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ORIGINAL ARTICLE

The inflammatory response to percutaneous coronary intervention is related to the technique of stenting and not the type of stent

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KEYWORDS

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Abstract *Introduction:* Several studies have demonstrated that percutaneous coronary intervention (PCI) induces the release of multiple inflammatory markers which is associated with a later poor prognosis. We aimed to evaluate the inflammatory response to PCI via the assessment of the pre- and post-PCI serum levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1 in relation to the technique of stenting (predilation versus direct stenting [DS]), the type of stent (bare-metal [BMS] versus drug-eluting stents [DES]), the various coronary lesion characteristics, and the other PCI procedural variables.
Methods: We studied 75 consecutive patients (aged 54.2 ± 9.1 years, 54 men) enrolled between March and September 2012. BMS and DES were deployed in 46 and 29 patients respectively; via predilation technique in 37 patients and DS technique in 38 patients. Patients were evaluated monthly in the cardiology outpatient clinic for 6 months.
Results: The procedural increase in hsCRP and ICAM-1 was statistically significant in high risk coronary lesions (total occlusions, bifurcation lesions, and in-stent restenosis). The PCI-induced change of mean hsCRP, IL-6, and ICAM-1 levels was statistically significant in relation to the technique of stenting (predilation leads to augmented inflammatory response compared to DS) but was unrelated to the type of stent (BMS or DES).
Conclusions: Predilation significantly augments the inflammatory response to PCI than DS irrespective of the type of stent (BMS or DES). So, if predilation is required before any type of stent, measures to improve the patient's inflammatory profile should be carried out in advance.

1. Introduction

Several studies have demonstrated that percutaneous coronary intervention (PCI) induces the release of multiple inflammatory markers[1–3] which is associated with poor prognosis[4] and might interfere with the clinical outcome when surgical or

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medical treatments are subsequently required.[5] In humans, coronary stents have been shown to elicit an initial acute inflammatory cell response within 0–3 days, centered at the stent struts.[5] The stimulus for the inflammatory process is the disruption of the coronary endothelial layer with a subsequent prompt activation of the inflammatory cells, with early neutrophil recruitment to the site of injury, followed by prolonged macrophage accumulation.[6]

In this study, we aimed to evaluate the inflammatory response to PCI via the assessment of the pre- and post-PCI serum levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1 in relation to the technique of stenting (predilation versus direct stenting [DS]), the type of stent (bare-metal [BMS] versus drug-eluting stents [DES]), the various lesion characteristics, and the other PCI procedural variables.

2. Patients and methods

2.1. Patient selection

We studied 75 consecutive patients enrolled between March and September 2012 from Medicine Specialized Hospital (Mansoura University, Egypt). Patients who underwent coronary stenting in our institution were included in the study unless they met at least one of the following exclusion criteria: left ventricular (LV) ejection fraction $<30\%$, severe heart failure, cardiogenic shock, significant renal impairment (serum creatinine >2 mg/dl), clinical evidence of acute inflammation, malignancy, pregnancy, rheumatic conditions, hepatic decompensation, and treatment with steroids or immunosuppressive drugs.

2.2. Definitions of variables

Hypercholesterolemia was defined as serum total cholesterol (TC) $>$ 200 mg/dl or treatment with lipid-lowering drugs, diabetes as fasting blood glucose level >126 mg/dl on more than 2 occasions or treatment with insulin or oral hypoglycemic drug(s), and hypertension as blood pressure $\geqslant 140/90$ mm Hg on more than 2 occasions or current treatment with antihypertensive drug(s). Current smoking was defined as actively consuming $\geqslant 1$ cigarette/day on the time of admission or in the past year.

Major adverse cardiac events (MACE) were defined as the occurrence of death, acute coronary syndromes (unstable angina or myocardial infarction [MI]), or the need for coronary revascularization (via PCI or coronary artery bypass grafting [CABG] surgery) within a follow-up period of 6 months. In this context, unstable angina was defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of the following features: (1) occurring at rest (or on minimal exertion) and usually lasting >20 min (if not interrupted by the administration of a nitrate or an analgesic); (2) being severe and usually described as frank pain; or (3) occurring with a crescendo pattern (i.e., pain that awakens the patient from sleep or that is more severe, prolonged, or frequent than previously). Acute, evolving, or recent MI was diagnosed by typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of these criteria: (1) ischemic symptoms; (2) development of pathologic Q-waves in the ECG; (3) ECG changes indicative of ischemia (ST-segment elevation or depression); (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

2.3. Coronary intervention and sample acquisition

After local anesthesia, a sheath was placed into the femoral artery for insertion of coronary angiography and angioplasty catheters. All patients were pre-medicated with diazepam. Before intracoronary manipulations, an intravenous heparin bolus (80 IU/kg) was administered. A non-ionic contrast medium (Omnipaque, Nycomed Imaging, AS) was used in all processes.

The type of coronary stent, the need for predilation, and final balloon size for stent deployment were chosen by the operators to obtain an angiographic residual stenosis close to zero%. All patients were given aspirin 300 mg and clopidogrel 300 mg before angioplasty.

The PCI procedure was considered successful when the following criteria were fulfilled: (1) post-procedural stenosis $<10\%$ in the worst of 2 orthogonal views with normal contrast run-off in the stented artery, (2) no vascular complications during the procedure, (3) no clinical complications within 48 h after the procedure, and (4) no significant increase in the markers of myocardial necrosis (creatine kinase-MB and troponin-I) 24 and 48 h after the procedure.

After the procedure, the arterial sheath was manually removed when the activated clotting time was <150 s without the use of vascular closure devices; and the patients continued to receive 75 mg/day of aspirin indefinitely and 75 mg/day of clopidogrel for 12 months for DES (6 months for patients with BMS).

Blood samples were obtained within 1 h before and 24 h following PCI after 12 h overnight fasting. The inflammatory response to PCI was defined as the difference between baseline and post-procedural levels of the studied inflammatory marker (calculated as the serum level of the inflammatory marker after the procedure minus its level before the procedure).

2.4. Clinical and angiographic assessment

For follow-up and recording of clinical events, patients were required to visit the cardiac outpatient clinic monthly after the procedure, or when any anginal symptoms occurred. On each visit, the patients were examined clinically, with the addition of a simple exercise test when recommended.

Event-free survival was defined as freedom from MACE. Patients with symptoms or findings suggestive of myocardial ischemia underwent follow-up angiograms. In-segment angiographic restenosis was defined as the loss of $>50\%$ of the initial gain achieved with PCI anywhere within the stent or within the 5-mm borders proximal or distal to the stent.[7]

2.5. Laboratory assessment

Fasting venous blood samples (5 ml each) were obtained from all patients before and 24 h after PCI, and their sera were stored at -70 °C until later assessment for hsCRP, IL-6, and ICAM-1.

Serum levels of ICAM-1 were determined by Enzyme Linked Immuno-sorbent Assay (ELISA) kits obtained from