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Short communication

Cardiac troponin T and NT-proBNP for detecting myocardial ischemia in suspected chronic coronary syndrome

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ABSTRACT

Background: Elevated N-terminal pro-B-type natriuretic peptides (NT-proBNP) and cardiac troponin T (cTnT) are associated with poor outcome in patients with chronic coronary syndrome (CCS). The performance of these biomarkers in diagnosing ischemia, and their association with myocardial hypoperfusion and hypokinesis is unclear.

Methods: Patients with suspected CCS (history of angina, estimated cardiovascular risk >15% or a positive stress test) were included in the prospective, multi-center DOPPLER-CIP study. Patients underwent Single Positron Emission Computed Tomography for assessment of ischemia and NT-proBNP and cTnT were measured in venous blood samples.

Results: We included 430 patients (25% female) aged 64 ± 8 years. Reversible hypoperfusion and hypokinesis were present in 139 (32%) and 89 (21%), respectively. Concentrations of NT-proBNP and cTnT correlated moderately (rho = 0.50, $p < 0.001$). NT-proBNP and cTnT concentrations (median [IQR]) were higher in patients with versus without reversible ischemia: 150 (73–294) versus 87 (44–192) ng/L and 10 (6–13) versus 7 (4–11) ng/L, respectively ($p < 0.001$ for both), and the associations persisted after adjusting for possible confounders. The C-statistics to discriminate ischemia ranged from 63%–73%, were comparable for cTnT and NT-proBNP, and higher for hypokinesis than hypoperfusion, and both were superior to exercise electrocardiography and stress echocardiography. Very low concentrations (≤5 ng/L cTnT and ≤ 60 ng/L NT-proBNP) ruled out reversible hypokinesis with negative predictive value >90%.

Conclusion: cTnT and NT-proBNP are associated with irreversible and reversible ischemia in patients with suspected CCS, particularly hypokinesis. The diagnostic performance was comparable between the biomarkers, and very low concentrations may reliably rule out ischemia.

1. Introduction

Increased concentrations of cardiac troponins (cTn) and B-type natriuretic peptides (BNP) are associated with poor outcome and the presence of reversible myocardial ischemia in patients with chronic coronary syndrome (CCS) [1–4]. It is however unclear how these

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biomarkers perform in diagnosing ischemia when compared head-to-head, and compared to exercise electrocardiography and stress echocardiography. It is also unknown whether the association between these cardiac biomarkers and ischemia is by hypoperfusion per se, or if it is indirect and related to acute or chronic myocardial dysfunction. Very low concentrations of cTn and NT-proBNP are reliable for ruling out myocardial infarction (MI) and acute heart failure, respectively [5,6]. Whether very low concentrations of these biomarkers also can rule out myocardial ischemia in a stable setting is unknown.

To address these questions, we examined the associations between cTnT and N-terminal pro-BNP (NT-proBNP) and the presence of reversible and irreversible myocardial perfusion defects, regional wall motion abnormalities, and myocardial scar in patients with suspected CCS. We hypothesized that both biomarkers were independently associated with ischemia, that the discriminatory performance was superior to exercise electrocardiography and stress echocardiography, and that very low concentrations had a high negative predictive value (NPV).

2. Methods

We included 430 patients examined with Single Positron Emission Computed Tomography (SPECT) from the prospective, observational Determining Optimal non-invasive Parameters for the Prediction of Left vEntricular morphologic and functional Remodeling in Chronic Ischemic Patients (DOPPLER-CIP) study [2,7]. DOPPLER-CIP was conducted at 10 centers from seven European countries and was designed to investigate different noninvasive parameters for the prediction of LV morphologic and functional remodeling in patients with CCS. Inclusion criteria were suspected coronary artery disease defined as history of angina, and/or > 15% risk of cardiovascular events according to the European risk SCORE [8], and/or a previous positive stress test according to the individual center's criteria. Patients with life-expectancy <2 years, acute coronary events during the last 3 months, moderate or severe valvular heart disease, pacemaker with predominant pacing rhythm or permanent atrial fibrillation were excluded. Patients unable to undergo exercise testing (treadmill or bicycle) were subjected to pharmacologic stress protocols.

By protocol, β-blockers were withdrawn before the SPECT study. Perfusion defects were quantified for each segment and calculated as summed rest score (SRS), summed stress score (SSS, immediately after stress) and summed difference score (SDS, difference from stress to rest). Dichotomized measures of hypoperfusion were defined as SRS ≥ 2, SSS ≥4 and SDS ≥ 2 according to the Cedars-Sinai scoring system. [9] Similarly, the regional wall motion summed score was assessed during rest (SRSWM), stress (SSSWM) and difference from stress to rest (SDSWM). SRSWM≥3, SSSWM≥4 and SDSWM≥3 was defined as hypokinesis [10].

All patients underwent exercise electrocardiography and a subset also had stress echocardiography performed ($n = 266$). Left ventricular (LV) mass ($n = 396$) was calculated from LV end diastolic dimension and wall thickness in parasternal long axis by echocardiography. LV ejection fraction ($n = 378$) was calculated from LV end diastolic and end systolic volumes by SPECT, and myocardial scar by gadolinium enhanced magnetic resonance imaging ($n = 256$).

Blood samples were drawn on inclusion, prior to the stress test. cTnT was measured from frozen samples stored at −80 °C by the high sensitivity STAT assay and NT-proBNP by the proBNP II assay on an Elecsys platform (Roche Diagnostics), with analytical range as previously reported [11] [12]. Spearman correlation and multivariable logistic regression including the following known determinants for cTnT and NT-proBNP: age, sex, body mass index, blood pressure, estimated glomerular filtration rate, history of diabetes, MI and coronary revascularization were used to assess associations with ischemia. Stratified analysis for patients with and without previous MI was performed. C-statistics was used to assess the discriminatory ability, and the diagnostic performance (sensitivity, specificity and NPV) and calculated for cTnT and NT-proBNP at prespecified thresholds in the lower range.

Table 1
Baseline characteristics by the presence of reversible hypoperfusion.

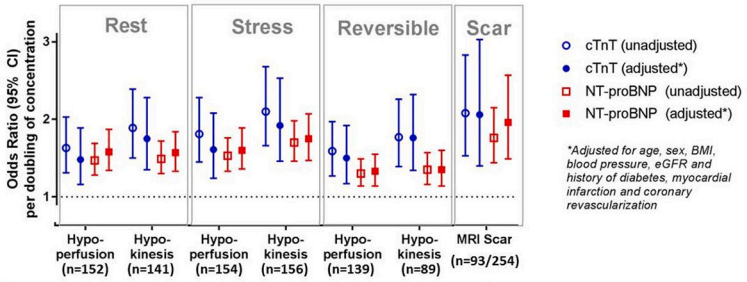
	No reversible hypoperfusion	Reversible hypoperfusion	
	n = 291 (68%)	*n = 139 (32%)*	*P*-value
Age (y)	63.8 ± 8.4	64.3 ± 8.5	0.55
Female gender	87 (29.9%)	22 (15.8%)	0.002
Body mass index (kg/m^2)	27.3 ± 3.6	27.6 ± 3.6	0.35
Smoking	38 (13.1%)	22 (15.8%)	0.45
Systolic blood pressure (mmHg)	138 ± 18	136 ± 20	0.52
Diastolic blood pressure (mmHg)	80 ± 10	79 ± 11	0.23
Heart rate (pr min)	68 ± 13	66 ± 10	0.06
NYHA class 3 or 4	41 (14.1%)	25 (18.0%)	0.29
Diabetes	37 (12.8%)	35 (25.2%)	0.001
Hypertension	176 (60.7%)	85 (61.2%)	0.93
Previous myocardial infarction	123 (42.4%)	76 (54.7%)	0.017
Previous coronary revascularization	141 (48.5%)	76 (54.7%)	0.23
Medications			
RASi	151 (51.9%)	87 (63.0%)	0.03
Nitrates	74 (25.4%)	53 (38.1%)	0.007
Aspirin	226 (77.7%)	125 (89.9%)	0.002
Statins	224 (77.0%)	116 (83.5%)	0.12
Cardiovascular Imaging			
LV end diastolic volume (ml)	105 ± 44	114 ± 41	0.06
LV ejection fraction (%)	57.3 ± 12.3	54.1 ± 11.3	0.016
LV mass (g)	193.9 ± 72.8	209.2 ± 59.1	0.041
Global longitudinal strain (%)	−16.8 ± 3.2	−16.5 ± 3.2	0.45
Left atrium dimension (mm)	41 ± 8	42 ± 7	0.27
E/e' ratio	10.0 ± 4.2	10.3 ± 4.4	0.5
Late gadolinium enhancement (CMR)	58 (32.4%)	35 (46.7%)	0.031
Circulating biomarkers			
Hemoglobin (g/dL)	143.3 ± 13.2	143.7 ± 12.3	0.79
Hemoglobin A1c (%)	5.6 ± 0.9	5.6 ± 0.9	0.78
White Blood Cell Count (x10^9/L)	7.2 ± 1.9	7.1 ± 2.4	0.92
LDL cholesterol (mmol/L)	2.6 ± 1.0	2.2 ± 0.8	<0.001
eGFR (mL/min/1.73m^2)	81.8 ± 15.9	82.3 ± 14.9	0.76

Abbreviations: NYHA = New York Heart Association; RASi = Renin-Angiotensin System inhibitor; LV = Left ventricular; CMR = Cardiac Magnetic Ressonance; LDL = Low-density lipoprotein; eGFR = estimate glomerular filtration rate.

3. Results

The 430 included patients were aged 64 ± 8 years, 25% were female and 46% had a previous MI. Reversible hypoperfusion (SDS ≥ 2) was present in 139 (32%) patients, and these were more often men ($p = 0.002$), had more diabetes ($p = 0.001$) and previous myocardial infarctions ($p = 0.02$), used more renin-angiotensin-system inhibitors ($p = 0.03$), nitrates ($p = 0.007$) and aspirin (p = 0.002) and had lower low-density lipoprotein-cholesterol ($p < 0.001$) than patients without reversible hypoperfusion (Table 1). Higher cTnT concentrations were associated with older age, male sex, higher BMI, worse renal function, diabetes, hypertension and previous MI. Higher NT-proBNP concentrations were associated with older age, worse renal function and previous MI. cTnT and NT-proBNP (median [IQR]) were higher in patients with versus without reversible hypoperfusion: 10 (6–13) versus 7 (4–11) ng/L and 150 (73–294) versus 87 (44–192) ng/L, respectively ($p < 0.001$ for both). cTnT and NT-proBNP correlated moderately (rho = 0.50, p < 0.001). Both biomarkers were associated with reversible and irreversible ischemia assessed by both hypoperfusion and hypokinesis, in addition to myocardial scar in unadjusted models, and after adjusting for age, sex,

A



ROC AUC

cTnT	0.64	0.68	0.66	0.70	0.63	0.66	0.73
NT-proBNP	0.67	0.67	0.68	0.72	0.63	0.64	0.72
P for difference	*0.35*	*0.82*	*0.55*	*0.57*	*0.80*	*0.55*	*0.93*

B

cTnT

		Reversible hypoperfusion			Reversible hypokinesis		
cTnT cut-off	N (%) below cut-off	Sens.	Spec.	NPV	Sens.	Spec.	NPV
4 ng/L	82 (19%)	91%	24%	85%	93%	22%	93%
5 ng/L	118 (27%)	86%	34%	83%	88%	31%	91%
6 ng/L	158 (37%)	76%	43%	79%	79%	41%	88%

NT-proBNP

		Reversible hypoperfusion			Reversible hypokinesis		
NT-proBNP cut-off	N (%) below cut-off	Sens.	Spec.	NPV	Sens.	Spec.	NPV
40 ng/L	82 (19%)	89%	23%	82%	93%	22%	93%
60 ng/L	124 (29%)	81%	33%	78%	89%	33%	92%
80 ng/L	139 (32%)	73%	48%	79%	79%	46%	89%

Fig. 1. Panel A. cTnT and NT-proBNP in association with reversible and irreversible ischemia.
Unadjusted and adjusted associations between cTnT, NT-proBNP as continuous variables and dichotomized measures of hypoperfusion and hypokinesis by Single Positron Emission Computed Tomography during rest, stress, difference from rest to stress; and myocardial scar by late gadolinium-enhanced magnetic resonance imaging in patients with suspected chronic coronary artery disease. Also shown is the C-statistics for cTnT and NT-proBNP in discriminating patients for each measure of ischemia.
Panel B. cTnT and NT-proBNP in ruling out myocardial ischemia.
Performance statistics of cardiac troponin T (cTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) at various thresholds for ruling out reversible hypoperfusion and reversible hypokinesis among patients with suspected chronic coronary artery disease.

body mass index, blood pressure, estimated glomerular filtration rate, history of diabetes, myocardial infarction and coronary revascularization (**Figure, Panel A**). These relationships remained significant after additional adjustment for LV mass and LV ejection fraction. Also, among the 161 patients free of myocardial scar on LGE CMR, both cTnT and NT-proBNP were higher in patients with versus without reversible perfusion defects and reversible hypokinesis, and these differences persisted in adjusted models.

The C-statistics discrimination between patients with- versus without ischemia ranged from 63%–73%, and were comparable for cTnT and NT-proBNP (P-for-difference $>$ 0.50 for all models; Fig. 1, **Panel A**). Both biomarkers performed better at discriminating hypokinesis than hypoperfusion and better at discriminating irreversible ischemia or scar than reversible ischemia. There was no improvement in C-statistics when adding cTnT to NT-proBNP, or vice versa ($P > 0.05$ for all models). The C-statistics for exercise electrocardiography and stress echocardiography were inferior to both biomarkers, ranging from 43%–56% and 52%–58%, respectively.

A stronger association between cTnT and ischemia, particularly hypokinesis, was observed in patients without compared to patients with previous MI: OR 2.36 (95%CI 1.55–3.57) vs OR 1.22 (95%CI 0.80–1.86), p-for-interaction = 0.03 for reversible hypokinesis and OR 2.31 (95%CI 1.54–3.46) vs OR 1.59 (95%CI 1.05–2.40), p-for-interaction = 0.09 for irreversible hypokinesis. The associations between NT-proBNP and ischemia were consistent in patients irrespective of previous MI (p-for-interaction>0.10 for all).

The performance of cTnT and NT-proBNP at different cut-offs for ruling out reversible hypoperfusion and reversible hypokinesis is presented in **Figure, Panel B**. Both biomarkers performed better for ruling out reversible hypokinesis, compared to hypoperfusion. Very low concentrations of either biomarker ($\leq$5 ng/L for cTnT [n = 118, 27%] and $\leq$ 60 ng/L for NT-proBNP [n = 124, 29%]) ruled out reversible hypokinesis with NPV 91% and 92% and reversible hypoperfusion with NPV 78% and 83%, respectively.

4. Discussion

Our findings suggest that cTnT and NT-proBNP are independently associated with myocardial ischemia in patients with suspected CCS, with comparable discriminatory performance, which was superior to exercise electrocardiography and stress echocardiography. Although cTnT and NT-proBNP correlated only moderately, their relationships with type of ischemia were comparable, and diagnostic performance was not enhanced by measuring both biomarkers.

We also provide novel insight to potential release mechanisms for cTnT and NT-proBNP by demonstrating a stronger association to hypokinesis and irreversible ischemia than hypoperfusion and reversible ischemia. Although our results suggest that reversible myocardial ischemia is a stimulus for release of cTnT and NT-proBNP independent of cardiac scarring and remodeling (LV mass and LV ejection fraction), the functional aspects of ischemia seem to be important for myocardial injury and stress. Furthermore, the association between cTnT and ischemia was stronger in patients without previous MI, suggesting that myocardial injury from post-MI cardiac remodeling complicates the interpretation of cTnT.

Both biomarkers were superior to exercise electrocardiography and stress echocardiography in detecting ischemia defined by SPECT. Still, the clinical implication of these findings does not suggest that cTnT and NT-proBNP should be used to diagnose ischemia in CCS given the only modest performance in discriminating patients. However, very low concentrations of cTnT and NT-proBNP may help the clinician to *rule out* ischemia when added to clinical evaluation. Although such concentrations only were present in about ¼ of patients, this strategy may be useful in selecting patients for further testing. This strategy is in agreement with findings from the large PROMISE trial, where cTn was not only associated with higher coronary artery calcium score in a population with suspected coronary artery disease [13], but patients in the lowest cTn-quartile had significantly lower 1-year risk of MI, UAP or death (0.8%) compared to the higher quartiles (1.5%, 2.4% and 3.2%, respectively) [14]. In patients presenting to the emergency department with suspected ACS, but who had MI excluded, CAD was 3-fold more prevalent in those with moderately elevated cTnI, compared to those with low concentrations (<5 ng/L) [15]. Thus, measurements of cardiac biomarkers integrated with thorough clinical assessment may be a readily available, low-cost strategy in managing patients with suspected coronary syndromes.

This study has limitations including a modest sample size, lack of information on which of the inclusion criteria the patients were enrolled

through and lack of follow-up data with respect to subsequent coronary angiography or optimization of medical therapy. The use of SPECT as the gold standard for ischemia is also a potential limitation.

5. Conclusion

cTnT and NT-proBNP are associated with irreversible and reversible ischemia in patients with suspected CCS. The diagnostic performance was comparable between the biomarkers, and very low concentrations may have a role in ruling out ischemia. Both biomarkers were more strongly associated with hypokinesis than hypoperfusion. These data support the use of cardiac biomarker in the management of patients with suspected CCS.

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Disclosures

Dr. Myhre has served on advisory boards and consulted for AmGen, AstraZeneca, Boehringer-Ingelheim, Novartis and Novo Nordisk, and received honoraria for this. Dr. Røsjø has received consultancy honoraria from SpinChip Diagnostics, Thermo Fisher BRAHMS and Cardinor AS. Dr. Omland has received consultancy and/or speaker honoraria from Abbott Diagnostics, Siemens Healthineers, Roche Diagnostics, and has received research support from AstraZeneca, Abbott Diagnostics, Novartis, Roche Diagnostics, and SomaLogic via Akershus University Hospital. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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References

[1] K. Bibbins-Domingo, M. Ansari, N.B. Schiller, B. Massie, M.A. Whooley, B-type natriuretic peptide and ischemia in patients with stable coronary disease: data from the Heart and Soul study, Circulation. 108 (2003) 2987–2992.
[2] P.L. Myhre, T. Omland, S.I. Sarvari, H. Ukkonen, F. Rademakers, J.E. Engvall, et al., Cardiac troponin T concentrations, reversible myocardial ischemia, and indices of left ventricular remodeling in patients with suspected stable angina pectoris: a DOPPLER-CIP substudy, Clin. Chem. 64 (2018) 1370–1379.
[3] T. Omland, J.A. de Lemos, M.S. Sabatine, C.A. Christophi, M.M. Rice, K. A. Jablonski, et al., A sensitive cardiac troponin T assay in stable coronary artery disease, N. Engl. J. Med. 361 (2009) 2538–2547.
[4] T. Omland, M.S. Sabatine, K.A. Jablonski, M.M. Rice, J. Hsia, R. Wergeland, et al., Prognostic value of B-type natriuretic peptides in patients with stable coronary artery disease: the PEACE trial, J. Am. Coll. Cardiol. 50 (2007) 205–214.
[5] K. Thygesen, J.S. Alpert, A.S. Jaffe, B.R. Chaitman, J.J. Bax, D.A. Morrow, et al., Fourth universal definition of myocardial infarction (2018), Circulation. 138 (2018) e618-e51.
[6] J.L. Januzzi Jr., C.A. Camargo, S. Anwaruddin, A.L. Baggish, A.A. Chen, D. G. Krauser, et al., The N-terminal Pro-BNP investigation of dyspnea in the emergency department (PRIDE) study, Am. J. Cardiol. 95 (2005) 948–954.
[7] F. Rademakers, J. Engvall, T. Edvardsen, M. Monaghan, R. Sicari, E. Nagel, et al., Determining optimal noninvasive parameters for the prediction of left ventricular remodeling in chronic ischemic patients, Scand. Cardiovasc. J. 47 (2013) 329–334.
[8] R.M. Conroy, K. Pyorala, A.P. Fitzgerald, S. Sans, A. Menotti, G. De Backer, et al., Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project, Eur. Heart J. 24 (2003) 987–1003.
[9] R. Hachamovitch, S.W. Hayes, J.D. Friedman, I. Cohen, D.S. Berman, Stress myocardial perfusion single-photon emission computed tomography is clinically effective and cost effective in risk stratification of patients with a high likelihood of coronary artery disease (CAD) but no known CAD, J. Am. Coll. Cardiol. 43 (2004) 200–208.
[10] L. Emmett, R.M. Iwanochko, M.R. Freeman, A. Barolet, D.S. Lee, M. Husain, Reversible regional wall motion abnormalities on exercise technetium-99m–gated cardiac single photon emission computed tomography predict high-grade angiographic stenoses, J. Am. Coll. Cardiol. 39 (2002) 991–998.
[11] E. Giannitsis, K. Kurz, K. Hallermayer, J. Jarausch, A.S. Jaffe, H.A. Katus, Analytical validation of a high-sensitivity cardiac troponin T assay, Clin. Chem. 56 (2010) 254–261.
[12] K.-T.J. Yeo, A.H.B. Wu, F.S. Apple, M.H. Kroll, R.H. Christenson, K. B. Lewandrowski, et al., Multicenter evaluation of the Roche NT-proBNP assay and comparison to the biosite triage BNP assay, Clin. Chim. Acta 338 (2003) 107–115.
[13] J.L. Januzzi Jr., S. Suchindran, A. Coles, M. Ferencik, M.R. Patel, U. Hoffmann, et al., High-sensitivity troponin I and coronary computed tomography in symptomatic outpatients with suspected CAD: insights from the PROMISE trial, J. Am. Coll. Cardiol. Img. 12 (2019) 1047–1055.
[14] J.L. Januzzi, S. Suchindran, U. Hoffmann, M.R. Patel, M. Ferencik, A. Coles, et al., Single-molecule hsTnI and short-term risk in stable patients with chest pain, J. Am. Coll. Cardiol. 73 (2019) 251–260.
[15] K.K. Lee, A. Bularga, R. O'Brien, A.V. Ferry, D. Doudesis, T. Fujisawa, et al., Troponin-guided coronary computed tomographic angiography after exclusion of myocardial infarction, J. Am. Coll. Cardiol. 78 (2021) 1407–1417.