ORIGINAL ARTICLE

High-sensitivity cardiac troponin T levels are increased in stable COPD

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ABSTRACT

Objective To assess the distribution of high-sensitivity cardiac troponin T (hs-cTnT) concentrations in stable chronic obstructive pulmonary disease (COPD), and whether hs-cTnT is associated with pulmonary function.

Design Prospectively designed, cross-sectional study.

Setting Outpatient clinic of Norwegian teaching hospital and community-based setting.

Participants Sample of 101 stable COPD patients from the hospital's outpatient clinic and 120 individuals derived from a random general population sample.

Main outcomes Ratio of hs-cTnT in stable COPD patients compared with references from the general population. Change in ratio of hs-cTnT per unit increase of relevant covariables.

Results The crude geometric means of circulating hs-cTnT in the cases and the references were 7.75 and 3.01 ng/l, respectively ($p<0.001$); that is, a relative ratio of 2.57 (95% CI 2.05 to 3.23). After adjustment for relevant confounders, this ratio was moderately attenuated to 1.65 (1.31–2.08). In the total study cohort, as well as among stable COPD patients, we found a significant positive association between hs-cTnT and interleukin-6 concentrations ($p<0.001$) and the presence of pathologic Q waves ($p=0.023$). Among stable COPD patients, one quartile increase in forced expiratory volume 1 was associated with a 39% decrease in hs-cTnT and patient category (Global Initiative of Obstructive Lung Disease classification 2011) was positively associated with hs-cTnT (p trend <0.001) after multivariate adjustment.

Conclusions Stable COPD is independently associated with higher hs-cTnT compared with randomly drawn subjects from the general population. In patients with stable COPD, higher hs-cTnT seems to be associated with immune activation and the severity of the disease.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. The international organisation, Global Initiative of Obstructive Lung Disease (GOLD), published their first definition of COPD in 2001. This definition focused almost exclusively on irreversible airflow limitation, airway inflammation and emphysema, in addition to tobacco smoking and environmental exposures. During the last few years, the inflammatory components and extrapulmonary comorbidities of COPD manifested as cardiovascular disease, osteoporosis or skeletal muscle wasting have attracted increasing attention.[1 2] In addition to the chronic progressive aspect of COPD, many COPD patients have acute worsening of their symptoms (ie, exacerbation), frequently leading to hospitalisation and increased mortality.[3] Retrospective, as well as prospective studies, have indicated that even modest troponin elevations among COPD patients hospitalised for exacerbation are associated with increased mortality.[4 5]

Detection of cardiac troponin T (cTnT) or cardiac troponin I (cTnI) above the 99th percentile of a reference population is a prerequisite for the diagnosis of acute myocardial infarction (MI).[6] In several chronic diseases, such as chronic renal failure and heart failure, chronically elevated cardiac troponin levels have been described in the stable state of the disease.[7] The new, highly sensitive (hs) assay for cardiac troponin T measures concentrations that are fivefold to tenfold lower than conventional assays, and the great majority of patients with stable coronary artery disease (CAD) have detectable levels of cTnT.[8] By contrast, with the conventional assay for cTnT, <1% of subjects in the general population have detectable levels.[9]

High-sensitivity cardiac troponin T (hs-cTnT) levels above the detection limit are associated with cardiac structure and impaired function, and predictive of heart failure, cardiovascular death and all-cause mortality.[10 11] Previous studies evaluating the association between COPD and troponin T have mainly focused on patients with COPD exacerbations, or have used COPD as a covariate for comorbidity. A recently published study showed that acute exacerbation of COPD is associated with higher hs-cTnT compared with stable COPD patients recruited at a rehabilitation hospital, and that hs-cTnT was associated with COPD severity.[12] To the best of our knowledge, there are, at present, no further studies evaluating hs-cTnT among COPD patients in the stable state. The objectives of the study were therefore to (A) compare the distribution of hs-cTnT among patients with stable COPD with a random sample from the general population and (B) assess the association between pulmonary function and hs-cTnT among patients with stable COPD.

MATERIALS AND METHODS

Study population

This is a prospectively designed, cross-sectional case-control study that includes a consecutive sample of 101 stable COPD patients from the Akershus University Hospital's outpatient clinic, and a random sample of 120 references from the general population from the Akershus University Hospital's catchment area. Patients with a history

of congestive heart failure (CHF), MI, angina pectoris, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) were not included. References with a diagnosis of COPD, or history of CHF, MI, PCI or CABG were excluded (n=9). The study protocol was approved by the committee for medical and health research ethics, Southeastern Norway, and all patients provided written informed consent.

Measurements

All subjects completed a questionnaire on smoking habits and respiratory symptoms according to the MMRC (Modified Medical Research Council) Dyspnea Scale. Spirometry with reversibility testing with salbutamol was performed at the outpatient clinic, as recommended by Miller.[13] COPD patients were classified into four categories (A–D) in accordance with the combined COPD assessment of the revised GOLD strategy document, including associations between symptoms (MMRC Scale), spirometric classifications and future risk of exacerbations.[14] Smoking habits were expressed as current smoking (yes/no) and cumulative tobacco exposure expressed as pack-years. Arterial and venous blood was sampled after an overnight fasting and tobacco-abstinent period; hs-cTnT was measured with the Elecsys 2010 troponin T hs STAT assay, and N-terminal-pro Brain Natriuretic Peptide (NT-proBNP) and Interleukin-6 (IL6) were measured with the Cobas e602 (Roche Diagnostics, Mannheim, Germany).

Statistical analyses

The statistical analyses were performed in three steps. First, all variables were compared between the cases and the references using a Student t test for continuous covariates and χ^2 test for categorical covariates. Second, we investigated the univariate associations between hs-cTnT and relevant covariates using a Student t test for dichotomous covariates. We used a least square univariate linear regression for continuous covariates categorised in quartiles with log-transformed hs-cTnT (ln (hs-cTnT)) as the dependent variable to detect linear trends. Pearson correlation analyses were also performed in order to investigate the association between relevant continuous determinants for hs-cTnT. Measurements below the limit of blank (LoB) and between the LoB and the limit of detection (LoD)[15] were replaced with LoB/2 and LoD/2, respectively. For each category of the covariate, hs-cTnT was expressed as the geometric mean. Third, we investigated the association between hs-cTnT and COPD using multiple ordinary least square regression adjusting for covariates that were associated with COPD, as well as hs-cTnT with corresponding p values less than 0.2. The initial full model was reduced by backward elimination if the p value for association between ln(hs-cTnT) and the covariate was ≥0.05, and if removal of the covariate did not change the association between ln(hs-cTnT) and COPD >20%. The results are given as the antilog of the coefficient of the corresponding covariate, which can be interpreted as the ratio between hs-cTnT and one unit increase of the corresponding covariate. In the analysis restricted to COPD patients, we used the same model using COPD patient categories A–D as the explanatory variable of interest. The analyses were performed using PASW Statistics 18 (SPSS, Inc, Chicago, Illinois, USA). For details please see online supplementary data.

RESULTS

Comparison of the cases and the references

The crude geometric means of circulating hs-cTnT in the cases and the references were 7.75 and 3.01 ng/l, respectively

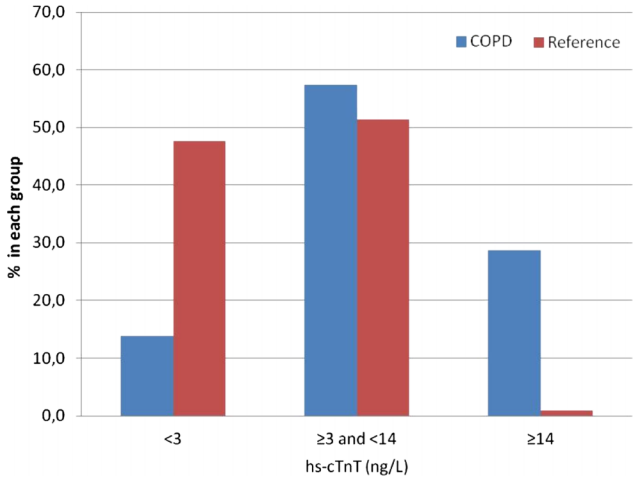

Figure 1 hs-cTnT, High-sensitivity cardiac troponin T; COPD, Chronic obstructive pulmonary disease; 3 ng/l, limit of blank and 14 ng/l, 99th percentile of healthy reference population.

(p<0.001); that is, a ratio of 2.57 (95% CI 2.05 to 3.23). The distribution of hs-cTnT related to the LoB and the 99th percentile in a healthy reference population is shown in figure 1. The crude analyses indicated a dose-response relationship between hs-cTnT and patient category (figure 2). The cumulative tobacco exposure (expressed as pack-years) was significantly higher among the patients than the references (table 1), whereas the prevalence of current smoking did not differ significantly between the cases and the references (p=0.127). Age, heart rate, NT-proBNP, IL6, neutrophils, history of arterial hypertension, indices of left ventricular hypertrophy (LVH) (Sokolow–Lyon criteria), and presence of pathological Q waves were significantly higher among the cases, although the absolute number of patients with LVH (n=6) or pathological Q waves (n=4) was low. None of the subjects had atrial fibrillation. The cases and the references did not markedly differ regarding gender, systolic blood pressure, diabetes, use of a statin, serum creatinine or presence of T wave inversion (p >0.2). The distributions of relevant covariates between the cases and the references are shown in table 1.

Univariate analysis of hs-cTnT

The univariate associations between hs-cTnT and covariates among cases and control subjects are shown in table 2 (dichotomous covariates) and table 3 (continuous covariates by quartiles). The majority of the dichotomous variables were

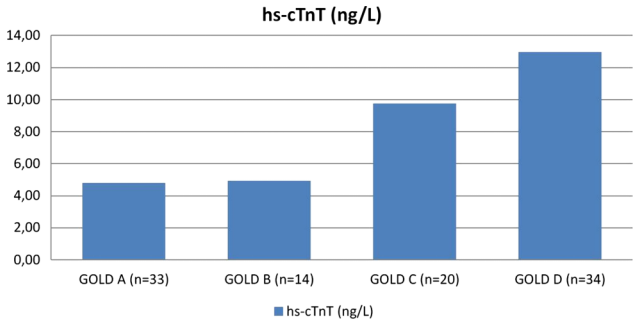

Figure 2 hs-cTnT, High-sensitivity cardiac troponin T; chronic obstructive pulmonary disease classification after the Global Initiative of Obstructive Lung Disease strategy document, revised 2011.

Table 1 Characteristics of the total cohort, stable chronic obstructive pulmonary disease patients and references

Covariate	Total	Cases	References	p Value
Total, n	212	101	111	<0.001
hs-cTnT, ≥3 ng/l, n (%)	145 (68.4)	87 (86.1)	58 (52.3)	<0.001
hs-cTnT, geometric mean	4.72	7.75	3.01	<0.001
Demographic data				
Age, years mean (SD)	59 (10.0)	64 (7.5)	54 (9.7)	<0.001
Female, n (%)	104 (49.1)	51 (50.5)	53 (47.7)	0.689
BMI, kg/m^2 mean (SD)	25.6 (4.6)	25.1 (4.9)	26.1 (4.4)	0.102
Smoking habit				
Pack-years, mean (SD)	21.3 (20.8)	36.6 (17.6)	7.3 (11.6)	<0.001
Current smoker, n (%)	47 (22.2)	27 (26.7)	20 (18.0)	0.127
Spirometry				
FVC, litre mean (SD)	3.5 (1.4)	2.7 (1)	4.3 (1.3)	<0.001
FEV1, litre mean (SD)	2.3 (1.3)	1.3 (0.6)	3.2 (1)	<0.001
FEV1/FVC, % mean (SD)	62.6 (17.5)	47.4 (12.8)	76.3 (6.4)	<0.001
FEV1/height^2, litre/m^2 mean (SD)	0.8 (0.4)	0.4 (0.2)	1.1 (0.2)	<0.001
Clinical data				
Syst BP, mm Hg mean (SD)	136.4 (20)	137.8 (21.4)	135.3 (18.7)	0.360
Arterial HT, n (%)	48 (22.6)	35 (34.7)	13 (11.7)	<0.001
Diabetes mellitus, n (%)	8 (3.8)	3 (3.0)	5 (4.5)	0.558
Statin, n (%)	20 (9.4)	10 (9.9)	10 (9)	0.824
Laboratory data				
Haemoglobin, g/dl mean (SD)	14.3 (1.2)	13.8 (1.1)	14.8 (1.1)	<0.001
NT-pro BNP, pmol/l, median (IQR)	7.8 (12.7)	13.4 (15.1)	5.5 (7.7)	<0.001
IL6, pg/ml, median (IQR)	0.8 (2.1)	2.1 (3.2)	0.8 (0.9)	0.016
Neutrophils, 10^9/l mean (SD)	3.8 (1.4)	4.3 (1.5)	3.3(1.2)	<0.001
Creatinine, mg/dl mean (SD)	0.8 (0.2)	0.8 (0.2)	0.8 (0.1)	0.331
ECG				
Heart rate, n/min mean (SD)	67 (12.0)	70 (12.4)	65 (10.5)	0.005
Pathological Q wave, n (%)	4 (1.9)	4 (4)	0 (0)	0.034
T wave inversion, n (%)	7 (3.3)	3 (3.0)	4 (3.6)	0.797
Left ventricular hypertrophy, n (%)	7 (3.3)	6 (5.9)	1 (0.9)	0.040
Right ventricular hypertrophy, n (%)	3 (1.4)	3 (3.0)	0 (0)	0.067
P pulmonale, n (%)	7 (3.3)	7 (6.9)	0 (0)	0.005

BMI, body mass index; FEV, forced expiratory volume; FVC, forced vital capacity; HT, hypertension; hs-cTnT, high-sensitivity cardiac troponin T; IL, interleukin; NT-pro BNP, N-terminal probrain natriuretric pepride; one pack-year, 20 cigarettes daily during 1 year, Syst BP: systolic blood pressure.

Table 2 Geometric mean of high-sensitive cardiac troponin T (hs-cTnT in ng/l) by dichotomous covariates, and the ratio of geometric mean of hs-cTnT

Covariate	Covariate present		Ratio	p Value
	Yes	No		
Demographic data				
Female	3.80	5.81	0.65	<0.001
Smoking habit				
Current smoker	4.24	4.87	0.87	0.289
Clinical data				
COPD	7.75	3.01	2.57	<0.001
Hypertension	7.18	4.18	1.72	<0.001
Laboratory data				
IL6 (≥1.5 pg/ml)	7.50	3.29	2.28	<0.001
Electrocardiogram				
Pathological Q wave	19.38	4.60	4.21	0.013
Left ventricular hypertrophy	15.60	4.53	3.44	0.003
Right ventricular hypertrophy	28.90	4.60	6.28	0.005

COPD, chronic obstructive pulmonary disease; IL6, interleukin 6.

associated with hs-cTnT, except current smoking. Among the continuous variables, body mass index, heart rate, blood haemoglobin and serum creatinine were not significantly associated with hs-cTnT (table 3). Creatinine was, however, included in the initial multivariate regression model, as creatinine is an established factor associated with circulating troponin levels.

Multivariate analysis

In the final multivariate model, we found that the ratio of hs-cTnT between cases and references was 1.65 (1.31–2.08, p<0.001). We also found a significant relation between hs-cTnT and forced expiratory volume in one second (FEV 1) (ratio (95% CI): 0.74 (0.65 to 0.83), p=0.001 in the total cohort, and that hs-cTnT was significantly higher among subjects with pathological Q waves and ECG signs of LVH as compared with their counterparts. Moreover, hs-cTnT was significantly lower in females than in males, and increased significantly with higher age. The coefficient for the product of age and population group (case/reference) was not significant. Subjects with IL6 levels above the detection limit (LoD=1.5 pg/ml) had significantly higher hs-cTnT than subjects with IL6 below the detection limit. We found, however, no significant independent association between hs-cTnT and cumulative tobacco use

Table 3 Geometric mean of high-sensitivity cardiac troponin T (hs-cTnT) by quartiles of continuous covariates

Covariate	Quartile (Qn) of covariate				Ratio	p Value
	Q1	Q2	Q3	Q4		
Demographic data						
Age, (52; 60; 66) years	2.64	4.23	5.78	8.58	1.47	<0.001
BMI, (22; 25.2; 28.7) kg/m^2	5.45	4.31	4.57	4.64	0.96	0.483
Pack-years (0; 19.3; 35.1)	2.86	4.35	6.26	6.95	1.36	<0.001
Clinical data						
Heart rate, (57; 66; 75) 1/min	4.68	4.19	4.01	6.23	1.09	0.155
Systolic BP, (125; 135; 150) mm Hg	3.31	4.87	6.01	5.78	1.23	0.001
Spirometry						
FVC, (2.50; 3.32; 4.36) litre	8.14	4.97	3.23	3.79	0.76	<0.001
FEV_1, (1.28; 2.30; 3.10) litre	11.34	4.60	2.69	3.50	0.67	<0.001
FEV_1/FVC, (47; 68; 77) %	11.34	4.38	3.32	2.99	0.65	<0.001
Laboratory data						
NT-proBNP, (3.7; 7.8; 16.4) pmol/l	3.56	3.51	5.08	7.80	1.31	<0.001
Neutrophils, (2.8; 3.5; 4.5) 10^9/l	3.53	4.04	4.64	7.64	1.28	<0.001
Haemoglobin, (13.5; 14.3; 15.1) g/dl	6.56	4.15	4.49	4.36	0.90	0.087
Creatinine, (0.72; 0.80; 0.93) mg/dl	4.71	3.90	5.14	5.24	1.06	0.352

Ratio: $(\text{hs-cTnT})_{Qn}/(\text{hs-cTnT})_{Qn-1}$. Quartile limits in parentheses.
BMI; body mass index; BP, blood pressure; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s.

(p=0.123), current smoking (p=0.195), history of hypertension (p=0.594), serum NT-proBNP concentration (p=0.111), heart rate (p=0.684), blood neutrophil count (p=0.682) or serum creatinine concentration (p=0.926), when added to the final model. The ratio of hs-cTnT was attentuated to 1.61 (1.28–2.04) when p pulmonale was added to the final model, but p pulmonale was not independently associated with hs-cTnT in the total study cohort.

hs-cTnT among COPD patients

In the analysis restricted to the COPD patients, we found a significant positive association between hs-cTnT and the severity of disease. In COPD patients, the crude analyses indicated a dose-response relationship between hs-cTnT and patient categories A–D (figure 2). This positive association remained significant after multivariate adjustment (p trend <0.001). A similar relation was observed between hs-cTnT and FEV1 (ratio: 0.61 (0.48–0.79), p=0.001). The significant positive association between FEV1 and hs-cTnT among the patients only was not changed after inclusion of p pulmonale in the model. The associations between hs-cTnT and age, gender, pack-years and indices of left and right ventricular hypertrophy were not significant among stable COPD patients. Arterial blood oxygen and carbon dioxide tension, diffusing capacity for carbon monoxide and presence of p pulmonale were not significantly associated with hs-cTnT in our patient group. The association between hs-cTnT and IL6 levels (p <0.001) and the presence of pathological Q waves (p=0.023) were highly significant among stable COPD patients. Among the reference subjects, there was no significant association between hs-cTnT and pulmonary function (FEV1), and a weak significant association with IL6 above LoD (p=0.040). We found, however, significant associations between hs-cTnT and age or gender among the references (table 4).

DISCUSSION

Principal findings

The new and salient finding of this study is that COPD patients in their stable state without a history of coronary heart disease have higher circulating levels of troponin T than a reference population drawn randomly from the general population. This association remained highly significant after multivariate adjustment. Among the cases, we found a dose-response relationship

Table 4 The relative change in high-sensitive cardiac troponin T (hs-cTnT) (95% CI) by relevant covariates

Covariate (C)	Change of C (Δx)	$\text{Hs-cTnT}_{x+\Delta x}/\text{hs-cTnT}_x$		
		Total cohort	COPD cases	References
COPD	Yes versus no	1.65 (1.31–2.08)	–	–
FEV1	Quartiles	–	0.61 (0.48–0.79)	1.08 (0.83–1.41)
Age	Quartiles	1.23 (1.12–1.36)	1.07 (0.89–1.27)	1.36 (1.19–1.55)
Female	Yes versus no	0.63 (0.52–0.77)	0.71 (0.51–1.00)	0.52 (0.38–0.70)
IL6 ≥LoD	Yes versus no	1.48 (1.19–1.84)	1.79 (1.28–2.51)	1.32 (1.01–1.72)
Q wave	Yes versus no	2.35 (1.11–4.94)	2.56 (1.14–5.71)	NA
LVH	Yes versus no	2.01 (1.13–3.54)	1.97 (1.00–3.80)	NA
RVH	Yes versus no	3.06 (1.30–7.16)	2.31 (0.92–5.85)	NA

COPD, chronic obstructive pulmonary disease; FEV, forced expiratory volume in 1 s; LoD, limit of detection; LVH, left ventricular hypertrophy; NA, not available (0–1 patient only); RVH, right ventricular hypertrophy.

between hs-cTnT and the severity of disease. To our knowledge, this is the first study to show that high-sensitivity cardiac troponin T levels in peripheral blood are increased in stable COPD patients compared with their healthy references.

Pathophysiology of COPD and chronic, low-grade myocardial injury

COPD appears to be an important independent determinant of circulating troponin, expressed as hs-cTnT. Several underlying mechanisms for the association between COPD and troponin T should be considered. First, the prevalence of cardiovascular disease is higher in COPD patients than in the general population.[16 17] Existing explanatory models for a relation between COPD and cardiovascular disease (CVD) include inflammation, hyperinflation and shared risk factors and genetics.[18] The inflammatory process in COPD involves neutrophils, macrophages and T lymphocytes, and augmented concentrations of inflammatory markers, such as IL6 have been reported.[19 20] Spillover of inflammatory mediators from the lungs to the systemic circulation has been proposed as a possible link between COPD and comorbidities.[2]

Concerning measurement of hs-cTnT, large-scale population-based epidemiological studies have shown that multiple factors are associated with chronic, low-grade troponin elevation;[10 11] thus, increasing age, male gender, hypertension, diabetes mellitus and reduced renal function have all been shown to be associated with higher hs-cTnT levels in the general population.[10 21] Moreover, significant associations between cTnT and biomarkers of inflammation have been observed.[11] In the current study, patients with a history of CAD were not included. Due to common risk factors between COPD and CAD, subclinical atherosclerosis still may be common in patients with COPD.[18] Accordingly, it is not surprising that almost 4% of the patients had pathological Q waves in their ECG, and that Q wave, as well as LVH, was significantly associated with hs-cTnT even after adjustment for relevant covariates. However, NT-proBNP concentrations were not significantly associated with hs-cTnT in the current study population. B-type natriuretic peptides are markers of haemodynamic stress[22] and powerful markers of outcome across the spectrum of cardiovascular disease.[23] In the current study, NT-proBNP concentrations were significantly higher in cases than in references, but there were no individuals with measurements above the normal range, suggesting that our COPD patients did not have unrecognised heart failure. Cases had a higher prevalence of hypertension, but the mean systolic blood pressure was within normal range, suggesting that the hypertension was fairly well controlled.

Hypoxaemia has been suggested as an explanatory factor for myocardial damage and leakage of troponin in the setting of pulmonary embolism.[24] We did not, however, find any association between hs-cTnT and arterial oxygen or carbon dioxide tension among the COPD patients (data not shown). This could be due to the fact that the mean oxygen tension was higher than 8.0 kPa, and that the lowest value was 7.2 kPa. Admittedly, the lack of association between hypoxaemia and hs-cTnT could also be explained by insufficient study power. However, in a retrospective and prospective study of troponin in COPD exacerbation, we also failed to find any association between hypoxaemia and troponin levels.[25 26]

Another mechanism contributing to troponin elevation in COPD may be increased inflammatory activity. Elevated troponin levels are frequently found in acute disease with a major inflammatory component, such as sepsis.[27] Previous studies suggest that IL6 might play a salient role in the inflammatory responses in COPD[28] as well as in cardiovascular disease.[29] Our results indicate that IL6 above the detection limit is a significant determinant of hs-cTnT levels. This observation suggests that troponin release in COPD may, at least partially, be mediated by an inflammatory process that involves IL6. Theoretically, proinflammatory cytokines, like tumour necrosis factor (TNF-α), IL1β and IL6 derived from activated neutrophils could increase the permeability of the cell wall of cardiomyocytes and promote troponin release or apoptosis of cardiomyocytes.[30] In our model, neutrophils were not significantly associated with hs-cTnT, even after exclusion of IL6 from the model. This could be due to additional activity and IL6-secretion from, for instance T cells and macrophages.

Potential clinical implications

The fact that low-grade myocardial damage among COPD patients seems to be present even in the stable state of the disease strengthens the need to understand the pathogenic, especially immunologic, mechanisms in COPD and its comorbidities in order to be able to develop new strategies for the prevention and treatment of this condition. Although associated with increased risk, there is at present no consensus for the use of hs-cTnT as a screening tool, and there are no established cut-off points for hs-cTnT to guide therapy in settings other than acute coronary syndromes. Since chronic, low-grade increase of circulating troponin can be due to both ischaemic and non-ischaemic causes, it is important to be able to distinguish between these aetiologies. Stable COPD patients without previously known coronary heart disease or CHF presenting with elevated levels of hs-cTnT may, therefore, be candidates for cardiac investigations, such as echocardiography and stress testing. Such a strategy may prove effective in identifying a subgroup of stable COPD patients who potentially could benefit from cardiovascular interventions and therapies, such as antiplatelet therapy, treatment with statins or referral for coronary angiography. However, further validation of the current results, definition of appropriate cut-off values for troponins for referral to cardiac investigations, and clinical trials to demonstrate efficacy and cost-effectiveness are clearly required before such a strategy can be recommended in clinical practice.

Strengths and limitations

Major strengths of the study include the participation of stable COPD patients, including patients in all GOLD stages. Several prior studies have included COPD patients hospitalised with an acute exacerbation, but those results may not be extrapolated to the stable state. First, an acute exacerbation is commonly associated with respiratory infection and inflammation that could influence the rate of troponin release. Second, there is increasing evidence that patients with frequent COPD exacerbations may represent a separate phenotype distinct from stable patients. Other strengths of our study include the relatively similar sizes of patients and references as well as balanced representation of men and women. Smokers are well represented among the references. The main limitation of the study is the cross-sectional design that precludes any causative interpretation of the results. The fact that the COPD group had a prevalence of 4% pathological Q waves, suggesting unrecognised cardiac injury in a small minority of patients, is another limitation. However, a sensitivity analysis excluding these subjects did not reveal a significant change in the association between hs-cTnT and the relevant covariates.

The selection of COPD patients from the outpatient clinic may have resulted in a group of patients with more severe

symptoms, including comorbidities, than non-selected COPD patients from a general population. The latter issue is, however, of minor concern as we have registered the majority of variables that constitute broad aspects of the health problems in COPD patients. The representativeness of the references may also be questioned. Thus, we compared the distribution of age and gender in the source population in the same period, that is, from 2006 to 2010. It turned out that 50% of the population in this age group in Akershus County were female, and the distribution of subjects of the age groups 40–49, 50–64 and 65 years or older was 39%, 45% and 17%, respectively (accessed from the Norwegian Central Statistics Office, table 07459, July 2011). Hence, our sample is likely to be representative for the source population.

CONCLUSION

Stable COPD is associated with elevated cardiac troponin T levels, and the hs-cTnT levels increase with the severity of airflow limitation. Higher hs-cTnT levels are associated with higher IL6 concentrations and pathological Q waves, suggesting that inflammatory activity, as well as unrecognised MI, may contribute to higher hs-cTnT concentrations in stable COPD.

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