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Oxidative Stress and Myocardial Damage during Elective Percutaneous Coronary Interventions and Coronary Angiography

A Comparison of Blood-borne Isoprostane and Troponin Release

KIRSTI BERG[a,*], RUNE WISETH[b], KRISTIAN BJERVE[c], HEIDI BRUROK[a], SIGURD GUNNES[a], SISSEL SKARRA[a], PER JYNGE[a] and SAMAR BASU[d]

[a]*Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Medisinsk teknisk senter N-7489, Trondheim, Norway;* [b]*Department of Heart Diseases, St. Olavs Hospital, Trondheim, Norway;* [c]*Department of Laboratory Medicine, St. Olavs Hospital, Trondheim, Norway;* [d]*Department of Public Health/Geriatrics and Clinical Nutrition Research, Uppsala University Hospital, Uppsala, Sweden*

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The role of oxidative stress in clinical cardiology is still controversial. The aims of the present study were to examine if minor ischaemic episodes as may occur during elective percutaneous coronary intervention (PCI) induce oxidative stress and, eventually, if oxygen stress correlates with myocardial injury.

Thirty eight and nine patients underwent PCI and diagnostic coronary angiography, respectively. Peripheral blood was sampled at different time points for plasma analyses of: 8-iso-$PGF_{2\alpha}$ (free radical-mediated oxidative stress); 15-keto-dihydro-$PGF_{2\alpha}$ (cyclooxygenase-mediated inflammation); troponin-T (myocardial injury); hsCRP, vitamin A and vitamin E; and, total antioxidants status (TAS). In both groups 8-iso-$PGF_{2\alpha}$ increased transiently by approximately 80% ($p < 0.001$) during the procedure. There was a minor troponin-T release ($p < 0.001$) after PCI, but no correlation with 8-iso-$PGF_{2\alpha}$. Troponin-T did not increase after angiography. 15-keto-dihydro-$PGF_{2\alpha}$ decreased by 50% after ended procedure, but increased by 100% after 24 h compared to baseline. hsCRP increased significantly ($p < 0.001$) from baseline to the next day in the PCI-group, but not in the angiography group. Vitamins and TAS decreased slightly after the procedures.

It is concluded that a moderate oxidative stress was induced by both elective PCI and coronary angiography but that no correlation was found between oxidative stress and myocardial injury in this setting. This indicates that other mechanisms than ischaemia–reperfusion episodes caused an elevation in plasma isoprostane such like the injury at a vascular site mutual for both procedures. A secondary finding from the study was elevated markers of early inflammatory response, not only after PCI, but also after angiography.

Keywords: Ischaemia–reperfusion; Reactive oxygen species; Isoprostanes; Percutaneous coronary intervention; Coronary angiography

INTRODUCTION

Percutaneous coronary intervention (PCI) is a rapidly expanding treatment for both chronic and acute stages of coronary artery disease. PCI has become a main-line therapy and is generally recognised as a versatile and safe technique. Repeated balloon inflations make PCI a clinical model of myocardial ischaemia–reperfusion and following PCI elevation in markers of myocardial damage occurs frequently.[1–4] Both oxidative injury[5] and inflammatory processes[6] are thought to play an important factor in reperfusion injury. However, the presence and potential role of oxidative stress during PCI remain controversial.[7–17]

One major reason for not recognising oxidative stress *in vivo* is the escaping nature of reactive oxygen species (ROS) and the limitation in available, specific and sensitive indices for both direct and indirect assessments. Techniques for direct detection

*Corresponding author. Tel.: +47-73-55-02-78. Fax: +47-73-59-86-13. E-mail: kirsti.berg@medisin.ntnu.no

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of ROS like electron spin resonance (ESR) with use of spin trap agents are hardly applicable in routine clinical work, and indirect ROS detection by measuring lipid peroxide products like malondialdehyde (MDA) has been hampered by inaccuracies.[18,19] A more reliable method of assessing oxidative stress *in vivo* is measurement of isoprostanes by mass-spectroscopy or immunological techniques.[19–23] Isoprostanes represent a group of stable products formed *in vivo* from phospholipids mainly by a non-enzymatic free radical-catalysed oxidation of arachidonic acid.[20,23] Studies have indicated that a major isoprostane, 8-iso-$PGF_{2\alpha}$, is particularly useful as *in vivo* biomarker of oxidative stress.[11,20,23,24] 8-iso-$PGF_{2\alpha}$ is also a potent vasoconstrictor with a yet undefined role in physiology.[19]

Enzymatic oxidation of arachidonic acid by cyclooxygenase (COX) leads to release of prostaglandins that induce an inflammatory response. 15-keto-dihydro-$PGF_{2\alpha}$, a major metabolite of $PGF_{2\alpha}$, is elevated following tissue injury and can be used as an indicator of inflammation and of *in vivo* lipid peroxidation occurring via the COX pathway.[25–27] The recent adoption of highly sensitive assays to measure cardiac troponins in plasma has led to detection of even minor myocardial injuries or infarction. Following PCI, troponin elevation ($>0.1\,\mu g/l$) may occur in as many as 18% of patients.[28]

The main aim of the present study was to investigate the involvement of oxidative stress and of early inflammation in patients undergoing elective PCI in a daily clinical practice. A second aim was to examine if there was any correlation between oxidative stress assessed by 8-iso-$PGF_{2\alpha}$ and myocardial injury assessed by elevation of troponin-T. Patients undergoing coronary angiography served as control. The study was based on repeated measurements of 8-iso-$PGF_{2\alpha}$ and 15-keto-dihydro-$PGF_{2\alpha}$ in peripheral blood samples, thus avoiding the insertion of catheters in the coronary sinus or in the urinary bladder. In addition, plasma levels of antioxidants and high sensitive C-reactive protein (hsCRP) were measured as supplementary parameters of oxidative stress and inflammation, respectively.[29,30]

METHODS

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

Patients (Tables I and II)

A total number of 41 and 11 patients undergoing PCI and coronary angiography (angiography), respectively, were consecutively enrolled. One patient in the PCI group was excluded because of unsuccessful procedure. Two PCI patients and one angiography patient were excluded because of elevated troponin T ($>0.1\,\mu g/l$) at baseline. Thus, the study groups consisted of 38 PCI and 9 angiography patients, respectively (Table I). The two groups were well balanced regarding age and sex. The majority of patients (90% in both groups) presented with stable angina. The two groups were similar with respect to risk factors, lipids and medications (Table II). All in the angiography group and all but one in the PCI group were treated with acetylsalicylic acid (low-dose aspirin). All patients except three in the PCI group were on statin therapy.

TABLE I Clinical characteristics of patients

Characteristic	PCI (n=38)	Angiography (n=9)
Age, y (range)	61 (39–84)	61 (51–72)
Female, *n* (%)	9 (24)	1 (11)
Male, *n* (%)	29 (76)	8 (89)
Stabile angina, *n* (%)	33 (87)	8 (89)
Unstable angina, *n* (%)	5 (13)	1 (11)
Previous AMI, *n* (%)	31 (82)	5 (56)
Previous CABG, *n* (%)	5 (13)	0 (0)
One-vessel procedure, *n* (%)	36 (95)	–
Two-vessel procedure, *n* (%)	2 (5)	–

AMI = acute myocardial infarction
CABG = coronary artery bypass grafting

PCI and Coronary Angiography

PCI and coronary angiography are parallel procedures with PCI more demanding due to transient balloon inflations and insertion of intracoronary stents. Both procedures were performed according

TABLE II Risk factors and medications

	PCI (n=38)	Angiography (n=9)
Risk factors		
Known diabetes, *n* (%)	3 (8)	0 (0)
Hypertension,* *n* (%)	5 (13)	2 (22)
Cigarette smoking		
No, *n* (%)	23 (61)	7 (78)
Yes, *n* (%)	13 (34)	2 (22)
Unknown	2 (5)	
Cholesterol (mM), mean (SD)	5.0 (1.4)	5.0 (1.0)
Medications		
Acetylsalicylic acid (ASA), *n* (%)	37 (97)	9 (100)
Beta-blocker, *n* (%)	36 (95)	8 (89)
Nitroglycerin (long acting), *n* (%)	16 (42)	4 (44)
Calcium antagonist, *n* (%)	7 (18)	2 (22)
ACE-inhibitor, *n* (%)	5 (13)	1 (11)
Statin, *n* (%)	35 (92)	9 (100)
Clopidogrel, *n* (%)	38 (100)	8 (89)

* Admission blood pressure (systolic) > 160 mmHg.

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to a standardised protocol with a femoral approach and use of 6 Fr introducers. Diazepam, 5–10 mg, was given for premedication and lidocaine hydrochloride was used for local anesthesia. During PCI the patients were anticoagulated with heparin (10,000 IU). A non-ionic X-ray contrast agent (Iomeprol 350, Astra Tech AB, Sweden) was used. During PCI procedures intracoronary nitroglycerin was given according to the operator's decision. Following PCI the introducer was removed after 3 h, following angiography the introducer was removed immediately. Radiation exposure was assessed both by fluoroscopy time and by total area dose (cGy/cm^2) automatically measured by the X-ray equipment (Hicor, Siemens, Germany).

Collection and Handling of Blood Samples

Blood samples were collected at four time points: At baseline, just after arterial puncture but before heparin was introduced (t_0); immediately after the last balloon dilatation (t_1); 3 h following the procedure (t_2); and finally 24 h after end of the procedure (t_3). Two patients (one from each group) were discharged from the hospital before the last sample was taken (t_3). After the introducer was removed, blood samples were collected from the antecubital vein. Blood from the syringe was immediately transferred into tubes with K_3EDTA and centrifuged (10 min, + 4°C, 3000*g*). Plasma was stored at − 80°C until analysis.

Biochemical Assessments

Non-esterified 8-iso-$PGF_{2\alpha}$ was measured by a validated radioimmunoassay without any extraction procedure as described by Basu.[23] An antibody was raised in rabbits by immunization with 8-iso-$PGF_{2\alpha}$ coupled to bovine serum albumin at the carboxylic acid by the 1,1′-carbonyl-diimmidazole method. The cross-reactivity of 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 limit of the assay was 23 pM.

15-keto-dihydro-$PGF_{2\alpha}$ was measured by a validated radioimmunoassay as described by Basu.[25] An antibody was raised in rabbits by immunisation with 15-keto-dihydro-$PGF_{2\alpha}$ coupled to bovine serum albumin at the carboxylic acid by the 1,1′-carbonyl-diimmidazole method. The cross-reactivity of the 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 of the assay was 45 pM. Troponin-T was measured by electrochemiluminiscence with Elecsys 2010 analyser (Roche Diagnostics, Mannheim, Germany). The detection limit of the assay was 0.01 μg/l. Retinol, carotenoids ($\alpha + \beta$) and tocopherols ($\alpha + \gamma$) were assayed by high performance liquid chromatography (HPLC) with UV-detection based on methods described by Nierenberg *et al.* and Comstock *et al.*[31,32] Total antioxidant status (TAS), a measure of peroxyl-scavenging capacity, was measured spectrophotometrically on a Cobas Mira S analyser with use of an enzymatic assay (Randox Laboratories Ltd., Crumlin, UK). hsCRP was measured by latex-enhanced immuno-turbidimetry on a Hitachi 917 analyser (CRP (Latex) HS, Roche Diagnostics, Mannheim, Germany). The detection limit of the assay was 0.03 mg/l (analytical sensitive).

Statistical Analysis

All data analyses were performed with the Statistical Package for Social Sciences (SPSS 11.5, Chicago, IL, USA). Data are shown as median with range. Owing to relatively small groups and non-normal distribution of data, non-parametric methods were used, except when otherwise stated. Differences between groups were analysed by the Friedman test for related data. The Wilcoxon signed-rank test was used for comparison of two related variables or the Mann–Whitney test when independent samples.

RESULTS

Procedures (Table III)

In the PCI group 35 coronary arteries and 4 saphenous vein grafts were dilated, and 35 out of 38 patients received intracoronary stents. The number of balloon inflations in this group varied from 1 to 19 with 3 as median value. The accumulated median balloon inflation (ischaemia) time was 90 (37–481) s. When PCI was compared to angiography, duration of procedure ($p < 0.001$) and fluoroscopy time ($p = 0.004$) were longer, and radiation exposure ($p = 0.005$) and volume of contrast agent ($p = 0.001$) were higher.

Biochemical Assessments

8-iso-$PGF_{2\alpha}$ (Fig. 1)

The median baseline values (measured at t_0) of 8-iso-$PGF_{2\alpha}$ were 62 (23–149) and 57 (23–147) pM in the PCI and angiography groups, respectively (ns). 8-iso-$PGF_{2\alpha}$ showed a significant rise by 87% (PCI, $p < 0.001$) and 76% (angiography, $p = 0.02$)

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TABLE III Procedural variables

	PCI (n=38)	Angiography (n=9)	p-Value
Dilated vessel			
LAD (left anterior descending artery), *n* (%)	18 (47)	–	
LCX (left circumflex artery), *n* (%)	7 (18)	–	
RCA (right coronary artery), *n* (%)	10 (26)	–	
SVG (saphenous vein graft), *n* (%)	4 (11)	–	
Stent (yes), *n* (%)	35 (92)	–	
Medications during procedure		–	
Intracoronary nitroglycerin, *n* (%)	28 (74)	1 (11)	
GP IIb/IIIa-antagonist, *n* (%)	6 (16)	–	
Time of procedure,* min	55 (20–130)	20 (10–50)	<0.001
Balloon inflations, *n*	3 (1–19)	–	
Balloon inflation time, *s*	90 (37–481)	–	
Radiation exposure, cGy/cm^2	583 (215–2107)	252 (34–879)	0.005
Fluoroscopy time, min	13.1 (3.0–46.1)	4.5 (1.3–23.3)	0.004
Contrast volume (ml)	295 (70–760)	120 (40–600)	0.001

Data are shown as median with range in parentheses or absolute numbers with relative frequencies. *Time from insertion of the arterial introducer to the end of procedures (immediately post procedure).

at the end of procedures (t_1). After 24 h the level of 8-iso-$PGF_{2\alpha}$ were back to baseline in both groups. No statistically significance between PCI and angiography were noted at any of the time intervals.

15-keto-dihydro-$PGF_{2\alpha}$ (Fig. 2)

15-keto-dihydro-$PGF_{2\alpha}$ showed a more complex response. Median baseline values were 299 (118–851) and 286 (97–869) pM for PCI and angiography, respectively (ns). For both groups 15-keto-dihydro-$PGF_{2\alpha}$ decreased to values significantly below baseline immediately following the procedure; PCI to 142 (63–351) ($p < 0.001$) and angiography to 128 (73–185) ($p = 0.011$). After 24 h the values were raised significantly above baseline: PCI to 674 (185–3784) pM ($p < 0.001$); and, angiography to 494 (251–1152) pM ($p = 0.012$).

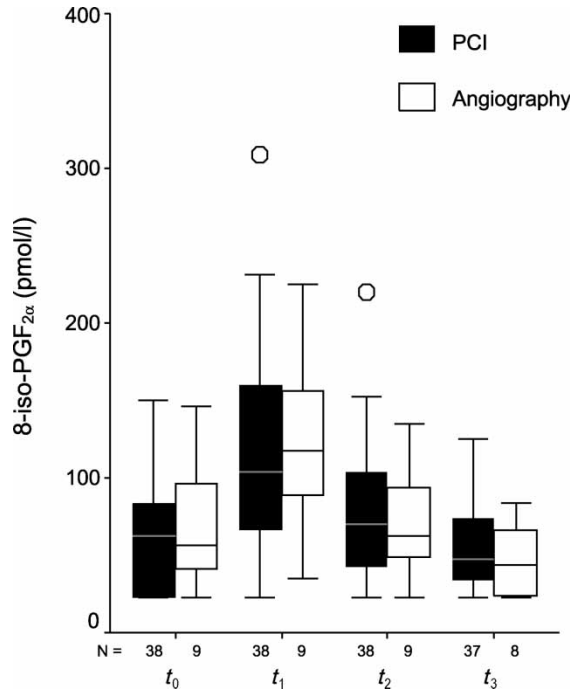

FIGURE 1 8-iso-$PGF_{2\alpha}$ in plasma before and after PCI and coronary angiography. Sampling times: t_0, baseline; t_1, immediately after the procedures; t_2, 3 h after t_1 and t_3, 24 h after t_1. The boxplot is showing the 25th, 50th (median) and the 75th percentiles. A boxplot *outlier* (O) is a value more than 1.5 box-lengths away from the box. N = number of patients.

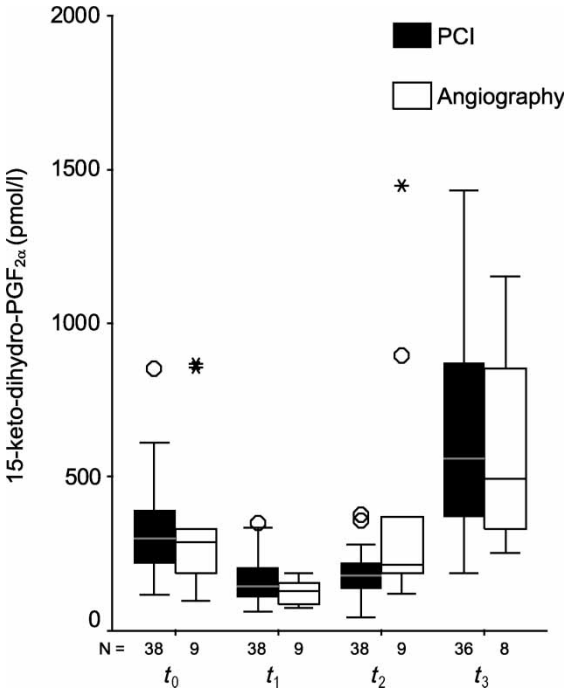

FIGURE 2 15-keto-dihydro-$PGF_{2\alpha}$ in plasma before and after PCI and coronary angiography. Sampling times: t_0, baseline; t_1, immediately after the procedures; t_2, 3 h after t_1 and t_3, 24 h after t_1. The boxplot is showing the 25th, 50th (median) and the 75th percentiles. A boxplot *outlier* (O) is a value more than 1.5 box-lengths away from the box, and an *extreme value* (*) as more than 3 box-lengths away from the box. N = number of patients.

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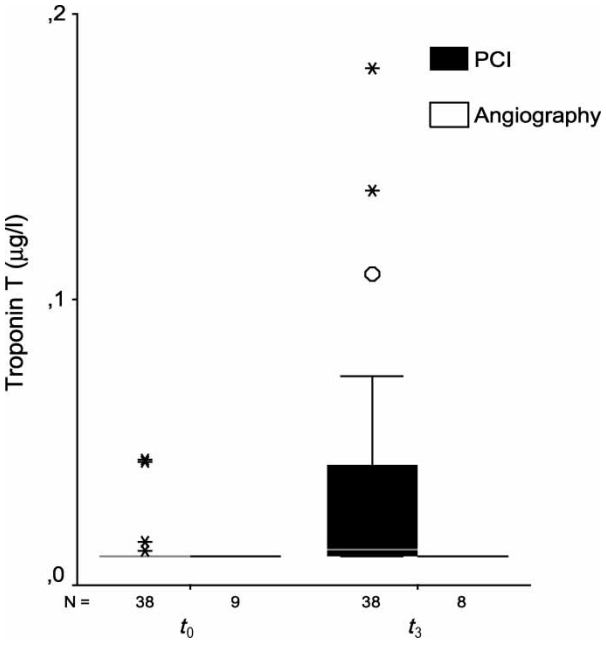

FIGURE 3 Troponin T in plasma before (t_0) and 24 h (t_3) after PCI and coronary angiography. The boxplot is showing the 25th, 50th (median) and the 75th percentiles. A boxplot *outlier* (O) is a value more than 1.5 box-lengths away from the box and an extreme value (*) as more than 3 box-lengths away from the box. N = number of patients.

Troponin-T (Fig. 3)

Troponin-T was assessed at baseline (t_0) and 24 h after the procedure (t_3). At baseline only four patients in the PCI-group (max level 0.044 µg/l) and none in the angiography group were above the detection limit of 0.01 µg/l. Twenty four hours after the procedure 13 patients in the PCI group measured levels of troponin-T above the detection level, but only 3 patients had values above 0.1 µg/l. No patient in the angiography group had troponin-T at or above 0.01 µg/l after the procedure.

Other Oxidative Stress Markers (Table IV)

In the PCI group the plasma total antioxidant capacity (TAS) showed a slight, but statistically significant biphasic response during the time of observation. Compared to baseline (t_0) TAS values were lower at the end of procedure (t_1) ($p = 0.02$), normalised 3 h later (t_2) and elevated at 24 h (t_3) ($p < 0.001$). The angiography group showed a similar trend, but no significant differences were observed. The concentrations of the antioxidant vitamins A and E (retinols, carotenoids, α- and γ-tocopherol) in plasma were measured at two time points: at baseline (t_0); and, after 24 h (t_3). α- and γ-tocopherol showed a significant ($p = 0.015$ and 0.029, respectively) decrease in the sample taken after 24 h in the PCI group, but not in the angiography group. Retinols and carotenoids were not changed in any direction during the period in either group.

hsCRP (Table V)

hsCRP was assessed at baseline (t_0) and 24 h following the procedure (t_3). No differences were observed between the groups at baseline. After 24 h hsCRP rose significantly in the PCI-group ($p < 0.001$) but not in the angiography group ($p = 0.263$).

TABLE IV Antioxidant parameters in plasma at baseline and post procedure with PCI and angiography

	PCI (n=38)	p-Value*	Angiography (n=9)	p-Value*
Total antioxidant status				
t_0†	1.27 ± 0.08		1.29 ± 0.07	
t_1‡	1.22 ± 0.09	0.002	1.25 ± 0.07	ns
t_2¶	1.26 ± 0.16	ns	1.40 ± 0.06	0.021
t_3§	1.35 ± 0.09	<0.001	1.37 ± 0.05	ns
α-tochopherol				
t_0	17.40 ± 5.03		17.50 ± 3.40	
t_3	16.51 ± 4.78	0.015	17.10 ± 3.17	ns
γ-tochopherol				
t_0	2.65 ± 1.03		2.81 ± 0.95	
t_3	2.56 ± 0.96	0.029	2.88 ± 0.63	ns
Retinol				
t_0	1.65 ± 0.45		1.39 ± 0.31	
t_3	1.66 ± 0.38	ns	1.56 ± 0.32	0.024
Carotene (α and β)				
t_0	0.23 ± 0.17		0.30 ± 0.26	
t_3	0.24 ± 0.17	ns	0.30 ± 0.26	ns

Data are shown as the mean ± SEM. *Compared to baseline level (t_0). ns: $p > 0.05$. † t_0: baseline level. ‡ t_1: immediately after ended procedure. ¶ t_2: 2–3 h after t_1. § t_3: 24 h after t_1.

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TABLE V HsCRP (mg/l)

	PCI (n=38)	Angiography (n=9)	p-Value*
t_0 (*before procedure*)			
Mean	3.06	2,28	0.978
Median	1.14	1,41	
Range (min–max)	(0.10–33.66)	(0.10–8.88)	
t_3 (*day after procedure*)			
Mean	7.35	3.05	0.086
Median	3.44	2.06	
range (min–max)	(0.10–42.62)	(0.76–6.29)	
p-Value†	<0.001	0.263	

*Between groups. †Compared to baseline level (t_0).

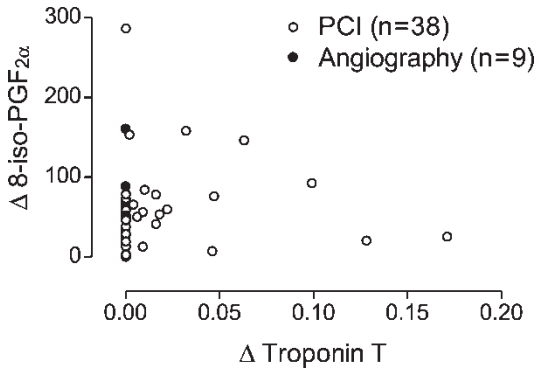

FIGURE 4 Scatterplot of Δ Troponin T (t_3-t_0) and Δ 8-iso-$PGF_{2\alpha}$ (t_1-t_0) in individual patients. Sampling times: t_0, baseline; t_1, immediately after the procedures and t_3, 24 h after t_1.

DISCUSSION

In the present study, the main aims were to diagnose oxidative stress in patients undergoing elective PCI in a daily clinical practice, make use of peripheral blood measurements of the indirect ROS marker 8-iso-$PGF_{2\alpha}$, and, eventually, relate positive findings with the established myocardial injury marker troponin-T. Our results indicate that a transient oxidative stress occurred in PCI as manifested by an early 87% elevation of plasma 8-iso-$PGF_{2\alpha}$. Minor transient reductions in plasma antioxidant capacity (TAS) and α- and γ-tocopherols support this conclusion. As expected for the PCI patients cardiac troponin-T release underwent a significant small elevation from day 1 to day 2. Accordingly, our basic hypotheses of oxidative stress occurring during elective PCI with brief intermittent coronary occlusions and of a relationship between a preferably mild oxidative stress and a minor myocardial injury were apparently confirmed. Additionally, on day 2 the $PGF_{2\alpha}$, metabolite, 15-keto-dihydro-$PGF_{2\alpha}$ was elevated as a sign of an early inflammatory response through COX pathway previously shown in both acute and chronic inflammation studies.[26,27,33] Of note is that a similar oxidative stress as in PCI was evidenced by a 76% rise in 8-iso-$PGF_{2\alpha}$ in the angiography group. Also TAS and tocopherols tended to show a similar biphasic response as in PCI. Thus, the present study has not established any causal relationship between a mild ROS attack and a minor myocardial injury following elective PCI. In line with this, Fig. 4 shows that there was no individual correlation between the rises in respectively isoprostane and troponin-T in the PCI-group. The study, however, can not rule out a relationship between cardiac injury and local oxidation processes in the myocardium as the samples were not taken from the coronary sinus blood, and as both PCI and angiography generated a vascular injury. Angiography resulted in a similar rise in 15-keto-dihydro-$PGF_{2\alpha}$ on day 2 as did PCI. This indicates that some mutual and initiating inflammatory events took place in both patient groups.

These main findings both contradict and confirm those reported by others. Studies that failed to demonstrate the existence of oxidative stress in PCI[14,16,17] have used ROS related analyses of less specific and sensitive markers than isoprostanes. In a recent study of PCI patients,[34] blood samples from peripheral blood were analysed for ischaemia-modified-albumin (IMA), a new myocardial injury marker with a probable ROS origin. IMA levels were elevated at 30 min post PCI, whereas 8-iso-$PGF_{2\alpha}$ measured by a commercial immunoassay showed no significant elevation. It was concluded that IMA is a more sensitive marker of PCI-induced injury than 8-iso-$PGF_{2\alpha}$.

Positive reports of oxidative stress have so far made use of analyses from samples of coronary sinus blood[7–10,12,13,16] or of urine.[11] Most of these have employed 8-iso-$PGF_{2\alpha}$ as an oxidative stress marker. Clearly, coronary sinus sampling could have revealed more clear-cut evidence for a myocardial origin of ROS, and sampling of urine could also have been more rewarding by circumventing eventual short-lasting plasma peaks in peripheral blood. However, the present study is the first to detect an oxidative stress during elective PCI and during coronary angiography by 8-iso-$PGF_{2\alpha}$ measurements from repeated peripheral blood samples. There were two other novel aspects with the present study. To our knowledge no report has yet matched indices of oxidative stress with the highly sensitive marker troponin-T of myocardial injury. Furthermore, our study has also indicated that not only PCI, but also angiography led to a potentially proinflammatory condition, as shown by elevated values for 15-keto-dihydro-$PGF_{2\alpha}$.

An intriguing finding that finds no direct explanation was that the oxidative stress was equally present in both groups studied. This confirms an earlier documentation[11] of a rise in the urinary

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content of 8-iso-$PGF_{2\alpha}$ following angiography as well as following PCI. However, both PCI and angiography are complex procedures that may affect cardiovascular and whole body physiology. The vascular trauma cannot be disregarded as an initiator of ROS attack and of a later inflammatory process. The presence of a catheter sheath (introducer) into the femoral artery and the repeated catheter movements and contrast medium injections into atherosclerotic coronary arteries in both patient groups could theoretically induce transient damage to vessel walls and contribute to the generation of ROS from endothelial cells or activated leukocytes.[35]

Another ROS related factor is that X-ray exposure may generate free radicals.[36] However, in a recent study by Andreassi *et al.* there was no evidence of X-ray induced oxidative damage of deoxyribonucleic acid in lymphocytes following PCI.[37] There is a paucity, though, of studies elucidating the potential role of X-ray exposure in generating oxidative stress during cardiological interventional procedures. Judged from fluoroscopy time and dose in our study this factor was more prominent in PCI than in angiography. If vascular trauma and X-rays contribute to ROS generation, the similar oxidative stress level in both PCI and angiography finds no obvious explanation except for differences in the use of therapeutic or diagnostic adjuncts. Only the patients in the PCI group received heparin at start of the procedure. Heparin is known as an indirect scavenger of ROS, with stimulation of extracellular superoxide dismutase.[38] Another interesting factor is related to X-ray contrast media, which were used in larger quantities in PCI than in angiography. Although these substances are tolerated at a non-comparable scale with other intravenously applied drugs,[39] they are not inert but may affect vascular tone, cardiac electrophysiology and coagulation.[39,40] Also the cause of transient renal insufficiency induced by contrast media in susceptible patient groups like diabetics with reduced renal function is not well understood, but ROS may in some ways be involved.[41]

15-keto-dihydro-$PGF_{2\alpha}$ showed a time course inverse to that of 8-iso-$PGF_{2\alpha}$ but again there were no differences between PCI and angiography. After 24 h, when 8-iso-$PGF_{2\alpha}$ level was normalised, 15-keto-dihydro-$PGF_{2\alpha}$ was elevated compared to baseline in both groups which supports a potential inflammatory reaction.[20,21] Given the parallelism between the two groups, the injury plus inflammation locus is most probably identical such as the entry site in femoral arteries and the examined or treated coronary arteries. Further inferred, this underlines that the myocardium was a less likely source for generation of ROS in the present study. In contrast to 15-keto-dihydro-PGF hsCRP demonstrated significant differences between the study groups. Thus hsCRP was elevated above a closely similar baseline level in the PCI group only. The elevation most probably reflects the somewhat larger injury potential in PCI than in angiography, and confirms that hsCRP is a sensitive injury and inflammation marker.

In this study, we have used the highly sensitive myocardial injury marker troponin-T.[42] Values above 0.1 μg/l were found in only 3 of the 38 patients (8%) undergoing PCI. Seven other patients had troponin-T larger than 0.06 μg/l indicating a minor cell injury. These values indicate that the ischaemia induced during PCI was minor. The absence of any substantial myocardial injury may explain the similarity between the PCI and angiography groups regarding indices of oxidative stress.

Whereas balloon inflation with rupturing of atheroscletic plaques represents an injurious process, which might easily lead to reduced reflow and transient ischaemia, the repetitiveness may on the other hand induce an endogenous cardioprotective cascade. Thus the initial brief coronary artery occlusion may activate signal pathways that ameliorate myocardial ischaemia–reperfusion injury (myocardial preconditioning) during subsequent balloon inflations.[43] In our study, treated vessels were balloon inflated in average about 5 times. With preconditioning present it is to be expected that both myocardial damage and local ROS mediated reactions could have been moderated. Most likely, however, a major reason for the modest rise in troponin-T in our study is that the patient material only included patients with elective PCI undergoing uncomplicated procedures with only minor ischaemic episodes.

In conclusion, isoprostanes are sensitive parameters of oxidative stress in PCI and can be detected in peripheral blood samples. Since a moderate oxidative stress was induced by both elective PCI and coronary angiography, but minor myocardial injuries were only observed after PCI, no obvious link was established between oxidative stress and myocardial injury in the present study. An early inflammatory response in both groups most probably resulted from mutual injuries to vessel walls.

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