Høiseth et al.: Serial measurement of high-sensitivity cardiac troponin T in acute exacerbations of chronic obstructive pulmonary disease

Additional material - details regarding patient inclusion, data collection, and description of procedures and analytical methods.

The study was conducted at Akershus University Hospital (AUH), Norway, a secondary teaching hospital that, with the exception of severe trauma and patients with ST-elevation myocardial infarctions, receives all medical emergencies from its catchment area. At the time the study was conducted, the hospital served a population of about 300.000 inhabitants living in urban, suburban and rural communities.

Patients were included from January 3rd 2005 through to November 30th 2006 and followed until December 31st 2008 or death. All patients admitted with assumed AECOPD were eligible for preliminary inclusion in the emergency room, prior to the emergency physicians' knowledge of any blood tests. The research fellow contacted the patient on the ward within a day to retrieve written informed consent and medical history. Exclusion criteria were: age <50 years, metastatic cancer and ECOG performance status grade ≥2, neuromuscular disease with respiratory failure, and non-cooperability. The diagnosis of AECOPD, as defined by the British Thoracic Society in 2004, was later verified by two study doctors by independent review of the hospital records, blinded for the result of the troponin analysis. In case of disagreement, the diagnosis was settled by consensus. Mortality data were gathered from the National Population Registry.

On admission, data were obtained from 234 patients admitted with assumed AECOPD. Out of these, 114 were not included either because the research fellow was absent or because he had not been informed of the patients' arrival. Of the remaining 120 patients, nine failed to fulfill study entry criteria, leaving 111 consenting patients. Nine patients were excluded as review of their spirometry

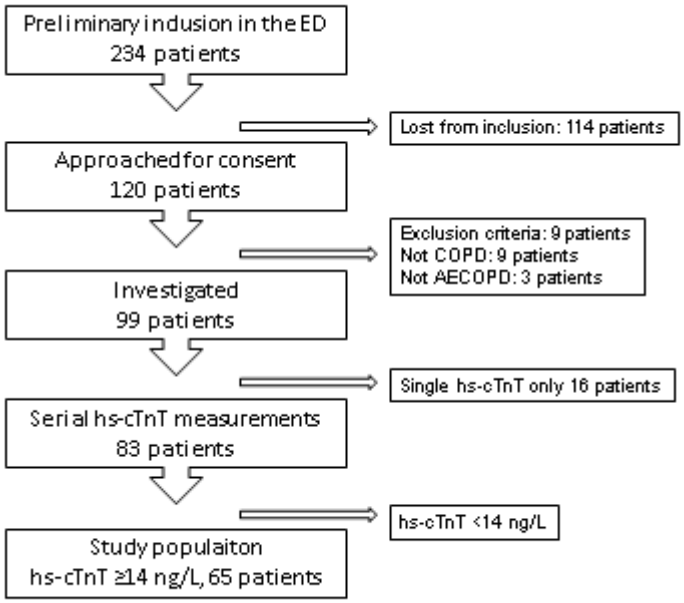
showed that they did not have COPD. Three patients with COPD were excluded as the primary cause of hospitalisation was pulmonary embolism or pneumothorax, leaving 99 patients for analysis.

Spirometries from stable phase only were recorded, and recordings from the outpatient clinic prior to inclusion were preferred. To make the data as complete as possible, we retrieved spirometry reports from collaborating hospitals in some cases. Median time from spirometry (n=88) to inclusion was 179 days (interquartile range 11–416 days), including both before (maximum 1250 days) and after (maximum 341 days) inclusion. In the lung outpatient clinic, spirometry with reversibility testing is the routine, and post bronchodilatation results were used in the analyses. There was no significant difference in NT-proBNP concentrations between the patients who had spirometry available and those who had not. Of the 11 patients who did not have spirometry available, eight died during follow-up.

During the index admissions, no patients were diagnosed with heart failure. Two patients received diagnosis of heart failure during subsequent admissions, and both patients died. One patient received a discharge diagnosis of an acute coronary syndrome (ACS) during the index hospitalization, and our patients received the diagnosis of ACS during subsequent admissions. All five patients survived.

After venepuncture and processing, serum and plasma were stored at -80°C for subsequent analysis of serum creatinine, NT-proBNP and hs-cTnT, using a Cobas e411 analyzer. The Elecsys hs-cTnT assay (Roche Diagnostics, Mannheim, Germany) had a reported lower limit of detection of 3.0 ng/L, a 99th percentile in healthy individuals at 14 ng/L and a coefficient of variation <10% for concentrations >13 ng/L at the time of biochemical and statistical analysis. Later, a limit of blank at 3.0 ng/L and a limit of detection of 5.0 ng/L has been reported. NT-proBNP was also analyzed with a Roche kit. According to the manufacturer, the assay had a limit of detection of 5.0 pg/mL. The coefficients of variation were reported to be 4.2%, 2.4% and 1.3% at concentrations of 44 pg/mL, 126 pg/mL and 2410 pg/mL, respectively. These study specific analyses were performed by a dedicated biochemist using the

same batch. Glomerular filtration rate was estimated (eGFR) by the MDRD formula. 15.5% of the samples had eGFR <60 mL/min/1.73 m^2, and 2% were <30 mL/min/1.73 m^2. When stratifying for renal function, the mortality rate ratios were 2.4 and 2.2 for creatinine <100 and ≥100 µmol/L, respectively (p=0.882 for interaction).



Supplementary figure 1: Flowchart showing the derivation of the study population.