.01 |
| Resection           | 0.88 | 0.73–1.06 | 0.92 | 0.79–1.07 | 0.89 | 0.78–1.02 | 0.96 | 0.88–1.06 |
| Model 2<sup>b</sup> |       |        |       |        |       |        |       |        |
| Minimal surgery     | 1 (reference)   | 1 (reference)   | 1 (reference)   | 1 (reference)   |
| Resection/vagotomy  | 0.87 | 0.72–1.05 | 0.93 | 0.80–1.09 | 1.00 | 0.87–1.14 | 1.05 | 0.95–1.16 |
| Resection           | 0.94 | 0.78–1.14 | 0.99 | 0.85–1.17 | 0.99 | 0.86–1.14 | 1.08 | 0.97–1.19 |
| Propensity score model |   |        |       |        |       |        |       |        |
| Minimal surgery     | 1 (reference)   | 1 (reference)   | 1 (reference)   | reference      |
| Resection/vagotomy  | 1.01 | 0.82–1.24 | 1.04 | 0.87–1.23 | 1.10 | 0.95–1.28 | 1.08 | 0.97–1.21 |
| Resection           | 0.95 | 0.76–1.18 | 1.01 | 0.84–1.22 | 0.99 | 0.85–1.16 | 1.08 | 0.96–1.22 |

<sup>a</sup> Model adjusted for age and sex. <sup>b</sup> Model adjusted for age, sex, comorbidities, hospital volume, endoscopic intervention, ulcer history and calendar period.

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**Table 3.** Risk of all-cause mortality after surgery for peptic ulcer bleeding before and after year 2000, expressed as HR with 95% CI

|                     | 30-day mortality | 90-day mortality | 1-year mortality | 5-year mortality |
|---------------------|------------------|------------------|------------------|------------------|
|                     | HR   | 95% CI | HR   | 95% CI | HR   | 95% CI | HR   | 95% CI |
| Year 1987–1999      |       |        |       |        |       |        |       |        |
| Regression model<sup>a</sup> |       |        |       |        |       |        |       |        |
| Minimal surgery     | reference |        | reference |        | reference |        | reference |        |
| Definitive surgery  | 0.84  | 0.70–1.02 | 0.90  | 0.77–1.06 | 0.98  | 0.85–1.13 | 1.03 | 0.93–1.15 |
| Propensity score model |        |        |       |        |       |        |       |        |
| Minimal surgery     | reference |        | reference |        | reference |        | reference |        |
| Definitive surgery  | 0.96  | 0.77–1.19 | 0.98  | 0.81–1.17 | 1.06  | 0.91–1.24 | 1.05 | 0.93–1.18 |
| Year 2000–2008      |       |        |       |        |       |        |       |        |
| Regression model<sup>a</sup> |       |        |       |        |       |        |       |        |
| Minimal surgery     | reference |        | reference |        | reference |        | reference |        |
| Definitive surgery  | 1.05  | 0.65–1.69 | 1.18  | 0.81–1.73 | 1.17  | 0.84–1.62 | 1.27 | 0.99–1.63 |
| Propensity score model<sup>b</sup> |       |        |       |        |       |        |       |        |
| Minimal surgery     | reference |        | reference |        | reference |        | reference |        |
| Definitive surgery  | 1.59  | 0.81–3.12 | 1.69  | 0.98–2.92 | 1.56  | 0.99–2.48 | 1.39 | 0.99–1.94 |

<sup>a</sup> Logistic regression model adjusted for age, sex, comorbidities, hospital volume, endoscopic intervention and ulcer history. <sup>b</sup> Adjusted for propensity score.
inherent difficulties of randomizing and blinding surgical procedures. We did, however, adjust for several potentially important confounding factors, and included both an adjusted logistic regression model and a propensity score-matched analysis to counteract the influence of confounding. However, as in any observational study, residual confounding from the adjusted variables or confounding from unknown factors cannot be excluded. For example, radiologic interventions are not included in the Swedish Patient Register and could not be adjusted for. The number of performed endoscopies in the Patient Register, even in the later calendar period, is somewhat lower than we expected (fig. 1). This could be due to slight underreporting of these procedures among patients undergoing open surgery during the same hospitalization. This is because endoscopy is sometimes not seen as a surgical procedure. Focus at discharge is probably put on the more extensive procedure performed, and not on less extensive actions preceding it, including endoscopy. It may also to some extent reflect that not all hospitals have 24-hour endoscopy service.

Few previous studies have compared surgical procedures for acute peptic ulcer bleeding in relation to survival, and the available results vary widely. Moreover, there is a lack of studies conducted in the modern era of novel endoscopic, pharmacologic and angiographic treatment. Two randomized studies have addressed this subject. A randomized multicenter trial from the UK from 1991 compared minimal surgery (underrunning of the bleeding vessel or ulcer excision) with definitive surgery (vagotomy and pyloroplasty or gastric resection) in 137 patients, and found a statistically nonsignificantly higher mortality among patients treated with minimal surgery (16 deaths in 62 patients) compared to definitive surgery (13 deaths in 67) [12]. A French multicenter trial from 1993 compared underrunning of the ulcer plus vagotomy with gastric resection in bleeding duodenal ulcers in 202 patients, and found no difference in mortality [13]. A recent study from the US retrospectively compared simple ulcer oversuturing with vagotomy and drainage. The results of that study indicated that vagotomy and drainage was associated with lower postoperative mortality than simple oversuturing [14]. The authors did not find a significant difference in 30-day mortality when comparing oversuturing with resection surgery. A US retrospective cohort study from 2006 compared vagotomy plus drainage with vagotomy plus resection, with no significant differences in mortality or morbidity [15]. A US case series of 19 patients who underwent surgery for peptic ulcer bleeding showed that definitive surgery procedures for peptic ulcer surgery had declined between 1990–1999 and 2000–2009 without any corresponding increase in adverse outcomes [16]. In a French study of 22 consecutive patients who had undergone minimal emergency surgery for peptic ulcer bleeding, none of the patients had recurrent bleeding after surgery, and the authors concluded that minimal surgery in combination with continuous PPI was effective [17]. A retrospective study of 61 patients showed that patients operated on with only underrunning sutures had a lower mortality (10%) than those who received underrunning sutures plus vagotomy (45%), or those who underwent gastric resection (26%) [18]. Taken together, the results of the previous literature and the present study indicate that a minimal surgery approach can be recommended in most patients.

The main argument for performing resection surgery instead of minimal surgery would be to avoid deaths due to rebleeding if the underrunning sutures are insufficient. However, rebleeding is uncommon. The main causes of death among peptic ulcer bleeding patients are pulmonary or cardiovascular rather than rebleeding [1]. This supports advocating a minimal surgery strategy. In selected cases, combination therapy with transarterial embolization after minimal surgery can probably be of value, but this needs to be studied further. If the ulcer is very large or if, for example, damaged surrounding tissue makes safe suturing difficult, resection surgery can still be necessary.

The patients in the minimal surgery group seem to be a selection of older individuals with more comorbidities than in the definitive surgery group, which probably re-
fects that surgeons are more hesitant to perform more extensive procedures on such patients. However, survival was similar in the two groups after adjustment for confounding by age among other factors.

In conclusion, this population-based cohort study found no benefit in survival after resection surgery compared with a minimal surgical approach for treatment of peptic ulcer bleeding, and suggested a possibly better survival in the minimal surgery group during the more recent calendar period. A minimal approach with underrunning of the ulcer is probably sufficient in most cases.

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