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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 surgeries. 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 trombospondin 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 ≥ 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 the-rapy. 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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