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Preoperative Factors Predicting Clinical Outcome Following Laparoscopic Fundoplication

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Abstract

Background Antireflux surgery is effective for the treatment of gastroesophageal reflux, but not all patients benefit equally from it. The challenge is to identify the patients who will ultimately benefit from antireflux surgery. The aim of this study was to identify preoperative factors that predict clinical outcome after antireflux surgery, with special interest in the influence of socioeconomic factors.

Methods Preoperative clinical and socioeconomic data from 1,650 patients who were to undergo laparoscopic fundoplication were collected prospectively. Clinical outcome measures (persistent heartburn, dysphagia, satisfaction) were assessed at short-term (1 year) and longer-term (≥3 years) follow-up.

Results At early follow-up, male gender (relative risk [RR] 1.091, $p < 0.001$) and the presence of a hiatus hernia (RR 1.065, $p = 0.002$) were independently associated with less heartburn. Male gender was also associated with higher overall satisfaction (RR 1.046, $p = 0.034$). An association was found between postoperative dysphagia and age (RR 0.988, $p = 0.007$) and the absence of a hiatus hernia (RR 0.767, $p = 0.001$). At longer-term follow-up, only male gender (RR 1.125, $p < 0.001$) was an independent prognostic factor for heartburn control. Male gender (RR 0.761, $p = 0.001$), the presence of a hiatus hernia (RR 0.823, $p = 0.014$), and cerebrovascular comorbidities (RR 1.306, $p = 0.019$) were independent prognosticators for dysphagia at longer-term follow-up. A hiatus hernia was the only factor associated with better overall satisfaction. Socioeconomic factors did not influence any clinical outcomes at short- and longer-term follow-up.

Conclusion Male gender and hiatus hernia are associated with a better clinical outcome following laparoscopic fundoplication, whereas socioeconomic status does not influence outcome.

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Introduction

Chronic gastroesophageal reflux disease (GERD) is the commonest benign upper gastrointestinal tract pathology in the Western world, with a prevalence of 10–20 % [1]. The role of surgery for the treatment of GERD is well established. Antireflux surgery is at least as effective as medical management with respect to reflux control and costs [2–7]. The gold standard for antireflux surgery is now laparoscopic fundoplication. Under the umbrella of laparoscopic fundoplication there are a number of technical variants, and the optimal procedure still remains to be determined [8]. The 360° Nissen and the 270° posterior partial (Toupet) fundoplications are currently considered to be the surgical

approaches of choice [8, 9]. Other techniques such as the anterior 180° partial fundoplication have also been shown to provide effective treatment [10, 11].

Not all patients benefit equally from antireflux surgery. Dissatisfaction can follow recurrent reflux symptoms, persistent heartburn, or new onset post-fundoplication symptoms such as dysphagia, abdominal bloating, and flatulence [12, 13]. Identification of factors that might predict the likelihood of a good versus poorer outcome would allow better selection of the patients that would most likely benefit from surgical treatment. However, data addressing predictors of outcome following laparoscopic fundoplication are scarce. Some factors have been shown to be predictors of outcome. However, many studies lack a large enough number of patients, and others analyze only a limited number of possible factors or include only univariate analyses [14–17].

In particular, there is limited knowledge about the patient's socioeconomic status as a potential predictor of outcome following laparoscopic fundoplication. An earlier study from our group suggested that patients from higher socioeconomic groups had a better outcome than patients from lower socioeconomic groups [15]. However, the overall study group was not large (262 patients), and socioeconomic status was derived from the patient's physical address. Other studies in other surgical fields have also found an association between socioeconomic status and cancer incidence, mortality, and survival [18–20]. Data on the association between socioeconomic status and surgical outcome the literature are scarce.

The aim of the present study was to investigate potential preoperative predictors of the clinical outcome of laparoscopic fundoplication in a very large cohort of patients. In addition, this study analyzed the association between the detailed socioeconomic status and clinical outcome of the patients. We hypothesized that patients with low socioeconomic status would have a less favorable clinical outcome after fundoplication.

Patients and methods

Between October 1991 and January 2010, a total of 1,650 patients underwent a laparoscopic fundoplication for GERD at the Royal Adelaide Hospital, Flinders Medical Centre, and associated private hospitals in Adelaide, South Australia. Patients were excluded from this study if they had a very large hiatus hernia (more than 50 % of the stomach in the thorax), or their first operation in our department was a revisional antireflux surgery procedure.

The laparoscopic fundoplication procedure was performed with either a total wrap or a partial wrap as described previously [21], with the choice of which fundoplication to use made by the surgeon or by patient preference. The indication for surgery was either poorly controlled reflux symptoms (volume regurgitation, heartburn, or a combination of both) or well-controlled reflux symptoms in patients not wanting to take antireflux medication on a continuous basis. The latter comprised a small minority of the overall patient group. All patients underwent clinical evaluation before surgery, as well as upper gastrointestinal endoscopy and esophageal manometry. Twenty-four-hour pH monitoring was performed selectively for patients without endoscopic evidence of esophagitis or patients with atypical symptoms. Barium contrast radiology was not part of the standard workup for these patients.

Patient-specific characteristics such as gender, age, body weight, home address, health insurance status, comorbidities, anatomical hiatal abnormalities, duration of reflux symptoms, and details about previous abdominal surgery were collected preoperatively and managed on a dedicated database (FileMaker Pro ver. 11, FileMaker Inc., Santa Clara, CA, USA). The database and the study were approved by the respective institutional ethical committees. Additionally, a number of objective variables, determined at upper gastrointestinal endoscopy, barium contrast radiology (if undertaken), esophageal manometry, and 24 h pH monitoring, were collected. The highest Savary-Miller grade of esophagitis was determined at any preoperative endoscopy and then the esophagitis was classified as no esophagitis, uncomplicated erosive esophagitis, or complicated esophagitis (esophageal stricture or Barrett's esophagus). The manometry variables, lower esophageal sphincter pressure (LOSP), and the peristaltic wave contractions in the body of the esophagus were analyzed. The continuous data collected were transformed into categorical data, as previously done by Power et al. [22]: Nadir LOSP <10 mmHg = normal, 11–19 mmHg = mild hypertensive sphincter pressure, and ≥20 mmHg = increased hypertensive sphincter pressure; peristaltic wave contraction >80 % = normal, 40–80 % = mild peristaltic disorder, and <40 % = relevant peristaltic disorder. The percentage of total, upright, and supine time with pH <4 in the distal esophagus during 24 h pH monitoring (which was categorized as normal), pH 4–7 (which was categorized as mild reflux), and pH >7 (which was categorized as severe reflux) was calculated. Data from preoperative 24 h pH monitoring studies were available for a subgroup of approximately 50 % patients.

Socioeconomic status was determined using the Socio-Economic Indexes for Areas (SEIFA) of the Australian Bureau of Statistics [23]. SEIFA indexes are summary measures of a number of variables that represent different aspects of relative socioeconomic disadvantage in a geographical area. Every area in Australia is ranked using this summary measure. There are three different indexes:

relative socioeconomic advantage and disadvantage, economic resources, and education and occupation. For each index, every geographical area defined by postcodes is given a score number, a rank number, a decile number, and a percentile number. According to postcodes, these numbers all rank areas according to disadvantage but are used for different purposes, as described in the SEIFA manual [23]. Socioeconomic status was evaluated for each patient in our study using the SEIFA indexes. As suggested by the Bureau of Statistics, we used the decile number as the outcome number.

The main outcome measures were degree of persistent heartburn, degree of dysphagia, and overall satisfaction after the antireflux surgery. Surgical outcome measures were determined at the 1 year (short term) and ≥3 years (longer term) follow-ups using a clinical questionnaire based on widely used analog scales. The aim was to assess the subjective outcome measures of heartburn, dysphagia, and overall satisfaction after surgery. The questionnaire used yes/no questions and separate 0–10 visual analog scales to evaluate each of these parameters separately. Heartburn and dysphagia scores ranged from 0 = no symptoms to 10 = severe symptoms, whereas the satisfaction score ranged from 0 = dissatisfied to 10 = highly satisfied. To simplify the regression analysis, the continuous data were transformed to categorical data: for heartburn, a score of 0–3 was good heartburn control and 4–10 was insufficient heartburn control; for dysphagia, a score of 0–3 meant no or minimal dysphagia and 4–10 was significant dysphagia; and for satisfaction, a score of 0–6 meant dissatisfied and 7–10 meant satisfied.

Statistical analysis

Statistical analysis was performed using MedCalc for Windows ver. 9 (Mariakerke, Belgium) and Stata ver. 11 (StataCorp., College Station, TX, USA). Data are presented as median with range or mean with standard deviation (SD), as appropriate. Log binomial generalized linear models were used determine predictors of the outcome variables. For each outcome variable, individual predictor variables were first regressed against it (univariate analysis). The best joint predictors (multivariable analysis) were then determined, with the initial model, including any variable significant at the univariate level at 0.05 or less. In cases of problems with convergence of the model, a robust Poisson model was used instead.

Results

A total of 1,650 patients were included in this study. Follow-up data at 1 year after surgery was available for 1,529 patients. Two patients had died and 119 (7.2 %) patients did not provide follow-up data at that time point. At the 3 years (longer-term) follow-up, data from 1,455 patients were available. Forty-three patients from the original group did not reach the 3 years follow-up, 33 patients had died and 119 (8.2 %) patients were lost to follow-up. Of those patients followed for three or more years, follow-up ranged from 3 to 11 years (mean = 5 years). Patient characteristics and preoperative clinical parameters are summarized in Table 1.

Short term follow-up (1 year)

Table 2 summarizes the association between various preoperative factors versus heartburn control at 1 year. Univariate analysis showed that male gender, the presence of a hiatus hernia, and prior abdominal surgery were predictors of heartburn control. Also, the presence of cardiovascular comorbidities was a predictive factor. In multivariate analysis, only male gender and the presence of a hiatus hernia were independent predictors of less heartburn symptoms at 1 year.

Table 3 summarizes the association between the dysphagia score and preoperative clinical and demographic parameters. Univariate analysis showed the following factors to be predictive for dysphagia: male gender, age, the presence of a hiatus hernia, and prior surgery. Also, respiratory comorbidities were a predictive factor. In the multivariate model, male gender was associated with significantly less dysphagia. There was also an association between the severity of dysphagia and patient age and the absence of a hiatus hernia.

Regression analysis of satisfaction with the overall outcome also showed that patients with a hiatus hernia and male patients were more satisfied with the overall outcome following surgery (Table 4). The type of indication for surgery also predicted satisfaction, but only in the univariate analysis.

Longer-term follow-up (≥3 years)

Table 5 summarizes preoperative factors versus heartburn control at the longer-term follow-up. In univariate analysis, male gender, duration of symptoms, and surgery in a private hospital were associated with a better outcome for heartburn control. The presence of a hiatus hernia did not have an impact on longer-term heartburn symptoms. In multivariate analysis, only male gender remained an independent prognostic factor.

A number of factors were significant predictors of the presence of dysphagia at the longer-term follow-up. Again, male gender, the presence of a hiatus hernia, the presence of cerebrovascular comorbidities, and prior

Table 1 Baseline characteristics and preoperative clinical parameters

Variable	Code/unit	Count	%/Mean (range)
Sex	Female	769	53
	Male	880	47
Age	Years		49.6 (18–87)
Hospital type	Public	821	51
	Private	801	49
Indication	Regurgitation	104	13
	Reflux poorly controlled by PPI	329	42
	Reflux poorly controlled by PPI + ENT throat symptoms	23	3
	Reflux well controlled but not wanting to use PPIs	48	6
	ENT throat symptoms only	29	4
	Regurgitation + ENT throat symptoms	18	2
	Regurgitation and reflux poorly controlled by PPI	227	29
Duration symptoms	Years		9.6 (1–66)
Hiatus hernia	No	686	44
	Yes	867	56
BMI	kg/m^2		29.0 (15.5–55.1)
Patient included in a randomized trial	No	1,246	76
	Yes	404	24
Prior abdominal surgery	No	870	60
	Yes	404	24
Diabetes	No	1,399	98
	Yes	31	2
Respiratory comorbidity	No	1,199	85
	Yes	218	15
Renal comorbidity	No	1,345	98
	Yes	23	2
CVD comorbidity	No	1,170	90
	Yes	125	10
pH category	<4	117	14
	4–7	231	28
	8+	477	58
Esophagitis grade	Grade		2 (0–6)
Preop esophageal peristalsis category	>80	932	68
	40–80	322	24
	<40	113	8
LESP category	<10	902	66
	11–19	320	23
	20+	152	11

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic

abdominal surgery were negatively associated with dysphagia. In the multivariate model, all these factors were independent predictors, with the exception of prior surgery (Table 6).

As summarized in Table 7, univariate analysis showed hiatus hernia, prior surgery, and diabetes were associated with overall satisfaction. Hiatus hernia was the only independent factor that predicted higher levels of satisfaction with the outcome at longer-term follow-up. Male gender did not affect this outcome.

Influence of socioeconomic factors on the outcomes

Within both the early and late follow-up analyses, socioeconomic variables failed to predict any outcome parameters as shown in the corresponding tables.

Table 2 Results of univariate and multivariate analyses for heartburn control after 1 year follow-up (good heartburn control vs. insufficient heartburn control)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	1.002	0.996–1.010	0.446			
Relative SE resources	Decile	1.002	0.995–1.008	0.618			
Relative SE education	Decile	1.002	0.996–1.008	0.566			
Sex	Female	1.000			1.000		
	Male	1.089	1.048–1.131	<0.001	1.091	1.049–1.134	<0.001
Age	Years	0.999	0.998–1.001	0.286			
Hospital type	Public	1.000					
	Private	1.017	0.979–1.055	0.391			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	1.042	0.941–1.153	0.432			
	Reflux poorly controlled by PPI + ENT throat symptoms	1.078	0.907–1.280	0.395			
	Reflux well controlled but not wanting to use PPIs	1.110	0.979–0.258	0.104			
	ENT throat symptoms only	1.013	0.840–1.222	0.891			
	Regurgitation + ENT throat symptoms	1.048	0.852–1.288	0.658			
	Regurgitation and reflux poorly controlled by PPI	0.980	0.875–1.096	0.720			
Duration symptoms	Years	1.000	0.992–0.1007	0.922			
Hiatus hernia	No	1.000			1.000		
	Yes	1.056	1.016–1.098	0.006	1.065	1.024–1.107	0.002
BMI	kg/m^2	1.001	0.996–1.006	0.595			
Patient included in a randomized trial	No	1.000					
	Yes	1.043	1.004–1.084	0.030			
Prior abdominal surgery	No	1.000					
	Yes	0.940	0.902–0.981	0.004			
Diabetes	No	1.000					
	Yes	0.984	0.854–1.134	0.824			
Respiratory comorbidity	No	1.000					
	Yes	0.982	0.925–1.042	0.541			
Renal comorbidity	No	1.000					
	Yes	0.923	0.729–1.169	0.506			
Cardiovascular comorbidity	No	1.000					
	Yes	0.904	0.823–0.993	0.036			
pH category	<4	1.000					
	4–7	0.954	0.865–1.051	0.339			
	8+	0.969	0.896–1.047	0.433			

Table 2 continued

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Esophagitis grade	Grade	1.007	0.998–1.017	0.132			
Preop esophageal peristalsis category	>80	1.000					
	40–80	0.982	0.928–1.039	0.532			
	<40	0.966	0.889–1.049	0.410			
LESP category	<10	1.000					
	11–19	0.950	0.902–1.001	0.057			
	20+	0.963	0.894–1.037	0.316			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* Ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

Discussion

Laparoscopic fundoplication is a well-established procedure for the treatment of GERD [2–7], although selecting the right individuals for surgery can at times be difficult. Within a large cohort of patients who were to undergo laparoscopic fundoplication, this study analyzed a range of possible factors that were identifiable before surgery and compared them with prospectively collected standardized clinical outcomes. The main predictors of a better outcome at early follow-up, i.e., 1 year after surgery, were male gender and the presence of a hiatus hernia. These two factors independently predicted heartburn control, the presence of dysphagia, and overall satisfaction with the outcome of surgery. At longer-term follow-up (≥3 years after surgery), male gender remained an independent predictor of heartburn control and the presence of dysphagia but not for overall satisfaction. The presence of a hiatus hernia was also a predictor of less postoperative dysphagia and better overall satisfaction.

Laparoscopic fundoplication seems to yield a better outcome in males, a finding that we have observed in the past [15]. One possible reason might be the fact that men cope better with postoperative side effects such as dysphagia or bloating, thus reporting a higher satisfaction with the surgical outcome. The presence of a hiatus hernia is also often associated with a more mechanically defective lower esophageal sphincter, and the consequent surgical repair might more positively influence the outcome in these patients. Our findings are different than those of the study by Power et al. [22], who found the presence of a hiatus hernia greater than 3 cm was an independent risk factor for failure after laparoscopic Nissen fundoplication. However, in their study, only 14 of 131 patients were in the "failure" group and the interpretation of any statistical analysis using such small numbers needs to be done with care. The far larger cohort of 1,650 patients in our current study provides significantly more robust data.

A number of other studies have addressed the problem of patient selection for primary surgical therapy for GERD, or for surgical therapy for recurrent GERD or dysphagia after fundoplication. A large number of factors have been tested and include patient-related factors such as BMI, gender, or the presence of psychiatric disorders, operative factors such as the surgical approach, and the results of preoperative clinical investigations such as pH measurements or manometry [15–17, 24–27]. The results are contradictory. Campos et al. [16] described a 24 h pH score, typical reflux symptoms, and a good clinical response to antacid medication as independent predictors of outcome. The median follow-up in their study was short (15 months) and their cohort of 199 patients was too small for multivariate logistic regression analysis. The presence of typical

Table 3 Results of univariate and multivariate analyses for dysphagia after 1 year follow-up (significant dysphagia vs. no or minimal dysphagia)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	1.001	0.973–1.030	0.946			
Relative SE resources	Decile	1.005	0.976–1.035	0.723			
Relative SE education	Decile	0.991	0.965–1.017	0.493			
Sex	Female	1.000			1.000		
	Male	0.753	0.647–0.875	<0.001	0.800	0.672–0.951	0.012
Age	Years	0.994	0.988–0.999	0.016	0.988	0.979–0.997	0.007
Hospital type	Public	1.000					
	Private	1.076	0.923–1.254	0.350			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	0.921	0.667–1.273	0.618			
	Reflux poorly controlled by PPI + ENT throat symptoms	0.403	0.110–1.472	0.169			
	Reflux well controlled but not wanting to use PPIs	0.484	0.225–1.040	0.063			
	ENT throat symptoms only	1.280	0.759–2.162	0.354			
	Regurgitation + ENT throat symptoms	1.210	0.646–2.265	0.552			
	Regurgitation and reflux poorly controlled by PPI	1.288	0.938–1.767	0.117			
Duration symptoms	Years	0.964	0.938–0.990	0.007			
Hiatus hernia	No	1.000					
	Yes	0.789	0.675–0.923	0.003	0.767	0.652–0.902	0.001
BMI	kg/m^2	0.973	0.947–1.000	0.046			
Patient included in a randomized trial	No	1.000					
	Yes	0.892	0.743–1.070	0.217			
Prior abdominal surgery	No	1.000					
	Yes	1.325	1.132–1.552	<0.001	1.257	1.057–1.493	0.001
Diabetes	No	1.000					
	Yes	1.398	0.933–2.095	0.105			
Respiratory comorbidity	No	1.000					
	Yes	1.257	1.029–1.534	0.025			
Renal comorbidity	No	1.000					
	Yes	1.124	0.539–2.344	0.756			
CVD comorbidity	No	1.000					
	Yes	1.213	0.935–1.574	0.145			
pH category	<4	1.000					
	4–7	0.823	0.598–1.133	0.231			
	8+	0.880	0.681–1.137	0.327			
Esophagitis grade	Grade	0.960	0.920–1.002	0.060			
Preop esophageal peristalsis category	>80	1.000					
	40–80	1.064	0.854–1.324	0.580			
	<40	0.915	0.650–1.288	0.611			
LESP category	<10	1.000					
	11–19	1.263	1.057–1.509	0.010			
	20+	0.755	0.533–1.068	0.113			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

Table 4 Results of univariate and multivariate analyses for satisfaction after 1 year follow-up (satisfaction vs. no satisfaction)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	1.000	0.992–1.008	0.983			
Relative SE resources	Decile	0.998	0.990–1.006	0.602			
Relative SE education	Decile	0.997	0.991–1.004	0.469			
Sex	Female	1.000					
	Male	1.048	1.005–1.092	0.027	1.046	1.000–1.091	0.034
Age	Years	1.000	0.999–1.002	0.529			
Hospital type	Public	1.000					
	Private	1.040	0.998–1.084	0.065			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	1.141	1.015–1.282	0.027			
	Reflux poorly controlled by PPI + ENT throat symptoms	1.089	0.879–1.350	0.433			
	Reflux well controlled but not wanting to use PPIs	1.186	1.030–1.364	0.017			
	ENT throat symptoms only	0.902	0.690–1.179	0.451			
	Regurgitation + ENT throat symptoms	1.282	1.149–1.429	<0.001			
	Regurgitation and reflux poorly controlled by PPI	1.064	0.938–1.207	0.336			
Duration symptoms	Years	1.000	0.993–1.007	0.954			
Hiatus hernia	No	1.000					
	Yes	1.056	1.012–1.102	0.011	1.060	1.016–1.106	0.007
BMI	kg/m^2	1.003	0.997–1.010	0.318			
Patient included in a randomized trial	No	1.000					
	Yes	1.009	0.964–1.056	0.699			
Prior abdominal surgery	No	1.000					
	Yes	0.987	0.944–1.033	0.575			
Diabetes	No	1.000					
	Yes	0.967	0.823–1.127	0.686			
Respiratory comorbidity	No	1.000					
	Yes	0.968	0.907–1.034	0.334			
Renal comorbidity	No	1.000					
	Yes	0.790	0.582–1.073	0.132			
CVD comorbidity	No	1.000					
	Yes	0.998	0.923–1.078	0.950			
pH category	<4	1.000					
	4–7	0.923	0.827–1.030	0.153			
	8+	0.964	0.886–1.049	0.399			
Esophagitis grade	Grade	1.002	0.991–1.013	0.732			
Preop esophageal peristalsis category	>80	1.000					
	40–80	0.960	0.900–1.024	0.218			
	<40	0.925	0.838–1.022	0.125			
LESP category	<10	1.000					
	11–19	0.968	0.915–1.024	0.262			
	20+	1.037	0.973–1.106	0.263			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* Ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

Table 5 Results of univariate and multivariate analyses for heartburn control after 3 years follow-up (good heartburn control vs. insufficient heartburn control)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	1.001	0.996–1.010	0.882			
Relative SE resources	Decile	1.002	0.991–1.012	0.760			
Relative SE education	Decile	0.998	0.989–1.007	0.695			
Sex	Female	1.000					
	Male	1.144	1.083–1.209	<0.001	1.125	1.061–1.193	<0.001
Age	Years	0.999	0.997–1.001	0.251			
Hospital type	Public	1.000					
	Private	1.063	1.008–1.121	0.024			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	0.964	0.854–1.090	0.566			
	Reflux poorly controlled by PPI + ENT throat symptoms	0.809	0.557–1.175	0.265			
	Reflux well controlled but not wanting to use PPIs	1.051	0.882–1.253	0.576			
	ENT throat symptoms only	0.937	0.730–1.204	0.612			
	Regurgitation + ENT throat symptoms	0.867	0.612–1.227	0.420			
	Regurgitation and reflux poorly controlled by PPI	0.910	0.769–1.052	0.202			
Duration symptoms	Years	1.009	1.000–1.018	0.038			
Hiatus hernia	No	1.000					
	Yes	1.014	0.961–1.071	0.611			
BMI	kg/m^2	1.000	0.993–1.007	0.990			
Patient included in a randomised trial	No	1.000					
	Yes	1.008	0.952–1.068	0.776			
Prior abdominal surgery	No	1.000					
	Yes	0.901	0.848–0.958	0.001			
Diabetes	No	1.000					
	Yes	0.821	0.626–1.112	0.203			
Respiratory comorbidity	No	1.000					
	Yes	0.956	0.875–1.044	0.319			
Renal comorbidity	No	1.000					
	Yes	0.858	0.596–1.234	0.409			
CVD comorbidity	No	1.000					
	Yes	0.966	0.860–1.085	0.560			
pH category	<4	1.000					
	4–7	0.875	0.766–0.999	0.049			
	8+	0.944	0.858–1.040	0.244			
Esophagitis grade	Grade	1.007	0.993–1.022	0.304			
Preop esophageal peristalsis category	>80	1.000					
	40–80	0.942	0.866–1.025	0.164			
	<40	0.893	0.782–1.019	0.093			
LESP category	<10	1.000					
	11–19	0.930	0.862–1.004	0.062			
	20+	1.028	0.842–1.122	0.536			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* ear, nose, throat; PPI proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

Table 6 Results of univariate and multivariate analyses for dysphagia after 3 years follow-up (significant dysphagia vs. no or minimal dysphagia)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	0.985	0.961–1.010	0.230			
Relative SE resources	Decile	0.994	0.969–1.020	0.653			
Relative SE education	Decile	0.986	0.965–1.009	0.225			
Sex	Female	1.000					
	Male	0.740	0.647–0.846	<0.001	0.761	0.647–0.895	0.001
Age	Years	0.998	0.994–1.003	0.485			
Hospital type	Public	1.000					
	Private	1.020	0.891–1.168	0.771			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	0.827	0.641–1.067	0.144			
	Reflux poorly controlled by PPI + ENT throat symptoms	0.804	0.430–1.505	0.496			
	Reflux well controlled but not wanting to use PPIs	0.606	0.333–1.105	0.102			
	ENT throat symptoms only	0.871	0.523–1.452	0.597			
	Regurgitation + ENT throat symptoms	1.268	0.831–1.933	0.271			
	Regurgitation and reflux poorly controlled by PPI	1.077	0.829–1.400	0.577			
Duration symptoms	Years	1.003	0.987–1.019	0.730			
Hiatus hernia	No	1.000					
	Yes	0.824	0.717–0.948	0.007	0.823	0.705–0.961	0.014
BMI	kg/m^2	1.006	0.987–1.025	0.571			
Patient included in a randomized trial	No	1.000					
	Yes	0.988	0.849–1.149	0.871			
Prior abdominal surgery	No	1.000					
	Yes	1.231	1.070–1.416	0.004			
Diabetes	No	1.000					
	Yes	0.962	0.523–1.770	0.902			
Respiratory comorbidity	No	1.000					
	Yes	1.192	0.991–1.435	0.063			
Renal comorbidity	No	1.000					
	Yes	0.608	0.231–1.600	0.313			
CVD comorbidity	No	1.000					
	Yes	1.360	1.103–1.677	0.004	1.306	1.046–1.630	0.019
pH category	<4	1.000					
	4–7	0.832	0.621–1.116	0.220			
	8+	0.850	0.675–1.071	0.168			
Esophagitis grade	Grade	0.971	0.935–1.008	0.122			
Preop esophageal peristalsis category	>80	1.000					
	40–80	1.225	1.024–1.467	0.027			
	<40	1.080	0.831–1.404	0.563			
LESP category	<10	1.000					
	11–19	1.091	0.919–1.295	0.321			
	20+	0.987	0.755–1.290	0.924			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

Table 7 Results of univariate and multivariate analyses for satisfaction grade after 3 years follow-up (satisfaction vs. no satisfaction)

Variable	Code/unit	Univariate			Multivariate		
		RR	95 % CI (RR)	*p*	RR	95 % CI (RR)	*p*
Relative SE advantage	Decile	0.999	0.989–1.009	0.887			
Relative SE resources	Decile	0.994	0.984–1.005	0.267			
Relative SE education	Decile	0.999	0.990–1.008	0.799			
Sex	Female	1.000					
	Male	1.032	0.977–1.090	0.255			
Age	Years	1.000	0.998–1.001	0.657			
Hospital type	Public	1.000					
	Private	1.041	0.986–1.099	0.150			
Indication	Regurgitation	1.000					
	Reflux poorly controlled by PPI	1.075	0.932–1.239	0.320			
	Reflux poorly controlled by PPI + ENT throat symptoms	0.969	0.695–1.350	0.853			
	Reflux well controlled but not wanting to use PPIs	1.189	0.997–1.418	0.054			
	ENT throat symptoms only	1.021	0.786–1.326	0.875			
	Regurgitation + ENT throat symptoms	1.227	1.010–1.491	0.039			
	Regurgitation and reflux poorly controlled by PPI	1.001	0.851–1.178	0.987			
Duration symptoms	Years	1.002	0.993–1.011	0.687			
Hiatus hernia	No	1.000					
	Yes	1.099	1.038–1.162	0.001	1.111	1.047–1.179	<0.001
BMI	kg/m^2	0.999	0.991–1.008	0.824			
Patient included in a randomized trial	No	1.000					
	Yes	1.012	0.955–1.073				
Prior abdominal surgery	No	1.000					
	Yes	0.935	0.881–0.994	0.030			
Diabetes	No	1.000					
	Yes	0.643	0.427–0.968	0.034			
Respiratory comorbidity	No	1.000					
	Yes	0.968	0.888–1.056	0.467			
Renal comorbidity	No	1.000					
	Yes	0.759	0.494–1.169	0.211			
CVD comorbidity	No	1.000					
	Yes	0.878	0.764–1.008	0.065			
pH category	<4	1.000					
	4–7	0.973	0.837–1.132	0.726			
	8+	1.005	0.889–1.136	0.934			
Esophagitis grade	Grade	1.009	0.995–1.024	0.197			
Preop esophageal peristalsis category	>80	1.000					
	40–80	0.906	0.825–0.994	0.037			
	<40	0.876	0.762–1.006	0.061			
LESP category	<10	1.000					
	11–19	0.959	0.890–1.034	0.278			
	20+	0.935	0.832–1.051	0.258			

BMI body mass index, *CVD* cardiovascular disease, *LESP* lower esophageal sphincter pressure, *ENT* ear, nose, throat, *PPI* proton pump inhibitors, *SE* socioeconomic, *RR* relative risk

symptoms and response to antireflux medication were also predictive factors in a study by Morgenthal et al. [17]. However, the authors performed only univariate analysis of the factors; adding a multivariate analysis might have changed the results. In our study, we stratified the indication for surgery in a more detailed fashion and found no association between indication and outcome.

In our study, a number of new variables were shown to independently predict some of the outcome measures. For example, previous abdominal surgery predicted post-fundoplication dysphagia. Interestingly, neither preoperative 24 h pH monitoring results nor esophageal manometry outcomes (esophageal peristalsis or LOSP) predicted the clinical outcome, in contrast to the results of Campos et al. [16]. The indication for surgery was not an independent factor of either short- or long-term outcome. However, the majority of patients in our study had typical reflux symptoms that were poorly controlled by PPI medication; only a minority reported atypical reflux symptoms. In a previous study from our group, we specifically analyzed the influence of the indications of antireflux surgery on outcome [28]. We hypothesized that patients with regurgitation might have better outcomes compared with patients with poorly controlled reflux or atypical reflux. However, no difference in outcome was detected.

Socioeconomic status did not influence outcome. We used the Australian Bureau of Statistics indices, which represent an accurate analysis of each individual's socioeconomic status in terms of relative advantage, available resources, and status of education [23]. To our knowledge, this is the first report to evaluate the influence of socioeconomic factors on the subjective outcome of antireflux surgery. Socioeconomic status has been demonstrated to be associated with the risk of colorectal cancer, the incidence of and patient survival of breast cancer, and mortality after a diagnosis of non-Hodgkin's lymphoma [18–20]. With respect to the outcome of surgery, the literature is scarce and contradictory. Whereas some data suggest higher mortality after cardiovascular surgery, others report that socioeconomic status does not influence short- or long-term mortality after lower-extremity bypass surgery [29, 30]. We hypothesized that higher socioeconomic status patients would have a better outcome after antireflux surgery, as differences in general health, frequency of smoking- and alcohol-related diseases, and nutritional behavior probably differ among socioeconomic groups. However, this hypothesis was not substantiated. Similarly, where the surgery took place, i.e. private versus public hospital, did not influence outcome, in contrast to an earlier report from our group [15].

Differences in outcome measurements make it difficult to compare studies. In our current study, we chose three subjective outcome measures. Heartburn control and overall satisfaction are, in our opinion, the most important outcome measures that define whether the fundoplication has successfully treated GERD. Postoperative dysphagia is the most high-profile side effect of fundoplication. For this study it was not practical to employ pH measurements or contrast studies to evaluate the postoperative outcome. However, standardized clinical outcomes across multiple time points in a large cohort of patients should still be informative and provide a better measure of clinically relevant outcomes than objective outcomes from studies with incomplete follow-up in smaller patient cohorts. We also did not apply the use of proton pump inhibitors (PPI) after fundoplication as an outcome variable, as other studies have shown that PPIs after fundoplication is not a strong indicator of recurrent reflux: only 33 % of individuals using PPIs after fundoplication have an actual reflux problem and more than 60 % of those patients have a normal postoperative pH study [31–34].

In conclusion, male gender and the presence of hiatus hernia were the sole independent factors predicting a better subjective outcome after laparoscopic fundoplication. Socioeconomic status did not influence the clinical outcome.

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