Is elevated troponin associated with in-hospital mortality in emergency department patients admitted with chronic obstructive pulmonary disease?

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The aim of this study was to determine the prevalence and prognostic value of troponin elevation at emergency department (ED) presentation in patients admitted with an exacerbation of chronic obstructive pulmonary disease (COPD). A retrospective cohort study of ED patients with acute exacerbations of COPD who were admitted to hospital and in whom troponin was assayed at ED presentation. Other data collected included demographics, clinical characteristics, test results, and outcome. Outcome of interest was in-hospital mortality. A total of 252 patients were studied, median age 73 years, 61% men. In-hospital mortality was 4.4% [*n* = 11; 95% confidence interval (CI) 2.5–7.7%]. Seventy-eight patients had elevated troponin of greater than 99th centile (31%, 95% CI 26–37%). Factors independently associated with mortality were troponin elevation [odds ratio (OR) 8.3, 95% CI 1.58–43.7], pH less than 7.2 (OR 12.7, 95% CI 1.86–86.4), and requirement for noninvasive ventilation (OR 8.09, 95% CI 1.61–40.8). In conclusion, troponin elevation is associated with increased in-hospital mortality in ED patients with acute exacerbation of COPD. *European Journal of Emergency Medicine* **00:000–000**

European Journal of Emergency Medicine 2012, **00**:000–000

Keywords: chronic obstructive pulmonary disease, mortality, troponin

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Received 9 August 2011 **Accepted** 1 December 2011

Introduction

Originally thought to be 'specific' for cardiac disease, serum troponin concentration has been found to be of prognostic significance in a diverse range of acute conditions. For patients with chronic obstructive pulmonary disease (COPD), studies report that troponin elevation is common [1] and an association between elevated troponin levels and mortality at 30 days [2] and long term has been shown [3,4]. To date, there are little data on the association between serum troponin level at emergency department (ED) presentation and in-hospital mortality. The aim of this study was to determine the prevalence and prognostic value of troponin elevation at ED presentation.

Methods

This was a retrospective cohort study of a convenience sample of patients treated in the ED of Sunshine or Western Hospitals in Melbourne Australia for acute exacerbations of COPD between October 2009 and October 2010. These are community teaching hospitals with a combined adult ED census of approximately 85 000 per annum. Patients with a working diagnosis of acute exacerbation of COPD were identified prospectively by clinical staff at ED presentation and a single troponin I (TnI) sample was drawn for analysis. The final cohort, defined by hospital admission and hospital discharge diagnosis 'exacerbation of COPD' or equivalents (assigned by the treating clinician who was not aware of the study), was identified from a patient management database. Patients with a TnI assay at ED presentation comprised the sample for analysis.

Nursing staff were instructed to draw a single sample for analysis of TnI level with presentation blood tests on all patients with a suspected diagnosis of COPD. For included patients, data were collected explicitly from medical records, pathology, and radiology databases. This included demographics, observations at ED arrival, chest radiograph and ECG results, TnI assay results, arterial blood gas analysis (if performed), noninvasive ventilation (NIV) in ED, and in-hospital outcome. Patients with missing TnI values were excluded from analysis; however, in order to test the representativeness of the sample, ethics approval allowed acquisition of age, sex, and in-hospital mortality data.

The TnI assay used was TnI-Ultra by Siemens Diagnostics (Erlangen, Germany) performed on an Advia Centaur analyzer (Siemens). The test has a reported range of 0.006–50 ng/ml. The 99th centile of the test is 0.04 ng/ml [95% confidence interval (CI) 0.03–0.05 ng/ml] (information provided by manufacturer). Levels of greater than 99th centile were considered elevated. All treatment decisions and subsequent investigation decisions were at the discretion of the treating physician.

The primary outcome of interest was in-hospital mortality. The secondary outcomes were the prevalence of TnI elevation at ED presentation, and factors associated with in-hospital mortality. Data were analyzed using descriptive

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statistics, χ^2 and Fisher's exact tests, odds ratios (OR), stepwise logistic regression, and receiver operating curve analyses using Analyze-It (Leeds, UK) and Minitab software (State College, Pennsylvania, USA). Sample size estimation showed that to detect a difference in mortality of 20% (30 vs. 10%), assuming a prevalence of troponin elevation of 25% as reported by Harvey and Hancox [1], approximately 240 patients were needed. Ten percent was the mortality reported for troponin-negative patients by Høiseth *et al.* [3].

The study was approved by the institutional Human Research Ethics Panel. Specific patient consent was not required.

Results

A total of 252 patients met the study criteria and 188 patients were missed (TnI was not drawn) (Fig. 1). Their characteristics are shown in Table 1.

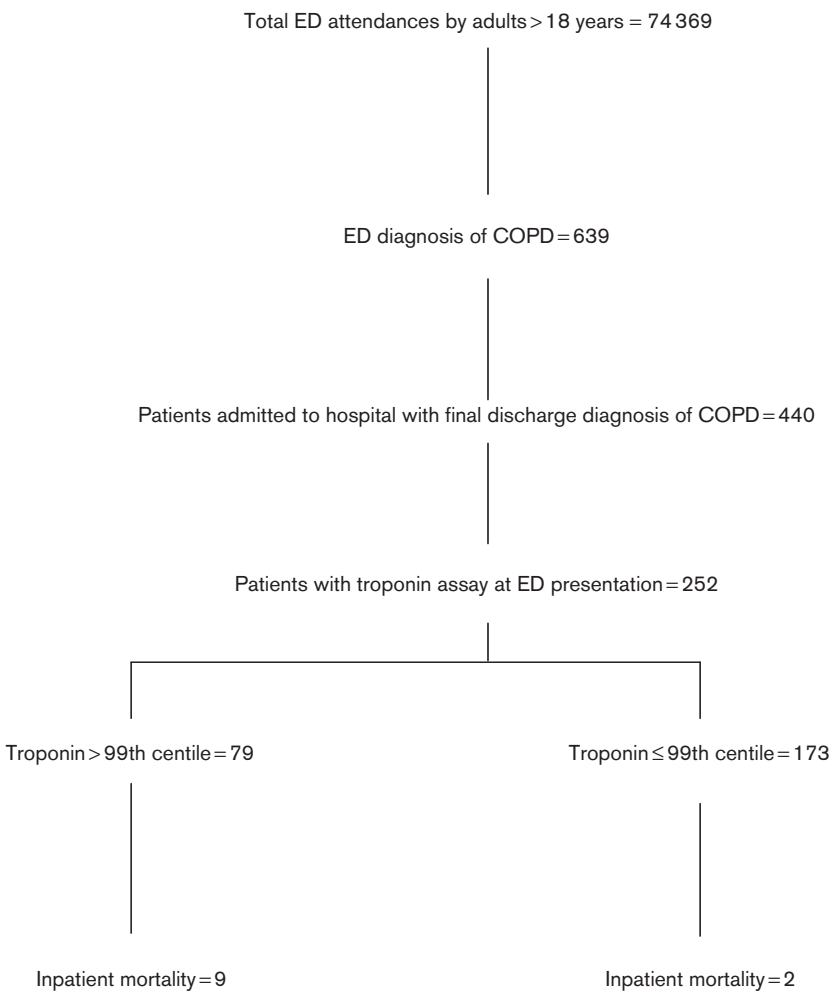
The prevalence of TnI elevation was 79/252 (31%, 95% CI 26–38%). There were 11 deaths (4.4%, 2.5–7.7%), nine of whom had TnI of greater than 99th centile. Mortality in patients with elevated troponin was 11.4% (9/79; 95% CI 6.1–20.3%) compared with 1.2% in those without troponin elevation (2/173; 95% CI 0.3–4.1%).

On multivariate analysis, factors associated with in-hospital mortality were pH of less than 7.2 (OR 12.7; 95% CI 1.86–86.4, reference pH 7.35–7.45), TnI elevation of more than 0.04 ng/l (OR 8.3, 95% CI 1.58–43.7), and requirement for NIV in ED (OR 8.09, 95% CI 1.61–40.8). The prognostic performance of TnI as a predictor of mortality is shown in Fig. 2. The *c*-statistic is 0.77 (95% CI 0.65–0.90).

Discussion

Our data show that like other serious acute illnesses, TnI elevation at ED presentation is common and is associated

Fig. 1



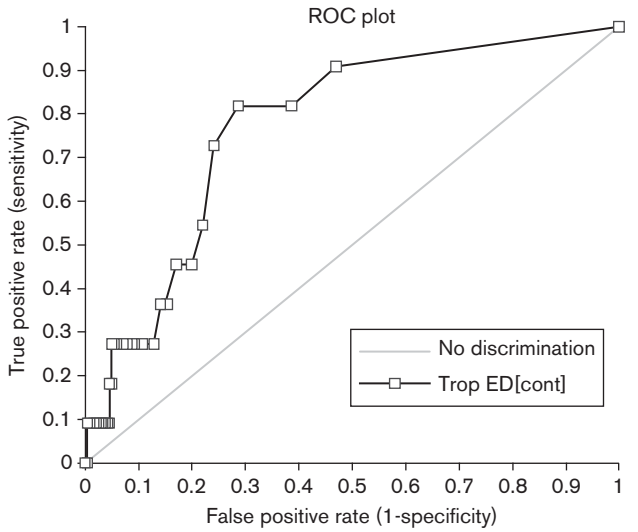
Sample derivation. COPD, chronic obstructive pulmonary disease; ED, emergency department.

Table 1 Characteristics of the sample

Parameter	Troponin assay obtained ($N=252$)	Troponin assay not obtained ($N=188$)	Statistical significance
Age (years, median, IQR)	73,65–80	70.5, 62–80	$P=0.08$
Men (*N*, %)	154, 61%	105, 56%	$P=0.15$
In-hospital deaths (*N*, %, 95% CI)	11, 4.4%, 2.5–7.7%	7, 3.7%, 1.8–7.5%	$P=0.47$
TnI (median, IQR)	0.03, 0.02–0.06	–	–
TnI > 0.04 ng/l (*N*, %, 95% CI)	78, 31%, 26–37%	–	–
NIV in ED (*N*, %)	67, 27%	–	–
pH (median, IQR, 32 missing data)	7.34, 7.28–7.40	–	–
pH < 7.2 (*N*, %)	15, 6%	–	–

CI, confidence interval; ED, emergency department; IQR, interquartile range; NIV, noninvasive ventilation; TnI, troponin I.

Fig. 2



Receiver operating curve (ROC) analysis for troponin elevation above the 99th centile as a predictor of in-hospital mortality.

with higher mortality. The TnI elevation prevalence finding in our study is in the middle of previous reports, which range from 16.5 to 74%, with a mean of 46% [1,2,5]. The strength of association with mortality is similar to that reported by Chang *et al*. [2] for 30-day mortality. The findings that severe acidosis and requirement for NIV in ED were associated with mortality were not surprising as both are indicators of severe illness.

The pathophysiological processes underlying TnI elevations in COPD are not well understood, nor how these elevations relate to cause of death. It is plausible that hypoxia and pulmonary vasoconstriction could lead to pulmonary hypertension and right ventricular dysfunction [6]. Alternatively, patients with COPD often have coexisting coronary artery disease [7]. It is plausible that hypoxia, inflammation, increased afterload from hyperinflation, and tachycardia could contribute to coronary ischemia, manifesting as either myocardial infarction (type I or type II) or heart failure. This is supported by registry data that report that the risk of myocardial infarction and stroke is increased significantly in the 5 days after a COPD exacerbation [8]. It is also plausible that TnI elevation is associated with undiagnosed pulmonary embolism.

Knowing that TnI elevation is associated with in-hospital mortality is only of academic interest unless it can be used to guide an intervention to mitigate that risk. For example, treatment of associated cardiac failure would be supported by evidence suggesting that it is a major cause of early death in patients hospitalized with COPD [9] and that patients with elevated troponin and *N*-terminal pro-brain natriuretic peptide showed a 15-fold increase in 30-day mortality compared with patients with normal values [2].

This study has some limitations that should be considered. This was a convenience sample at a single health service; thus, generalizability cannot be assumed. Selection bias is a risk in this type of study due to failure to recruit a significant proportion of eligible patients. Missed patients were, however, similar to included patients on limited data comparisons, suggesting that this risk of selection bias is small. Ethics approval conditions precluded the collection of further clinical data for comparison. Not all patients had serial troponin assays, as this was at the discretion of the treating clinicians. We were therefore unable to accurately identify concurrent NSTEMI for inclusion in the factor analysis. Although patients were identified prospectively, some data were collected retrospectively from medical records. This carries the well-described risks of missing data [10]. We tried to minimize this by explicit data collection processes. Clinicians were not blinded to TnI results and this may have influenced care in ways we did not measure.

Conclusion

Troponin elevation is associated with increased in-hospital mortality in patients attending ED with an acute exacerbation of COPD.

Acknowledgements

The authors thank Dr Sandy Clarke, Statistical Consulting Centre, and Professor Stephen Farish of The

University of Melbourne for assistance with statistical analysis. The authors also thank the nurses who participated by enthusiastically collecting the specimens. This project was supported by departmental funds only.

Conflicts of interest

There are no conflicts of interest.

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