Biomarkers, 2010; 15(4): 325–331

informa
healthcare

ORIGINAL ARTICLE

Procalcitonin as a prognostic marker in patients with acute myocardial infarction

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Abstract

Background: Procalcitonin is involved in the inflammatory response and is associated with adverse prognosis in certain conditions.

Aims: To investigate the association between procalcitonin and major adverse cardiac events (MACE), left ventricular (LV) function and remodelling following acute myocardial infarction (AMI).

Methods: Plasma procalcitonin was measured in 977 patients with AMI. Subjects were followed for MACE (median 671 days). A subgroup underwent echocardiography at discharge and follow-up LV function and volume assessment.

Results: Procalcitonin was associated with MACE on uni- and multivariable analysis. Kaplan–Meier assessment revealed an adverse outcome in subjects with procalcitonin above the median. Procalcitonin was related to markers of LV dysfunction and remodelling.

Conclusion: Procalcitonin is associated with MACE, LV dysfunction and remodelling post-AMI.

Keywords: *Myocardial infarction; heart failure; biomarkers; procalcitonin*

Introduction

Risk stratification following acute myocardial infarction (AMI) has an important role in helping to select treatment regimes for patients. Current tools available to clinicians include clinical factors, which are incorporated into scoring systems such as the Global Registry of Acute Coronary Events (GRACE) or Thrombolysis In Myocardial Infarction (TIMI) risk scores. Biochemical markers such as troponins and more recently B-type natriuretic peptide (BNP) are also useful and give important prognostic information. Procalcitonin (PCT) is a 116-amino acid polypeptide precursor of calcitonin (Maruna et al. 2000) and is raised in several conditions associated with bacterial infections, such as sepsis (Schuetz et al. 2007, Charles et al. 2008) and also postcardiac surgery (Sponholz et al. 2006). The pathophysiological significance of PCT in cardiovascular disease is poorly described. As AMI is itself associated with an inflammatory response it may be expected that PCT may be elevated in this setting. Senturk et al. (2007) investigated PCT levels in subjects with acute coronary syndromes, but no association could be demonstrated between PCT levels and severity of disease or prognosis. Remskar et al. (2002) have shown PCT to remain low in uncomplicated AMI while being raised in those subjects with pulmonary oedema, cardiogenic shock or in those with concomitant bacterial infection. Kafkas et al. (2008) recently described the temporal profile of PCT release post-AMI and showed correlations with known prognostic markers such as interleukin (IL)-6 and C-reactive protein (CRP). No previous studies have investigated the relationship between PCT and outcome following MI and previous studies employed relatively insensitive PCT assays.

The aim of the current study was to investigate the association between PCT, measured using an

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(Received 18 December 2009; revised 03 February 2010; accepted 03 February 2010)

ISSN 1354-750X print/ISSN 1366-5804 online © 2010 Informa UK Ltd
DOI: 10.3109/13547501003675084

ultrasensitive assay, and the occurrence of major adverse cardiac events (MACE) following AMI. We also assessed the relationship between PCT and markers of left ventricular (LV) function and subsequent remodelling in a subgroup of subjects.

Methods

Subjects and setting

We conducted a prospective, cohort study enrolling 977 patients with AMI admitted to the coronary care units (CCU) of the University Hospitals of Leicester NHS Trust between 1 March 2000 and 30 April 2007. The hospitals provide emergency and elective care for a catchment population of approximately 940 000. The diagnosis was based on admitting symptoms consistent with AMI in conjunction with appropriate, dynamic ECG changes (ST segment elevation, STEMI, 79.8%) or ST segment/T wave changes (NSTEMI, 20.2%) and elevation in plasma markers of myocardial necrosis (creatine kinase or troponin I). We excluded patients with coexisting illness likely to alter PCT levels such as sepsis. No subjects suffered AMI as a consequence of cocaine abuse. Venous blood was sampled immediately prior to discharge from hospital following the index admission for the assay of plasma PCT concentration (median 5 days). The predefined primary outcome measure was the composite of all-cause mortality, recurrent MI or heart failure episode during follow-up (median 671 (range 1–2837 days). Heart failure episode was defined as an unplanned hospital admission (>12 h) for which the primary reason was clinical heart failure requiring high-dose diuretic (>40 mg i.v. furosemide), intravenous nitrate or inotropic support. Secondary outcomes were the individual components of the primary outcome. Clinical endpoints were identified through the hospital patient tracking system, with review of medical records for each endpoint. Checks were made by telephone contact with all surviving patients at the end of the study to ensure complete capture of all events. The local research ethics review committee approved the study and all patients gave written consent to participation. The conduct of the study was in keeping with the declaration of Helsinki.

Echocardiographic assessment

Detailed echocardiographic examination was performed in a subset of 273 subjects (215 STEMI and 58 NSTEMI) immediately prior to discharge and at 4 months post-event (median time to follow-up echo of 155 days (range 124–378)) by a single operator (D.K.) using a Sonos 5500 or IE33 scanner (Philips Medical Systems, Reigate, UK). Subjects who died prior to follow-up echocardiography were excluded from the echocardiographic remodelling assessment. LV end systolic volume (LVESV), LV end diastolic volume (LVEDV) and LV ejection fraction (LVEF) were estimated using the biplanar modified Simpson's rule from apical 2- and 4-chamber views. LV wall motion index score (WMIS) was measured using a standard 16-segment model from parasternal long and short axis and apical 2- and 4-chamber views.

The degree of ventricular remodelling after AMI was assessed from the change in LVEDV (ΔEDV) and LVESV (ΔESV) between predischarge and follow-up examinations, expressed as a percentage of the predischarge measurement.

When assessing remodelling, we considered data pertaining only to patients with adequate echocardiographic examinations both predischarge and at follow-up. Intraobserver variation, assessed in a subset ($n = 45$; mean ± SD) was 0.36% ± 1.75 for WMIS, 5.2% ± 3.9 for EDV, 6.0% ± 6.6 for ESV and 6.7% ± 7.6 for LVEF. Pearson's correlation between analyses were all >0.9, $p < 0.001$. Investigators were blinded to the results of PCT assays at the time of echo interpretation.

Laboratory methods

PCT was measured with a novel highly sensitive commercial assay (BRAHMS PCT sensitive LIA; B.R.A.H.M.S. AG, Hennigsdorf, Germany) as described (Morgenthaler et al. 2002). Briefly, tubes were coated with a monoclonal antibody directed against the katacalcin moiety of PCT. A purified sheep polyclonal antibody directed against the calcitonin moiety of PCT was labelled with MACN-acridinium-NHS-ester (InVent GmbH, Braunschweig, Germany) and used as a tracer. Dilutions of a recombinant PCT variant in normal horse serum served as standards. The immunoassay was performed by incubating 100 µl of samples/standards in the tubes for 30 min, followed by the addition of 200 µl tracer and an incubation of 2 h at room temperature. Tubes were washed four times with 1 ml of LIA wash solution (B.R.A.H.M.S. AG), and bound chemiluminescence was measured using a LB952T luminometer (Berthold, Bad Wildbad, Germany). The lower detection limit of the assay was 6 pg ml^{-1} and the interassay CV was 8% at 30 pg ml^{-1} and 6% at 100 pg ml^{-1}.

Statistical analysis

For all variables with non-Gaussian distribution (PCT, creatine kinase, troponin I, WMIS), log-transformed values were used in analyses. The association of PCT levels with categorical variables was assessed using the paired *t*-test or Mann–Whitney *U* test for non-parametric data, and with continuous variables using Pearson's correlation coefficient. Differences between groups experiencing or not experiencing each clinical endpoint were

assessed using χ^2 analysis for categorical variables and Mann–Whitney *U* test for continuous variables. For each patient, the GRACE score, a measure of risk of adverse outcome based upon clinical variables (Eagle et al. 2004) was calculated. Factors included in the GRACE score are: patient age, heart rate at presentation, systolic blood pressure, creatinine, Killip class, cardiac arrest at admission, ST segment deviation and elevation of cardiac enzymes. Factors with univariate association with each endpoint at significance level of $p < 0.1$ were entered into a multivariable Cox proportional hazards model. The strength of association with endpoints is expressed as a hazards ratio (HR) per log-transformed unit increase in plasma concentration of PCT. When considering the primary endpoint of death or heart failure we assessed time to first event.

Median values of PCT for the whole population were calculated and used as a cut-off point to predict adverse outcome using the Kaplan–Meier assessment. For all analyses, $p < 0.05$ was regarded as significant and two-sided tests were used where appropriate. Statistical analyses were carried out using SPSS version 14. The authors had full access to the data, accept responsibility for their validity, and have read and agreed to the manuscript as submitted.

Results

Admission demographic features of the study population are shown in Table 1. Approximately 73% of the patients were male, median creatine kinase was 628 IU l^{-1}. Seven hundred and eighty patients (79.8%) presented with STEMI, of whom 539 (69%) received thrombolytic therapy with intravenous streptokinase or tenecteplase. No patient received primary percutaneous revascularization.

Medications at discharge are shown in Table 1. Compared with NSTEMI, STEMI subjects were younger and fewer had a previous history of hypertension. At discharge aspirin, angiotensin-converting enzyme inhibitors/angiotensin-receptor blocker (ACE-I/ARB) and statin use was higher in subjects with STEMI whereas diuretic use was lower. There was no difference in PCT levels between STEMI versus NSTEMI groups.

No patient was lost to clinical follow-up over a median of 671 (range 1–2837) days. During follow-up a total of 246 patients underwent revascularization (coronary artery bypass or percutaneous transluminal coronary angioplasty). For patients alive at the end of the study, minimum follow-up was 125 days with a range of 125–2837.

Predictors of plasma PCT

Predischarge PCT correlated with patient age ($r = 0.275$, $p < 0.001$), GRACE risk score ($r = 0.385$, $p < 0.001$) and admission serum glucose ($r = 0.263$, $p < 0.001$) and was inversely correlated to estimated glomerular filtration rate (eGFR) ($r = -0.355$, $p < 0.001$). Levels were higher in females versus males (median 45.0 vs 35.0 pg ml^{-1}, $p < 0.001$) and in subjects with a previous history of hypertension (39.0 vs 35.0 pg ml^{-1}, $p = 0.014$), MI (42.5

Table 1. Population demographics at admission.

	All patients	STEMI	NSTEMI	*p*-Value
Number	977	780	197	
Age (years) (range)	66 (24–97)	65(24–95)	69 (38–93)	**0.002**
Male, *n* (%)	716 (73.3)	575 (73.7)	141 (71.6)	0.543
Previous medical history, n (%)				
Diabetes, *n* (%)	213 (21.8)	171 (21.9)	42 (21.3)	0.848
Hypertension, *n* (%)	427 (43.7)	319 (40.9)	108 (54.8)	**<0.001**
Previous MI, *n* (%)	164 (16.8)	123 (15.8)	41 (20.8)	0.091
STEMI, *n* (%)	780 (79.8)	–	–	–
Anterior territory, *n* (%)	414 (42.4)	308 (39.5)	–	–
Thrombolysis, *n* (%)	539 (55.2)	539 (69.1)	–	–
Current smoker, *n* (%)	613 (62.7)	494 (63.3)	119 (60.4)	0.415
Peak CK (range)	628 (21–9523)	807 (21–9523)	244 (35–3118)	
Troponin I (range)	6.8 (0.02150)	10.3 (0.06–150)	1.74 (0.02–59.8)	
eGFR (range)	67.7 (14.9–166)	67.9 (26.2–166.0)	65.5 (14.9–115.8)	
Medications				
Aspirin, *n* (%)	877 (89.8)	710 (91.0)	167 (84.8)	**0.010**
Beta-blocker, *n* (%)	768 (78.6)	622 (79.7)	146 (74.1)	0.079
ACE-I/ARB, *n* (%)	689 (70.5)	584 (74.9)	105 (53.3)	**<0.001**
Statin, *n* (%)	690 (70.6)	567 (72.7)	123 (62.4)	**0.005**
Furosemide, *n* (%)	329 (33.7)	251 (32.2)	78 (39.6)	**0.05**

CK, creatine kinase; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

vs 36.0 pg ml^{-1}, $p = 0.017$) or diabetes mellitus (47.0 vs 34.0 pg ml^{-1}, $p < 0.001$). There was no association with peak creatine kinase ($r = 0.082$) or troponin ($r = -0.11$) and their levels were similar between STEMI versus NSTEMI (36.0 vs 39.0 pg ml^{-1}, $p = 0.396$) or between anterior versus inferior territory infarcts (36.5 vs 37.0 pg ml^{-1}, $p = 0.728$).

Echocardiographic assessment

Echocardiographic analysis was conducted in a subgroup of subjects ($n = 273$). Of subjects undergoing echo analysis, prior to discharge, LVEF and WMIS were measurable in 237 (86.8%) and 240 (87.9%) of patients, respectively. Forty-two subjects did not attend for follow-up echocardiography (22 deaths, 20 refused) with LVEF and WMIS available in 207 (89.6%) and 205 (88.7%), respectively. Prior to discharge median WMIS was 1.31 (range 1–2.69) falling to 1.19 (range 1–2.63) at follow-up and median LVEF was 43% (range 12–78) increasing to 47% (range 10–82). LV end diastolic and systolic volumes were 91 ml (range 29–263) and 49 ml (range 13–223), respectively, prior to discharge and 89 ml (29–252) and 46 ml (13–223) at follow-up. Correlation between plasma PCT and echocardiographic markers prior to discharge and at follow-up are shown in Table 2. Prior to discharge PCT showed a weak association with LV dysfunction with inverse correlation with LVEF and direct correlation with WMIS. At follow-up echo PCT again showed a weak association with LV dysfunction with inverse and direct correlations with LVEF and WMIS, respectively. PCT was also associated with LV volumes at this time. In addition PCT held some association with the degree of change in LV volumes between discharge and follow-up with correlation with ΔESV ($r = 0.145$, $p = 0.039$).

Table 2. Correlation between plasma procalcitonin and echocardiographic markers prior to discharge and at follow-up.

	LVEF	WMIS	LVEDd	LVESd	LVEDV	LVESV
Prior to discharge						
Correlation (r)	−0.20	0.20	0.004	0.054	0.074	0.153
Significance (p)	0.003	0.002	0.943	0.395	0.249	0.017
At follow-up						
Correlation (r)	−0.286	0.233	0.029	0.137	0.139	0.244
Significance (p)	<0.001	0.001	0.670	0.047	0.04	<0.001

LVEF, left ventricular ejection fraction; WMIS, wall motion index score; LVESV, LV end systolic volume; LVEDV, LV end diastolic volume.

Clinical endpoints

During follow-up 200 (20.4%) patients died, 127 (13.0%) suffered a further MI and 82 (8.4%) experienced a heart failure episode. Overall 336 (34.4%) patients reached the combined primary endpoint of death, MI or heart failure episode.

Primary endpoint: association of PCT with MACE (death, recurrent MI or heart failure episode)

Factors showing univariable association ($p < 0.1$) and biological plausibility with the primary endpoint (Table 3) were entered into multivariable Cox proportional hazards analyses for the prediction of outcome. Factors with independent association with MACE were GRACE risk score (HR per unit increase 1.01, 95% CI 1.01–1.02, $p < 0.001$) and a previous history of hypertension (HR 1.29, 95% CI 1.03–1.61, $p = 0.027$) or diabetes mellitus (HR 1.39, 95% CI 1.07–1.80, $p = 0.013$). Log-PCT retained independent association with our primary outcome (HR per unit increase in log-transformed PCT 1.39, 95% CI 1.13–1.71, $p = 0.002$).

On Kaplan–Meier assessment subjects with PCT above the median value (37.0 pg ml^{-1}) had a significantly worse prognosis (log rank 27.43, $p < 0.001$) (Figure 1).

Table 3. Univariable and multivariable Cox proportional hazards regression for major adverse cardiac events in all subjects.

	Univariable analysis		Multivariable analysis	
	Hazard ratio (95% CI)	p-Value	Hazard ratio (95% CI)	p-Value
Male	0.74 (0.59–0.92)	**0.008**	1.0 (0.77–1.29)	0.977
Previous medical history				
AMI	2.13 (1.66–2.71)	**<0.001**	1.24 (0.97–1.58)	0.806
Hypertension	1.56 (1.26–1.93)	**<0.001**	1.39 (1.09–1.76)	**0.007**
Diabetes	1.79 (1.42–2.26)	**<0.001**	1.39 (1.07–1.80)	**0.013**
Smoking	0.74 (0.59–0.92)	**0.006**	0.84 (0.66–1.07)	0.154
Anterior MI	1.07 (0.87–1.33)	0.515	–	
STEMI	0.96 (0.74–1.24)	0.756	–	
Revascularization	1.13 (0.84–1.53)	0.413	–	
GRACE score	1.01(1.01–1.02)	**<0.001**	1.01 (1.01–1.02)	**<0.001**
ACE-1/ARB	0.97 (0.78–1.23)	0.824	–	
Beta-blocker	0.53 (0.42–0.67)	**<0.001**	0.90 (0.68–1.18)	0.428
Log PCT	1.98 (1.67–2.34)	**<0.001**	1.39 (1.13–1.71)	**0.002**

MI, myocardial infarction; GRACE, Global Registry of Acute Coronary Events; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; PCT, procalcitonin.

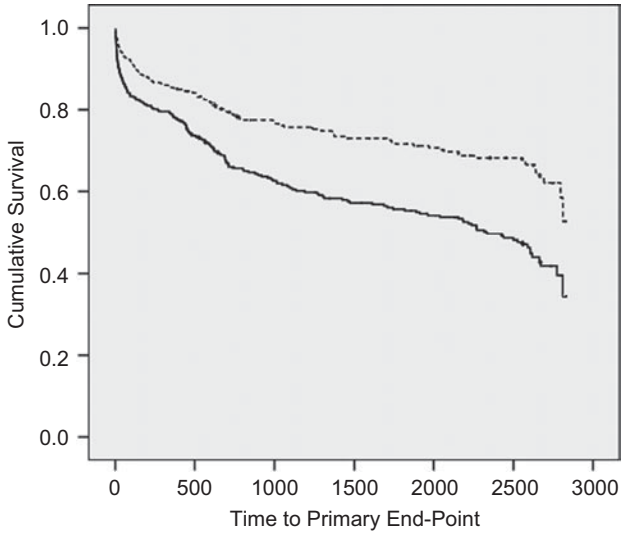

Figure 1. Kaplan–Meier survival curves for subjects stratified by procalcitonin (PCT) above (complete line) versus below (dotted line) the median value – all subjects.

Secondary endpoints: PCT as predictor of death, recurrent MI or heart failure episode as individual endpoints

Considering the individual components of the endpoint, on Cox regression analysis PCT retained association with death (HR 1.50, 95% CI 1.16–1.95, $p = 0.001$). Other factors with independent association with death were GRACE risk score (HR 1.02, 95% CI 1.01–1.02, $p < 0.001$), previous history of myocardial infarction (HR 1.43, 95% CI 1.04–1.96, $p = 0.03$) and beta-blocker usage prior to admission (HR 0.68, 95% CI 0.48–0.87, $p = 0.024$).

Recurrent MI was associated with a history of diabetes mellitus (HR 1.77, 95% CI 1.18–2.63, $p = 0.05$) or hypertension (HR 1.52, 95% CI 1.05–2.19, $p = 0.025$) and beta-blocker usage prior to admission (HR 1.93, 95% CI 1.52–3.39, $p = 0.021$). There was no independent association between PCT and recurrent MI.

Heart failure episode was associated with GRACE risk score (HR 1.01, 95% CI 1.01–1.02, $p < 0.001$) and previous history of diabetes (HR 1.70, 95% CI 1.02–2.81, $p = 0.04$). There was no independent association between PCT and heart failure episodes.

Discussion

Our study demonstrates the potential use of a new prognostic marker after AMI, PCT. While PCT is known to be elevated in subjects with systemic inflammation, especially if associated with bacterial infections, its role in cardiovascular disease is poorly understood. AMI invokes an acute inflammatory response with elevation in markers such as CRP and IL-6 (Buratti et al 2001). While previous studies have also shown PCT to be elevated post-AMI (Remskar et al 2002, Kafkas et al 2008, Senturk et al 2007) interpretation of these studies is difficult, as barely quantifiable PCT concentrations were reported. Our use of an ultrasensitive assay allows us to report a relationship between PCT and the occurrence of MACE post-AMI. The concentrations of PCT in our population of post-MI patients are considerably lower compared with patients with sepsis, but still allow risk stratification after AMI. Subjects with PCT levels above the median have an almost 50% higher relative risk of MACE at 12 months post-MI. In addition this association persists in the long term, with continued separation of the Kaplan–Meier curves to at least 5 years. Moreover maintenance of the relationship between PCT and adverse outcome when incorporated into a robust multifactorial Cox proportional hazards model including the well-validated, GRACE risk score indicates that PCT adds additional information above many clinical factors.

Analysis of the secondary outcomes demonstrates that PCT is predominantly associated with patient death during follow-up. There was no significant association seen with either recurrent MI or heart failure episode. The lack of relationship with heart failure is perhaps surprising in view of previous studies suggesting that PCT is raised in subjects with complications of MI such as pulmonary oedema or cardiogenic shock (Remskar et al. 2002). However in this previous study, this relationship was most powerful in subjects with concomitant sepsis. Our echocardiographic subgroup analysis observes a relationship between PCT and LV volumes, function and remodelling; it must be noted that these relationships are relatively weak and require further investigation in further studies. It may be suggested that the weak associations seen between PCT and LV function and LV remodelling may be due to the imaging modality used in this study. Echocardiography is a readily available technique used in most cardiac centres. The data provided are limited by factors such as patient obesity and airways disease. The use of other modalities such as cardiac MRI in determining the association between PCT and post-MI ventricular remodelling would provide more accurate and reproducible data and should be the aim of future studies.

The pathophysiological mechanisms linking PCT with adverse outcome are likely to be multifactorial. PCT may be stimulated by several cytokines involved in the acute inflammatory response (Nijsten & Hoekstra 2001). This is mediated by inflammatory response elements within the CALC gene promoter leading to induction of PCT mRNA and hence production of PCT. Once expressed, PCT may lead to modulation of the inducible nitric oxide synthase (iNOS) pathway. Indeed Hoffman *et al.* have suggested that PCT inhibits the iNOS-inducing effects of the proinflammatory cytokines tumour necrosis factor (TNF)-α/interferon (IFN)-γ in a dose-dependent

manner (Hoffmann et al. 2001). These interactions with the iNOS pathway are likely to lead to downstream effects on ischaemic reperfusion injury and late preconditioning. In addition, PCT may act competitively via the calcitonin gene-related peptide receptor leading to alterations in cardiac contractility and vascular tone (Katori et al. 2005).

Our data have several important clinical implications. First, we demonstrate a potential biomarker in prognostication post-AMI. Identification of subjects at risk of adverse outcome is of utmost importance. This identification may steer patient management potentially leading to more aggressive therapy for those at high risk. It is unlikely that PCT alone would have sufficient sensitivity and specificity to be used as a prognostic biomarker alone; however it may add additional data to a multivariable approach to patient assessment, e.g. in combination with the GRACE score.

In addition PCT may represent a potential therapeutic target to improve outcomes. Indeed if our observation of an association with LV remodelling was to be corroborated in further studies we suggest that PCT inhibition may prevent LV dysfunction and remodelling in the post-MI period and this inhibition may hence translate to improved patient prognosis. Indeed PCT neutralization has been shown to be feasible and of benefit in sepsis as a method of manipulating the acute inflammatory response (Martinez et al 2001). However no studies to date have investigated PCT neutralization in the context of acute coronary syndromes.

We acknowledge that our study does have several limitations. We performed a single-centre study and as such we cannot extrapolate our data to other populations and further multicentre studies are required to validate our findings. Our cohort included a high percentage of STEMI which reflects our CCU admission criteria; however, we do not present data regarding success of reperfusion therapy which may influence prognosis. In addition our unit did not provide primary percutaneous coronary intervention at the time of these studies, and validation of similar results should be sought in such a population. We acknowledge the relatively low correlation coefficient between PCT and our echocardiographic markers. However our data are internally consistent and low correlation coefficients are common in the 'real-life' situation. In addition we also acknowledge the limitations of transthoracic echocardiography in such a situation with adequate echocardiographic data being absent in a percentage of our subjects. Also follow-up echocardiographic data are absent in those subjects who died prior to this point but it may be hypothesized that these subjects were likely to have the greatest degree of LV remodelling and their loss only dilutes any potential observations. Our echo data were interpreted by a single reader and although intraobserver variability was low may account for a degree of error. Further studies using more accurate measures of LV function such as cardiac MRI or the use of echocardiographic contrast agents to improve LV wall visualization may be warranted.

We acknowledge that differences in pharmacological therapy may bias results. However prior to admission few subjects were receiving cardiovascular medications and therapy at discharge was relatively uniform within infarct groups. We do not present data on therapy at follow-up which again may influence our findings. Further studies investigating the association of PCT immediately after admission may also demonstrate a potential use in early risk stratification and should be encouraged.

In summary we have described the relationship between PCT and adverse prognosis post-AMI. In addition we have seen a weak but statistically significant association with LV function and remodelling in the post-MI period. We propose that PCT may have clinical implications in the identification of subjects at risk post-MI and as a potential therapeutic target. We suggest that further investigation into the role of PCT post-MI is warranted based on our findings.

Acknowledgements

This study was supported by research grants from the Brandenburg Ministry of Economics, Germany and the European Regional Development Fund (EFRE/ERDF).

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

Buratti T, Ricevuti G, Pechlaner C, Joannidis M, Wiedermann FJ, Gritti D, Herold M, Wiedermann CJ. (2001). Plasma levels of procalcitonin and interleukin-6 in acute myocardial infarction. *Inflammation* 25:97–100.

Charles PE, Ladoire S, Aho S, Quenot JP, Doise JM, Prin S, Olsson NO, Blettery B. (2008). Serum procalcitonin elevation in critically ill patients at the onset of bacteremia caused by either gram negative or gram positive bacteria. *BMC Infect Dis* 8:38.

Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger CB, Steg PG, Gore JM, Budaj A, Avezum A, Flather MD, Fox KA. (2004). A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *JAMA* 291:2727–33.

Hoffmann G, Totzke G, Seibel M, Smolny M, Wiedermann FJ, Schobersberger W. (2001). *In vitro* modulation of inducible nitric oxide synthase gene expression and nitric oxide synthesis by procalcitonin. *Crit Care Med* 29:112–16.

Kafkas N, Venetsanou K, Patsilinakos S, Voudris V, Antonatos D, Kelesidis K, Baltopoulos G, Maniatis P, Cokkinos DV. (2008). Procalcitonin in acute myocardial infarction. *Acute Card Care* 10:30–6.

Katori T, Hoover DB, Ardell JL, Helm RH, Belardi DF, Tocchetti CG, Forfia PR, Kass DA, Paolocci N. (2005). Calcitonin gene-related peptide *in vivo* positive inotropy is attributable to regional sympatho-stimulation and is blunted in congestive heart failure. *Circ Res* 96:234–43.

Martinez JM, Wagner KE, Snider RH, Nylen ES, Muller B, Sarani B, Becker KL, White JC. (2001). Late immunoneutralization of procalcitonin arrests the progression of lethal porcine sepsis. *Surg Infect (Larchmt)* 2:193–202; discussion 202-3

Maruna P, Nedelnikova K, Gurlich R. (2000). Physiology and genetics of procalcitonin. *Physiol Res* 49 (Suppl. 1):S57–61.

Morgenthaler NG, Struck J, Fischer-Schulz C, Bergmann A. (2002). Sensitive immunoluminometric assay for the detection of procalcitonin. *Clin Chem* 48:788–90.

Nijsten MW, Hoekstra OP. (2001). *In vitro* and *in vivo* stimulation of procalcitonin by TNF alpha and IL-6. *J Anasthesie Intensivtherapie* 2:58–60.

Remskar M, Horvat M, Hojker S, Noc M. (2002). Procalcitonin in patients with acute myocardial infarction. *Wien Klin Wochenschr* 114:205–10.

Schuetz P, Mueller B, Trampuz A. (2007). Serum procalcitonin for discrimination of blood contamination from bloodstream infection due to coagulase-negative staphylococci. *Infection* 35:352–5.

Senturk T, Cordan J, Baran I, Ozdemir B, Gullulu S, Aydinlar A, Goral G. (2007), Procalcitonin in patients with acute coronary syndrome: correlation with high-sensitive C-reactive protein, prognosis and severity of coronary artery disease. *Acta Cardiol* 62:135–41.

Sponholz C, Sakr Y, Reinhart K, Brunkhorst F. (2006). Diagnostic value and prognostic implications of serum procalcitonin after cardiac surgery: a systematic review of the literature. *Crit Care* 10:R145.