

Impact of Chronic Obstructive Pulmonary Disease on Patients Undergoing Laryngectomy for Laryngeal Cancer

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Objectives/Hypothesis: Although chronic obstructive pulmonary disease (COPD) is a common comorbidity in patients undergoing laryngeal cancer surgery, the impact of this comorbidity in this setting is not well established. In this analysis, we used the Nationwide Inpatient Sample (NIS) to elucidate the impact of COPD on outcomes after laryngectomy for laryngeal cancer.

Methods: The NIS was queried for patients admitted from 1998 to 2010 with laryngeal cancer who underwent total or partial laryngectomy. Patient demographics, type of admission, length of stay, hospital charges, and concomitant diagnoses were analyzed.

Results: Our inclusion criteria yielded a cohort of 40,441 patients: 3,051 with COPD and 37,390 without. On average, COPD was associated with an additional \$12,500 ($P < 0.001$) in hospital charges and an additional 1.4 days ($P < 0.001$) of hospital stay. There was no significant difference in incidence of in-hospital mortality between the COPD and non-COPD groups after total laryngectomy (1.1% in COPD vs. 1.0% in non-COPD; $P = 0.776$); however, there was an increased incidence of in-hospital mortality in the COPD group compared to the non-COPD group after partial laryngectomy (3.4% in COPD vs. 0.4% in non-COPD; $P < 0.001$). Multivariate adjusted logistic regression revealed that COPD was associated with greater odds of pulmonary complications after both partial laryngectomy (odds ratio [OR] = 3.198; $P < 0.001$) and total laryngectomy (OR = 1.575; $P < 0.001$).

Conclusion: Chronic obstructive pulmonary disease appears to be associated with greater hospital charges, length of stay, and postoperative pulmonary complications in patients undergoing laryngectomy for laryngeal cancer. Chronic obstructive pulmonary disease after partial, but not total, laryngectomy appears to be associated with increased risk of in-hospital mortality.

Key Words: Chronic obstructive pulmonary disease (COPD), Nationwide Inpatient Sample (NIS), laryngeal cancer, partial laryngectomy, total laryngectomy, postoperative pulmonary complications.

Level of Evidence: 2C.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) and laryngeal cancer share smoking as their primary risk factor.^{1,2} Treatment of laryngeal cancer depends on the stage of the cancer and the characteristics of the patient, and may include radiotherapy and/or surgery with or without chemotherapy. Total and partial laryngectomy, which are employed in the treatment of this cancer, put patients at

risk of developing morbid and costly postoperative complications, including pulmonary complications.

Chronic obstructive pulmonary disease itself has also been shown to be a strong risk factor for the development of postoperative complications, particularly pulmonary complications such as atelectasis, pneumonia, and respiratory failure.³⁻⁵ Although COPD and laryngectomy are both linked to postoperative complications, there is a paucity of research exploring the impact of COPD status on laryngectomy for laryngeal cancer. Exploring this relationship might aid surgeons in risk stratification. In this study, we used the largest database of inpatient discharge data in the United States, the Nationwide Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality and the Healthcare Cost and Utilization Projection, to assess the impact of COPD on total and partial laryngectomy for laryngeal cancer.

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MATERIALS AND METHODS

The NIS is a publicly available sample of inpatient discharge data from roughly 20% of all non-federal hospitals in the United States.⁶

All NIS cases between 1998 and 2010 coding for patients ≥ 40 years with a primary diagnosis code of laryngeal cancer and a primary procedure code of total and partial laryngectomy

TABLE I.
ICD-9 Codes for Diagnoses, Procedures, and Comorbidities.

	ICD-9 Code
Diagnoses	
Malignant neoplasm of the larynx*	146.4, 146.5, 161.0, 161.1, 161.2, 161.3, 161.8, 161.9
Chronic obstructive pulmonary disease	490, 491.0, 491.1, 491.2, 491.20, 491.21, 491.22, 491.8, 491.9, 492.0, 492.8
Procedures	
Partial laryngectomy*	30.1, 30.29
Total laryngectomy/laryngopharyngectomy*	30.3, 30.4
Neck dissection*	40.40, 40.41, 40.42
Free flap reconstruction*	86.7, 86.70–86.75, 86.8, 86.89
Tracheostomy	31.1, 31.2, 31.21, 31.29
Comorbidities[†]	
Alcohol abuse	291.0–291.3, 291.5, 291.8, 291.81, 291.89, 291.9, 303.00–303.93, 305.00–305.03, V113
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 428.0, 428.1, 428.20, 428.22, 428.23, 428.30, 428.32, 428.33, 428.40, 428.42, 428.43, 428.9
Diabetes mellitus	250.00–250.33, 250.40–250.93
Hypertension	401.1, 401.9, 642.00–642.04
Hypothyroidism	243–244.2, 244.8, 244.9
Fluid and electrolyte disorder	276.0–276.9
Obesity	278.0, 278.00, 278.01
Chronic renal failure	585.1–585.9, 792.5, V42.0, V45.1, V55.1, V55.11, V55.12, V56.0–V56.8
Weight loss	260–263.9

*Adapted from Semenov et al.⁷

[†]Adapted from Healthcare Cost and Utilization Project comorbidity software comorbidity definitions.⁶
ICD-9 = International Classification of Diseases, Ninth Revision.

were isolated. International Classification of Diseases, Ninth Revision (ICD-9) codes used for the selection of this cohort (listed in Tables I and II) were adapted from Semenov et al.⁷ These inclusion criteria yielded a cohort of 40,441 patients, which was then stratified by the presence or absence of a diagnosis of COPD and the type of procedure (partial or complete laryngectomy). The COPD and non-COPD subgroups were compared with respect to demographic data, type of hospital admission, length of stay, hospital charges, in-hospital mortality, presence of comorbidities, and presence of postoperative complications in both the total and partial laryngectomy groups. The Rutgers New Jersey Medical School Institutional Review Board does not consider the use of de-identified data from the NIS to meet the regulatory definition of human subjects research provided in 45 Code of Federal Regulations (CFR) 46.102, and thus no approval was required for this NIS analysis.

Independent 2-tailed *t* test, cross-tabulation, chi-square, and 2-sided Fisher exact test were performed as appropriate. Binomial logistic regression analyses were performed using postoperative complications as the dependent variables. Variables with missing data for more than 5% of the population were given dummy variables to represent missing data in the regression analysis. Threshold of significance for all statistical tests was set at $P < 0.05$. All data were weighted using NIS discharge weights. SPSS 22 (IBM, Armonk, New York) was used for all statistical computations.

RESULTS

There were a total of 40,441 cases from 1998 through 2010 with a primary diagnosis of laryngeal cancer and primary procedure of laryngectomy. The rate of COPD was

7.7% in the total laryngectomy group versus 6.1% in the partial laryngectomy group ($P < 0.001$).

Patients with COPD were on average 2.1 years older ($P < 0.001$) than their non-COPD counterparts in the total laryngectomy group and 3.3 years older ($P < 0.001$) in the partial laryngectomy group (Table III). There was a significantly greater fraction of patients with COPD in the oldest age cohort (> 80 years) in the partial laryngectomy group but not in the total laryngectomy group (Table III). There was no significant difference between the COPD and non-COPD groups in gender distribution in either the total or partial laryngectomy cohorts (Table III). All groups displayed a male predominance. Whites made up the majority of patients in both the total and partial laryngectomy groups (Table III).

The majority of admissions in both the total and partial laryngectomy groups were elective, with the COPD patients in the total laryngectomy group showing a significantly higher proportion of emergent/urgent admissions relative to their non-COPD counterparts (Table III). Neck dissection was not significantly different between the COPD and non-COPD groups for both procedures (Table III). Free flap reconstruction did not differ significantly in total laryngectomy patients when stratified by COPD status (Table III). No free flap reconstruction was performed in partial laryngectomy patients with COPD (Table III). Tracheostomy was significantly more common in the non-COPD group than the COPD group in partial laryngectomy patients, but the groups did not differ significantly among total laryngectomy patients (Table III).

TABLE II.
ICD-9 Codes: Postoperative Complications.

	ICD-9 Code
Acute Postoperative Pulmonary Complications	
Aspiration pneumonia*	507, 507.0
Infectious pneumonia*	480, 480.0–480.3, 480.8, 480.9, 481, 482, 482.0–482.3, 482.30–482.32, 482.39, 482.40–482.42, 482.49, 482.8, 482.81–482.84, 482.89, 482.9, 483, 483.1, 483.8, 484, 484.1, 484.3, 484.5, 584.6, 484.7, 484.8, 485, 487.0, V12.61
Pneumothorax, other air leak	512.0 – 512.2, 512.81, 512.82, 512.84, 512.89
Pulmonary collapse	518.0–518.2
Empyema, pleurisy, pleural effusion	510.0, 510.9, 511.0, 511.1, 511.8, 511.89, 511.9
Respiratory failure	517.3, 518.5, 518.51–518.53, 518.81–518.84, 799.1
Acute Postoperative Nonpulmonary Surgical Complications	
Postoperative fistula*	998.6
Postoperative infection*	998.5, 998.51, 998.59
Shock*	998.00–998.09
Bleeding*	998.1, 998.11, 998.12, 998.13
Nonhealing surgical wound*	998.83
Wound dehiscence*	998.3, 998.30, 998.31, 998.32, 998.33
Acute Postoperative Nonpulmonary Medical Complications	
Cardiac event*	410.0–410.9, 411.1, 411.8, 415.0, 420.0, 420.9, 421.0, 421.1, 421.9, 422.0, 422.9, 427.0–427.5, 428.0, 428.1, 428.21, 428.23, 428.31, 428.33, 428.41, 428.43, 428.9
Venous thromboembolism	415.11, 415.13, 415.19, 453.40, 453.41, 453.42
Cerebrovascular event*	997.00, 997.01, 997.02, 997.09
Urinary tract infection*	599.0, 996.64, 996.31, V13.02
Sepsis*	995.9, 038.0–038.4, 999.3
Hepatic failure*	570
Renal failure*	584.5–584.9

*Adapted from Semenov et al.⁶
ICD-9 = International Classification of Diseases, Ninth Revision.

All comorbidities that were significantly different between the COPD and non-COPD groups for a given procedure were more prevalent in the COPD group (Table IV). These included congestive heart failure and fluid and electrolyte disorders in both groups, alcohol abuse and weight loss in the total laryngectomy group, and hypothyroidism and chronic renal failure in the partial laryngectomy group. The most common comorbidity for both procedures was hypertension, for which there was no difference between the COPD and non-COPD groups.

Although COPD patients did not stay in the hospital significantly longer than non-COPD patients after partial laryngectomy, they stayed on average 1.4 days longer ($P < 0.001$) after total laryngectomy (Table III). Chronic obstructive pulmonary disease was associated with a significant increase in hospital charges for both total laryngectomy (increase of \$11,389; $P < 0.001$) and partial laryngectomy (increase of \$15,978; $P < 0.001$). In-hospital mortality rate was not significantly different between COPD and non-COPD groups after total laryngectomy; however, it was significantly more common in COPD patients after partial laryngectomy (3.4% in COPD vs. 0.4% in non-COPD; $P < 0.001$).

Postoperative complications were grouped according to whether they were pulmonary or non-pulmonary compli-

cations. Non-pulmonary complications were further subdivided into surgical and medical complications. The most common pulmonary complication in the COPD cohort after both total and partial laryngectomy was respiratory failure (12.9% and 17.2%, respectively) (Table V). The second most common pulmonary complications in the COPD cohorts were infectious pneumonia (9.7%) after total laryngectomy and aspiration pneumonia (10.1%) after partial laryngectomy. Postoperative fistula was the most common non-pulmonary surgical complication after both total and partial laryngectomy, whereas acute cardiac complications was the most common non-pulmonary medical complication.

Multivariate logistic regression analyses were performed to determine odds of postoperative complications resulting from COPD status. Covariates entered into each model were age, race, gender, type of admission (elective vs. nonelective), presence/absence of neck dissection, free flap reconstruction, tracheostomy, COPD, alcohol abuse, congestive heart failure, diabetes mellitus, hypertension, hypothyroidism, fluid/electrolyte disorders, obesity, chronic renal failure, and weight loss. Chronic obstructive pulmonary disease status was associated with greater odds of pulmonary complications after both partial (odds ratio [OR] = 3.198; $P < 0.001$) (Table VI) and total laryngectomy (OR = 1.575; $P < 0.001$) (Table VII).

TABLE III.
Characteristics of Non-COPD Versus COPD Patient Cohorts.

Characteristic	Total Laryngectomy			Partial Laryngectomy		
	Non-COPD (n = 32,819)	COPD (n = 2,754)	P Value	Non-COPD (n = 4,571)	COPD (n = 297)	P Value
Age y, mean ± SD	63.0 ± 10.5	65.1 ± 9.3	<0.001*	61.7 ± 9.9	65.0 ± 10.8	<0.001*
Age cohorts, %			<0.001* [†]			<0.001* [†]
40–59 years	38.9	25.4	<0.001*	41.6	34.0	0.011*
60–79 years	54.9	68.7	<0.001*	54.4	53.2	0.763
≥ 80 years	6.2	6.0	0.647	4.0	12.8	<0.001*
Sex, %			0.938			0.535
Male	81.1	81.2		75.0	73.4	
Female	18.9	18.8		25.0	26.6	
Race, %			<0.001* [†]			0.002* [†]
White	56.8	55.6	0.215	62.6	58.6	0.194
Black	10.9	8.2	<0.001*	6.1	5.4	0.707
Hispanic	4.5	2.5	<0.001*	3.2	3.4	0.865
Asian or Pacific Islander	0.8	0.0	<0.001*	0.9	3.4	0.001*
Other	1.9	1.3	0.052	1.6	1.6	0.814
Unknown	25.1	32.4	—	25.6	27.6	—
Type of Hospital Admission, %			<0.001* [†]			0.011* [†]
Emergent/urgent	20.0	27.9	<0.001*	12.4	15.2	0.174
Elective	72.4	65.9	<0.001*	79.9	81.4	0.550
Unknown	7.6	6.2	—	7.7	3.4	—
Neck dissection, %	5.8	4.9	0.052	28.3	31.0	0.320
Free flap reconstruction, %	7.1	7.2	0.791	1.4	0.0	0.033*
Tracheostomy, %	12.5	13.7	0.093	38.8	20.9	<0.001*
Mean length of stay, d	12.1	13.5	<0.001*	7.1	7.4	0.444
Mean hospital charge, \$	64,440	75,829	<0.001*	37,995	53,973	<0.001*
In-hospital mortality, %	1.0	1.1	0.776	0.4	3.4	<0.001*

*Statistically significant.

[†]Analysis among groups of a given variable.

COPD = chronic obstructive pulmonary disease; SD = standard deviation.

DISCUSSION

In 2013, Gupta et al. used the National Surgical Quality Improvement Program (NSQIP) database to study

the effect of COPD on postoperative outcomes and found that COPD patients have an increased frequency of preoperative comorbidities and postoperative pulmonary and

TABLE IV.
Comorbidity Frequency in Non-COPD Versus COPD Patient Cohorts in Percentage.

Comorbidity	Total Laryngectomy			Partial Laryngectomy		
	Non-COPD (n = 32,819)	COPD (n = 2,754)	P Value	Non-COPD (n = 4,571)	COPD (n = 297)	P Value
Alcohol abuse	8.8	11.8	<0.001*	5.6	4.7	0.601
Congestive heart failure	4.6	8.9	<0.001*	2.7	11.1	<0.001*
Diabetes mellitus	14.8	14.0	0.275	9.8	11.5	0.316
Hypertension	40.3	41.6	0.157	37.7	38.7	0.758
Hypothyroidism	6.9	6.0	0.061	4.9	8.1	0.020*
Fluid and electrolyte disorder	13.8	18.6	<0.001*	4.8	14.1	<0.001*
Obesity	1.6	1.9	0.353	1.9	0.0	0.010*
Chronic renal failure	1.1	1.2	0.641	0.7	5.1	<0.001*
Weight loss	7.5	14.8	<0.001*	2.5	1.7	0.556

*Statistically significant.

COPD = chronic obstructive pulmonary disease.

TABLE V.
Frequency of Postoperative Pulmonary Complications in Non-COPD Versus COPD Patient Cohorts.

Acute Complications	Total Laryngectomy			Partial Laryngectomy		
	Non-COPD (n = 32,819)	COPD (n = 2,754)	P Value	Non-COPD (n = 4,571)	COPD (n = 297)	P Value
Acute Pulmonary Complications, %						
Aspiration pneumonia	2.0	4.0	<0.001*	2.4	10.1	<0.001*
Infectious pneumonia	4.8	9.7	<0.001*	2.7	5.4	0.011*
Pneumothorax, other air leak	0.6	0.3	0.134	0.3	1.7	0.006*
Pulmonary collapse	5.6	7.4	<0.001*	3.7	7.7	0.002*
Empyema, pleurisy, pleural effusion	2.3	2.8	0.096	0.9	0.0	0.174
Respiratory failure	6.9	12.9	<0.001*	3.6	17.2	<0.001*
Acute Nonpulmonary Surgical Complications, %						
Postoperative fistula	4.1	5.2	<0.007*	0.5	3.4	<0.001*
Postoperative infection	4.1	4.4	0.342	1.4	0.0	0.032*
Shock	0.1	0.2	0.108	0.0	0.0	—
Bleeding	4.1	5.2	<0.007*	3.0	2.0	0.477
Wound dehiscence	2.9	3.1	0.557	0.2	0.0	1.000
Acute Nonpulmonary Medical Complications, %						
Cardiac events	8.0	10.2	<0.001*	5.5	13.5	<0.001*
Venous thromboembolism	0.5	1.1	0.001*	0.1	0.0	1.000
Cerebrovascular accident	0.3	0.0	<0.001*	0.3	0.0	1.000
Urinary tract infection	2.4	3.4	0.001*	2.0	0.0	0.006*
Sepsis	0.1	0.2	0.040*	0.1	0.0	1.000
Hepatic failure	0.1	0.0	0.395	0.0	0.0	—
Renal failure	1.3	1.7	0.066	0.7	3.7	<0.001*

*Statistically significant.
COPD = chronic obstructive pulmonary disease.

nonpulmonary complications.⁵ Although the effects of COPD on pulmonary complications for thoracic and abdominal surgery have been explored in the literature, there have been few studies in the realm of head and neck cancer surgery.^{3,8,9} In this study, we utilized NIS data to analyze the impact of COPD on laryngectomy for laryngeal cancer. To our knowledge, this is the first study to use a national database to specifically evaluate the effect of COPD on postoperative complications of laryngectomy. The 2011 Behavioral Risk Factor Surveillance System survey estimated the national prevalence of COPD to be 6.2%.^{10,11} In comparison, the estimated prevalence of COPD in this national sample of laryngeal cancer surgery patients was 7.7% in total laryngectomy patients and 6.1% in partial laryngectomy patients.

A meta-analysis in 2006 by Smetana et al. determined that both COPD and head and neck surgery are among the strongest predictors of pulmonary complications.⁴ In our analysis, COPD status resulted in a significantly increased frequency of four out of the six pulmonary complications after total laryngectomy, and five out of the six pulmonary complications after partial laryngectomy. Furthermore, our multivariate adjusted binomial logistic regression analysis showed that COPD status was associated with increased odds of developing pulmonary complications in patients undergoing both partial and total laryngectomy.

Gupta et al. also found that COPD was associated with increased postoperative mortality.⁵ In our study, there was no significant difference in mortality between

TABLE VI.
Logistic Analysis: Relationship of COPD Status to Acute Postoperative Complications in Partial Laryngectomy Group.

Acute Complications	Unadjusted OR (95% CI)	P Value	Multivariate-Adjusted OR (95% CI)	P Value
Pulmonary complications	3.226 (2.460–4.231)	<0.001*	3.198 (2.340–4.371)	<0.001*
Nonpulmonary surgical complications	1.149 (0.678–1.947)	0.607	1.126 (0.612–2.074)	0.703
Nonpulmonary medical complications	2.016 (1.455–2.813)	<0.001*	1.222 (0.821–1.818)	0.323

*Statistically significant.
CI = confidence interval; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

TABLE VII.
Logistic Analysis: Relationship of COPD Status to Acute Postoperative Complications in Total Laryngectomy Group.

Acute Complications	Unadjusted OR (95% CI)	P Value	Multivariate-Adjusted OR (95% CI)	P Value
Pulmonary complications	1.858 (1.700–2.030)	<0.001*	1.575 (1.431–1.734)	<0.001*
Nonpulmonary surgical complications	1.197 (1.068–1.341)	0.002*	1.124 (0.999–1.263)	0.052
Nonpulmonary medical complications	1.313 (1.176–1.466)	<0.001*	1.007 (0.894–1.134)	0.912

*Statistically significant.

CI = confidence interval; COPD = chronic obstructive pulmonary disease; OR = odds ratio.

the COPD and non-COPD groups after total laryngectomy. In contrast, there was a significant increase in mortality seen in the COPD group after partial laryngectomy, where the mortality rate increased from 0.4% to 3.4%. This may be due to the fact that after partial laryngectomy, patients rely on adequate pulmonary function (including an adequate cough and proper pulmonary ciliary function) to expectorate aspirated material. In patients undergoing total laryngectomy, mechanical tracheobronchial clearance may be performed more effectively via the tracheostoma, although this is speculative.

The total national cost of care attributable to COPD in 2010 has been estimated to be \$32.1 billion, over half of which was paid for by Medicare.¹² This cost is expected to rise to \$49.0 billion by 2020. Consistent with this finding, COPD in our study was associated with an increase in hospital charges after both total and partial laryngectomy, and a longer hospital stay after total laryngectomy. These increases might reflect the increased incidence of pulmonary complications in the COPD cohort; one analysis of NSQIP data found that postoperative pulmonary complications resulted in a greater cost of care and length of stay than cardiovascular, thromboembolic, or infectious complications.¹³ Emphasis on appropriate management and preoperative planning for the COPD patient undergoing laryngectomy is necessary to minimize these associated costs. In order to minimize the effect of COPD on postoperative outcomes of laryngectomy, we recommend the following suggestions based on guidelines put forth by the American Thoracic Society: smoking cessation 4 to 8 weeks preoperatively, optimization of pulmonary function with inhaled bronchodilators, early postoperative mobilization facilitated by effective analgesia, deep breathing, intermittent positive-pressure ventilation, and incentive spirometry.¹⁴

The nature of data coding in the NIS database puts limitations on how we were able to analyze the effect of COPD on laryngectomy. The NIS only uses ICD-9 codes to code diagnoses and procedures; thus, we were not able to determine the effect of COPD severity, cancer stage and grade of differentiation, residual tumor classification, specific surgical approach, and preoperative COPD management on postoperative outcomes. There is a remote possibility that the increase in postoperative complication, seen in the COPD group compared to the non-COPD group, reflects stage/grade/resection margin-status, which themselves are correlated to COPD status rather than the COPD status itself. Because the ICD-9 codes do not differentiate between open partial laryngectomy and transoral

laser microsurgery (TLM) resection, potential differences in outcomes after open partial laryngectomy versus TLM resection were unable to be examined. It is conceivable that the minimally invasive nature of TLM resection might offer better protection from postoperative pulmonary complications than open partial laryngectomy in patients with COPD; however, further research is needed to explore this possibility.

The use of ICD-9 codes in our research also requires the assumption of correct coding, leading our analysis susceptible to miscoding bias. Inherent to the use of NIS data is an inability to determine causal relationships; thus, we were limited to determining associations that may reflect other covariates such as additional comorbidities. Additionally, because the NIS database only contains data from the index admission, complications diagnosed at follow-up visits may not have been included in our data. Despite these limitations, our NIS sample was large and distributed across the country, suggesting high external validity of our results. Findings of this study may help surgeons evaluate the risks and costs associated with laryngectomy in the subset of patients with COPD. Further research is needed to evaluate the impact of presurgical treatment options on the outcomes studied in this article.

CONCLUSION

In summary, this analysis of the NIS database suggests that COPD may be a significant risk factor for the development of postoperative complications and increased hospital charges in laryngeal cancer surgery patients. Multivariate regression analysis, grouping complications into subsets, showed COPD status after laryngectomy to be associated with greater odds of pulmonary but not non-pulmonary surgical or nonpulmonary medical complications. Finally, after partial but not total laryngectomy, COPD status is associated with increased in-hospital mortality.

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