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CLINICAL—ALIMENTARY TRACT

Mortality, Reoperation, and Hospital Stay Within 90 Days of Primary and Secondary Antireflux Surgery in a Population-Based Multinational Study

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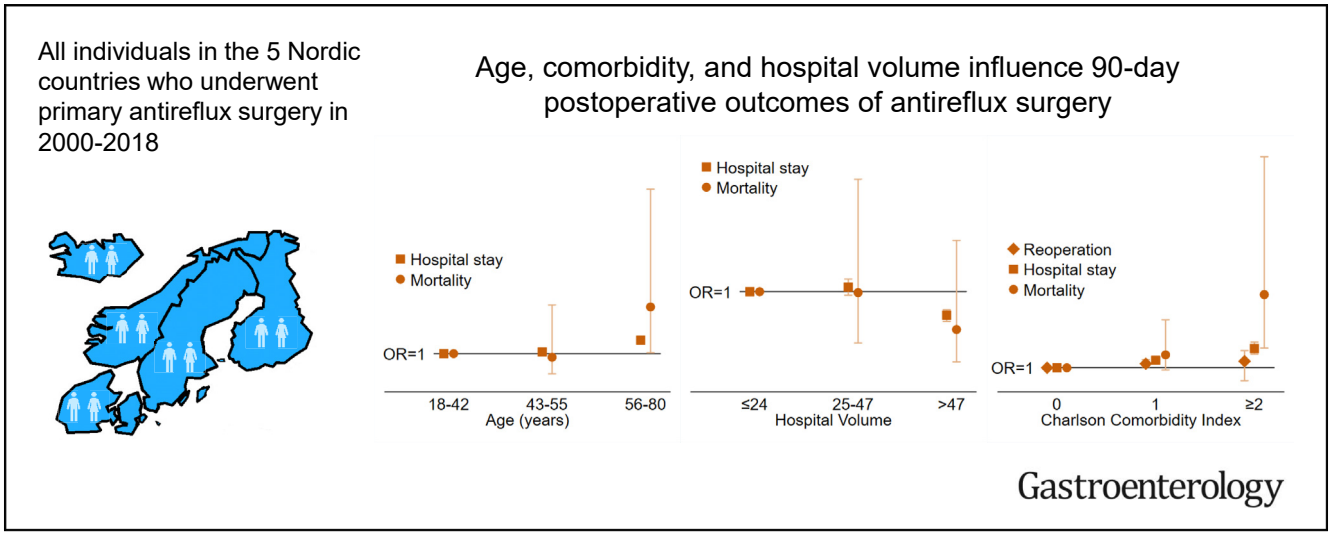
This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e18. Learning Objective:Upon completion of this CME activity, successful learners will be able to discuss the incidence of antireflux surgery, recurrence of gastroesophageal reflux disease after antireflux surgery, and how laparoscopic antireflux surgery compares with open antireflux surgery.



BACKGROUND & AIMS: Absolute rates and risk factors of short-term outcomes after antireflux surgery remain largely unknown. We aimed to clarify absolute risks and risk factors for poor 90-day outcomes of primary laparoscopic and secondary antireflux surgery. **METHODS:** This population-based cohort study included patients who had primary laparoscopic or secondary antireflux surgery in the 5 Nordic countries in 2000-2018. In addition to absolute rates, we analyzed age, sex, comorbidity, hospital volume, and calendar period in relation to all-cause 90-day mortality (main outcome), 90-day reoperation, and prolonged hospital stay (≥2 days over median stay). Multivariable logistic regression provided odds ratios (ORs) with 95% confidence intervals (95% CI), adjusted for confounders. **RESULTS:** Among 26,193 patients who underwent primary laparoscopic antireflux surgery, postoperative 90-day mortality and 90-day reoperation rates were 0.13% (n = 35) and 3.0% (n = 750), respectively. The corresponding rates after secondary antireflux surgery (n = 1 618) were 0.19% (n = 3) and 6.2% (n = 94). Higher age (56-80 years vs 18-42 years: OR, 2.66; 95% CI 1.03-6.85) and comorbidity (Charlson Comorbidity Index ≥2 vs 0: OR, 6.25; 95% CI 2.42-16.14) increased risk of 90-day mortality after primary surgery, and higher hospital volume suggested a decreased risk (highest vs lowest tertile: OR, 0.58; 95% CI, 0.22-1.57). Comorbidity increased the risk of 90-day reoperation. Higher age and comorbidity increased risk of prolonged hospital stay after both primary and secondary surgery. Higher annual hospital volume

decreased the risk of prolonged hospital stay after primary surgery (highest vs lowest tertile: OR, 0.74; 95% CI, 0.67-0.80). **CONCLUSION:** These findings suggest that laparoscopic antireflux surgery has an overall favorable safety profile in the treatment of gastroesophageal reflux disease, particularly in younger patients without severe comorbidity who undergo surgery at high-volume centers.

Keywords: Gastroesophageal Reflux Disease; GERD; GORD; Fundoplication; Laparoscopic.

Antireflux surgery with laparoscopic fundoplication is a viable treatment option for selected patients with objectively confirmed gastroesophageal reflux disease (GERD), particularly for those who do not respond adequately to antireflux therapy with a proton pump inhibitor (PPI) or do not want or tolerate long-term PPI use. Compared with PPI therapy, antireflux surgery seems to be superior regarding reflux symptom control, esophageal acid exposure time, quality of life, and cost-effectiveness.[1,2] However, apart from the risk of postoperative recurrence of reflux symptoms,[3,4] antireflux surgery carries a risk of serious complications,[1,5] which has contributed to its decreased use.[5–7] The reported postoperative mortality rates in Western populations are up to 0.6% after primary laparoscopic antireflux surgery and up to 0.8% after secondary antireflux surgery, and severe nonlethal complications occur in up to 4.8% of cases.[3,5,8–12]

However, the validity of these estimates is unclear for a number of reasons. First, they are based on few or no deaths, leading to low statistical precision. Second, most studies have assessed 30-day outcomes or in-hospital mortality, although 90-day outcomes are now regarded as more valid because of developments in perioperative health care and improvements in rescue strategies. Third and last, selection bias is a concern because few studies have been population-based.

There is little knowledge about risk factors for poor postoperative outcomes after primary antireflux surgery and less so for secondary antireflux surgery. In an attempt to overcome these limitations of the existing evidence, we examined the absolute risks and risk factors for poor 90-day outcomes of primary laparoscopic antireflux surgery and secondary antireflux surgery from a modern period in a population-based multinational cohort.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Absolute rates and risk factors of poor short-term outcomes after antireflux surgery remain largely unknown, but are important for clinical decision-making in patients with gastroesophageal reflux disease (GERD).

NEW FINDINGS

This multinational cohort of primary laparoscopic (n=26,193) and secondary (n=1,618) antireflux surgery, showed low 90-day mortality (0.13% and 0.19%, respectively). Following primary surgery, comorbidity and older age increased 90-day mortality and hospital stay, while higher hospital volume decreased hospital stay. After secondary surgery, higher age and comorbidity increased hospital stay.

LIMITATIONS

The main limitation of the present study is the lack of direct data on covariates that might contribute to confounding, such as obesity and smoking.

IMPACT

Antireflux surgery is a safe treatment option for GERD, particularly in younger patients without severe comorbidity who undergo surgery at high-volume centers.

Methods

Design

This population-based cohort study included all individuals aged between 18 and 80 years who had undergone elective primary (first) laparoscopic (no open surgery) antireflux surgery for GERD according to any of the national patient registries in the 5 Nordic countries of Denmark, Finland, Iceland, Norway, or Sweden. The overall study period was January 1, 2000, to December 31, 2018, but with different start and end years for each country (2000–2014 in Denmark, 2000–2018 in Sweden, 2000–2018 in Finland, and 2008–2013 in Norway).

Participants were included if the primary laparoscopic procedure was conducted at least 90 days before the end of the study period (December 31, 2018) to ensure 90 days of follow-up for each patient. A subcohort included patients who underwent elective secondary antireflux surgery (laparoscopic or open), defined as a second antireflux surgery procedure after a primary laparoscopic antireflux procedure.

The study investigated absolute rates of mortality and reoperation within 90 days of surgery, risk factors for the outcomes all-cause mortality (main), reoperation, and prolonged hospital stay within 90 days of primary laparoscopic antireflux surgery, and risk factors for reoperation and prolonged hospital stay within 90 days of secondary antireflux surgery (there were too few deaths after secondary antireflux surgery to allow analyses of risk factors for this outcome). The study was approved by all relevant ethical review boards, data inspectorates, and governmental agencies in the 5 Nordic countries.[13]

Cohort

The study cohort was an updated version of the Nordic Antireflux Surgery Cohort (NordASCo), which has been described in detail in a separate cohort profile paper.[13] In brief, NordASCo consists of merged data from well-established and nationwide health data registries in the Nordic countries, consisting of patient registries, cancer registries, and cause of death registries.[13] The similarity in structure of these registries and the system of personal identity codes of all Nordic residents allowed precise linkages of individuals' data between the registries.[13,14]

Abbreviations used in this paper: **CI, confidence interval; GERD, gastroesophageal reflux disease; IQR, interquartile range; NordASCo, Nordic Antireflux Surgery Cohort; OR, odds ratio; PPI, proton pump inhibitor.**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All patients in NordASCo had a GERD diagnosis or elective antireflux surgery in any of the Nordic patient registries (with codes defined in Supplementary Table 1). Complete national coverage of the patient registries was reached in 1970s (Finland), 1978 (Denmark), 1987 (Sweden), 1999 (Iceland), and 2008 (Norway). The data in these registries have high validity, with most diagnoses and surgical procedures having a positive predictive value close to 100%.[15–17] Patients who underwent paraesophageal repair without a concomitant antireflux surgery procedure were not included, and patients with incarcerated hernia (International Classification of Diseases, Tenth Revision, codes K44.0, K44.1) or those who underwent emergency antireflux surgery (Nordic Medico-Statistical Committee Classification of Surgical Procedures code ZXD00) were excluded.

Exposures

The analyses assessed 5 potential risk factors (exposures) for the study outcomes: age at surgery (categorized into 3 similarly sized groups; ie, tertiles), sex (male or female), comorbidity (Charlson Comorbidity Index 0, 1, or ≥2), annual hospital volume of primary laparoscopic antireflux surgery (tertiles), and calendar period (tertiles). The Charlson Comorbidity Index was developed for assessing how comorbidity influences outcomes after surgical procedures, and the most recent and well-validated version of this index was used in this study.[18,19] The index was based on diagnoses recorded in the patient registries up to 3 years before inclusion into the cohort. This time restriction was made to consider only the most relevant comorbidities at the time of antireflux surgery.

Annual hospital volume of primary laparoscopic antireflux surgery and secondary antireflux surgery was calculated using a 4-year moving average, counting the procedures at each hospital during the year of surgery and the 3 previous years. The analyses of annual hospital volume did not include patients from Iceland or Norway, because of the lack of such data in these countries.

Outcomes

The main outcome was all-cause 90-day postoperative mortality. The cause of death registries provided causes of death and death dates through December 31, 2018, with virtually 100% complete and accurate recording.[14,20] A secondary outcome was reoperation within 90 days of surgery. The specific procedures used for defining reoperation are presented in Supplementary Table 2. The other secondary outcome was prolonged hospital stay, defined as ≥2 days longer than the median length of hospital stay after primary laparoscopic or secondary antireflux surgery, calculated separately. Length of hospital stay was assessed using admission and discharge dates in the patient registries. Any new admission to in-hospital care within 1 day of the discharge date was regarded as a continuation of the initial postoperative hospital stay.

Statistical Analysis

The absolute rates of mortality and reoperation were calculated as frequencies, and length of hospital stay was calculated as the median with the interquartile range (IQR). To assess the influence of the 5 potential risk factors on the outcomes, multivariable logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CIs). The ORs were adjusted for age at surgery (categorized into tertiles), sex (male or female), comorbidity (Charlson Comorbidity Index 0, 1, or ≥2), calendar period (tertiles), and country (Finland, Sweden, or Denmark, and Iceland and Norway combined). In the analysis of prolonged hospital stay, where the statistical power was higher than for the other outcomes, the influence of the continuous variables of age, year of surgery, and annual hospital volume on the odds of the outcome was modeled with cubic splines, adjusted for the other exposures. These results are reported in graphs as probabilities using the following reference values: age 43 to 55 years, male sex, Charlson Comorbidity Index 0, calendar year 2000 to 2003, and Finland. All statistical analyses were conducted using IBM SPSS Statistics 24 software (IBM Corp, Armonk, NY) and were guided by an experienced biostatistician (G.S.).

Results

Patients

The study cohort included 26,193 patients who had undergone elective primary laparoscopic antireflux surgery for GERD, and the subcohort included 1618 patients who had undergone elective secondary antireflux surgery. Characteristics of the study participants are presented in Table 1. In the primary laparoscopic antireflux surgery cohort, the median age was 50 years (IQR, 39–59 years), 53% were women, and 85% had no comorbidity included in the Charlson Comorbidity Index. In the secondary antireflux surgery subcohort, the median age was 53 years (IQR, 43–62 years), 57% were women, and 79% had no comorbidity.

Mortality

The absolute all-cause 90-day mortality rate was 0.13% (n = 35) after primary laparoscopic antireflux surgery and 0.19% (n = 3) after secondary antireflux surgery. The corresponding rates for 30-day mortality were 0.08% (n = 22) and 0.06% (n = 1), respectively. The most frequent causes of death were secondary to cardiovascular disease and suicide or intoxication (Table 2).

Table 3 presents the ORs of 90-day all-cause mortality in the primary laparoscopic antireflux surgery cohort. The adjusted ORs were increased in patients of higher age (highest vs lowest tertile: OR, 2.66; 95% CI, 1.03–6.85) and in those with comorbidity (Charlson Comorbidity Index ≥2 vs 0: OR, 6.25; 95% CI, 2.42–16.14), whereas sex did not influence the risk. The point estimates decreased with higher hospital volume (highest vs lowest tertile: OR, 0.58; 95% CI, 0.22–1.57) and increased over calendar periods, but none of these estimates reached statistical significance.

Reoperation

The 90-day reoperation rate was 3.0% (n = 750) after primary laparoscopic antireflux surgery and 6.2% (n = 94) after secondary antireflux surgery.

Comorbidity was associated with an increased OR of reoperation within 90 days of primary laparoscopic antireflux surgery (Charlson Comorbidity Index ≥2 vs 0: OR, 1.47; 95% CI, 0.97–2.23; and Charlson Comorbidity Index 1 vs 0: OR, 1.29; 95% CI, 1.05–1.58). There were no statistically significant associations between the other exposures (age, sex, hospital volume, or calendar periods) and the risk of reoperation (Table 3).

Table 1. Characteristics of Patients Who Underwent Primary Laparoscopic or Secondary Antireflux Surgery in a Nordic Country in 2000 to 2018

Variable	Primary laparoscopic antireflux surgery Number (%)	Secondary antireflux surgery Number (%)
Total	26,193 (100)	1618 (100)
Age (tertiles[a])		
Lowest	8374 (33.4)	515 (31.8)
Intermediate	9073 (34.6)	551 (34.1)
Highest	8746 (32.0)	552 (34.1)
Sex		
Male	13,841 (47.2)	695 (43.0)
Female	12,352 (52.8)	923 (57.0)
Charlson Comorbidity Index		
0	22,325 (85.2)	1279 (79.0)
1	3265 (12.5)	277 (17.1)
≥2	603 (2.3)	62 (3.8)
Annual hospital volume[b] (tertiles[c])		
Lowest	7899 (33.3)	484 (33.1)
Intermediate	7848 (33.1)	497 (34.0)
Highest	7943 (33.5)	481 (32.9)
Calendar period (tertiles[d])		
Earliest	9023 (34.4)	516 (31.9)
Intermediate	8744 (33.4)	559 (34.5)
Latest	8426 (32.2)	543 (33.6)
Country		
Denmark	3119 (11.9)	272 (16.8)
Finland	13,255 (50.6)	782 (48.3)
Iceland	1300 (4.96)	101 (6.24)
Norway	1203 (4.59)	55 (3.40)
Sweden	7316 (27.9)	408 (25.2)
30–day mortality	22 (0.08)	1 (0.06)[e]
90–day mortality	35 (0.13)	3 (0.19)
Reoperation within 90 days of surgery[f]	750 (3.0)	94 (6.2)

[a]Primary surgery: lowest, 18–42 years; intermediate, 43–55 years; highest, 56–80 years; secondary surgery: lowest, 18–46 years; intermediate, 47–58 years; highest, 59–80 years.
[b]Restricted to 23,690 participants from Denmark, Finland, and Sweden with data on hospital volume.
[c]Primary surgery: lowest ≤24, intermediate 25–47, highest >47; secondary surgery: lowest ≤26, intermediate 27–47, highest >47.
[d]Primary surgery: lowest 2000–2003, intermediate 2004–2008, highest 2009–2018; secondary surgery: lowest 2000–2006, intermediate 2007–2011, highest 2012–2018.
[e]Observed study participant is not from Denmark.
[f]Restricted to 24,893 participants from Denmark, Finland, Norway, and Sweden with data on reoperation.

There were no statistically significant associations for any of the 5 exposures in relation to the risk of reoperation within 90 days of secondary antireflux surgery (Table 4).

Table 2. Causes of Death Within 90 Days of Primary Laparoscopic Antireflux Surgery

Cause of death	Primary laparoscopic antireflux surgery Number (%)
All	35 (100)
Intraoperative-related complications	6 (17)
Infectious disease	<3[a]
Respiratory disease	4 (11)
Cardiovascular disease	8 (23)
Gastrointestinal disease[b]	6 (17)
Suicide or intoxication	7 (20)
Cancer	<3[a]

[a]Danish law does not allow reporting of absolute numbers <3 in studies including participants from Danish health registries.
[b]Includes diagnosis codes representing pancreatitis, peritonitis, gastrointestinal bleeding, and gastrointestinal perforation.

Prolonged Hospital Stay

The median length of hospital stay was 3 days (IQR, 2–4 days) after primary laparoscopic antireflux surgery and 4 days (IQR, 2–6 days) after secondary antireflux surgery. Prolonged hospital stay (≥2 days longer than the median length of hospital stay) was observed in 5252 patients (20%) after primary surgery and in 477 patients (29%) after secondary surgery.

Table 3 gives the adjusted ORs of prolonged hospital stay. After primary laparoscopic antireflux surgery, the ORs increased with older age (age 56–80 vs 18–42 years: OR, 1.48; 95% CI, 1.37–1.61), and an upward deflection in probability was found around the age of 60 years (Figure 1). Higher hospital volume was followed by a decreased OR (highest vs lowest tertile: OR, 0.74; 95% CI, 0.67–0.80), and the probability of prolonged hospital stay declined in a seemingly continuous manner with increasing hospital volume (Figure 2). The OR was slightly higher in women compared with men (OR, 1.09; 95% CI, 1.02–1.16). Comorbidity was associated with increased ORs (Charlson Comorbidity Index ≥2 vs 0: OR, 2.38; 95% CI, 1.98–2.85). The ORs of prolonged hospital stay decreased over calendar periods (2009–2018 vs 2000–2003: OR, 0.48; 95% CI, 0.44–0.52), which seemed to plateau around the year 2010 (Figure 3).

After secondary antireflux surgery, older age and comorbidity were associated with increased ORs of prolonged hospital stay, whereas later calendar period was associated with decreased ORs, and sex and hospital volume did not influence the ORs of prolonged hospital stay (Table 4).

Discussion

This population-based study shows low 90-day rates of all-cause mortality and reoperation and short median hospital stays after primary laparoscopic and secondary

Table 3. Odds Ratios and 95% Confidence Intervals of 90-Day Mortality, 90-Day Reoperation, and Prolonged Hospital Stay After Primary Laparoscopic Antireflux Surgery

Variable	90-day mortality		90-day reoperation		Prolonged hospital stay[a]	
	Patients (n)	Adjusted OR[b] (95% CI)	Patients (n)	Adjusted OR[b] (95% CI)	Patients (n)	Adjusted OR[b] (95% CI)
Age, *y*						
18–42	6	1.00 [Reference]	241	1.00 [Reference]	1504	1.00 [Reference]
43–55	6	0.87 (0.28–2.73)	245	0.92 (0.78–1.11)	1694	1.06 (0.98–1.15)
56–80	23	2.66 (1.03–6.85)	264	0.98 (0.81–1.18)	2054	1.48 (1.37–1.61)
Sex						
Male	15	1.00 [Reference]	389	1.00 [Reference]	2630	1.00 [Reference]
Female	20	1.08 (0.54–2.14)	361	1.04 (0.89–1.20)	2622	1.09 (1.02–1.16)
Charlson Comorbidity Index						
0	21	1.00 [Reference]	608	1.00 [Reference]	4200	1.00 [Reference]
1	8	1.93 (0.84–4.44)	117	1.29 (1.05–1.58)	845	1.54 (1.40–1.68)
≥2	6	6.25 (2.42–16.14)	25	1.47 (0.97–2.23)	207	2.38 (1.98–2.85)
Annual hospital volume[c]						
≤24	13	1.00 [Reference]	252	1.00 [Reference]	1560	1.00 [Reference]
25–47	14	0.99 (0.43–2.25)	224	0.84 (0.70–1.02)	2184	1.05 (0.96–1.14)
>47	6	0.58 (0.22–1.57)	252	1.10 (0.91–1.32)	1289	0.74 (0.67–0.80)
Calendar period (in years)						
2000–2003	6	1.00 [Reference]	229	1.00 [Reference]	2229	1.00 [Reference]
2004–2008	10	1.51 (0.55–4.20)	246	1.07 (0.89–1.29)	1587	0.61 (0.56–0.65)
2009–2018	19	2.33 (0.91–5.98)	275	1.15 (0.95–1.38)	1436	0.48 (0.44–0.52)

[a]Defined as ≥2 days longer than the median length of hospital stay after surgery.
[b]Adjusted for age, sex, Charlson Comorbidity Index, calendar period, and country.
[c]Restricted to 23,690 participants from Denmark, Finland, and Sweden with data on hospital volume.

antireflux surgery. For primary laparoscopic antireflux surgery, comorbidity increased the risk of all postoperative outcomes, older age increased the risk of 90-day mortality and prolonged hospital stay, and male sex, higher annual hospital volume, and later calendar period decreased the risk of prolonged hospital stay. For secondary antireflux surgery, older age and comorbidity increased the risk of prolonged hospital stay, and later calendar period decreased this risk.

Strengths of this study include the population-based design, the large sample size, the use of data with high quality and validity, and the complete follow-up. Because the study encompassed virtually all patients who underwent primary laparoscopic or secondary antireflux surgery in any of the 5 Nordic countries from year 2000 onward, it was possible to reflect on unselected clinical practice in a modern era and to support generalization of the findings to other Western populations.

There are also weaknesses. Despite the adjustment for several confounders, residual or unmeasured confounding cannot be ruled out. This might be particularly relevant for the variables of body mass index and tobacco smoking, where we did not have direct data in the registries, because these can increase the risk of postoperative complications. However, tobacco smoking was indirectly controlled for by adjustment for the Charlson Comorbidity Index, which includes diseases closely associated with heavy tobacco smoking (eg, chronic obstructive pulmonary disease).

Although individuals who underwent antireflux surgery due to incarcerated hernia or emergency surgery were excluded, another limitation is that factors that might increase the technical difficulty of the antireflux surgery, such as visceral adiposity and abdominal adhesions from previous surgery, could not be accounted for. Yet, the influence of obesity was counteracted by the adjustment for Charlson Comorbidity Index, which includes diagnoses closely related to obesity, such as diabetes type 2.[21] Data on specific types of antireflux surgery techniques were not available, but the dominant techniques in the Nordic countries are laparoscopic Nissen (360° wrap) and Toupet (270° posterior wrap). Finally, despite the large sample size, the statistical power was low in some of the analyses.

Few studies have investigated the absolute rate of mortality within 90 days of primary laparoscopic antireflux surgery, and even fewer of secondary antireflux surgery, and the largest studies have had insufficient sample sizes for robust analyses. Nevertheless, the 90-day mortality rate (0.13%) after primary laparoscopic antireflux surgery in the present study was similar to a Swedish study in 1997 to 2013 of 8947 patients of (0.08% [n = 7]).[5] However, this rate was higher in a Danish study in 2000 to 2017 of 3717 patients (0.6% [n = 22]),[8] which could be due to the inclusion of emergency surgery and surgery due to incarcerated hernia, which were excluded in the present study. The same Danish study also reported 90-day mortality (0.6% [n < 5]) in 541 patients who underwent secondary antireflux surgery, whereas a Swedish study reported 0 deaths in 549 patients after such surgery.[3,8] While these previous studies

Table 4. Odds Ratios and 95% Confidence Intervals of 90-Day Reoperation and Prolonged Hospital Stay After Secondary Antireflux Surgery

Variable	90-day reoperation		Prolonged hospital stay[a]	
	Patients (n)	Adjusted OR[b] (95% CI)	Patients (n)	Adjusted OR[b] (95% CI)
Age, *y*				
18–46	34	1.00 [Reference]	141	1.00 [Reference]
47–58	32	0.91 (0.55–1.51)	146	0.93 (0.70–1.23)
59–80	28	0.79 (0.46–1.36)	190	1.57 (1.18–2.08)
Sex				
Male	47	1.00 [Reference]	201	1.00 [Reference]
Female	47	0.79 (0.51–1.21)	276	1.01 (0.81–1.27)
Charlson Comorbidity Index				
0	72	1.00 [Reference]	1279	1.00 [Reference]
1	20	1.41 (0.83–2.38)	277	1.23 (0.92–1.64)
≥2	2[c]	0.63 (0.15–2.67)	62	1.97 (1.15–3.38)
Annual hospital volume[d]				
<26	30	1.00 [Reference]	129	1.00 [Reference]
27–47	29	0.93 (0.53–1.62)	183	1.15 (0.86–1.55)
>47	31	0.99 (0.57–1.72)	150	0.97 (0.71–1.31)
Calendar period (in years)				
2000–2006	32	1.00 [Reference]	191	1.00 [Reference]
2007–2011	29	0.86 (0.50–1.48)	164	0.56 (0.43–0.73)
2012–2018	33	1.03 (0.60–1.74)	122	0.38 (0.29–0.51)

[a]Defined as ≥2 days longer than the median length of hospital stay after surgery.
[b]Adjusted for age, sex, Charlson Comorbidity Index, calendar period, and country.
[c]Observed study participants are not from Denmark.
[d]Restricted to 1462 participants from Denmark, Finland, and Sweden with data on hospital volume.

used data that were in part included in the cohort of the present study, the present study has an unselected cohort from a more recent period and a much larger sample size, providing reassurance in the low mortality rates found.

To our knowledge, this is the first study examining risk factors of short-term mortality after antireflux surgery. This gap of knowledge is probably due to the low mortality rates, which require very large-scale studies. The risk of 90-day mortality after primary laparoscopic antireflux surgery was greatly increased in patients of older age and with comorbidity and was possibly decreased by higher annual volume (statistically nonsignificant), whereas sex, hospital volume, and calendar period did not reach statistical significance in influencing this risk.

The association with age seemed to start from 60 years. The associations with age and comorbidity are probably due to

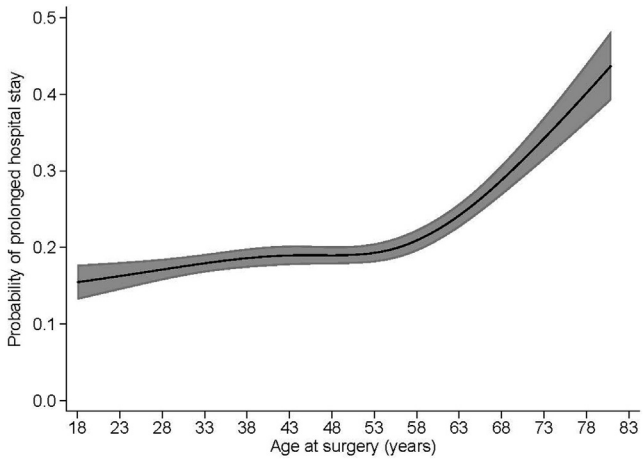

Figure 1. Probability (*black line*) with 95% confidence intervals (*grey area*) of prolonged hospital stay by age at surgery after primary laparoscopic antireflux surgery.

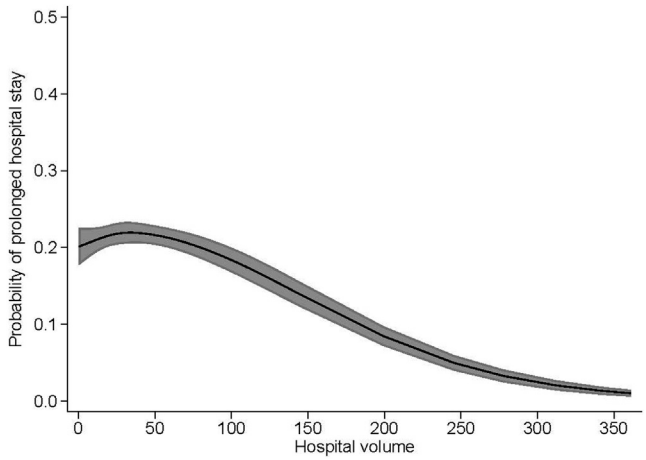

Figure 2. Probability (*black line*) with 95% confidence intervals (*grey area*) of prolonged hospital stay by hospital volume after primary laparoscopic antireflux surgery.

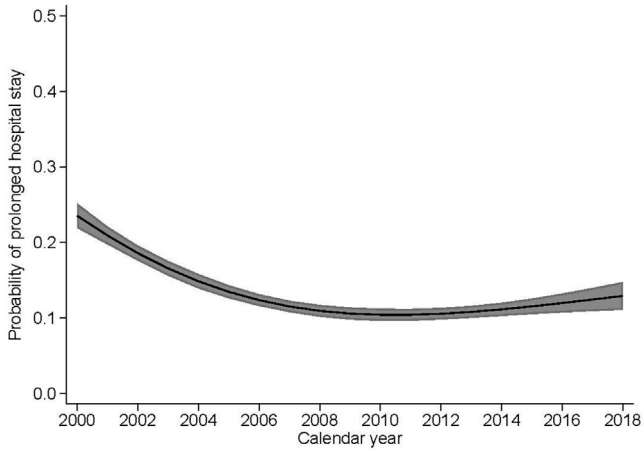

Figure 3. Probability (*black line*) with 95% confidence intervals (*grey area*) of prolonged hospital stay over time after primary laparoscopic antireflux surgery.

higher frailty and likelihood of life-threatening postoperative complications. The potential association with higher annual volume indicates a beneficial influence of the experience of the surgeon and the surgical team on postoperative outcomes. This may be explained by stricter selection of surgical candidates, more specialized surgeons conducting these procedures, and more tailored perioperative healthcare.

Only 1 previous study, from Sweden (n = 8947), has investigated the 90-day reoperation rate after primary laparoscopic antireflux surgery and found a lower rate (0.4%) than in the present study (3.0%).[5] This difference is probably due to the broader inclusion of reoperation codes in the present study. No other study has investigated the 90-day reoperation rate after secondary antireflux surgery, but the present study indicates a rather low rate.

The median length of hospital stay after primary laparoscopic antireflux surgery and secondary antireflux surgery was similar to some other studies.[3,5] The present study found an increased risk of prolonged hospital stay in patients with older age and comorbidity, and a decreased risk in high-volume hospitals and with later calendar period. Older age and comorbidity predispose to a longer hospital stay in general, and these patients also have an increased risk of postoperative complications and slower recovery compared with younger and more fit patients. The lower risk of prolonged hospital stay after primary antireflux surgery in high-volume hospitals may be explained by the same reasons as those described above. The shorter hospital stays with later calendar period could be at least partly explained by the development in perioperative health care.

Compared with the other Nordic countries included in the study cohort, Finland had a higher number of antireflux surgery patients, which is mainly explained by the differences in the start and end years of each country's contribution to the study cohort. The remaining slightly higher rate of antireflux surgery in Finland is well in line with the findings of previous studies on antireflux surgery trends in the Nordic countries.[5,7,11]

The similar rates of 90-day mortality and prolonged hospital stay after primary and secondary antireflux surgery are probably due to referrals to more specialized high-volume centers for secondary surgery and a reflection of clinical selection of more fit patients for secondary surgery instead of advising antireflux medication. Additionally, all study participants who underwent secondary antireflux surgery did so after laparoscopic primary antireflux surgery, which results in less scarring and adhesions compared with open surgery.

Some studies have suggested similar or slightly superior reflux control comparing antireflux surgery and PPI in the treatment of GERD,[22–24] and a recent population-based cohort study from our group found that only a limited proportion (17.7%) of patients with GERD had reflux recurrence after primary laparoscopic antireflux surgery.[4] Although the present study suggests that severe complications after antireflux surgery are rare, they do exist, which is not the case after initiation of PPI treatment. Therefore, in view of the benign nature of GERD and the availability of effective antireflux medication with PPIs,[1,25–27] caution should be exercised when considering antireflux surgery as a treatment option for GERD in patients with risk factors for poor postoperative outcomes, such as age >60 years and serious comorbidity, as found in the present study. Nonetheless, in patients with objectively confirmed GERD without these risk factors, laparoscopic antireflux surgery at high-volume centers is a safe treatment option. Finally, the finding of suicide or intoxication as causes of 90-day mortality after antireflux surgery suggests a value of psychologic evaluation in selected patients.

Conclusion

This population-based multinational cohort study indicates that laparoscopic antireflux surgery is an overall safe treatment option of GERD and that risk of poor short-term outcomes may be reduced by centralization to high-volume specialized centers and by selection of patients aged <60 years without severe comorbidity.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2021.02.035.

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