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Low levels of circulating CD25high CD127low regulatory T cells predict perioperative major cardiovascular and cerebrovascular events after non-cardiac surgery

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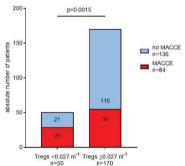
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Background: Perioperative major cardiovascular and cerebrovascular events (MACCE) are common after non-cardiac surgery and contribute to 30-day post-operative mortality. Preoperative risk prediction tools are limited. Murine experiments revealed that immunological reactions have a substantial impact on perioperative atherosclerotic plaque stability. Regulatory T cells (Tregs) have been shown to prevent progression of atherosclerosis and to promote plaque stabilizing effects. The "Leukocytes and Cardiovascular Perioperative Events-1" (LeukoCAPE-1) study demonstrated an association between preoperative levels Tregs and perioperative cardiovascular events.

Purpose: The aim of the here presented LeukoCAPE-2 study was to validate the previously derived cut off of 0.027 Tregs/nl for prediction of perioperative cardiovascular events (NCT03105427, ethic committee approval: S-351/2016).

Methods: In this single-center prospective observational cohort study, 233 elevated risk, coronary artery disease patients scheduled for non-cardiars surgery were recruited. Blood was drawn prior to surgery to quantify circulating CD25highCD127low Tregs by flow cytometry. High-sensitivity cardiac Troponin T (hs-cTnT) was measured preoperatively and on postoperative day one to three to detect MINS (defined as postoperative hs-cTnT >20 pg/ml and <65 pg/ml with an increase of 5 pg/ml or ≥65 pg/ml). ECGs were recorded preoperatively and on postoperative day 3. The primary endpoint was a composite of cardiac death, myocardial infarction, myocardial ischemia, myocardial injury after non-cardiac surgery (MINS) and stroke and was registered until postoperative day 30. Categorical data were analyzed using Fisher's exact test. Non-parametric Mann-Whitney U test was used for comparison between two groups. Risk prediction based on preoperative Tregs was evaluated using receiver operating characteristic (ROC) analysis. Cut off values were calculated using Youden's index.

Results: In the final analysis set the composite primary endpoint occurred in 84 of 220 patients (38%). The cut off value of 0.027 Tregs/nl derived from the LeukoCAPE-1 study was predictive for MACCE and reached a sensitivity of 35% and specificity of 85% (OR=2.89 [1.52; 5.39]; p=0.0015). ROC analyses support the predictive value of Tregs for MACCE (AUC=0.64; 95% CI [0.559; 0.711]; p=0.0008). Using Youden's index for LeukoCAPE-2 study the highest sensitivity (76%) and specificity (49%) was calculated for a cut off value of 0.05137 Tregs/nl (OR=3.02 [1.62; 5.63]; p=0.0003). Patients with MACCE showed significantly lower preoperative Treg values compared to patients without MACCE (Median [IQR] 0.049 [0.031; 0.068] vs. 0.038 [0.022; 0.051] Tregs/nl; p=0.0007).



Tregs <0.027 nl⁻¹ correctly identified 29 of 50 patients at risk for MACCE (positive predictive value 0.58).

Tregs ≥0.027 nl⁻¹ correctly identified 115 of 170 patients without risk for MACCE (negative predictive value 0.68). p=0.0015

Predictive value of Treas

Conclusion: Preoperative low levels of CD25highCD127low Tregs predict perioperative major cardiovascular and cerebrovascular events after non-cardiac surgery. Whether reduced Tregs play a causative role for perioperative cardiovascular events needs to be determined.

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Coronary angiography and revascularization in patients with peripheral artery disease undergoing percutaneous transluminal angioplasty

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Background: Clinical evaluation and noninvasive stress tests have reduced ac-

curacy for the identification of obstructive coronary artery disease (CAD) in patients with peripheral artery disease (PAD). At our institution according to internal hospital protocols implemented by a multidisciplinary vascular team all Percutaneous Transluminal Angioplasty (PTA) procedures both for carotid and low extremity artery disease (LEAD) are performed in conjunction by vascular surgeons and interventional cardiologists in the catheterization laboratory and are preceded by selective coronary angiography (CA) on the same angiographic session.

Purpose: To determine the prevalence and severity of CAD and the impact of systematic CA on the management and short-term outcome of patients undergoing PTA for PAD.

Methods: Patients scheduled for elective PTA from June 2017 to February 2018 were enrolled. CA was performed through the same femoral arterial sheath used for PTA. CA was not performed in patients with a recent (<12 months) angiogram unless significant clinical variations occurred. All patients were on dual antiplatelet therapy with aspirin (100 mg/day) and clopidogrel (75 mg/day). Indications for coronary revascularization were symptoms or high-risk anatomy (≥50% left main stenosis, 3-vessel disease with stenosis ≥70%, or 2-vessel disease involving the proximal left anterior descending artery (LAD). The prevalence, extension and treatment approach of CAD were compared with those of PAD.

Results: 93 consecutive patients (66 M/27F; mean age 75.4±8.03 years) were enrolled. The most frequent indications for PTA were carotid artery disease (n=58, 45%) and LEAD (n=34, 26%). CA was performed in 65 (69%) patients. Critical CAD was found in 45 (69%) patients: 21 (32%) had 3-vessel disease, 6 (9%) left main stenosis and 8 (12%) 2-vessel disease with involvement of the proximal LAD. In 2 patients the scheduled PTA procedure was deferred after myocardial revascularization for a very high-risk coronary anatomy. Coronary angioplasty was performed in 19 patients 3±2 days after PTA. In 4 patients a noninvasive test was indicated to assess the extension of inducible ischemia, 3 patients underwent coronary artery bypass surgery, and the remaining 14 patients received medical therapy. Neither major complication nor major cardiovascular events were recorded within 30 days of admission. Only male gender was statistically correlated with the evidence of high-risk coronary anatomy (correlation coefficient = 0.262: p=0.03).

Conclusions: The prevalence of significant CAD with complex lesions is high in patients with carotid disease or LEAD scheduled for PTA. A multidisciplinary approach combining PTA and CA is feasible (albeit it requires structural and logistic organization), safe (no complications following coronary procedures have been observed) and convenient to the patient (receiving no additional arterial puncture and medical therapy to that required for PTA).

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Incidence and outcome of perioperative myocardial injury after noncardiac surgeries diagnosed by different high sensitivity troponin assays

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Background: In order to differentiate perioperative myocardial injury (PMI) after noncardiac surgery from preexisting cardiomyocyte injury from chronic disorders, recent studies have shown the importance of using an acute absolute increase as criteria for PMI. For high-sensitivity troponin T (hs-cTnT), PMI defined as an absolute increase of 14ng/L (the 99th percentile) has been shown to be strongly associated with 30-day mortality. We hypothesized that using hs-cTnI and the respective 99th percentile of that assay as PMI criteria, a similar incidence of PMI and similar association with 30-day mortality would emerge.

Purpose: To evaluate the incidence and outcome of PMI diagnosed by hs-cTnI and by hs-cTnT assays after non-cardiac surgery.

Results: Patients had median age of 73 years and 58% were male. The primary outcome occurred in 5% of patients within 30 days of surgery and, 14% within one year. After surgery, 19% of patients had hs-cTnl values above the 99th percentile, and 13% fulfilled PMI diagnostic criterion. Considering hs-cTnT concentrations, 61% of patients had values above the 99th percentile and 16% had PMI. Patients with PMI diagnosed by hs-cTnl had higher rates of MACE than patients without PMI at 30 days (15%vs.3%; OR 5.2 Cl95% 2.7–10.0; P<0.001) and, at one-year follow-up (30%vs.10%; OR 3.3 Cl95% 2.2–5.0; P<0.001). Patients with PMI diagnosed by hs-cTnT also had higher rates of MACE than patients without PMI at 30 days (14%vs.3%; OR 5.9 Cl95% 3.3–10.5; P<0.001) and at one year (28%vs.11%; OR 3.0 Cl95% 2.1- 4.3; P<0.001)

Conclusion: PMI is frequent and associated with high rates of MACE in short-