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Peri-operative Myocardial Infarction/Injury after Peripheral Artery Disease Revascularization

ABSTRACT

KEY WORDS: peri-operative myocardial infarction/injury, myocardial injury after non-cardiac surgery, peripheral artery disease, critical limb ischemia, revascularization, troponin, major adverse cardiovascular events

The use of a serial high-sensitivity troponin assays enables the diagnosis of a peri-operative myocardial infarction/injury (PMI), which proved to be a valuable peri-operative prognostic marker. An absolute increase of post-operative high-sensitivity cardiac troponin T or I in more than the upper limit of normal above the pre-operative concentration was associated with an important increase in 30-day and long-term mortality and cardiovascular events. In patients after revascularization, the incidence of PMI is approximately 20% which is higher than after non-cardiac surgery in general. Only a minority of patients with PMI after revascularization have clinical symptoms or ECG changes suggestive of myocardial ischemia. Therefore, active surveillance is mandatory to promptly address their residual atherosclerotic risk.

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INTRODUCTION

The presence of peripheral artery disease (PAD) confers a three- to six-fold higher risk for major adverse cardiovascular events (MACE) compared to the general population. The prognosis of patients with critical limb ischemia is especially poor, with a 25–% mortality expected in one year. This may be linked to the presence of concomitant coronary artery disease (presumably in 50–60% patients) (1). Recently, troponin values before and after a PAD revascularization procedure showed to enable peri-procedural risk stratification that is based on the detection of so-called peri-operative myocardial infarction/injury (PMI).

DEFINITION AND RECOMMENDATIONS

PMI is described as a post-operative high-sensitivity cardiac troponin T or I (hs-cTn T/I) release that indicates acute cardiomyocyte damage, not necessarily being accompanied by concordant symptoms, ischemic ECG changes, or imaging findings. It is defined as an absolute increase in the hs-cTn T/I concentration of more than the upper limit of normal on days one or two after a procedure. The hs-cTn T concentration complements clinical evaluation and ECG in risk prediction and is therefore recommended in patients who undergo high-risk or intermediate-risk procedures, the latter including peripheral arterial angioplasty.

Based on emerging data, serial troponin assessment is advised in the European Society of Cardiology (ESC) guidelines as an IB recommendation (2). Symptomatic and asymptomatic PMI have the same impact on 30-day mortality.

INCIDENCE AND PROGNOSTIC VALUE

Large prospective studies have confirmed the association of PMI with an increased risk of 30-day and one-year mortality and non-fatal MACE after non-cardiac surg-

eries. Approximately 16% of high-risk patients develop PMI. Among those, 30-day mortality was 8.9% and one-year mortality was 22.5% (compared to 1.5% and 9.3% in patients without PMI). PMI is a heterogeneous syndrome that can result from various cardiac and non-cardiac causes. Invasive coronary angiography was advised only in 10% of patients being managed for PMI (3).

In the Puelacher report, only 7% of all PMI cases were type 1 myocardial infarction (MI), of those 41% developed clinically overt MACE and 27% died in one year. The most common presentation of PMI was type 2 MI, in this group, 25% of patients developed overt MACE and 17% died in one year, compared to 7% and 9%, respectively in non-PMI patients. Other etiologies of PMI were extra-cardiac, tachy-arrhythmia, and acute heart failure (4). The baseline hs-cTn T/I value, when increased, already proved to be a strong independent predictor of combined cardiovascular endpoints.

PERI-OPERATIVE MYOCARDIAL INFARCTION/INJURY AFTER VASCULAR SURGERY AND ENDOVASCULAR LIMB REVASCULARIZATION

There is a discrepancy between different studies regarding the definition of PMI. Many are using the term MINS – myocardial injury after non-cardiac surgery – that excludes cardiac non-coronary aetiology, the assessment of troponin (I or T, being high sensitivity) and troponin threshold or absolute/relative increase values. In a study that evaluated troponin (that was not high sensitivity) in patients after lower extremity revascularization, there was a 23.7% incidence of MINS after open surgical revascularization, 19.5% after endovascular revascularization, and 36% after a hybrid procedure. Transcriptome profiling analysis was performed and found gene upregulation for thrombospondin 1 that was associ-

ated with long-term cardiovascular events. This is only one of possible mechanisms explaining increased risk in patients with PAD exhibiting PMI (5).

A study of vascular surgical patients (after thoracic aorta, aorto-iliac or peripheral artery reconstruction, extracranial cerebrovascular surgery, and endovascular aortic repair), which defined MINS as an elevated troponin T value within 30 days after the operation, found that without screening, MINS would not be recognized in 74.1% patients. The incidence of MINS was 19.1%. 30-day all-cause mortality was 12.5% (versus 1.5% in patients without MINS) and was similar in MINS patients with and without ischemic feature (6).

In a study that investigated chronic limb ischemia patients after endovascular limb revascularization, the incidence of PMI was 25.5%. The value of hs-cTn T was determined on admission, three to six hours after revascularization, and the next morning. PMI was defined as a hs-cTn T value above 14 ng/L with a relative increase $\geq 30\%$ from the baseline. One year mortality in patients with critical limb ischemia that manifested with PMI was 14.2%, and one year occurrence of MACE was 20.5%. Interestingly, 62.1% of patients had a baseline hsTnT value above the threshold level. Only 14.8% patients with PMI after endovascular revascularization had clinical symptoms or ECG changes suggestive of myocardial ischemia (1).

THE MANAGEMENT OF PERI-OPERATIVE MYOCARDIAL INFARCTION/INJURY IN VASCULAR PATIENTS

A transthoracic echocardiography should be performed on the day of PMI detection. An invasive coronary angiography is indicated in case of type 1 MI or in certain clinical settings of type 2 MI or missed type 1 MI. The last two could also be scheduled for

outpatient stress imaging or coronary CT angiography. In case of severe anaemia, other triggers of type 2 MI (such as hypoxemia, tachycardia, and hypertension), other cardiac causes (e.g. acute heart failure, aortic valve stenosis) or non-cardiac causes (e.g. sepsis, pulmonary embolism, stroke) should be treated (2).

Patients with PAD with confirmed PMI require even stronger clinical attention in terms of optimal medical therapy. Acetylsalicylic acid (ASA) and statins are already part of their regular therapy. Additional measures are required when target LDL cholesterol is below 1.4 mmol/L and at least 50% LDL cholesterol reduction from baseline are not met (adding ezetimibe and consequently a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor) (7). PAD patients without relevant contraindications are candidates for the addition of a low dose rivaroxaban (2.5 mg twice a day) to ASA according to the VOYAGER PAD study (8).

Based on the MANAGE study, the addition of dabigatran 110 mg twice a day may be considered about one week after non-cardiac surgery in patients with a low risk of bleeding as the study showed a 28% relative reduction of major vascular complications. Patients who developed MINS after orthopaedic, general, or vascular surgery were randomized to receive dabigatran 110 mg twice a day or a placebo (with initiation six days after operation) and were followed approximately nine months. 60% of patients already had ASA or an adenosine diphosphate receptor P2Y₁₂ inhibitor as part of their therapy. The composite primary outcome of vascular mortality, MI, non-haemorrhagic stroke, peripheral arterial thrombosis, amputation and symptomatic venous thromboembolism was 11% in the dabigatran group and 15% in the placebo group. There was no difference in major bleeding (9).

CONCLUSIONS

PAD patients have significant atherosclerotic burden involving coronary arteries that predisposes them to a worse cardiovascular prognosis. Determining PMI

among PAD patients is beneficial and should be used as a diagnostic and prognostic tool leading to personalized short- and long-term post-procedural treatment.

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