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Oxidative stress and inflammatory response during and following coronary interventions for acute myocardial infarction

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Abstract

Background: In acute myocardial infarction (AMI) treated with percutaneous coronary intervention (PCI), myocardial injury results from complex processes during both ischemia and reperfusion. Release of reactive oxygen species (ROS) may contribute to the accumulated myocardial damage.

Aims: To examine by frequent sampling of peripheral blood oxidative stress and early inflammation in patients undergoing primary PCI for AMI. Secondly, to assess whether a correlation exists between these parameters and the extent of myocardial damage.

Methods: Sixteen patients undergoing primary PCI within 6 h of AMI onset were included. Peripheral blood was sampled at start of procedure (t_0) and repeatedly over 24 h following reperfusion. Main plasma analyses were: 8-iso-$PGF_{2\alpha}$ (oxidative stress), 15-keto-dihydro-$PGF_{2\alpha}$ (cyclooxygenase-mediated inflammation); and troponin-T (myocardial injury). Additional analyses included: total antioxidant status (TAS); vitamins; hsCRP and lipids.

Results: 8-Iso-$PGF_{2\alpha}$ increased following restoration of blood flow, returned to t_0 values after 3 h and was reduced below t_0 the following day. TAS decreased significantly from t_0 to the next day. There was no significant correlation between 8-iso-$PGF_{2\alpha}$ and troponin T values. 15-Keto-dihydro-$PGF_{2\alpha}$ was elevated during the first hour. There was a major rise in hsCRP after 24 h.

Conclusion: Following reperfusion by primary PCI in AMI, oxidative stress and an inflammatory response are induced immediately. A rise in 8-iso-$PGF_{2\alpha}$ during ischemia indicate that ROS generation may also take place during severely reduced coronary blood flow and hypoxia. No direct relationship between 8-iso-$PGF_{2\alpha}$ or 15-keto-dihydro-$PGF_{2\alpha}$ and troponin T was evident. The present study adds to the increasingly complex pathophysiological roles of ROS acting both as signal molecules and as mediators of tissue injury.

Keywords: *Oxidative stress, isoprostanes, inflammation, myocardial infarction, PCI*

Introduction

Primary percutaneous coronary intervention (PCI) is now established as the preferred reperfusion strategy in acute myocardial infarction (AMI) [1–4]. However, following primary PCI, insufficient myocardial reperfusion is often present despite a successful opening of the thrombotic occluded epicardial artery, and microcirculatory failure still remains as a major challenge [5,6]. Reduced coronary flow following primary PCI may be caused by several mechanisms including embolization of thrombotic material maintaining distal ischemia and generation of reactive oxygen species (ROS) and inflammatory mediators inducing microcirculatory failure [7–9].

Over the last decade, oxidative stress following restoration of myocardial flow in humans has been studied in detail [10–16] but the results are conflicting [17]. While ischemia-reperfusion studies in animals

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have shown protective effects of antioxidants [18–20], the use of antioxidants in acute coronary syndromes in humans has been disappointing [9,21–23]. The limitations in available, specific and sensitive indices for both direct and indirect assessments of ROS *in vivo* have been suggested as one possible explanation of the conflicting results between experimental and human studies.

Isoprostanes represent a group of relatively stable products formed *in vivo* from phospholipids mainly by a non-enzymatic free radical-catalyzed oxidation of arachidonic acid [24]. Studies have indicated that a major isoprostane, 8-iso-prostaglandin(PG)$F_{2\alpha}$, is a reliable indicator of *in vivo* oxidative stress [16,24,25]. Reperfusion of ischemic myocardium is followed by an inflammatory response that occurs as a consequence of the accumulated injury during ischemia and reperfusion [8,26]. Prostaglandins and thromboxanes are bioactive compounds derived from arachidonic acid through catalysation by cyclooxygenases (COX), and are important mediators of inflammation. 15-Keto-dihydro-$PGF_{2\alpha}$, a major metabolite of $PGF_{2\alpha}$, is elevated following tissue injury and may be used as an indicator of early inflammatory response and *in vivo* lipid peroxidation occurring via COX pathways [27–30].

The aim of the present study was to investigate the appearance and severity of oxidative stress and early inflammation in patients undergoing primary PCI for AMI by repeated measurements in peripheral blood of 8-iso-$PGF_{2\alpha}$ and 15-keto-dihydro-$PGF_{2\alpha}$, respectively. Secondly, we wanted to examine potential correlations between oxidative stress, inflammation and the extent of myocardial damage assessed by the cell injury marker troponin T.

Methods

The study was performed according to the Helsinki declaration. The Regional Ethics Committee approved the protocol, and written informed consent was obtained from all patients.

Patients

Sixteen patients with AMI treated with primary PCI within six hours of symptom onset were enrolled in the study. ST-segment elevation ≥ 1 mm in two standard ECG leads or ≥ 2 mm in two precordial leads were observed in all patients. An additional inclusion criterion was TIMI flow grade ≤ 1 (see below) at the first angiographic picture, that is a functionally occluded infarct related artery.

PCI

Primary PCI was performed according to a standardized protocol with a femoral artery approach and use of six French catheters introduced via an arterial sheath. Lidocaine hydrochloride was used for local anaesthesia. During the PCI procedure patients were anticoagulated with heparin (10.000 IU). A non-ionic x-ray contrast agent (Omnipaque® 350, Amersham Health, UK) was used. During PCI intracoronary nitroglycerine was given according to the operator's decision. Following PCI the introducer was removed after three hours. Coronary blood flow was assessed from coronary angiograms by the use of a semi-quantitative thrombolysis in myocardial infarction (TIMI) scale with 0 and 3 signifying zero or normal flow, respectively. Reperfusion arrhythmias were registered and categorized semiquantitatively by the PCI operator; (1) No or a few, (2) Moderate or (3) Severe.

Collection and handling of blood samples

Peripheral blood samples were collected at twelve time points: After arterial puncture but prior to reperfusion (t_0); immediately after restoration of flow in the infarct related artery (start of reperfusion) (t_1); 5, 10, 20, 30, 60, 120 and 180 min after reperfusion (t_2–t_8); and then 3,6,12 and 24 h after end of the PCI procedure (t_9–t_{12}). Samples t_0–t_8 were obtained from the introducer in the femoral artery while samples t_9–t_{12} were obtained from the antecubital vein. Blood from the syringes was transferred into precooled tubes with K_3EDTA and immediately centrifuged (10min, $+4$°C, 3000 × *g*). Plasma was stored at -80°C until analysis.

Biochemical assessments

Nonesterified 8-iso-$PGF_{2\alpha}$ and 15-keto-dihydro-$PGF_{2\alpha}$ were measured by a validated radioimmunoassay without any extraction procedure as described by Basu [27,31]. In brief, the cross-reactivity of the 8-iso-$PGF_{2\alpha}$ antibody with 15-keto-13, 14-dihydro-8-iso-$PGF_{2\alpha}$, 8-iso-$PGF_{2\beta}$, $PGF_{2\alpha}$, 15-keto-$PGF_{2\alpha}$, 15-keto-13,14-dihydro-$PGF_{2\alpha}$, TXB_2, 11β- $PGF_{2\alpha}$, 9β- $PGF_{2\alpha}$ and 8-iso-$PGF_{3\alpha}$ was 1.7, 9.8, 1.1, 0.01, 0.01, 0.1, 0.03, 1.8 and 0.6%, respectively. The detection limits of the 8-iso-$PGF_{2\alpha}$ assay was 23 pM. The cross-reactivity of the 15-keto-dihydro-$PGF_{2\alpha}$ antibody with $PGF_{2\alpha}$, 15-keto-$PGF_{2\alpha}$, PGE_2, 15-keto-13,14-dihydro-PGE_2, 8-iso-15-keto-13,14-dihydro-$PGF_{2\alpha}$, 11β-$PGF_{2\alpha}$, 9β-$PGF_{2\alpha}$, TXB_2 and 8-iso-$PGF_{3\alpha}$ was 0.02, 0.43, <0.001, 0.5, 1.7, <0.001, <0.001, <0.001 and 0.01%, respectively. The detection limit was 45 pM. Concentrations were corrected for hemodilution by analysing albumin concentrations at each time point. The correction for hemodilution was made by the formula: Plasma concentration (t_x) *x* albumin (t_0)/albumin (t_x), where t_x indicates at what time the sample was taken. Total antioxidant status (TAS) was measured by photometry on a Cobas Mira S Analyser by an enzymatic assay

(TAS, Randox Laboratories Ltd., Crumlin, United Kingdom). Troponin-T was measured on an Elecsys 2010 Analyser (Roche Diagnostics, Mannheim, Germany). The detection limit of the assay was 0.01 μg/l. High sensitive CRP (hsCRP) was measured by latex-enhanced immuno-turbidimetry on a Hitachi 917 Analyser (CRP (Latex) HS, Roche Diagnostics). Detection limit of the assay was 0.03 mg/l (analytical sensitive). Albumin, total cholesterol, HDL cholesterol, triglycerides, retinol, carotenoids ($\alpha + \beta$) and tocopherols ($\alpha + \gamma$) were measured by standard laboratory techniques.

Statistical analysis

Data analyses were performed with the statistical package for social sciences (SPSS 11.5, Chicago, Illinois) or GraphPad Prism Software (GraphPad Software 4.01, Inc., San Diego, CA, USA). Because of non-Gaussian distribution of most data, non-parametric tests and median values with interquartile ranges (25 and 75%) were chosen for presentation. Wilcoxon signed ranks test was performed for comparison between two dependent groups. For correlation analyses Spearman's correlation coefficient (rho) was used. For all analyses values below detection limit were set to detection limit at calculation. Values for $p < 0.05$ were considered significant.

Results

Patients

Patient characteristics are presented in Table I. Of the 16 patients with a median age of 60 years there was a male dominance (13) and few with previous AMI (2). They presented a low drug profile with prior use of ASA, β-blocker, Ca antagonists and statins in only 1, 2, 1, and 1 patient(s), respectively.

Table I. Characteristics of patients ($n = 16$).

Characteristics		
Male, *n* (%)	13	(81)
Median age, years (min–max)	60	(38–78)
Previous myocardial infarction, *n* (%)	2	(13)
Current smoking, *n* (%)	5	(31)
Known diabetes, *n* (%)	1	(6)
Known hypertension, *n* (%)	4	(25)
Total cholesterol (mM), mean (SD)	4.9	(1.0)
Medications at admission		
Acetylsalicylic acid (ASA), *n* (%)	1	(6)
β-blocker, *n* (%)	2	(13)
Ca antagonist, *n* (%)	1	(6)
Statins, *n* (%)	1	(6)
Infarct localisation		
Anterior wall, *n* (%)	6	(38)
Inferior wall, *n* (%)	9	(56)
Posterior wall, *n* (%)	1	(6)

Procedural variables are presented in Table II. Time from onset of chest pain signifying start of ischemia to reperfusion (t_1) was 198 (63–405) minutes. PCI was successful with TIMI flow grades ≥ 2 obtained in all patients. Intracoronary stents were implanted in all cases. There was a close concordance between infarct localization by ECG and the occluded culprit arteries.

All patients were given 300 mg ASA just prior to PCI. Eleven of 16 patients received intracoronary nitroglycerin during the procedure. Severe but transient reperfusion arrhythmias were registered in five patients, with rapidly convertible ventricular fibrillation in one. There was no hospital mortality.

Biochemical assessments

Oxidative stress assessed by 8-Iso- $PGF_{2\alpha}$ (Figure 1). Reperfusion resulted in a rise in 8-iso- $PGF_{2\alpha}$ in peripheral blood in all except two patients, but interindividual variations were large. For the entire group 8-iso- $PGF_{2\alpha}$ rose significantly from the median values of 31 (<23–60) at t_0 to 90 (57–115) pM at t_1 ($p = 0.001$). 8-iso-$PGF_{2\alpha}$ remained elevated during the first hour following reperfusion, subsequently it decreased. At 12 and 24 h the median value was <23 pM and thus below t_0 ($p = 0.007$). This might indicate that t_0 did not represent a true baseline and that generation of ROS did start during ischemia prior to reperfusion. There was a positive correlation between 8-iso-$PGF_{2\alpha}$ and duration of ischemia (rho = 0.694, $p = 0.006$), but no correlation with the occurrence of severe reperfusion arrhythmias.

Total antioxidant status (TAS), vitamin A and E (Table III). TAS, vitamin A (retinol and carotenoids ($\alpha + \beta$)) and vitamin E (tocopherols ($\alpha + \gamma$)) were measured at t_0 and 24 h after primary PCI. A significant decrease in TAS was seen from 1.22 (1.15–1.40) at t_0 to 1.13 (1.06–1.27) mM at t_{11} ($p = 0.001$). The concentrations of the antioxidant vitamins A and E (retinols, carotenoids, α- and γ-tocopherols) did not change during this period.

Inflammatory response assessed by 15-keto-dihydro-$PGF_{2\alpha}$ and hsCRP (Figure 2, Table III). 15-Keto-dihydro-$PGF_{2\alpha}$ showed large interindividual variations. For the entire group reperfusion resulted in an immediate increase from 81 (55–156) at t_0 to 111 (84–211) pM at t_1 ($p < 0.001$). The increase was sustained during the first hour after reperfusion with a subsequent fall to the t_0 level. A minor rise in 15-keto-dihydro-$PGF_{2\alpha}$ occured at 24 h ($p = 0.023$). The 15-keto-dihydro-$PGF_{2\alpha}$ levels at t_0 correlated closely with the duration of ischemia prior to reperfusion (rho = 0.65, $p = 0.007$) indicating that also an inflammatory response might have been initiated

Table II. Procedural variables ($n = 16$).

Variables		
Main culprit artery (dilated vessel)		
Left anterior descending artery (LAD), *n* (%)	5	(31)
Right coronary artery (RCA), *n* (%)	7	(44)
Left circumflex artery (LCX), *n* (%)	3	(19)
Diagonal on LAD, *n* (%)	1	(6)
Stent		
One, *n* (%)	14	(88)
Two, *n* (%)	2	(13)
Stent diameter (mm), median (min–max)	3.0	(2.25 – 4.00)
Medications during procedure		
Acetylsalicylic acid (ASA) (300mg), *n* (%)	16	(100)
Clopidogrel, *n* (%)	16	(100)
Heparin, *n* (%)	16	(100)
GP IIb/IIIa-antagonist, *n* (%)	15	(94)
Intracoronary nitroglycerin, *n* (%)	11	(69)
Reperfusion arrythmias		
No or a few, *n* (%)	3	(19)
Moderate, *n* (%)	8	(50)
Severe, *n* (%)	5	(31)
Ischemia time (min)*, median (min–max)	198	(63–405)
Fluoroscopy time (min), median (min–max)	6.9	(2.5–24.4)
Contrast volume (ml), median (min–max)	210	(60–450)

* Lapse time between debut of symptoms to successful reperfusion (TIMI flow grade ≥ 2).

during ischemia. A marked increase in hsCRP from 2.0 (1.1–4.0) at t_0 to 9.7 (5.3–25.5) mg/l at t_{11} ($p < 0.001$) was observed.

Myocardial damage assessed by troponin T (Figure 3). The median values of troponin T before reperfusion (t_0) were below detection level, <0.01 (<0.01–0.06) μg/l. Troponin T remained closely above the detection level in 2 patients, and became markedly elevated in the other 14 patients. For the entire group troponin T rose gradually with a maximum peak at 6–12 h after opening of the occluded artery and then subsided. Both peak levels and total release (area under the curve) of troponin T, 8-iso-$PGF_{2\alpha}$ and 15-keto-dihydro-$PGF_{2\alpha}$ were compared, but there was no correlation between myocardial damage and oxidative stress nor inflammation assessed by these three parameters.

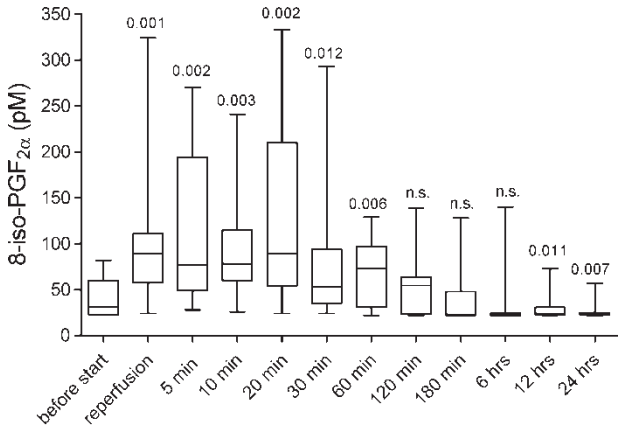

Figure 1. Plasma 8-iso-$PGF_{2\alpha}$ levels in AMI patients before and after primary PCI (reperfusion). Number of patients = 16. The boxes extend from the 25th to the 75th percentiles with horizontal lines at the median. Whiskers show the highest and the lowest values. The number above the upper whiskers illustrates the *p*-value between 8-iso-$PGF_{2\alpha}$ at the actual time points compared to before reperfusion (t_0) estimated by Wilcoxon signed ranks test. (n.s. = not significant).

Albumin and lipids (Table III). Albumin was measured at all time points to quantify hemodilution during the PCI procedure. The concentration of albumin decreased with 12% immediately following reperfusion ($p < 0.001$). Maximum hemodilution was observed 20 min after reperfusion with 16% decrease in albumin compared to t_0 ($p < 0.001$). The following day the concentration of albumin was only 3% below t_0 ($p = 0.018$). Plasma lipids did not reveal significant changes from t_0 to the next day, except for a minor reduction in total cholesterol.

Discussion

The present study included patients with little prior history or drug treatment for ischemic heart disease before the onset of AMI. With an average duration of preceding ischemia of about 3 h prior to PCI, this is a situation in which a major oxidative stress and inflammatory response may be expected. A major finding was that of a significant rise in 8-iso-$PGF_{2\alpha}$ during the first hour. This was supported by a decrease

Table III. Total antioxidant status (TAS), vitamins, hsCRP, lipids and albumin before start (t_0) and 24 h after ended PCI procedure (t_{11}).

	t_0		t_{11}		*p*-value⋆
TAS (mM)	1.22	(1.15–1.40)†	1.13	(1.06–1.27)‡	0.001
α-tocopherol (μM)	19.2	(16.7–22.2)	19.2	(15.3–21.9)	0.234
γ-tocopherol (μM)	2.5	(2.1–3.5)	2.2	(1.9–2.8)	0.099
Retinol (μM)	1.7	(1.4–1.8)	1.4	(1.2–1.7)	0.077
Carotene (α,β) (μM)		0.24 (0.16–0.37)	0.22	(0.15–0.41)	0.327
HsCRP (mg/l)	2.0	(1.10 – 3.97)	9.7	(5.3 – 25.5)	< 0.001
Total cholesterol (mM)	4.9	(4.3 – 5.6)	4.6	(4.1 – 5.8)	0.049
HDL-cholesterol (mM)	1.03	(0.93 – 1.13)	0.98	(0.88 – 1.07)	0.055
Triglycerides¶ (mM)	1.2	(1.03 – 1.48)	1.3	(1.10 – 1.80)	0.139
Albumin (g/l)	38	(36 – 40)	37.0	(36 d– 37)	0.018

All results are presented as median with (25 and 75% percentile), $n = 16$.
⋆ Wilcoxon signed ranks test.
† $n = 14$.
‡ $n = 13$.
¶ not fasting.

in TAS levels the following day. Thus an oxidative stress was induced by myocardial ischemia-reperfusion *per se* or by a general body response to a serious disease condition. A further interpretation might be that elevation of 8-iso-$PGF_{2\alpha}$ was caused by the technical procedure of PCI only. Concerning the latter possibility, a previous study [32] in patients undergoing elective PCI or coronary angiography for angina pectoris, showed elevation of 8-iso-$PGF_{2\alpha}$ in peripheral blood without significant differences between the two groups. It was assumed that the 8-iso-$PGF_{2\alpha}$ response could result from the purely vascular interventions involving an introducer into the femoral artery and the mutual catheterization and angiography of coronary arteries. However, the present situation with longstanding ischemia and the diagnosis of AMI indicates a more serious condition than in the previous PCI study.

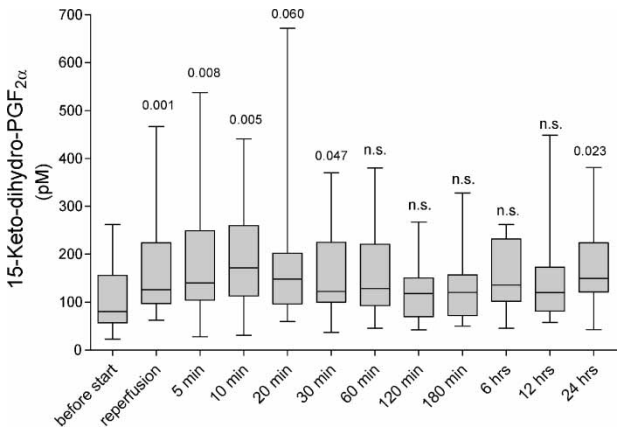

Figure 2. Plasma 15-keto-dihydro-$PGF_{2\alpha}$ levels in AMI patients before and after primary PCI (reperfusion). Number of patients = 16. The boxes extend from the 25th to the 75th percentiles with horizontal lines at the median. Whiskers show the highest and the lowest values. The number above the upper whiskers illustrates the *p*-value between 15-keto-dihydro-$PGF_{2\alpha}$ at the actual time points compared to before reperfusion (t_0) estimated by Wilcoxon signed ranks test. (n.s. = not significant).

The elevation of 8-iso-$PGF_{2\alpha}$ was sustained for the first hour after restoration of blood flow and then gradually subsided. Another finding was that 8-iso-$PGF_{2\alpha}$ presented significantly lower values on the following day than at the arrival in hospital (t_0). This indicates a lower and more true baseline level for 8-iso-$PGF_{2\alpha}$ than observed at t_0. It might therefore be that ROS was generated at an early stage while the myocardium was still ischemic. Thus, experimental evidence exists for ROS production in ischemic cardiomyocytes with superoxide leaking from the respiratory chain in hypoxic mitochondria [33–35]. Such an interpretation may explain that the duration of ischemia correlated with elevated 8-iso-$PGF_{2\alpha}$ before reperfusion (t_0) in the present study. However, there was no correlation between duration of ischemia and peak levels of 8-iso-$PGF_{2\alpha}$ during the first hour thereafter (t_1–t_6). Thus reperfusion processes or other accompanying factors led to the generation of ROS following PCI.

In the present study we found an increase (median values in individual patients in %) by 88% of 8-iso-$PGF_{2\alpha}$ following PCI (t_1–t_6) compared to the start level (t_0). This represents a similar elevation compared to that observed in an earlier study by our group where oxidative stress was examined during elective PCI and diagnostic angiography [32]. Different observations were made in a study by Reilly et al. (1996) [16] where elective PCI in patients with angina was compared with thrombolysis and rescue PCI in patients with AMI. In this study the differences in release of 8-iso-$PGF_{2\alpha}$ (measured in urine) were more marked than observed in our two studies. However, when we relate the level of 8-iso-$PGF_{2\alpha}$ after reperfusion with the minimum level taken the following day, a close to 300% increase was observed following primary PCI.

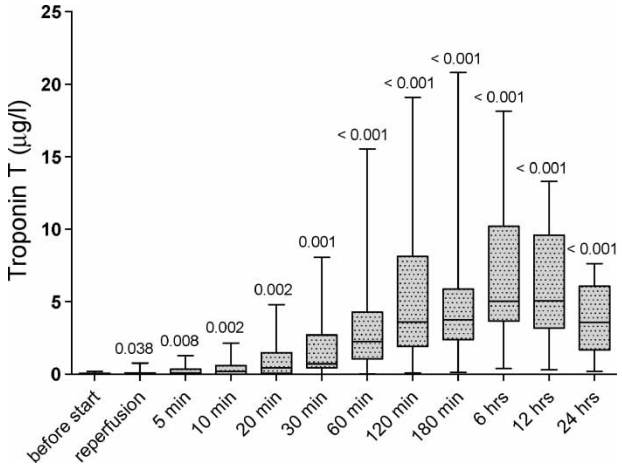

Figure 3. Plasma troponin T levels in AMI patients before and after primary PCI (reperfusion). Number of patients = 16. The boxes extend from the 25th to the 75th percentiles with horizontal lines at the median. Whiskers show the highest and the lowest values. The number above the upper whiskers illustrates the *p*-value between troponin T at the actual time points compared to before reperfusion (t_0) estimated by Wilcoxon signed ranks test. (n.s. = not significant).

Another particular finding was that the values for 8-iso-$PGF_{2\alpha}$ prior to and immediately after PCI were about 25% lower in the present than in our previous study [32] in purely elective patients with no sign of AMI. Although speculative, this might indicate that the present patients were protected against ROS release or lipid peroxidation. Two different mechanisms may support this. Thus the release of ROS during the ischemic phase might have activated signalling cascades in cardiomyocytes enhancing their defence against cell damage. Accordingly, the phenomenon of ischemic preconditioning [35–37] may have provided protection against ROS release or ROS induced lipid peroxidation on reperfusion. Another possibility is the parallel drug treatment. Two thirds of the patients received intracoronary infusion of nitroglycerine which is a nitric oxide (NO) donor, and NO is a potent scavenger [38,39]. A more likely possibility is that the single 300 mg dose of ASA given to all patients just prior to PCI was rapidly metabolized to salicylic acid which is an effective scavenger of hydroxyl radicals [40,41].

COX and cytokine mediated pathways are important in evaluating inflammatory responses *in vivo*. In this study plasma levels of both COX and cytokine mediated markers like 15-keto-dihydro-$PGF_{2\alpha}$ and hsCRP, were significantly elevated following the procedure. However, with 15-keto-dihydro-$PGF_{2\alpha}$ the plasma levels prior to PCI were only 1/3 of those previously reported by us in elective PCI and coronary angiography [32] indicating a stronger influence of COX inhibition by a higher and more recent dose of ASA [42,43]. In contrast, the cytokine related parameter hsCRP is not affected by COX and showed a much larger increase, times 4, compared to 15-keto-dihydro-$PGF_{2\alpha}$ the day after primary PCI.

To the best of our knowledge, this is the first clinical study to undertake a systematic evaluation comparing oxidative stress with myocardial damage. However, no significant correlation was observed between 8-iso-$PGF_{2\alpha}$ and the now established myocardial injury marker troponin T [44–46]. In contrast to this, the temporal release kinetics of 8-iso-$PGF_{2\alpha}$ and troponin T presented as mean (±SEM) plasma values in Figure 4, clearly demonstrates an early oxidative burst on reperfusion to be followed by a later release of troponin T. However, the overall picture with ROS and tissue injury has become increasingly complex with ROS attaining different roles as signal molecules in both endogenous protective [35] and apoptotic pathways [47] and as injurious agents. Furthermore, ROS may reveal different aspects of these roles during at least three different stages: Ischemia, initial reperfusion and subsequent prolonged inflammation. A particular problem adding to the complexity is the apparent lack of clinical success with potentially effective therapeutic antioxidants [4,9,21].

In conclusion, oxidative stress is induced during and following primary PCI for AMI as shown by increased levels of lipid peroxides in peripheral blood. The release of ROS products seems to start already during the phase of ischemia and thus before onset of reperfusion. The study also indicated that inflammatory responses were both an early event on reperfusion and a late event during the subsequent 24 h follow up. A direct relationship could not be established between oxidative stress and

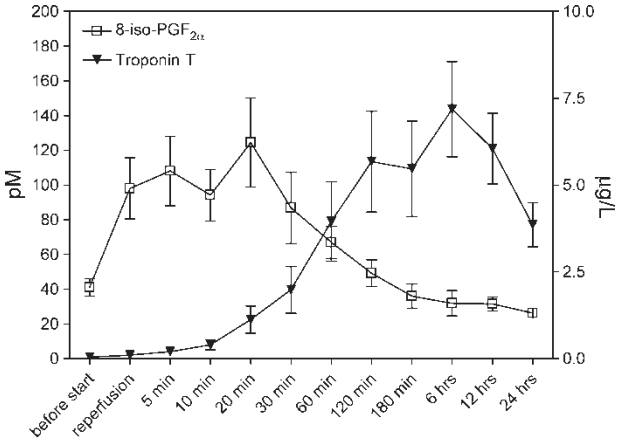

Figure 4. Plasma 8-iso-$PGF_{2\alpha}$ vs. troponin T. The figure illustrates the early release of 8-iso-$PGF_{2\alpha}$ (square) followed by the later release of troponin T (triangle) in plasma samples taken from AMI patients following primary PCI. Mean ± standard error of the means (SEM) is shown. In spite of an apparent interrelationship, no individual correlation was observed between these two variables either compared with the maximum levels or total amounts (area under the curve) of each variable; Spearman's rho = 0.374 and 0.914 respectively.

inflammation on the one hand and myocardial damage on the other.

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