Severity of chronic obstructive pulmonary disease is associated with adverse outcomes in patients undergoing elective abdominal aortic aneurysm repair

David H. Stone, MD,[a] Philip P. Goodney, MD, MS,[a,b] Jeffrey Kalish, MD,[c] Andres Schanzer, MD,[d] Jeffrey Indes, MD,[e] Daniel B. Walsh, MD,[a] Jack L. Cronenwett, MD,[a,b] and Brian W. Nolan, MD, MS,[a,b] for the Vascular Study Group of New England, *Lebanon, NH; Boston and Worcester, Mass; and New Haven, Conn*

Introduction: Although chronic obstructive pulmonary disease (COPD) has been implicated as a risk factor for abdominal aortic aneurysm (AAA) rupture, its effect on surgical repair is less defined. Consequently, variation in practice persists regarding patient selection and surgical management. The purpose of this study was to analyze the effect of COPD on patients undergoing AAA repair.

Methods: We reviewed a prospective regional registry of 3455 patients undergoing elective open AAA repair (OAR) and endovascular AAA repair (EVAR) from 23 centers in the Vascular Study Group of New England from 2003 to 2011. COPD was categorized as none, medical (medically treated but not oxygen [O_2]-dependent), and O_2-dependent. End points included in-hospital death, pulmonary complications, major postoperative adverse events (MAEs), extubation in the operating room, and 5-year survival. Survival was determined using life-table analysis based on the Social Security Death Index. Predictors of in-hospital and long-term mortality were determined by multivariate logistic regression and Cox proportional hazards analysis.

Results: During the study interval, 2043 patients underwent EVAR and 1412 patients underwent OAR with a nearly equal prevalence of COPD (35% EVAR vs 36% OAR). O_2-dependent COPD (4%) was associated with significantly increased in-hospital mortality, pulmonary complications, and MAE and was also associated with significantly decreased extubation in the operating room among patients undergoing both EVAR and OAR. Five-year survival was significantly diminished among all patients undergoing AAA repair with COPD (none, 78%; medical, 72%; O_2-dependent, 42%; $P < .001$). By multivariate analysis, O_2-dependent COPD was independently associated with in-hospital mortality (odds ratio 2.02, 95% confidence interval, 1.0-4.0; $P = .04$) and diminished 5-year survival (hazard ratio, 3.02; 95% confidence interval, 2.2-4.1; $P < .001$).

Conclusions: Patients with O_2-dependent COPD undergoing AAA repair suffer increased pulmonary complications, overall MAE, and diminished long-term survival. This must be carefully factored into the risk-benefit analysis before recommending elective AAA repair in these patients. (J Vasc Surg 2013;57:1531-6.)

The clinical management of patients with severe chronic obstructive pulmonary disease (COPD) in the setting of abdominal aortic aneurysms (AAA) remains an ongoing challenge in contemporary practice. Oxygen (O_2)-dependent COPD has been documented in several

older studies to be associated with poor clinical outcomes after open AAA repair (OAR) and is also an independent predictor of AAA rupture.[1-3] Accordingly, patient selection for elective AAA repair in patients with COPD is more difficult, and variation in practice persists in patient selection and surgical management. Moreover, clinical decision making in treatment of patients with COPD and AAA is perhaps further complicated by the application and evolution of endovascular AAA repair (EVAR), which has affected the perioperative morbidity profile in treating AAA.[4-8]

Despite a substantial body of literature devoted to COPD, there is a relative paucity of surgical literature about the effect of clinically significant COPD on AAA repair in the modern, endovascular era. In addition, comparisons with historical control groups of AAA cohorts often reflect AAA patients who were treated before the widespread adoption of statin therapy, which may improve survival and affect the natural history of AAA. This study used a prospective regional registry to analyze the effect of COPD on patients undergoing AAA repair in contemporary real-world practice.

METHODS

Patients and database. This study reflects data collected in the prospectively compiled regional registry of the Vascular Study Group of New England (VSGNE).[9] The use of deidentified data for this analysis was approved by the Committee for the Protection of Human Subjects of Dartmouth Medical School. All patients undergoing elective OAR and EVAR repair from 23 centers in New England from 2003 to 2011 were reviewed (n = 3455). The analysis excluded ruptured and symptomatic AAA and juxtarenal and suprarenal aneurysms. There was a small difference in mean maximal AAA diameter among those undergoing EVAR vs OAR (57 vs 60 mm). Selection of EVAR or OAR was at the discretion of the operating surgeon.

Outcomes and variable definitions. COPD was categorized as none, medical (medically treated but not O_2-dependent), and O_2-dependent. The end points of this study included in-hospital death, pulmonary complications (pneumonia/ventilatory failure), major postoperative adverse events (MAEs), extubation in the operating room, and 5-year survival, which was determined by matching patients in the VSGNE database with the Social Security Death Index. MAEs included in-hospital death, postoperative myocardial infarction, new-onset congestive heart failure or cardiac dysrhythmia, respiratory failure, decline in renal function (by at least 20%), lower extremity ischemia, mesenteric ischemia, or unplanned reoperation. Chronic renal insufficiency was defined as a creatinine value of ≥1.8 mg/dL. Ventilatory failure reflected a composite of pulmonary complications, including reintubation and prolonged ventilator support.

Statistical analysis. Data were compared using χ^2 analysis for dichotomous and categoric variables and the *t*-test or analysis of variance (ANOVA) for continuous variables. Comparisons were made across all groups, comparing O_2-dependent patients with those with no COPD and those with medically managed disease. Survival was determined using life-table analysis. Variables associated with end points were initially identified by univariate analysis using χ^2 test, with the Fisher exact test substituted where needed.

Variables significant at $P < .10$ were entered into a multivariable model using backwards stepwise logistic regression. Predictors of in-hospital and long-term mortality were determined by multivariate logistic regression (in-hospital mortality) and Cox proportional hazards analysis (5-year survival). Hazard ratios (HR), odds ratios (OR), and 95% confidence intervals (CIs) were generated for significant end point predictors.

RESULTS

During the study interval, 3455 patients underwent elective AAA repair. Among them, 2043 patients underwent EVAR and 1412 underwent OAR with near equal prevalence of COPD (35% EVAR vs 36% OAR). Of the study cohort, 2238 patients (65%) had no COPD, 1082 (31%) had medically managed COPD, and 135 (4%) had O_2-dependent COPD. Demographic details and comorbidities of patients stratified by COPD severity are summarized in Table I.

In-hospital mortality was significantly increased among patients with any COPD undergoing AAA repair (none, 1%; medically managed, 2.1%, O_2-dependent, 2.0%; $P = .02$). Further analysis of this cohort when stratified by repair type revealed that in-hospital death did not differ among patients undergoing EVAR. By comparison, in-hospital death was significantly higher among O_2-dependent patients undergoing OAR. For each category of COPD severity, in-hospital mortality was significantly higher among those undergoing OAR (Fig 1).

Postoperative pulmonary complications were significantly higher among all O_2-dependent patients undergoing AAA repair (none, 4.3%; medically managed, 8.7%; O_2-dependent, 10.4%; $P < .001$). When analyzed by operation type (EVAR vs OAR), O_2-dependent patients experienced significantly higher rates of pulmonary complications after EVAR and OAR. For each category of COPD severity, pulmonary complications were significantly higher among those undergoing OAR (Fig 2).

MAEs were also significantly higher among patients with O_2-dependent COPD than in patients without COPD (none, 14.9%; medically managed, 21%; O_2-dependent, 22.6%; $P < .001$). When assessed by specific repair type, the number of patients experiencing MAEs was significantly increased among those with O_2 dependence for EVAR and OAR. In addition, for each category of COPD severity, MAEs were significantly higher among those undergoing OAR (Fig 3).

The incidence of successful extubation in the operating room was substantially diminished among those with O_2-dependent COPD than in non−O_2-dependent patients (none, 87.3%; medically managed, 81.5%; O_2-dependent, 79.4%; $P < .001$). Patients with O_2 dependence also experienced lower rates of extubation in the operating room, irrespective of repair type. Similar to other end points, extubation in the OR was significantly decreased among patients for each category of COPD severity undergoing OAR (Fig 4). The 280 patients who underwent EVAR under regional anesthesia were excluded from this specific subanalysis.

Survival at 5 years was significantly decreased among patients with O_2-dependent COPD undergoing AAA repair compared with those with no COPD or medically managed disease (none, 79%; medical, 72%; O_2-dependent, 42%; $P < .001$; Fig 5). In addition, when 5-year survival was stratified by procedure type, a small but statistically significant difference was found between OAR (78%) and EVAR patients (72%) at 5 years ($P = .047$).

Multivariate logistic regression confirmed that O_2-dependent COPD was an independent predictor of in-hospital death (OR, 2.0; $P = .04$). In addition, age >80 years (OR, 3.8; $P = .004$), coronary artery disease (OR, 1.8; $P = .05$), and OAR (OR, 5.1; $P < .001$) were also independent predictors of in-hospital death. Cox proportional
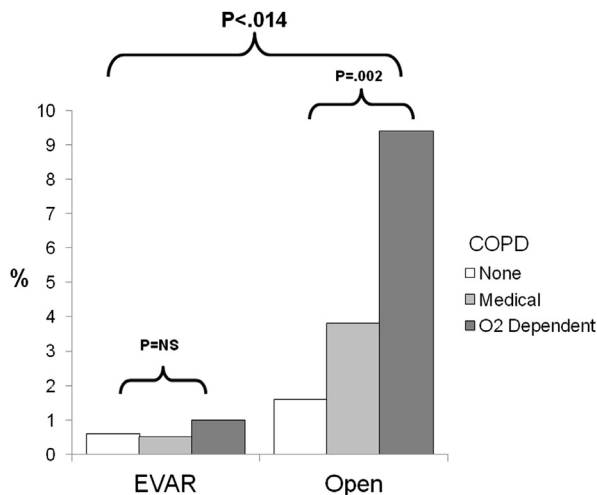
Table I. Patient demographics and comorbidities for total study cohort stratified by COPD severity

Variable[a]	COPD			P[b]
	None (n = 2238)	Medical (n = 1082)	O2 dependent (n = 135)	
Age, years	72 ± 8.9	72 ± 7.9	75 ± 7.3	.005
Female sex	19 (425)	26 (281)	36 (49)	.001
Coronary artery disease	31 (694)	39 (422)	38 (51)	.001
Congestive heart failure	6 (134)	12 (130)	24 (32)	.001
Smoking	85 (1902)	97 (1050)	93 (126)	.001
Diabetes mellitus	17 (380)	29 (206)	19 (26)	.38
Hypertension	84 (1880)	84 (909)	87 (117)	.49
CRI (Cr > 1.8 mg/dL)	7 (157)	6 (65)	6 (8)	.72
Aspirin	72 (1613)	72 (779)	65 (88)	.21
Statin	69 (1545)	66 (715)	64 (87)	.15
β-blocker	80 (1786)	82 (885)	64 (87)	.0001

COPD, Chronic obstructive pulmonary disease; *Cr,* creatinine; *CRI,* chronic renal insufficiency; *SD,* standard deviation.
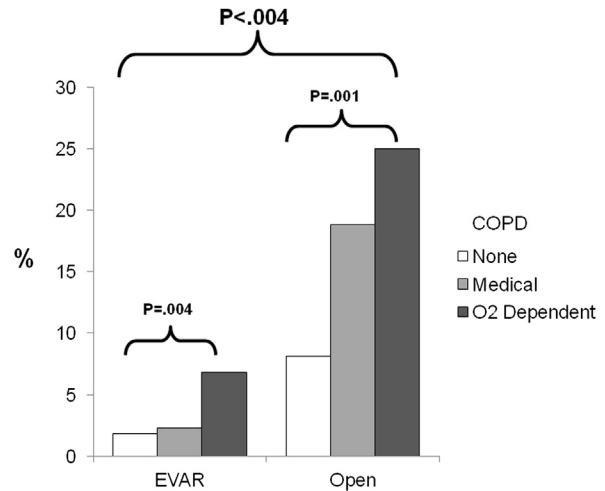
[a]Categoric data are shown as number (%) and continuous data as mean ± standard deviation.

[b]P values reflect a χ^2 analysis across all three cohorts.

Fig 2. Rates of pulmonary complications are shown stratified by chronic obstructive pulmonary disease (*COPD*) severity and endovascular (*EVAR*) or open abdominal aortic aneurysm repair. Pulmonary complications were defined as pneumonia or respiratory failure.

Fig 1. Rates of in-hospital death are shown stratified by chronic obstructive pulmonary disease (*COPD*) severity and endovascular (*EVAR*) or open abdominal aortic aneurysm repair.

hazards analysis revealed that O_2-dependent COPD was also independently associated with decreased 5-year survival (HR, 3.0; $P < .001$). Other independent predictors of diminished 5-year survival were age >80 years (HR, 2.69; $P < .001$), chronic renal insufficiency (HR, 1.91; $P < .001$), coronary artery disease (HR, 1.46; $P < .001$), congestive heart failure (HR, 1.46; $P = .002$), and medically managed COPD (HR, 1.22; $P = .02$). Aspirin (HR, 0.78; $P = .005$) and statin therapy (HR, 0.79, $P = .007$) were independently associated with improved 5-year survival (Table II).

DISCUSSION

This study, using a prospective regional registry, is among the first to better define real-world outcomes of patients with O_2-dependent COPD undergoing AAA repair in the endovascular era. Multiple studies have investigated the effect of clinically significant COPD on rupture risk, operative outcomes, and long-term survival; however, many remain single-center retrospective studies with statistically modest sample sizes and thus are more finite in their conclusions guiding clinical decision making.[1,10-12] In addition, many of these studies antedate the evolution and widespread application of EVAR, which has altered the morbidity and mortality profile of AAA repair.[4-7]

Patient selection for operative AAA repair remains predicated on a careful assessment of current risks and benefits. Driving this decision is the longitudinal risk of rupture vs the risks of elective perioperative morbidity and mortality as well as long-term survival. Some studies have demonstrated increased operative mortality and morbidity in patients with COPD, but others have documented no differences in associated death.[8,10,11,13-16] Axelrod et al,[11] using the Veterans Affairs Department Patient Treatment File for 1997 to 1998, found no associated difference in mortality after elective repair among patients with COPD vs those without (3.7% vs 3.7%, $P = .99$). However, this study did demonstrate an increased risk of prolonged ventilation, increased length of stay, and increased intensive care unit length of stay in the COPD cohort.[11] Unfortunately, this study did not distinguish EVAR vs OAR. Moreover, the Veterans Affairs database used in this analysis was unable to stratify patients by COPD severity. Thus, results pertaining to mortality may have reflected the inevitable inclusion of patients with
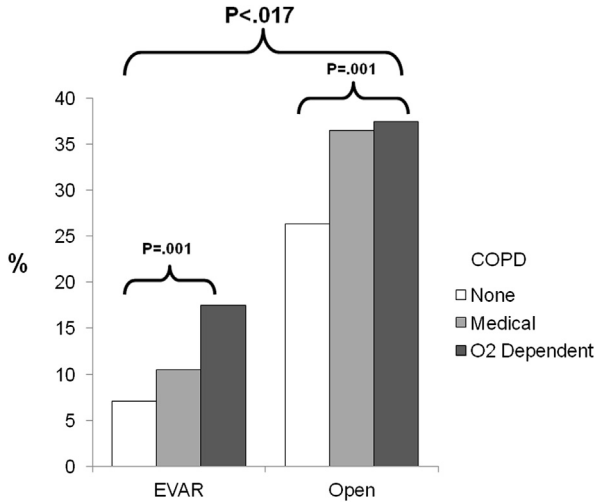
Fig 3. Rates of major adverse events are shown stratified by chronic obstructive pulmonary disease (*COPD*) severity and endovascular (*EVAR*) or open abdominal aortic aneurysm repair. Major adverse events reflected a composite of in-hospital death, postoperative myocardial infarction, new-onset congestive heart failure or cardiac dysrhythmia, respiratory failure, decline in renal function (by at least 20%), lower extremity ischemia, mesenteric ischemia, or unplanned reoperation.
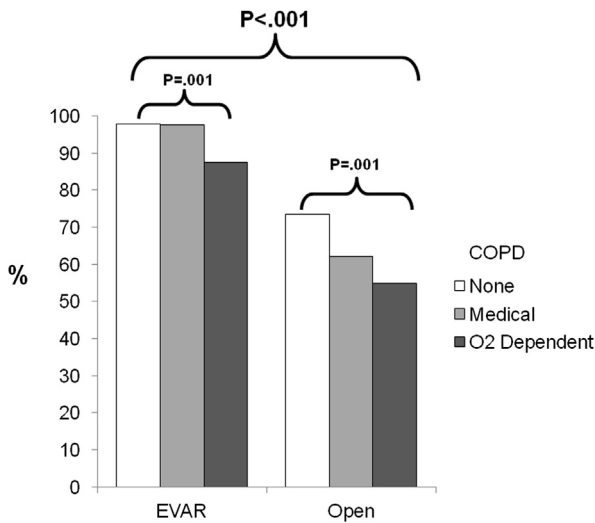
Fig 4. Rates of extubation in the operating room are shown stratified by chronic obstructive pulmonary disease (*COPD*) severity and endovascular (*EVAR*) or open abdominal aortic aneurysm repair.

only mildly diminished pulmonary function, thereby limiting the study's ability to stratify outcomes across disease severity.

Upchurch et al,[12] in a single-center review of 158 patients treated with OAR, similarly concluded that COPD alone should not be considered a deterrent in offering surgical treatment. Although the authors were able to provide
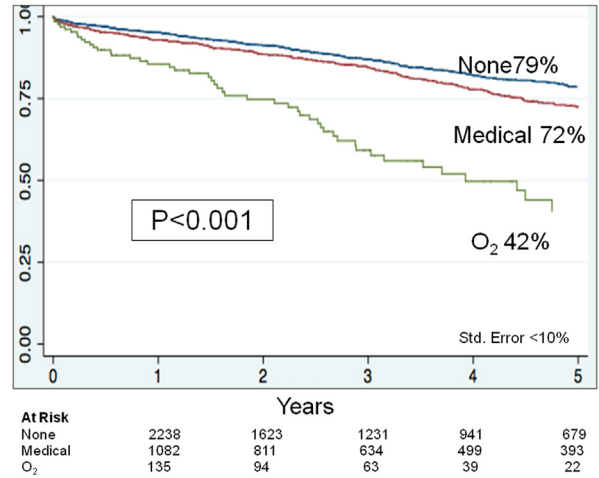
Fig 5. Kaplan-Meier life table analysis shows 5-year survival stratified by severity of chronic obstructive pulmonary disease. All standard error was <10%.

spirometric and arterial blood gas information, their analytic cohort reflected only 8% O_2-dependent patients in the uncomplicated outcome group and 12% in the complicated outcome group. This amounted to 13 patients on home O_2 available for analysis; thus, results might have been driven predominantly by those with less severe pulmonary compromise.[12] Furthermore, their study reflected only those patients undergoing OAR but not EVAR. Accordingly, debate persists about patient selection for AAA repair, especially among O_2-dependent patients.

More recently, Compton et al[1] reported 44 patients with O_2-dependent COPD undergoing EVAR (n = 24) and OAR (n = 20) during an 8-year period. They reported 0% operative mortality and suggested that overall survival in this group compared favorably with historical estimates of the survival of untreated patients with 6-cm AAA. As in previous reports, length of stay was extended in O_2-dependent patients compared with standard-risk patients for EVAR and OAR. Although the authors conclude that EVAR and OAR can both be safely offered to home O_2-dependent COPD patients, the limited sample size makes a type II error quite likely.

Our study successfully documents the effect of O_2-dependent COPD in a larger number of patients than previously reported undergoing EVAR and OAR. In looking at our overall cohort of 3455 patients, O_2-dependence was associated with increased in-hospital death, pulmonary complications, MAEs, diminished early extubation, and decreased 5-year survival. These findings were similar in direction but larger in magnitude for OAR than for EVAR.

As noted, O_2-dependence was associated with diminished 5-year overall survival. In addition, a small but statistically significant difference was noted between OAR (78%) and EVAR (72%), possibly reflecting that EVAR is offered more readily to frail O_2-dependent patients or to those with more comorbidities who would have otherwise been

Table II. Multivariate (Cox proportional hazards) analysis for 5-year survival

Variable	*HR (95% CI)*	P
O_2-dependent COPD	3.02 (2.2-4.1)	<.001
Age >80 years	2.69 (2.2-3.4)	<.001
Renal insufficiency	1.91 (1.5-2.5)	<.001
Coronary artery disease	1.46 (1.2-1.7)	<.001
Congestive heart failure	1.46 (1.1-1.9)	.002
Medical COPD	1.22 (1-1.5)	.02
Aspirin	0.78 (0.7-0.9)	.005
Statin	0.79 (0.7-0.9)	.007

CI, Confidence interval; *COPD*, chronic obstructive pulmonary disease; *HR*, hazard ratio.

denied OAR. This study further demonstrated that O_2-dependence was an independent predictor of increased in-hospital death and decreased 5-year survival, whereas some previous reports failed to independently associate this risk factor with death.[11,12] Accordingly, clinical decision making must reflect a careful stratification of perioperative risk factors as well as long-term survival rather than a sole comparison of longitudinal mortality. Furthermore, such analyses may prove to be increasingly challenging in a cost-containment era or in accountable care organizations where procedure-associated costs will be potentially more scrutinized and finite.

This study does have several intrinsic limitations. First, we are unable to correlate our COPD clinical severity scoring with objective pulmonary function testing. Nevertheless, we believe that O_2-dependence serves as an objective measure of severe COPD. Furthermore, the medically managed group may reflect a modest variation in pulmonary function. As with many registry and administrative data sets, we remain more limited in our ability to derive certain patient-specific factors such as a specific inhaler vs medication use. Nevertheless, we do believe this group reflects an intermediate category of disease and likely reflects a cohort less debilitated than those with a documented oxygen requirement.

In addition, the size of our O_2-dependent cohort remains modest at 4% (n = 135). However, this sample size still reflects more than a threefold increase in O_2-dependent patients compared with previous reports. Furthermore, patients most debilitated by severe O_2-dependence were likely not offered surgery, and we cannot further stratify the severity of O_2-dependence of patients in this series.

Finally, the end point, extubation in the operating room, may be affected by variation in practice among surgeons, with some preferentially opting to extubate patients in a delayed fashion after an OAR. Despite this potential confounder, the findings of this study still demonstrated a reproducible significant trend of COPD severity on this end point, irrespective of procedure type, although amplified in the OAR cohort, suggesting a direct affect of pulmonary dysfunction on successful early extubation status.

CONCLUSIONS

O_2-dependent COPD is associated with increased pulmonary complications, MAEs, and diminished long-term survival among patients undergoing AAA repair. These findings were magnified in patients undergoing OAR but were also present after EVAR, despite a perception that EVAR would potentially abrogate the incidence of such morbidities. Furthermore, O_2-dependent COPD was an independent predictor of increased in-hospital death and decreased long-term survival. Although previous reports have highlighted the safety of AAA repair in COPD patients, we believe that AAA repair in the post-EVAR era, among patients with O_2-dependence, still warrants extremely prudent risk/benefit assessment.

AUTHOR CONTRIBUTIONS

Conception and design: DS, BN
Analysis and interpretation: DS, PG, JK, JS, JI, DW, JC, BN
Data collection: DS, BN
Writing the article: DS
Critical revision of the article: DS, PG, JK, JS, JI, DW, JC, BN
Final approval of the article: DS, BN
Statistical analysis: BN
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Overall responsibility: DS

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