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Diagnosis of myocardial infarction following hospitalisation for exacerbation of COPD

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Abstract

Background

Cardiovascular disease is common in COPD, and raised troponin is common in exacerbations. However, the prevalence of myocardial infarction following hospitalisation for exacerbation of COPD is unknown.

Methods

Patients aged ≥40 hospitalised with acute exacerbation of COPD (n=242) with ≥10 pack-years of cigarette smoking were included in a prospective case series conducted in four hospitals. Patients whose primary presenting complaint was chest pain, or who had an alternative diagnosis were excluded. Chest pain histories, serial electrocardiographs, and troponin levels were obtained.

Results

The mean (SD) age was 69 (9), 108 (45%) were male and almost half were current smokers. 124 (51%, 95% CI 48 to 58%) had chest pain, which was exertional in 62 (26%). 24 (10%) had raised troponin, among whom, 20 (8.3%, 95% CI 5.1 to 12.5) had chest pain and/or serial ECG changes, fulfilling the 2007 Universal Definition of Myocardial Infarction. Neither chest pain (P=0.77) nor serial ECG changes (P=0.39) were associated with raised troponin.

Conclusion

Raised troponin, chest pain and serial ECG changes are common in patients admitted to hospital with exacerbation of COPD. Overall 1 in 12 patients met the criteria for myocardial infarction. Whether these patients would benefit from further cardiac investigation is unknown.
Words 200

Introduction

Coronary heart disease is a major cause of mortality in chronic obstructive pulmonary disease (COPD)[1,2]. Both conditions share common risk factors such as smoking and socioeconomic status, and reduced FEV_1, a characteristic feature of COPD, is an independent risk factor for cardiovascular mortality[3].
In studies using routine clinical data, diagnosis with myocardial infarction (MI) appears commoner following exacerbations in patients with COPD[4,5], while raised troponin has been found to be associated with increased mortality in exacerbation of COPD [6-8],
Coronary events may present without chest pain [9], can be missed even in simple chest pain presentations [10], and may be more likely to be missed patients presenting with acute exacerbation of COPD who also report acute breathlessness and chest tightness.
Raised troponin is common in patients admitted to hospital with exacerbation of COPD [6-8], but we are unaware of any prospective study which has investigated this group for clinical or electrocardiography features of MI.
Therefore, we undertook a prospective case-series to identify the prevalence of MI in patients admitted to hospital with acute exacerbation of COPD.

Methods

Patients were recruited at four hospitals in Central Scotland: Royal Infirmary of Edinburgh, Glasgow Royal Infirmary, Monklands Hospital and Crosshouse Hospital. At each site the local investigator recruited patients from Emergency Medicine departments and acute medical (admission) units. Patients aged 40 or older, diagnosed with an acute exacerbation of COPD by a physician accredited in respiratory and/or general medicine, and with a ten or more pack-year history of cigarette smoking were recruited. Patients were excluded if chest pain was the primary presenting complaint, more than 48 hours had elapsed since admission, an alternative diagnosis was suggested by the admission chest x-ray, or pulmonary embolism was confirmed on computed tomography pulmonary angiogram.
In the 2007 "Universal Definition" statement, myocardial infarction was defined as a rise and/or fall of troponin concentration together with evidence of myocardial ischaemia (at least one of - symptoms of ischaemia, new ST-T changes or new left bundle branch block or development of pathological Q waves in the ECG) [11], We report the prevalence of MI diagnosed according to this definition, which does not imply a causal mechanism, and includes two subtypes: type 1 MI is due to a primary coronary event such as plaque rupture and type 2 MI is secondary to increased myocardial oxygen demand or decreased supply.
A detailed chest pain and exacerbation history was obtained and recorded on a standard form. If an admission ECG had been performed then this was obtained. If not, it was performed by the investigator, provided this could be done within 24 hours of admission. The ECG was repeated between 12 and 36 hours after the initial ECG.
A non-fasting blood sample was taken and serum troponin, HDL and total cholesterol, triglycerides, full blood count, and C-reactive protein were measured at each hospital laboratory. Where patients reported chest pain before or during the first 48 hours of admission, the sample was taken 12 hours after the onset of pain. If no chest pain was reported troponin was obtained between 12 and 48 hours following admission. Any

chest pain or raised troponin developing after 48 hours or longer following admission would not be identified in this study.
Spirometry results were either obtained from the patient's case notes, or from the local pulmonary function service. Research Ethics Committee Approval was obtained and patient consent was obtained for all study protocols and procedures (06/MRE10/78).
Troponin I (Abbott Architect, Illinois, USA) was measured in Royal Infirmary of Edinburgh and Glasgow Royal Infirmary, and troponin T (Roche, Basle, Switzerland) was measured in Monklands and Crosshouse Hospitals. The Universal definition of myocardial infarction recommends the use of the 99th percentile of the normal reference population to define raised troponin, and stipulates that the assay should have a co-efficient of variation of ≤ 10% (10%CV) at the 99th percentile value [11]. However, until recently, no troponin assay could achieve this level of precision. We followed the recommendation of Apple et al [12], and defined the cut-off as the lowest concentration measurable with <10% coefficient of variation. To facilitate reporting of results from multiple centres we have expressed troponin concentrations in multiples of the 10%CV level at each site [12].
All ECGs were coded using the Minnesota Code, the most widely used ECG coding system, which is used to assign codes to pathological and variant features in 12-lead ECGs in research studies [13]. A single reader (DM) coded all ECGs blinded to all clinical features, blood results and order of ECG recordings. In 48 ECGs collected at the Glasgow site Minnesota codes were also reported electronically [14]. Agreement for electronic and paper reads for the presence/absence of Q-waves, ST depression and T wave flattening/inversion was calculated (Kappa = 0.73, 0.61 and 0.57 respectively). Serial ECG changes indicative of an acute cardiac event were defined using the Minnesota code criteria for independently read serial ECGs [13(p204)].
Although the occurrence of MI in the absence of chest pain is well documented [9], certain features of the chest pain history are recognised as being high-risk or more indicative of myocardial ischaemia (pain which is "like a pressure", radiates to either shoulder or arm, or is related to exertion) while other features are considered low-risk (pleuritic, related to movement, reproduced by palpation, sharp or of very short or long duration [< 2 min or > 12 hours]) [15]. On this basis, patients were classified as having either low- or high-risk chest pain. Patients with neither low-risk nor high-risk features were categorised as indeterminate.
Each exacerbation was categorised as probably infectious or otherwise using the Anthonisen criteria (type 1 – three major infectious symptoms (increased sputum purulence, sputum volume and dyspnoea), type 2 – two of three major infectious symptoms, type 3 – one of three major infectious symptoms, plus additional minor symptoms) [16].
The prevalence of MI was calculated along with 95% confidence intervals using the exact binomial test. In exploratory analyses, associations between patient characteristics and raised troponin concentrations were examined using Fisher's exact test, for which we report all associations where the P-value was <0.10. Analyses were performed using SAS version 9.2 (Cary, North Carolina, USA) and R version 2.11.1 (Vienna, Austria).

Results

A total of 242 patients were recruited, 143 from Royal Infirmary of Edinburgh, 48 from Glasgow Royal Infirmary, 42 from Monklands Hospital and 9 from Crosshouse

Hospital. The mean (SD) age was 69 (9), 108 (45%) were male and almost half were current smokers, with the majority having severe or very severe airflow limitation on spirometry (Table 1). All patients were breathless on admission, increased sputum volume was present in 130 (54%) and sputum purulence in 141 (58%), leukocytosis in 113 (47%) and raised C-reactive protein (>6 mg/dL) in 158 (74%). All were treated with nebulised bronchodilators, 217 (90%) with oral prednisolone, and 164 (68%) with antibiotics. The median (IQR) length of stay was 5 (3-8) days and 21 (15%) of the 143 patients at the Edinburgh site (where follow-up was available via electronic records) died within 12 months of admission.

Twenty-four (10%) patients had elevated serum troponin, with 22 (9%) patients having a level greater than twice the cut-off (defined as the 10%CV level for the assay) and 15 (6%) having a serum troponin level greater than three times the cut-off. Twenty (8.3%, 95% CI 5.1 to 12.5) patients met the criteria for the Universal definition for MI (Figure 1) [11] as they had raised troponin along with ECG changes (new Q waves or serial changes in T-waves or ST segments) and/or chest pain. Six patients (2.5%, 95% CI 1.0 to 5.6) had raised troponin, chest pain and serial ST/T-wave ECG changes.

Overall, chest pain was common, with 124 (51%, 95% CI 48 to 58%) patients reporting chest pain, which was most commonly tight or sharp, but in 50 patients (40% of those with chest pain) the pain was 'high risk' for myocardial ischaemia (Table 2).

Sinus tachycardia was the commonest abnormality on admission ECG and was found in 112 (46%) patients. Fourteen (6%) patients had atrial fibrillation, 15 (6%) had right bundle branch block with 12 (5%) having left bundle branch block. Twenty (8%) had p-pulmonale. Q-waves considered 'diagnostic' in the Minnesota coding system and T-wave inversion were both common (34 (14%) and 37 (15%) respectively).

Eighteen (7.5%) patients had no ECG within the first 24 hours of admission, while 21 (8.6%) had no second ECG. Only 3 patients developed Q-waves during admission, but serial changes in T-wave inversion/flattening and ST depression were common (65 (32%) and 19 (9%) respectively). Thirteen (6%) had serial changes in ST elevation (Online supplement).

Neither chest pain, nor chest pain with exclusively high risk features, was associated with raised troponin (P=0.77 and P=0.29 respectively). Raised troponin may be commoner in patients with admission ECGs with Minnesota codes for MI (P=0.06) but there was no evidence that serial ECG changes were commoner (P=0.39, Table 3).

Cardiovascular risk factors were common (Table 4). Over 30% had a past medical history of ischaemic heart disease, 34 (14%) had previous stroke or peripheral vascular disease, with 101 (42%) having vascular disease at any site. Hypertension and hypercholesterolaemia were also common. Amongst the 141 patients without known vascular disease 19 (13%) had an estimated (Framingham) risk of a cardiac event within 10 years of 20% or greater [17]. Around a third of patients were on regular statin therapy, and 96 (40%) were on antiplatelet therapy, although only 5 (2%) were on a beta-blocker.

In exploratory analyses we examined the associations between raised troponin and a wide range of patient characteristics, including severity of airflow obstruction, performance status, smoking status, usual and acute therapy, anaemia, raised inflammatory markers and symptoms suggestive of infection, and arterial blood gases. There was a suggestion that diabetes, right bundle branch block, acidosis and methylxanthine therapy in patients with exacerbation of COPD may be associated with raised troponin.

Interestingly, the use of a long acting beta-agonist was less common in patients with raised troponin (Table 5).

Discussion

Cardiovascular disease is common in patients with COPD [1,2]. In a prospective case-series in patients admitted to hospital with acute exacerbation of COPD, we found that approximately one in twelve patients had raised troponin along with serial ECG changes and/or chest pain, meeting the criteria of the Universal definition for MI [11]. Two previous prospective studies report the prevalence of raised troponin in exacerbation of COPD. In one consecutive case-series of 71 patients admitted to an intensive care department with acute exacerbation of COPD 13 (18% (95% CI 11 to 29%) had raised troponin [6], and in a larger consecutive series of 250 patients with exacerbation of COPD admitted to a single-centre 17% had raised troponin [8]. In a study using routine data where troponin was measured in 441 of 996 patients admitted with exacerbation of COPD at the discretion of the treating clinician, troponin was raised in 27% (12% overall) [7]. Our findings suggest that most of these patients with raised troponin also have chest pain and/or serial ECG changes, and so meet the criteria for the Universal definition for MI [11].

A substantial proportion of these myocardial infarctions are likely to have developed secondary to increased myocardial demand / reduced oxygen supply. Under the Universal definition for MI such events, usually resulting in sub-endocardial rather than transmural infarction, are termed type 2 myocardial infarction [11]. Over half of our patients were tachycardic (with either sinus tachycardia or atrial fibrillation) which, together with hypoxaemia and increased afterload is likely to increase myocardial oxygen demand and reduce supply. Similarly, in a previous study among 441 patients where troponin was measured at clinical discretion, raised troponin was also found to be associated with lower haemoglobin and tachycardia favouring type 2 myocardial infarction [18].

During exacerbation of COPD, ischaemia secondary to increased afterload with consequent increased myocardial demand and reduced supply may also occur in the right heart, in a mechanism analogous to that proposed for the myocardial injury associated with acute pulmonary embolism [19]. Pulmonary hypertension is present in around a quarter of people with COPD awaiting lung transplant [20] with reversible increases in pulmonary artery pressure of around 20 mmHg having been described during acute respiratory failure in people with chronic bronchitis [21]. Such increases in pulmonary artery pressure may, in the context of tachycardia and underlying coronary disease, be sufficient to cause right ventricular ischemia and an increase in troponin.

Around a fifth of patients were taking cardiac medications but only 5 (2%) were taking beta-blockers. Mortality has been found to be lower among patients with COPD taking beta-blockers following admission to hospital with exacerbations [22] and during vascular surgery [23], and beta-blocker prescription has recently been found to be associated with a lower risk of hospitalisation for exacerbation of COPD [24]. Prevention of tachycardia-related myocardial damage may be one mechanism underlying these associations. None of the 5 patients in our case-series taking beta-blockers had raised troponin, although this observation should be interpreted very cautiously as this association was not statistically significant.

However, myocardial ischemia and infarction following acute exacerbations might well arise due to plaque rupture and coronary thrombosis (type 1 MI). Fifty percent of

patients in our sample either had known vascular disease or an estimated 10 year (Framingham) risk of a cardiac event of greater than 20%. Patients with COPD have an elevated risk of cardiovascular mortality [1,2] and two previous observational studies using routine healthcare data found that the risk of diagnosis with MI was two-fold higher in patients with COPD during and immediately following acute exacerbation [4,5]. Despite this the use of secondary prevention was surprisingly low among our patients, with only a third receiving statins.

Inflammation has been implicated in plaque rupture [25], and exacerbation of COPD is associated with raised C-reactive protein, interleukin-6 and fibrinogen [26,27]. Furthermore, we previously found that platelet activation was increased during exacerbations compared to the stable state [28], and an association between neutrophilia and raised troponin has been reported in acute exacerbation of COPD [18].

We believe that a proportion of patients with raised troponin in our case-series were likely to have had a primary coronary event (Type 1 myocardial infarction). Two (8%) patients of the of the 24 with elevated troponin also had ST-segment elevation or new Q-waves to indicate transmural infarction and perhaps may have benefited from coronary revascularision. The overlap in symptoms between exacerbation of COPD and myocardial infarction, and the absence of a simple diagnostic test to identify plaque rupture, represents a major diagnostic challenge for clinicians. This problem is likely to become more pressing as increasingly sensitive troponin assays with lower thresholds for detection of troponin are introduced into clinical practice [29].

Risk stratification on the basis of chest pain history and serial ECGs is problematic for a number of reasons. Previous authors have suggested that central chest pain typical of MI is rare in exacerbation of COPD [5], but we found that central chest pain was common and patients commonly reported exertional chest pain prior to admission. There was no association between symptoms of chest pain and increased troponin concentrations, even when we restricted the analysis to those patients with symptoms that were considered to be suggestive of cardiac ischaemia [15]. The character of chest pain is of limited prognostic value in patients presenting with chest pain alone [30], and our findings suggest that it may be less useful still in patients with exacerbation of COPD.

Similarly, abnormalities were common on the resting admission electrocardiograph in patients with exacerbation of COPD, a finding which is consistent with previous reports that ECG abnormalities predictive of long-term risk of MI are common in patients hospitalised with acute exacerbation of COPD [31], and are associated with reduced FEV_1[32]. We found that changes in the T-wave axis and dynamic ST segment depression on serial ECG testing were common, but were not associated with raised troponin. These changes may reflect transient myocardial ischaemia secondary to increased oxygen demand or reduced supply that is insufficient to induce myocardial infarction or alternatively may be artefactual and non-specific features of acute exacerbation. Consequently it is not clear in which patients, if any, we should measure troponin where the primary clinical presentation is exacerbation of COPD. Further observational studies are needed to better characterise which clinical features are associated with raised troponin and to determine the clinical significance of raised troponin in unselected patients with acute exacerbation of COPD, but randomised clinical trials of secondary prevention strategies are likely to be needed to address the diagnostic challenge of differentiating between primary acute coronary events and secondary myocardial ischemia.

Limitations

This was not a consecutive sample of patients admitted with acute exacerbation of COPD. However, we did include patients from secondary care and tertiary referral centres, and our group were very similar, including in the prevalence of known ischaemic heart disease, to that described in the 2008 British Thoracic Society Audit of patients consecutively admitted to hospital with acute exacerbation of COPD (Online supplement) [33].

Moreover, patients were not sampled on the basis of chest pain, troponin or ECG changes, and patients who presented to the treating clinician with evidence of myocardial infarction, even if this followed a severe exacerbation of COPD would not have been recruited to our study. Moreover, we report a lower proportion of patients with raised troponin than found in previous studies [6-8]. As such, the true risk of myocardial infarction in patients with severe exacerbation of COPD may be higher than suggested from our case-series of patients hospitalised with exacerbation of COPD.

The troponin measurements were conducted in different laboratories using different assays rather than in a single centre. However, studying patients across multiple centres was a strength of the study, a recommended method for summarising the results across multi-centre studies was employed, and results were not directly compared between centres [12].

Raised troponin has been reported following pulmonary embolism (PE) in patients with normal coronary arteries on angiography [34], and although we did not include patients diagnosed with PE in our case-series we cannot exclude sub-clinical PE as a cause of the raised troponin. However, PE is found in only 3% of patients admitted to hospital with exacerbation of COPD [35], while we found raised troponin in three times that number making it an unlikely explanation for raised troponin for the majority of patients.

The ECGs were obtained during admission in patients who were frequently acutely unwell and tachycardic, rather than in controlled conditions. As such, the accuracy of the coding is likely to have been reduced, particularly when evaluating the degree of ST segment changes, and this was reflected in the comparatively low agreement between paper and electronically coded ECGs. However, myocardial ischemia on the ECG is often transient and more likely to be present during the initial presentation, and therefore we feel that the use of ECGs obtained during routine clinical assessments was more appropriate and less likely to underestimate the prevalence of myocardial ischemia.

Conclusion

Raised troponin was found in approximately ten percent of patients admitted to hospital with acute exacerbation of COPD, and the majority of these patients meet the Universal definition of MI. The proportion of patients in whom myocardial infarction occurred as a consequence of plaque rupture and coronary thrombosis, or who would benefit from further cardiac investigation and secondary prevention is unknown.

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Table 1 Patient characteristics

N	242
Stable characteristics	
Age, years, mean (SD)	69 (9)
Male gender, n (%)	108 (45%)
Height, metres, mean (SD)	1.62 (0.10)
Current smoker, n (%)	115 (48%)
Pack years, median (IQR)	50 (33-63)
FEV1, litres, median (IQR)	0.90 (0.68-1.20)
FVC, litres, median (IQR)	2.05 (1.63-2.65)
FEV1/FVC ratio, median (IQR)	44 (35-55)
Severity of obstruction by GOLD criteria, n (%)	
Mild	10 (5%)
Moderate	59 (32%)
Severe	65 (35%)
Very severe	52 (28%)
Long-term oxygen therapy, n (%)	40 (17%)
Home nebulisers, n (%)	119 (49%)
Long-acting beta agonists, n (%)	172 (71%)
Long-acting anticholinergics, n (%)	120 (50%)
Methylxanthines, n (%)	34 (14%)
Inhaled corticosteroid, n (%)	195 (81%)
Long term oral steroids, n (%)	6 (2%)
Exacerbation characteristics	
Heart rate, mean (SD)	102 (20)
Respiratory rate, mean (SD)	24 (5)
BP systolic/diastolic, mean (SD)	135 (25) / 73 (16)
Arterial blood gases, mean (SD)	
Hydrogen (mmHg)	41 (8)
PaO2 (kPa)	11 (4)
PaCO2 (kPa)	6 (2)
Exacerbation (infection) type, n (%)	
Anthonisen type 1	110 (45%)
Anthonisen type 2	51 (21%)
Anthonisen type 3	67 (28%)
Leukocytosis (WCC >11) x 10^9/L	113 (47%)
Raised C-reactive protein (>6 mg/dl), n (%)	158 (74%)
Haemoglobin, g/dl, mean (SD)	135 (18)
Prescribed antibiotics, n (%)	164 (68%)
Prescribed oral prednisolone, n (%)	217 (90%)
Treated with non-invasive ventilation (NIV)	15 (6%)
Length of stay in days, median (IQR)	5 (3-8)
12 month mortality (Edinburgh), n (%)	21 (15%)

Table 2 Chest pain characteristics

	n (%)
Central	76 (61%)
Duration <2 min or > 12 hours†	19 (18%)
Radiated to arm or jaw*	13 (11%)
Character	
Tight	60 (48%)
Sharp†	24 (19%)
Dull	12 (10%)
Like a pressure*	11 (9%)
Heavy	4 (3%)
Burning	1 (2%)
Gripping	2 (2%)
Autonomic symptoms (volunteered)	8 (6%)
Precipitating factors	
Exertion*	62 (52%)
Exertion, but also present at rest	44 (36%)
Deep inspiration†	7 (6%)
Coughing	20 (16%)
Palpation (pain reproduced) †	11 (9%)
Relieving factors (partial or complete)	
Nitrate therapy	18 (15%)
Bronchodilator therapy	15 (12%)
Oxygen therapy	13 (10%)
Had similar pain previously	
During an exacerbation	67 (54%)
When stable	31 (25%)
Summary of chest pain	
High risk features only	50 (40%)
Low risk features only	21 (17%)
Low and high risk features	22 (18%)
Neither low nor high risk features	31 (25%)

† Chest pain features associated with low risk, *chest pain features associated with high risk

Table 3 Raised troponin relative to chest pain and ECG features

	> 3 x cut-off*	**> 1 cut-off***	**≤ cut-off***	**P-Value**
n	**15**	**9**	**218**	
Any chest pain	9 (60%)	4 (44%)	111 (51%)	0.77
High risk chest pain	2 (13%)	0	48 (22%)	0.29
First admission ECG				
Diagnostic ECG	4 (27%)	3 (33%)	28 (13%)	0.06
Equivocal ECG	5 (33%)	3 (33%)	80 (36%)	>0.99
Sinus tachycardia	8 (53%)	7 (78%)	97 (44%)	0.14
Left bundle block	0	0	12 (6%)	>0.99
Right bundle block	3 (20%)	0	12 (6%)	0.08
P-pulmonale	2 (13%)	1 (11%)	17 (8%)	0.36
Right axis deviation	2 (13%)	1 (11%)	17 (8%)	0.36
Serial ECG changes	7 (50%)	4 (50%)	72 (40%)	0.39

* cut-offs differed between sites and were based on the lowest concentration where the co-efficient of variation was <10% as recommended by the 2007 Universal definition; Royal Infirmary of Edinburgh (Abbot Architect assay), 0.15 ng/mL prior to introduction of a new assay (17th November 2007), and 0.05 ng/mL thereafter; Glasgow Royal Infirmary (Abbot Architect assay) 0.04 ng/mL; Monklands and Crosshouse Hospitals (Roche Troponin T assay), 0.03 ng/mL

Table 4 Cardiovascular risk factors and therapy

N	**242**
IHD, n (%)	
None	161 (69%)
Diagnosed by generalist	18 (8%)
Diagnosed by specialist	19 (9%)
Confirmed*	34 (15%)
Stroke or peripheral vascular disease, n (%)	34 (14%)
Hypertension, n (%)	90 (37%)
Hypercholesterolaemia, n (%)	76 (31%)
Diabetes, n (%)	30 (12%)
Family history of IHD, n (%)	76 (31%)
Creatinine > 120 μmol/L, n (%)	24 (10%)
Non-fasting lipids, mean (SD)	
HDL Cholesterol, mmol/l	1.73 (0.61)
Cholesterol:HDL Ratio	2.97 (1.07)
Triglycerides, mmol/l	1.45 (0.87)
Nitrate or nicorandil, n (%)	35 (14%)
Calcium channel blocker, n (%)	38 (16%)
Beta blocker, n (%)	5 (2%)
ACE-inhibitor/ AR2 blocker, n (%)	44 (18%)
Diuretic, n (%)	82 (34%)
Statin therapy, n (%)	85 (35%)
Antiplatelet therapy, n (%)	96 (40%)
Antidiabetic therapy, n (%)	13 (5%)

*Confirmed IHD refers to ischaemic heart disease confirmed through diagnostic exercise tolerance testing, angiography, or proven MI.

Table 5 Raised troponin relative selected characteristics

	> 3 x cut-off*	**> 1 cut-off***	**≤ cut-off***	**P-Value**
Airflow obstruction				
Mild	2 (20%)	0 (0%)	8 (5%)	
Moderate	2 (20%)	1 (20%)	56 (33%)	0.19
Severe	5 (50%)	1 (20%)	59 (35%)	
Very severe	1 (10%)	3 (60%)	48 (28%)	
Long-term oxygen	1 (7%)	1 (11%)	38 (17%)	0.67
Current smoker	7 (47%)	3 (33%)	105 (48%)	0.71
Diabetes	5 (33%)	1 (11%)	24 (11%)	0.05
COPD therapy				
Long acting beta agonists	7 (47%)	5 (56%)	160 (73%)	0.05
Methylxanthines	5 (33%)	4 (44%)	25 (11%)	0.002
Inhaled corticosteroids	10 (67%)	8 (89%)	177 (81%)	0.34
Arterial blood gases				
Acidosis	5 (33%)	3 (33%)	33 (15%)	0.04
Hypoxia	3 (20%)	1 (11%)	75 (34%)	0.24
Hypercapnia	5 (33%)	6 (67%)	95 (44%)	0.43

* cut-offs differed between sites and were based on the lowest concentration where the co-efficient of variation was <10% as recommended by the 2007 Universal definition; Royal Infirmary of Edinburgh (Abbot Architect assay), 0.15 ng/mL prior to introduction of a new assay (17th November 2007), and 0.05 ng/mL thereafter; Glasgow Royal Infirmary (Abbot Architect assay) 0.04 ng/mL; Monklands and Crosshouse Hospitals (Roche Troponin T assay), 0.03 ng/mL

Figure legends

Figure 1 Number of patients with chest pain, serial ECG changes and raised troponin