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ORIGINAL ARTICLE

Retrospective Study

Identification of independent risk factors for intraoperative gastroesophageal reflux in adult patients undergoing general anesthesia

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Abstract

BACKGROUND

Gastroesophageal reflux (GER) affects up to 20% of the adult population and is defined as troublesome and frequent symptoms of heartburn or regurgitation. GER produces significantly harmful impacts on quality of life and precipitates poor mental well-being. However, the potential risk factors for the incidence and extent of GER in adults undergoing general anesthesia remain unclear.

AIM

To explore independent risk factors for the incidence and extent of GER during general anesthesia induction.

METHODS

A retrospective study was conducted, and 601 adult patients received general anesthesia intubation or laryngeal mask surgery between July 2016 and January 2019 in Shanghai General Hospital of Nanjing Medical University. This study recruited a total of 601 adult patients undergoing general anesthesia, and the characteristics of patients and the incidence or extent of GER were recorded. The potential risk factors for the incidence of GER were explored using multivariate logistic regression, and the risk factors for the extent of GER were evaluated using multivariate linear regression.

set supporting the results of this article are included within the article.

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RESULTS

The current study included 601 adult patients, 82 patients with GER and 519 patients without GER. Overall, we noted significant differences between GER and non-GER for pharyngitis, history of GER, other digestive tract diseases, history of asthma, and the use of sufentanil ($P < 0.05$), while no significant differences between groups were observed for sex, age, type of surgery, operative time, body mass index, intraoperative blood loss, smoking status, alcohol intake, hypertension, diabetes mellitus, psychiatric history, history of respiratory infection, history of surgery, the use of lidocaine, palliative strategies, propofol, or rocuronium bromide, state anxiety inventory, trait anxiety inventory, and self-rating depression scale ($P > 0.05$). The results of multivariate logistic regression indicated that female sex [odds ratio (OR): 2.702; 95% confidence interval (CI): 1.144-6.378; $P = 0.023$], increased age (OR: 1.031; 95%CI: 1.008-1.056; $P = 0.009$), pharyngitis (OR: 31.388; 95%CI: 15.709-62.715; $P < 0.001$), and history of GER (OR: 11.925; 95%CI: 4.184-33.989; $P < 0.001$) were associated with an increased risk of GER, whereas the use of propofol could protect against the risk of GER (OR: 0.942; 95%CI: 0.892-0.994; $P = 0.031$). Finally, age ($P = 0.004$), operative time ($P < 0.001$), pharyngitis ($P < 0.001$), history of GER ($P = 0.024$), and hypertension ($P = 0.017$) were significantly associated with GER time.

CONCLUSION

This study identified the risk factors for GER in patients undergoing general anesthesia including female sex, increased age, pharyngitis, and history of GER.

Key Words: Gastroesophageal reflux; Intraoperative period; Risk factors; Anesthesia, General; Surgery; Retrospective studies

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Core Tip: The study included 82 patients who reported gastroesophageal reflux (GER) and 519 patients without GER. The results of multivariate logistic regression indicated sex, increased age, pharyngitis, and history of GER were associated with increased risk of GER, whereas the use of propofol could protect against the risk of GER. Finally, age, operative time, pharyngitis, history of GER, and hypertension were significantly associated with GER time.

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INTRODUCTION

Gastroesophageal reflux (GER) affects up to 20% of the adult population and is defined as troublesome and frequent symptoms of heartburn or regurgitation[1-3]. GER produces significantly harmful impacts on health-related quality and increases the risk for esophageal adenocarcinoma[4-6]. Currently, the identified risk factors for GER include overweight, tobacco smoking, low socioeconomic status, and heredity[7-9]. Moreover, GER is the most likely complication in perioperative patients, and early detection, diagnosis, and treatment can prevent serious adverse consequences. Acidic gastric juice reflux is associated with chemical damage to the airway mucosa and lung tissue, damages the normal respiratory membrane structure, and causes different degrees of bronchospasm, atelectasis, aspiration pneumonia, and even respiratory failure. Therefore, early identification of potential risk factors for the progression of GER in patients undergoing general anesthesia should be explored to improve the quality of anesthesia.

Several studies have explored the potential risk factors for GER. Taraszewska[10] indicated that intermediate physical activity might be associated with a reduced risk of GER in obese individuals, while this significant association was not observed in non-obese people. Maret-Ouda *et al*[11] suggested that older age, female sex, and comorbidity were associated with an increased risk of recurrent GER in patients who underwent antireflux surgery. Wang *et al*[12] recruited 56 patients who underwent peroral endoscopic myotomy and found that full-thickness myotomy and low post-operative 4-s integrated relaxation pressure induced more GER. Lindam *et al*[13] investigated 25844 participants and found that the relationship between sleep disturbances and GER seems to be bidirectional, and sleep disturbances seem to be a stronger risk factor for GER than the reverse. However, no study has focused on patients undergoing general anesthesia to identify the independent risk factors for the risk of GER and total GER time. Therefore, the current study was conducted to explore the potential risk factors for the progression of GER during general anesthesia induction.

MATERIALS AND METHODS

Patients inclusion and exclusion criteria

A retrospective study was conducted in 601 adult patients who underwent general anesthesia intubation or laryngeal mask surgery between July 2016 and January 2019 at the Shanghai General Hospital of Nanjing Medical University. The exclusion criteria of this study included patients diagnosed with nasal or upper esophageal obstruction, severe and uncontrolled clotting disease, bullae disease of the esophageal mucosa, unstable heart disease, or other poor tolerance to vagal stimulation. The general characteristics of the enrolled patients were collected using a pre-defined questionnaire, and the detailed medical history was collected through an anesthesiologist who made preoperative visits. This study was approved by the ethics committee of Nanjing Medical University. The purpose and procedures of the study were carefully explained, and written informed consent was obtained from all participants.

GER and variables

The definition of GER was based on assessment by Orion II-ohmega portable pH dynamic monitoring recorder (MMS, Enschede, The Netherlands), which was used to monitor the pH of the middle and lower esophagus, to observe whether reflux occurred, and to measure the occurrence frequency and duration[14]. The general characteristics of the patients included sex, age, body mass index, smoking status, and alcohol intake. The detailed medical history included pharyngitis, history of GER, other digestive tract diseases, hypertension, diabetes mellitus, history of asthma, psychiatric history, history of respiratory infection, history of surgery, state anxiety inventory (SAI), trait anxiety inventory (TAI), and self-rating depression scale (SDS). Moreover, the intraoperative parameters included type of surgery, operative time, intraoperative blood loss, and the use of lidocaine, palliative strategies, sufentanil, propofol, and rocuronium bromide.

Statistical analysis

The continuous data of patients' characteristics are presented as medians and quartiles because these data did not meet the normal distribution. Moreover, the category data are presented as event rates. Comparisons of continuous variables between non-GER and GER patients were calculated using Kruskal-Wallis tests due to the non-normal distributions, while the frequencies of data between groups were calculated using chi-squared tests. Multivariate logistic regression was applied to explore the risk factors for GER incidence after continued adjustment for potential confounders, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Moreover, the impact factors of GER time were explored using multivariate linear analyses. All reported P values were two-sided, and $P < 0.05$ was considered statistically significant. The data were analyzed using IBM SPSS Statistics for Windows, version 19.0 (SPSS 19.0, Armonk, NY, United States).

RESULTS

The characteristics of the enrolled patients are presented in Table 1. In total, 601 adult patients were enrolled, 82 patients with GER and 519 patients without GER. Overall, we noted significant differences between GER and non-GER for pharyngitis, history of GER, other digestive tract diseases, history of asthma, and the use of sufentanil ($P < 0.05$), while no significant differences were observed between groups for sex, age, type of surgery, operative time, body mass index, intraoperative blood loss, smoking status, alcohol intake, hypertension, diabetes mellitus, psychiatric history, history of respiratory infection, history of surgery, the use of lidocaine, palliative strategies, propofol, rocuronium bromide, SAI, TAI, and SDS ($P > 0.05$).

The results of logistic regression with multivariate adjustment for potential confounders indicated that female sex (OR: 2.702; 95%CI: 1.144-6.378; $P = 0.023$), older age (OR: 1.031; 95%CI: 1.008-1.056; $P = 0.009$), pharyngitis (OR: 31.388; 95%CI: 15.709-62.715; $P < 0.001$), and history of GER (OR: 11.925; 95%CI: 4.184-33.989; $P < 0.001$) were associated with an increased risk of GER, whereas increased propofol use was associated with a reduced risk of GER (OR: 0.942; 95%CI: 0.892-0.994; $P = 0.031$) (Table 2).

The results of the impact factors on GER time were evaluated using multivariate linear analyses and are shown in Table 3. Overall, we noted that older age ($P = 0.004$), longer operative time ($P < 0.001$), pharyngitis ($P < 0.001$), and history of GER ($P = 0.024$) were associated with longer GER time. Moreover, patients with hypertension were associated with a shorter GER time ($P = 0.017$).

DISCUSSION

This study reported that 13.6% of patients had GER. Risk factors for the incidence of GER include female sex, older age, pharyngitis, and history of GER, whereas the use of propofol was a protective factor. Moreover, older age, longer operative time, pharyngitis, and a history of GER produced longer GER time, whereas patients with hypertension were associated with shorter GER time.

The current study suggested that female sex was a potential risk factor for the incidence of GER; this result was consistent with a previous study[15] that recruited 23557 World Trade Center responders and found that women were associated with a greater risk of GER than men (hazard ratio: 1.25; 95%CI: 1.13-1.38). The potential reason for this could be that women present with more severe symptoms, leading to an easier diagnosis, whereas GER in men is mild compared to women, which may lead to a missed diagnosis[16,17]. Moreover, older age was associated with an increased risk of GER, which is consistent with a previous study[11]. The potential reason for this is that comorbidities of patients could affect the risk of GER. Furthermore, older people have poor esophageal acid clearance and decreased defense mechanisms against reflux of acid gastric contents on the esophageal mucosa[18,19].

Moreover, we noted that pharyngitis and a history of GER were associated with a greater risk of GER in patients undergoing general anesthesia. The 24-h pH monitoring for these patients should be employed to detect pathological reflux, and medical antireflux treatment should be used to prevent the progression of GER[20]. Moreover, the bidirectional associations of GER and pharyngitis, erosive esophagitis, esophageal strictures, Barrett's esophagus, and esophageal adenocarcinoma could be used to interpret these risk factors.

We noted that the use of propofol was associated with a lower risk of GER, whereas this result was variable compared with previous studies. Chawla *et al*[21] conducted 48-h pH tracings in 88 children and found that an increase in GER risk during the post-anesthesia period correlated with a direct effect of propofol or other related factors. However, the study conducted by Turan *et al*[22] found similar effects of dexmedetomidine and propofol on lower esophageal sphincter pressure and gastroesophageal pressure gradient. However, although a decrease in lower esophageal sphincter pressure at high concentrations was detected, there was no evidence that this effect could promote GER during sedation. Therefore, these effects should be verified in future prospective studies.

Numerous factors were not associated with the risk of GER, including type of surgery, operative time, body mass index, intraoperative blood loss, smoking status, alcohol intake, other digestive tract diseases, hypertension, diabetes mellitus, history of asthma, psychiatric history, history of respiratory infection (within 2 mo), history of surgery, lidocaine, the use of palliative strategies (dexmedetomidine *vs* midazolam),

Table 1 Baseline characteristics of recruited patients, *n* (%)

Variable	Non-GER	GER	*P* value
n	519	82	
Sex			
Male	260 (50.10)	32 (39.02)	0.085
Female	259 (49.90)	50 (60.98)	
Age (yr)	49.00 (35.00, 61.00)	60.00 (42.00, 68.00)	
Type of surgery			
Orthopedics	117 (22.54)	24 (29.27)	0.169
Abdominal	402 (77.46)	58 (70.73)	
Operative time (min)	85.00 (50.00, 140.00)	120.00 (75.00, 190.00)	
BMI (kg/m^2)	23.63 (20.96, 26.30)	24.77 (20.28, 26.22)	
Intraoperative blood loss (mL)	200.00 (100.00, 300.00)	250.00 (50.00, 350.00)	
Smoking status			
Never	446 (85.93)	64 (78.05)	0.116
Current or former	73 (14.07)	18 (21.95)	
Alcohol intake			
Never	477 (91.91)	73 (89.02)	0.436
Yes	42 (8.09)	9 (10.98)	
Pharyngitis			
Never	472 (90.94)	23 (28.05)	< 0.001
Yes	47 (9.06)	59 (71.95)	
History of GER			
Never	506 (97.50)	66 (80.49)	< 0.001
Yes	13 (2.50)	16 (19.51)	
Other digestive tract diseases			
Never	497 (95.76)	71 (86.59)	0.023
Yes	22 (4.24)	11 (13.41)	
Hypertension			
Never	413 (79.58)	66 (80.49)	0.846
Yes	106 (20.42)	16 (19.51)	
Diabetes mellitus			
Never	457 (88.05)	70 (85.37)	0.523
Yes	62 (11.95)	12 (14.63)	
History of asthma			
Never	501 (96.53)	73 (89.02)	0.041
Yes	18 (3.47)	9 (10.98)	
Psychiatric history			
Never	510 (98.27)	79 (96.34)	0.375
Yes	9 (1.73)	3 (3.66)	
History of respiratory infection (within 2 mo)			
Never	510 (98.27)	80 (97.56)	0.696
Yes	9 (1.73)	2 (2.44)	

History of surgery			
Never	500 (96.34)	76 (92.68)	0.229
Yes	19 (3.66)	6 (7.32)	
Lidocaine (2% mL)	3.00 (2.20, 3.50)	3.00 (2.30, 3.55)	
Palliative			
Midazolam	360 (69.36)	64 (78.05)	0.071
Dexmedetomidine	159 (30.64)	18 (21.95)	
Sufentanil (g)			
10	10 (1.93)	0 (0.00)	0.032
15	169 (32.56)	36 (43.90)	
20	340 (65.51)	46 (56.10)	
Propofol (mg)	100.00 (100.00, 100.00)	100.00 (90.00, 100.00)	
Rocuronium bromide	50.00 (40.00, 50.00)	50.00 (40.00, 50.00)	
Sufentanil	10.00 (10.00, 30.00)	30.00 (10.00, 30.00)	
SAI	46.01	46.10	
TAI	42.90	42.90	
SDS	42.59	42.50	

BMI: Body mass index; GER: Gastroesophageal reflux; SAI: State anxiety inventory; SDS: Self-rating depression scale; TAI: Trait anxiety inventory.

arden, rocuronium bromide, sufentanil, SAI, TAI, and SDS. A previous study indicated that anxiety and depression levels were significantly higher in subjects with GER[23] and pointed out that the potential reasons for this could be that psychological factors always precede the clinical manifestations of GER. Moreover, anxiety can induce acid reflux by lowering the pressure of the lower esophageal sphincter, changing esophageal motility or increasing gastric acid secretion[24,25].

The results of this study indicated that older age, longer operative time, pharyngitis, and history of GER produce longer GER time. The greater incidence of GER in patients during general anesthesia induction, which is associated with longer GER time, potentially leads to the longer operative time. Moreover, older age, pharyngitis, and history of GER are associated with a higher risk of GER, which correlates with long GER time. Interestingly, the results of this study indicated that hypertensive patients were associated with shorter GER time, which might be due to a potential beneficial effect of GER on hypertension in terms of inducing changes in the dietary habits of patients[26].

A strength of this study is that we systematically explored the risk factors for the incidence of GER in patients undergoing general anesthesia. Furthermore, this study is the first to explore factors affecting GER time, and the cohort data used in this study were of high completeness, accuracy, and quality. However, several limitations of this study should be mentioned: (1) The study design was retrospective, which might introduce uncontrolled biases that might lead to overestimated associations; (2) The severity of GER during general anesthesia induction was not explored in this study; and (3) Stratified analyses based on patients' characteristics were not conducted because all factors entered the regression models. Therefore, the specific factors affecting the risk of GER in patients with specific characteristics during general anesthesia should be explored in future prospective studies.

CONCLUSION

Among patients who underwent general anesthesia, 12.8% had one GER event, and 0.8% had two GER events. We noted that female sex, older age, pharyngitis, and history of GER were associated with an increased risk of GER, whereas the use of propofol could protect against the risk of GER. In addition, older age, longer operative time, pharyngitis, and history of GER produced longer GER time, whereas patients

Table 2 The risk factors for the incidence of gastroesophageal reflux by multivariate logistic regression analysis

Variables	*β* value	SD	Wald chi-square	OR (95%CI)	*P* value
Intercept 1	-10.518	182.127	0.003		0.954
Intercept 2	-14.558	182.128	0.006		0.936
Gender (female *vs* male)	0.994	0.438	5.144	2.702 (1.144-6.378)	0.023
Age (yr) (continuous)	0.031	0.012	6.824	1.031 (1.008-1.056)	0.009
Type of surgery	-0.018	0.382	0.002	0.982 (0.464-2.077)	0.963
Operative time (min) (continuous)	0.003	0.004	0.904	1.003 (0.996-1.010)	0.342
BMI (kg/m^2) (continuous)	-0.049	0.069	0.516	0.952 (0.832-1.089)	0.472
Intraoperative blood loss (mL) (continuous)	-0.000	0.001	0.081	1.000 (0.998-1.002)	0.776
Smoking status	0.802	0.474	2.859	2.230 (0.880-5.650)	0.091
Alcohol intake	0.602	0.565	1.135	1.826 (0.603-5.524)	0.287
Pharyngitis	3.446	0.353	95.234	31.388 (15.709-62.715)	< 0.001
History of GER	2.479	0.534	21.513	11.925 (4.184-33.989)	< 0.001
Other digestive tract diseases	0.028	0.570	0.002	1.028 (0.336-3.145)	0.961
Hypertension	-0.661	0.437	2.294	0.516 (0.219-1.215)	0.130
Diabetes mellitus	-0.854	0.533	2.568	0.426 (0.150-1.210)	0.109
History of asthma	0.313	0.594	0.278	1.368 (0.427-4.383)	0.598
Psychiatric history	0.467	0.827	0.319	1.596 (0.315-8.072)	0.572
History of respiratory infection (within 2 mo)	-0.560	1.155	0.235	0.571 (0.059-5.492)	0.628
History of surgery	1.181	0.692	2.915	3.258 (0.840-12.642)	0.088
Lidocaine (2% mL) (continuous)	0.016	0.121	0.018	1.017 (0.802-1.289)	0.892
Palliative (d *vs* midazolam)	0.005	0.416	0.000	1.005 (0.445-2.272)	0.990
Sufentanil (g)					.
10	-	-	-	Ref.	.
15	10.378	182.118	0.003	32155.18 (0.000-3.36E159)	0.955
20	10.653	182.121	0.003	42315.00 (0.000-4.44E159)	0.953
Propofol (mg) (continuous)	-0.060	0.028	4.680	0.942 (0.892-0.994)	0.031
Arden (mg) (continuous)	-0.185	0.236	0.619	0.831 (0.523-1.318)	0.431
Rocuronium bromide (continuous)	-0.005	0.050	0.009	0.995 (0.902-1.098)	0.926
Sufentanil (continuous)	0.016	0.025	0.383	1.016 (0.967-1.067)	0.536
SAI (continuous)	0.134	0.031	0.497	1.011 (0.976-1.044)	0.647
TAI (continuous)	0.006	0.029	0.516	1.004 (0.962-1.051)	0.712
SDS (continuous)	-0.072	0.013	0.311	0.982 (0.948-1.035)	0.562

BMI: Body mass index; CI: Confidence interval; GER: Gastroesophageal reflux; OR: Odds ratio; SAI: State anxiety inventory; SD: Standard deviation; SDS: Self-rating depression scale; TAI: Trait anxiety inventory.

with hypertension were associated with shorter GER time. These results require further prospective studies of patients undergoing general anesthesia.

Table 3 The factors associated with gastroesophageal reflux time by multivariate linear regression analyses

Variables	*β* value	SE	*t* value	*P* value
Intercept	12.061	17.616	0.685	0.494
Gender	1.732	3.079	0.563	0.574
Age (yr) (continuous)	0.277	0.095	2.903	0.004
Type of surgery	-0.898	3.178	-0.283	0.778
Operative time (min) (continuous)	0.103	0.031	3.378	< 0.001
BMI (kg/m^2) (continuous)	-0.667	0.517	-1.290	0.197
Intraoperative blood loss (mL) (continuous)	-0.007	0.007	-1.057	0.291
Smoking status	6.843	3.821	1.791	0.074
Alcohol intake	3.309	4.692	0.705	0.481
Pharyngitis	33.566	3.418	9.820	< 0.001
History of gastroesophageal reflux	13.809	6.111	2.260	0.024
Other digestive tract diseases	1.165	5.896	0.198	0.844
Hypertension	-8.575	3.593	-2.386	0.017
Diabetes mellitus	-2.448	4.280	-0.572	0.568
History of asthma	-2.465	6.177	-0.399	0.690
Psychiatric history	-5.423	9.060	-0.599	0.550
History of respiratory infection (within 2 mo)	-7.538	9.566	-0.788	0.431
History of surgery	4.426	6.443	0.687	0.492
Lidocaine (2% mL) (continuous)	-1.224	0.927	-1.320	0.187
Palliative (d *vs* midazolam)	4.683	3.009	1.556	0.120
Sufentanil (g)				
10	ref	-	-	-
15	1.823	11.849	0.154	0.878
20	2.301	13.692	0.168	0.867
Propofol (mg) (continuous)	-0.174	0.160	-1.093	0.275
Arden (mg) (continuous)	1.408	1.857	0.758	0.449
Rocuronium bromide (continuous)	-0.061	0.337	-0.182	0.856
Sufentanil (continuous)	-0.086	0.214	-0.401	0.689
SAI (continuous)	-0.053	0.031	-0.253	0.546
TAI (continuous)	-0.027	0.087	-0.436	0.658
SDS (continuous)	0.011	0.053	0.211	0.432

BMI: Body mass index; GER: Gastroesophageal reflux; SAI: State anxiety inventory; SE: Standard error; SDS: Self-rating depression scale; TAI: Trait anxiety inventory.

ARTICLE HIGHLIGHTS

Research background

Gastroesophageal reflux (GER) is the most likely complication in perioperative patients, and early detection, diagnosis, and treatment can prevent serious adverse consequences.

Research motivation

No previous study had investigated the independent risk factors for the risk of GER and total GER time for patients undergoing general anesthesia.

Research objectives

To explore independent risk factors for the incidence and extent of GER during general anesthesia induction.

Research methods

This is a retrospective study, and 601 adult patients who received general anesthesia intubation or laryngeal mask surgery were involved. The definition of GER was based on assessment by Orion II-ohmega portable pH dynamic monitoring recorder, which was used to monitor the pH of the middle and lower esophagus to observe whether reflux occurred and to measure the occurrence frequency and duration. The potential risk factors for the incidence of GER were explored using multivariate logistic regression, and the risk factors for the extent of GER were evaluated using multivariate linear regression.

Research results

This study found female sex, increased age, pharyngitis, and history of GER were associated with an increased risk of GER, whereas the use of propofol could protect against the risk of GER. Moreover, age, operative time, pharyngitis, history of GER, and hypertension were significantly associated with GER time.

Research conclusions

This study identified the risk factors for the incidence of GER in patients undergoing general anesthesia, including female sex, increased age, pharyngitis, and history of GER.

Research perspectives

Further prospective studies should be performed to verify these findings owing to the retrospective design of this study.

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