Impact of chronic obstructive pulmonary disease severity on surgical outcomes in patients undergoing non-emergent coronary artery bypass grafting †

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Abstract

OBJECTIVES: Although the association between chronic obstructive pulmonary disease (COPD) and adverse surgical outcomes has been previously demonstrated, the impact of COPD severity on postoperative mortality and morbidity remains unclear. Our objective was to analyse the prognostic implication of COPD stages as defined by the Global Initiative for Chronic Obstructive Lung Disease.

METHODS: Between September 1997 and April 2010, 13,638 patients undergoing first time isolated CABG were retrospectively reviewed, of whom 2421 patients were excluded due to lack of spirometry records or restrictive pattern on spirometry. The remaining 11,217 patients were divided into three groups: group 1 (including patients with normal spirometry and patients with mild COPD (FEV1/FVC ratio < 70%, FEV1 ≥ 80% predicted), group 2 (moderate COPD: FEV1/FVC ratio < 70%, 50% ≤ FEV1 < 80% predicted) and group 3 (severe COPD: FEV1/FVC ratio < 70%, FEV1 < 50% predicted). Logistic regression was used to examine the effect of COPD severity on early mortality and morbidity, after adjusting for differences in patient characteristics.

RESULTS: Early mortality in the three groups was 1.4, 2.9 and 5.7% respectively (P < 0.001). Similarly, a consistent trend of increasing frequency of postoperative complications with advanced COPD stage was noted. On multivariate analysis, severe COPD was found to be significantly associated with early mortality [adjusted OR, 2.31 (95% CI) (1.23–4.36), P = 0.01.

CONCLUSIONS: The severity of COPD as defined by spirometry can be a prognostic marker in patients undergoing CABG. Spirometric criteria may help refining currently used operative risk scores.

Keywords: COPD • CABG • In-hospital mortality

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has been conventionally recognized as a predictor of poorer early outcomes in patients undergoing coronary artery bypass grafting (CABG) [1–5]. Accordingly, the EuroSCORE includes chronic lung disease as an independent predictor of operative mortality, although with a generic definition not necessarily reflecting disease severity [6]. In contrast, some recent studies deny the association between COPD and increased early morbidity and mortality risk after CABG [7, 8].

Given the heterogeneity of clinical and/or spirometric variables used to define COPD by these different authors [1–8], and the continuous emphasis recent guidelines place on the importance of spirometry as the gold standard for the diagnosis and staging of severity in COPD patients (GOLD guidelines update available at http://www.goldcopd.org) [9], further investigation on this topic was deemed necessary. The purpose of this study was to analyse the impact of different COPD stages, as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric criteria [9], on the early surgical outcomes in patients undergoing primary isolated non-emergent CABG.

MATERIAL AND METHODS

Patient population and data

We retrospectively analysed a series of 13,638 consecutive patients who underwent primary isolated non-emergent CABG...
at our institution between April 1997 and September 2010. A total of 2421 patients were excluded due to lack of spirometry data, or restrictive pattern identified on preoperative spirometry. The remaining 11,217 patients composed the study population. The study was approved as an audit by the local ethics committee and patient consent was waived.

All data, including spirometric measurements, were collected prospectively in our cardiac surgery database during the patient’s admission as a part of routine practice. Definitions and data collection methods, unless otherwise specified have been previously published [10]. The different surgical techniques used in our patients, on-pump (n = 6836) and off-pump (n = 4381) have already been published [11].

The primary outcome variable was early mortality which was defined as death within 30 days of the operation due to any cause. Secondary outcomes included the need for inotropic support or intra-aortic balloon pump (IABP), renal failure, myocardial infarction (MI), atrial fibrillation, re-exploration for bleeding, stroke, deep sternal wound infection and prolonged mechanical ventilation. Prolonged mechanical ventilation was defined as the need for intubation and mechanical ventilation for more than 72 h, starting from completion of the operation. This includes both: patients with early and persistent ventilatory dependency who were not extubated within the initial 72 h and those who had one or more unsuccessful extubation attempts eventually accumulating more than 72 h of endotracheal intubation and mechanical ventilation.

**Spirometry and study groups**

Spirometry was performed as a part of the routine preoperative work-up in 11,324 patients, according to previously described guidelines [12]. Through the study period, two machines were used to assess spirometric results (Vitalograph S with PFT2 PLUS printer and Vitalograph 2120, Buckingham, UK). Restrictive disease was diagnosed when FEV1/FVC was <0.85, in 107 patients who were excluded from the study. Spirometric criteria compatible with a COPD diagnosis were found in 2895 patients (25.8%). Observed measurements were reported as a percentage of the predicted for individual patients. Depending on the degree of airflow limitation, the study population was divided into three groups: Group 1 (including patients with normal spirometry and those with mild COPD: FEV1/FVC ratio < 70%, FEV1 ≥ 80% predicted), Group 2 (moderate COPD: FEV1/FVC ratio < 70%, 50% ≤ FEV1 < 80% predicted) and Group 3 (severe COPD: FEV1/FVC ratio < 70%, FEV1 < 50% predicted).

**Statistical analysis**

Categorical data are presented as percentages and frequencies. Continuous data are presented as median with 25th and 75th percentiles. The COPD groups were compared using ANOVA tests with a Bonferroni correction to assess differences between groups. Standard statistical tests were used to calculate odds ratios (OR) and 95% CI. Logistic regression was used to examine the effect of COPD category on early mortality and morbidity, while adjusting for differences in patient characteristics. These characteristics were the variables (age, sex, left ventricular ejection fraction, left main stem stenosis, number of major coronary arteries with stenosis 70%, priority of surgery, peripheral vascular disease, diabetes, renal dysfunction and respiratory disease) suggested for risk adjustment of CAGB outcomes by Jones et al. [13] and the American College of Cardiology/American Heart Association practice guidelines [14]. This method was preferred over identification of those variables driving the outcome of interest and using these so-called risk factors for adjustment as a consequence of the low event rate and concerns regarding model over-specification. In all cases, a P-value < 0.05 was considered statistically significant. All statistical analyses were performed retrospectively using SAS for Windows v.9.2 (SAS Institute, Cary, NC, USA).

**RESULTS**

**Patient characteristics**

The baseline characteristics of the 11,217 patients included are outlined in Table 1. They compare well with the typical UK referral patterns (The Sixth National Adult Cardiac Database Report 2008 available at [http://www.scts.org/modules/resources/info.aspx?id=31]). Patients were mostly males (81%) with a median age of 65.9 (59.1–71.9) years, with a 22% incidence of diabetes and 8.5% of the study population having an ejection fraction less than 30%. The median logistic EuroSCORE was 2.6 (1.5–5.0).

Spirometric criteria compatible with a COPD diagnosis were found in 2895 patients (25.8%). The three study groups showed variable preoperative characteristics, risk factors with a statistically significant increasing trend mirroring COPD severity included left ventricular ejection fraction <30%, NYHA classes 3 and 4, respiratory disease and logistic EuroSCORE. A decreasing trend in left internal mammary artery (LIMA) use was observed as COPD severity increased. Factors where Groups 2 and 3 had significantly increased rates when compared with Group 1 included age, body mass index, peripheral vascular disease and urgent operations. Factors where Group 2 had significantly increased rates when compared with Group 1 included previous Q-wave MI, current smokers and left main stem disease. Patients in Group 3 had increased levels of hypertension when compared with Group 1 and greater instances of class IV angina when compared with both Groups 1 and 2. Risk factors with no significant differences between groups included gender, Q-wave MI within 30 days of operation, diabetes, hypercholesterolemia, cerebrovascular disease, renal dysfunction, triple-vessel disease, off-pump procedures and the number of distal anastomoses (Table 1).

Upon referral, while 20.6% (n = 1937) of the patients with normal spirometry or mild COPD had history of respiratory disease, 83.7% (n = 1285) of the moderate COPD group and 98.1% (n = 260) of the severe COPD group had history of respiratory disease (Table 1). Remarkably, only 15.3% (n = 445) of the patients with COPD diagnosis on spirometry fulfilled the EuroSCORE definition of chronic pulmonary disease being on respiratory medications. These represented 7.5% (n = 82), 17.7% (272) and 34.3% (91) of patients with mild, moderate or severe COPD, respectively.

**Postoperative outcomes**

A total of 187 patients suffered early mortality (1.7%), with a higher mortality proportion in patients with moderate (45 patients, 2.9%) and severe (15 patients, 5.7%) COPD. After Bonferroni correction,
there was a significantly higher incidence of postoperative complications with increasing COPD severity in inotropic support, acute renal failure and early mortality (Table 2).

**Crude and adjusted outcomes**

The crude and adjusted OR for outcomes following CABG are shown in Table 3. There was no association between COPD and MI, re-exploration for bleeding and postoperative stroke in either univariate or multivariate analysis.

In the univariate analysis, poorer COPD was associated with acute renal failure, prolonged mechanical ventilation and atrial fibrillation. Group 3 membership was also associated with increased IABP support. However, after adjustment for differences in patient characteristics these associations were not observed.

Groups 2 and 3 were also significantly associated with early mortality, inotropic support and the development of deep sternal wound infections in the univariate analysis. The multivariate analysis of these outcomes showed no association in Group 2, but did show an association in Group 3 (adjusted OR, 2.31; \( P = 0.01 \) for 30-day mortality; adjusted OR, 1.44; \( P = 0.008 \) for...
inotropic support; adjusted OR, 3.56, P < 0.001 for deep sternal wound infection).

**DISCUSSION**

Sharing smoking as a central risk factor, COPD and ischaemic heart disease commonly co-exist. Although essential for the diagnosis of COPD [9], spirometry seems to be underutilized in community practice, with the diagnosis solely relying on clinical grounds in a large number of cases [15, 16]. Given the imperfect relationship between the severity of airflow limitation and clinical symptoms, the estimation of severity of COPD may be significantly inaccurate when spirometric data are neglected [17, 18].

In the current study, we found the severity of COPD as defined by spirometry, to influence early surgical outcomes. While moderate COPD did not seem to be associated with worse outcomes on multivariate analysis, severe COPD (FEV1/FVC ratio < 70%, FEV1 < 50% predicted) was found to be significantly associated with early mortality following CABG [adjusted OR 2.31 (95% CI) (1.23–4.36), P = 0.01].

This is in parallel with the findings of some previous studies. Fuster et al. [5] found an FEV1 < 60%, rather than a clinical diagnosis of COPD, to be an independent predictor of early mortality following CABG. Adabag et al. [18] examined 1169 patients who had completed pulmonary function tests (PFTs) within one year prior to cardiac surgery and found mortality risk to be significantly higher in patients with moderate or severe COPD. The potential bias in their work, where PFTs were selectively performed, thus probably sampling a higher risk cohort, is absent from the current study where spirometry was done as a part of the routine preoperative work-up of all included patients.

Although a limited number of recent studies contradict the influence of COPD on early surgical outcomes, their findings should be interpreted cautiously. Angouras et al. [8] were unable to stratify COPD patients according to severity thus raising the possibility of their findings being attributable to a proportion of patients who, although fulfilling their definition for COPD, had rather mild forms of the disease. The work of Manganas et al although stratifying patients according to severity, included only 322 COPD patients. Patients with mild and moderate disease were added together in a single group of 153 patients compared with 68 patients with severe disease. Again, in contrast to the current study where spirometry was a standard preoperative practice, it was performed selectively in their practice, thus intuitively sampling more symptomatic patients [7].

Another important finding in the current study was the fact that 14.1% of the patients with moderate to severe airflow limitation on spirometry had no history of respiratory disease upon referral for surgery, and only 20.1% of them fulfilled the

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**Table 3:** Crude and adjusted odds ratio for outcomes

<table>
<thead>
<tr>
<th></th>
<th>Moderate COPD</th>
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<th>P-value</th>
<th>Severe COPD</th>
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<th>P-value</th>
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<td></td>
<td>ORa 95% CI</td>
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<td>ORa 95% CI</td>
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<td>Early mortality</td>
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<tr>
<td>Crude</td>
<td>2.21 1.57, 3.12</td>
<td>&lt;0.001</td>
<td></td>
<td>4.39 2.53, 7.60</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
<td>1.44 0.96, 2.18</td>
<td>0.08</td>
<td></td>
<td>2.31 1.23, 4.36</td>
<td>0.01</td>
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<tr>
<td>Inotropic support</td>
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<tr>
<td>Crude</td>
<td>1.20 1.07, 1.34</td>
<td>0.002</td>
<td></td>
<td>1.89 1.48, 2.42</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
<td>0.99 0.86, 1.13</td>
<td>0.82</td>
<td></td>
<td>1.44 1.10, 1.89</td>
<td>0.008</td>
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<td>IABP support</td>
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<tr>
<td>Crude</td>
<td>1.30 0.93, 1.83</td>
<td>0.12</td>
<td></td>
<td>2.61 1.50, 4.56</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
<td>0.98 0.66, 1.46</td>
<td>0.92</td>
<td></td>
<td>1.85 0.98, 3.47</td>
<td>0.06</td>
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<tr>
<td>Acute renal failure</td>
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<tr>
<td>Crude</td>
<td>1.35 1.06, 1.73</td>
<td>0.02</td>
<td></td>
<td>2.46 1.61, 3.77</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
<td>0.82 0.61, 1.10</td>
<td>0.17</td>
<td></td>
<td>1.41 0.87, 2.32</td>
<td>0.16</td>
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<tr>
<td>Deep sternal wound infection</td>
<td>1.69 1.02, 2.82</td>
<td>0.04</td>
<td></td>
<td>6.50 3.48, 12.15</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
<td>1.00 0.56, 1.78</td>
<td>&gt;0.99</td>
<td></td>
<td>3.56 1.74, 7.25</td>
<td>&lt;0.001</td>
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<tr>
<td>Myocardial infarction</td>
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<tr>
<td>Crude</td>
<td>1.07 0.74, 1.56</td>
<td>0.71</td>
<td></td>
<td>1.72 0.87, 3.39</td>
<td>0.12</td>
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<tr>
<td>Adjustedb</td>
<td>0.83 0.55, 1.26</td>
<td>0.39</td>
<td></td>
<td>1.32 0.64, 2.73</td>
<td>0.45</td>
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<td>Prolonged mechanical ventilation</td>
<td>1.60 1.18, 2.17</td>
<td>0.003</td>
<td></td>
<td>2.49 1.43, 4.35</td>
<td>&lt;0.001</td>
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<tr>
<td>Adjustedb</td>
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<td>0.96</td>
<td></td>
<td>1.34 0.74, 2.46</td>
<td>0.34</td>
<td></td>
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<tr>
<td>Re-exploration for bleeding</td>
<td>1.09 0.83, 1.45</td>
<td>0.54</td>
<td></td>
<td>1.16 0.63, 2.15</td>
<td>0.63</td>
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<tr>
<td>Adjustedb</td>
<td>0.99 0.72, 1.38</td>
<td>0.97</td>
<td></td>
<td>1.00 0.53, 1.93</td>
<td>0.99</td>
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<tr>
<td>Atrial fibrillation</td>
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<tr>
<td>Crude</td>
<td>1.27 1.13, 1.43</td>
<td>&lt;0.001</td>
<td></td>
<td>1.49 1.15, 1.94</td>
<td>0.002</td>
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<tr>
<td>Adjustedb</td>
<td>1.03 0.89, 1.18</td>
<td>0.72</td>
<td></td>
<td>1.15 0.87, 1.51</td>
<td>0.33</td>
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<tr>
<td>Stroke</td>
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<tr>
<td>Crude</td>
<td>1.11 0.70, 1.75</td>
<td>0.66</td>
<td></td>
<td>1.47 0.57, 3.61</td>
<td>0.40</td>
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</tr>
<tr>
<td>Adjustedb</td>
<td>0.80 0.48, 1.35</td>
<td>0.41</td>
<td></td>
<td>0.91 0.35, 2.36</td>
<td>0.84</td>
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</table>

*aGroup 1 (including normal spirometry and mild COPD) is the referent category.

*bAdjusted for age, sex, left ventricular ejection fraction, left main stem stenosis, number of major coronary arteries with stenosis >70%, priority of surgery, peripheral vascular disease, diabetes, renal dysfunction and respiratory disease.
EuroSCORE definition of chronic pulmonary disease providing a history of long-term use of bronchodilators or steroids. Ad et al. recently reported similar findings, with a discordant rate between clinical and spirometric criteria reaching 39.1%. The underestimated severity of lung disease reached 94% in 71 misclassified patients, which underlines the importance of spirometry to avoid underestimation of surgical risk in these patients [17]. Likewise, Adabag concluded that PFTs helped reclassify the COPD status of 364 patients (31%) undergoing cardiac surgery [16]. Although some authors argued against the value of preoperative PFTs [19], our findings as well as others [2, 5, 17, 18, 20] suggest that routine preoperative spirometry to confirm the diagnosis of COPD, and quantify its severity, may be important for better-informed decision-making regarding surgical risks. Meanwhile, preoperative spirometry continues to be performed at variable rates between different units, with some reporting less than 2% of their surgical patients having spirometry prior to cardiac surgical intervention [17].

Apart from potentially refining currently used risk scores, spirometric values may also help improving surgical outcomes in identified high-risk patients. Despite the evidence supporting the value of preoperative optimization of respiratory function in these patients [21, 22], such practices continue to be adopted only variably in surgical practice.

Regarding postoperative complications, the consistent rising trend of most postoperative morbidities in parallel with the increasing severity of COPD, also ran in parallel with an increasing prevalence of other comorbidities such as hypertension, peripheral vascular disease and poor left ventricular function. These comorbidities also seem to affect the long-term outcome in COPD patients [8]. The only associations to reach statistical significance on multivariate analysis were the association between severe COPD and a higher use of inotropes [adjusted OR, 1.44 (95% CI) (1.10–1.89)], P = 0.008, and a higher incidence of deep sternal wound infection [adjusted OR, 3.56 (95% CI) (1.74–7.25)], P < 0.001.

There was no difference in the distribution of on-pump versus off-pump procedures among different study groups (Table 1) and examining the previously demonstrated potential benefit of off-pump surgery in the high-risk respiratory patient [23] was not one of the aims of the current study. Among other reported operative variables was the rate of using the LIMA, which decreased from 94.1% in patients with normal PFTs to 83.4% in patients with severe COPD. This finding was noted in other studies [7], and may be related to previously documented greater impairment in PFTs associated with internal mammary artery harvesting [24], but may also be related to more elderly patients in the severe COPD group.

There are some limitations to the current study. It is a retrospective single centre study, and therefore the results may not be completely generalizable to other institutions. However, given the large cohort studied and the representativeness of this cohort, the potential for inaccuracy or bias should be minimal. The relatively long time period this study covers may carry along variable changes in operative and postoperative practices that might have affected outcomes. Finally, the fact that clinicians were not blinded to the results of spirometry, which might have possibly altered individual patients’ management, is another potential limitation. Nevertheless, to the best of our knowledge this is the largest study to date looking at the effect of objective measurement of COPD severity on outcomes following cardiac surgery.

In conclusion, the severity of COPD as defined by spirometry proved to be a prognostic marker in patients undergoing CABG. More advanced stages of COPD, rather than mild or moderate forms, were found to be significantly associated with early mortality following CABG. Spirometry confirming COPD diagnosis, and stratifying patients according to its severity, may thus help refining currently used operative risk scores.

Conflict of interest: none declared.

REFERENCES

APPENDIX. CONFERENCE DISCUSSION

Dr B. Mochtar (Maastricht, Netherlands): Mr Saleh, you have just elucidated on the burden of COPD in non-emergency coronary bypass surgery. You did a large retrospective study with prospective spirometric data. But more than 2,400 spirometry data were missing and the remaining study population comprised 11,000 patients. Could these missing data have influenced the variables of your baseline characteristics, such as female gender, body mass index, and age?

Dr Saleh Actually, we started looking into this data. What we tried to do was to compare, just to check whether these patients were entirely different from those that actually had their spirometry. And there were two subsets of patients, the largest being those who underwent elective surgery, and there was absolutely no statistical difference between those who underwent spirometry and those who didn’t. But in the case of the patients who underwent urgent CABG, there was a slight difference; you could see that there was a trend to being a higher risk group, but still it did not attain statistical significance.

Dr Mochtar And the second question: Do we have to adjust the operating risk management for this group of patients? According to your study, the EuroSCORE should then be adjusted, especially in the Group 4 patients, the Group 4 COPD with an FEV1 predicted less than 50%.

Dr Saleh Well, I think there was a similar study that was published earlier on, where they were looking prospectively at whether the spirometric criteria, if introduced into the STS risk model, would bring out any difference. And they found that in about more than 30%, the spirometric criteria were discordant with the clinical criteria. And once the spirometric criteria were introduced into the risk model, the whole risk model changed. So I think that’s quite a reasonable thing to look at.

Dr Mochtar Okay. But how do we have to handle it in daily practice, such as in the Heart Team discussion? How do we implement the thorough spirometric studies you have done in daily practice? Because you stated that there is enormous discordance between clinical and spirometric data in patient groups.

Dr Saleh That’s a difficult question, I’m sure, but it’s something to look into.

Dr T. Kieser (Calgary, AB, Canada): I have one little question. In what group might you see CO2 retention? Would it be Groups 3 and 4, and maybe this might be a marker, or only Group 4? Did you look at that?

Dr Saleh: Well, once again, I think the data we have is largely the spirometric data, and this is because we are in a unit where spirometry is being done routinely as part of the preoperative workup. Obviously, these patients are variable, so they are not really one clinical solid case. We might have variable clinical presentations.

Dr S. Shahabuddin (Karachi, Pakistan): I think we all know this special group of people and the high risk of postoperative morbidity and mortality. My question is whether you have looked into the cause of death in these patients who have increased mortality, whether it’s causally related to the respiratory complications, or maybe death was related to non-respiratory complications? It may be a coincidence that they were from a group of these patients but the cause of death may be different.

Dr Saleh: Well, actually, we didn’t look into that. But we have another piece of work that is currently under review where were looking into the predictors of prolonged mechanical ventilation in patients undergoing elective CABG. And the majority of these patients were patients with COPD. And on analysing the data, what we found was that once again the FEV1 was one of the independent predictors of prolonged mechanical ventilation postoperatively. And this group of patients who suffered prolonged postoperative mechanical ventilation had a mortality rate of more than 28% compared to a mortality rate of around 1% to 2% in the rest of the cohort. So it’s very difficult to dissect into these causes really.

Dr D. Pagano (Birmingham, UK): It’s all very well to look at predictors of in-hospital outcome, but coronary surgery is done also for long-term benefit. Have you looked at the impact of these variables on the long-term outcome of your patients?

Dr Saleh: No, we haven’t looked into long-term outcome.

Dr Wimmer-Greinecker (Bad Bevensen, Germany): One thing that I’m missing here is the discussion of on-pump and off-pump surgery. As I understand it, these are all on-pump CABGs, right?

Dr Saleh: Well, actually, in our unit, the off-pump practice is about one-third of the patients.

Dr Wimmer-Greinecker: Did you experience any difference in outcome there? Did you look at that?

Dr Saleh: We haven’t really. I mean, this study was not really designed to look into that. We had earlier published work in which our findings were similar to many other authors where off-pump was offering some benefit in patients with severe COPD, but that was not a part of this current study.

Dr Wimmer-Greinecker: So if a patient were in GOLD Group 4, he would not automatically go into the off-pump group?

Dr Saleh: If you look at the operative pattern, you’ll see that with the severe and very severe COPD group, there was a higher number of patients that had off-pump operations. But we don’t think that off-pump can be jeopardizing the findings in this current data.