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Pre-diabetes and the risk of contrast induced nephropathy in patients undergoing coronary angiography or percutaneous intervention

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ABSTRACT

Background: Contrast induced nephropathy (CIN) is a complication of coronary angiography/percutaneous intervention (PCI). It is known that diabetes is an independent risk factor for CIN, but we have no data regarding the association between CIN and glycemic levels in patients without diabetes. Aim of our study was to evaluate whether high level of glycated-haemoglobin in patients without diabetes is associated with an increased risk of CIN.

Methods: A total of 1324 patients without diabetes, undergoing elective/urgent coronary angiography/angioplasty were divided according to quartiles of baseline glycated-haemoglobin. CIN was defined as an absolute ≥0.5 mg/dL or a relative ≥25% increase in creatinine level at 24–48 h after the procedure.

Results: Patients with elevated glycated-haemoglobin were older, with hypertension, metabolic syndromes, previous history of AMI, PCI and CABG. They had higher gycaemia, fasting-glycaemia and triglycerides but lower HDL-cholesterol. Patients with higher glycated-haemoglobin were more often on therapy with statins, diuretics and calcium-antagonist at admission, had higher basal, 24 and 48 h creatinine, lower creatinine clearance and lower ejection fraction. They had the highest incidence of PCI and contrast volume-eGFR rate. CIN occurred in 10.6% of patients with a linear association with glycated-haemoglobin ($p = 0.001$). No relationship was found between glycaemia/fasting glycaemia at admission and CIN. The multivariate analysis confirmed the association between elevated glycated haemoglobin (above the median value 5.7%) and the risk of CIN after adjustment for baseline confounding factors (Adjusted OR [95% CI] = 1.69 [1.14–2.51], $p = 0.009$). In fact, the results were consistent in major high-risk subgroups.

Conclusion: This is the first study showing that among patients without diabetes undergoing coronary angiography/PCI elevated glycated-haemoglobin but not glucose levels is independently associated with the risk of CIN.

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1. Introduction

Contrast induced nephropathy (CIN) is one of the major complications of procedures that foresee the use of contrast media and is associated with a poor long-term clinical outcome [1,2]. In particular, in patients undergoing diagnostic and/or therapeutic coronary angiography it has been shown to occur in up to 20–25% [3,2], especially in high-risk patients, who, due to the improvement in stent technology and antithrombotic therapies [4–9], represent a yearly growing proportion of patients revascularized percutaneously. The pathogenesis of CIN is the result of endothelial dysfunction, cellular toxicity from the contrast agent and tubular apoptosis resulting from hypoxic damage or reactive oxygen species [10]. The use of contrast media superimposed acute vasoconstriction, caused by the release of adenosine and endothelin, with the reduction in renal blood flow to the outer medulla, consequent medullary hypoxia, ischemic injury and death of renal tubular cells [11]. Hyperglycaemia leads to increased endothelin and angiotensin levels, causing intrarenal vasoconstriction; it also modifies the regulation of intrarenal blood flow increasing the medullary lactate level, reducing pH and oxygen delivery and increasing reactive oxygen species and oxidative stress [12,13]. It is known that diabetes mellitus is an independent risk factor for CIN [14,15], because of altered renal oxygen supply and enhanced reactive oxygen species generation, but we have no data regarding the association between glycemic levels in patients without diabetes and the risk of CIN [16]. Therefore, the aim of the current study was to evaluate whether high level of glycated haemoglobin in patients without diabetes undergoing elective coronary angiography and/or percutaneous coronary intervention (PCI), is associated with an increased risk of CIN.

2. Material and methods

Our initial population is represented by consecutive patients undergoing coronary angiography and/or angioplasty at Catheterization Laboratory of AOU ''Maggiore della Carità'', Novara, from January 2007 to September 2011, who were included in our registry, that, as previously described [17], aimed at studying coronary atherosclerosis in a consecutive cohort of patients with clinical indication for angiography and/or PCI. All demographic, clinical, biochemistry and angiographic data were prospectively collected in a dedicated database protected by a password. We included in this study patients who did not meet the diagnostic criteria for diabetes mellitus, defined as previous diagnosis, specific treatment administration (oral or insulin), fasting glycemia >126 mg/dL or HbA^{1c} > 6.5%—47 mmol/mol [18]. Informed consent was obtained by all patients before angiography. The study was approved by our local ethical committee. Hypertension was defined as systolic pressure >140 mm Hg and/or diastolic pressure was >90 mm Hg or if the individual was taking antihypertensive medications. Metabolic syndrome was defined according to the guidelines of the International Diabetes Federation by the presence of three or more of these characteristics: obesity on the basis of waist circumference (males >94 cm, females >80 cm), tryglycerides >150 mg/dL, low HDL-cholesterol (M: <40 mg/dL; F: <50 mg/dL), hypertension (>130/>85 mmHg) and fasting glycaemia >110 mg/dL [19]. All patients were hydrated with saline solution 1 mL/kg/h 12 h before and after the procedure or with saline solution 0.5 mL/kg/h (ejection fraction ≤40%) or with sodium bicarbonate (154 mEq/L in dextrose and water received 3 mL/kg for 1 h before contrast exposure followed by an infusion of 1 mL/kg/h for 6 h after the procedure) for primary PCI. CIN was defined as an absolute ≥0.5 mg/dL or a relative ≥25% increase in the serum creatinine level at 24 or 48 h after the procedure.

Coronary angiography was routinely performed by the Judkins technique using 6-French right and left heart catheters through the femoral or radial approach. Quantitative coronary angiography (Siemens Acom Quantcor QCA, Erlangen, Germany) was performed by two experienced cardiologists who had no knowledge of the patients' clinical information [20]. Significant coronary artery disease was defined as at least 1 coronary stenosis more than 50%. Severe multivessel disease was defined as three-vessel disease and/or left main disease. Coronary angioplasty was performed with standard techniques [21]. Use of stents, type of stents and stent implantation techniques, as much as the use of directional or rotational atherectomy, IVUS, glycoprotein IIb-IIIa inhibitors, was left at the discretion of the operators. The contrast medium used was non-ionic, iso-osmolar (Optiray, Visipaque, Ultravist). All patients received, according to guidelines, high-dose bolus of clopidogrel (600 mg) at the time of hospitalization or before angioplasty.

3. Biochemical measurements

Blood samples were drawn at admission in patients undergoing elective (following a fasting period of 12 h) or urgent coronary angiography. Glucose, glycated haemoglobin, creatinine and haemochrome were determined by standard methods. Creatinine was measured at 12, 24 and 48 h after the procedure or longer in case of development of contrast induced nephropathy.

4. Statistical analysis

Statistical analysis was performed with the SPSS 15.0 statistical package. Continuous data were expressed as mean ±SD and categorical data as percentage. Analysis of variance and the chi-square test were used for continuous and categorical variables, respectively. A trend analysis was performed as previously described [22]. Multiple logistic regression analysis was performed to evaluate the relationship between glycated haemoglobin levels and CIN, after correction for baseline confounding factors (clinical and demographic variables with a p value <0.1 at univariate analysis), that were entered in the model in block.

5. Results

Our initial population is represented by consecutive 1831 patients without diabetes. A total of 507 patients were