

## **Abstract Peri-operative Cardiac Morbidity and Mortality**

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**Aim:** to give an update about perioperative cardiac morbidity and mortality, including myocardial injury after non-cardiac surgery (MINS), routine troponin measurements and treatment options

Although anesthetic and surgical advances have improved perioperative safety, more than 1 % of patients aged 45 years or older having noncardiac surgery die during initial hospitalization or within 30 days of surgery.<sup>1-4</sup> Cardiac complications after non-cardiac surgery are common, and up to 30 % of all surgical patients are having at least one cardiovascular risk factor.<sup>3</sup> Major cardiac adverse events including myocardial infarction and Myocardial Injury after Non-cardiac Surgery (MINS) are the single largest cause of death.

Perioperative myocardial infarction reflects a necrosis of myocardium and requires either ischemic symptoms like chest pain or ECG changes in addition to troponin elevation. Only the minority of patients with elevated troponin meet these universal diagnostic criteria of myocardial infarction.<sup>11</sup> This is especially challenging, as elevated troponin is the only clinical factor and there are no specific clinical symptoms. MINS is defined by elevated troponin being the single diagnostic criteria. Although the pathophysiologic mechanism is basically unclear, MINS is “presumably ischemic troponin elevation” and as such it may cover a spectrum from reversible myocardial injury to necrosis.

MINS is an adverse condition of great magnitude and prognostic relevance affecting millions of patients having noncardiac surgery annually. The risk of cardiac death at one year in patients having MINS ranges between 3 and 11 %, compared to 3 % in patients without MINS.<sup>6</sup> Importantly, prognosis of cardiac death depends on the magnitude of the perioperative troponin rise.

The Vision study included more than 15,000 patients and 8 % of the patients met the criteria of MINS. Overall mortality in patients experiencing MINS was 9.8 % compared to 1.1 % patients without MINS.<sup>1,11</sup> Importantly, the vast majority (84 %) of patients remained asymptomatic and only 42 % of the patients fulfilled the criteria for myocardial infarction. The study further demonstrated, that even low-level TnT concentrations to be predictive. Specifically, even a minor elevation of 0.02 ng/ml, being far below the routine diagnostic cut off, had an adjusted hazard ratio of 2.41 (95 % CI 1.33 – 3.77) compared to a concentration of 0.01 ng/ml. Higher concentration of TnT 0.03-0.29 ng/ml and > 0.3 ng/ml had an adjusted hazard ratio of 5.00 (95 % CI 3.72 to 6.76) and 10.48 (95 % CI 6.25 – 16.62) respectively. Mortality rates for 0.01, 0.02, 0.03-0.29 ng/ml, and > 0.3 ng/

ml were 1.0, 4.0, 9.3 and 16.9 %. Higher peak TnT concentrations exhibited shorter median time to death and nearly 75 % of deaths were in-hospital. <sup>1</sup>

Patients having noncardiac surgery and suffering MINS are at higher risk to die, but are further more at higher risk for nonfatal cardiac arrest (OROR, 14.58; 95% CI, 5.75–37.02; *P* < 0.001), congestive heart failure (OR, 10.34; 95% CI, 7.99–13.37; *P* < 0.001), and stroke (OR, 4.66; 95% CI, 2.87–7.58; *P* < 0.001) compared with patients who do not suffer MINS. The incidence of the composite of these major outcomes is 2.4 % in patients without MINS, compared to 18.8 % in patients suffering MINS [unadjusted OR 9.59 (95 % CI 7.99 – 11.51)].<sup>11</sup>

The by far largest study was the Vision 2 trial, including nearly 22,000 patients with routine hsTnT measurements.<sup>14</sup> Results of this study demonstrated, that among patients having noncardiac surgery, peak postoperative hsTnT during the initial 3 days after surgery is associated with 30-day mortality. Patients with an hsTnT of < 5 ng/dl are having a 30-day mortality of 0.4 %. Even a mild absolute increase of hsTnt to ≤ 5 to < 40 ng/ml is associated with an increase of mortality of 1.5 % [adjusted hazard ratio 2.81 (95 % CI 1.63 – 4.82)]. An even higher increase to ≥40 ng/ml is associated with a mortality of 9.7 % [adjusted hazard ratio 15.68 (95 % CI 8.94 – 27.51)].<sup>14</sup>

Investigators of the Vision2 trial were able to identify multiple hsTnT thresholds and associations to 30-day mortality through adjusted analysis (table below).<sup>14</sup>

**Table.** Peak postoperative hsTnT Thresholds associated with 30-day mortality<sup>14</sup>

|                                 | < 5 ng/ml | 5 to <14 ng/L    | 14 to <20ng/L       | 20 to < 65 ng/L     | 65 to < 1000 ng/L      | ≥1000 ng/L            |
|---------------------------------|-----------|------------------|---------------------|---------------------|------------------------|-----------------------|
| Deaths (%)                      | 0.1       | 0.5              | 1.1                 | 3.0                 | 9.1                    | 29.6                  |
| Adjusted hazard ratio (95 % CI) | 1         | 3.73 (1.58-8.82) | 9.11 (3.76 – 22.09) | 23.63 (10.32-54.09) | 70.34 (30.60 – 161.71) | 227.01 (87.35-589.92) |
| P value                         |           | .003             | <.001               | <.001               | <.001                  | <.001                 |

#### References:

1. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation Study I, Devereaux PJ, Chan MT, Alonso-Coello P, Walsh M, Berwanger O, Villar JC, Wang CY, Garutti RI, Jacka MJ, Sigamani A, Srinathan S, Biccard BM, Chow CK, Abraham V, Tiboni M, Pettit S, Szczeklik W, Lurati Buse G, Botto F, Guyatt G, Heels-Ansdell D, Sessler DI, Thorlund K, Garg AX, Mrkobrada M, Thomas S, Rodseth RN, Pearse RM, Thabane L, McQueen MJ, VanHelder T, Bhandari M, Bosch J, Kurz A, Polanczyk C, Malaga G, Nagele P, Le Manach Y, Leuwer M, Yusuf S: Association between

postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; 307: 2295-304

2. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S: Perioperative Major Adverse Cardiovascular and Cerebrovascular Events Associated With Noncardiac Surgery. *JAMA Cardiol* 2017; 2: 181-187
3. Kristensen SD, Knuuti J, Saraste A, Anker S, Botker HE, De Hert S, Ford I, Gonzalez Juanatey JR, Gorenek B, Heyndrickx GR, Hoeft A, Huber K, Jung B, Kjeldsen KP, Longrois D, Luescher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Uva MS, Voudris V, Funck-Brentano C, Authors/Task Force M: 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur J Anaesthesiol* 2014; 31: 517-73
4. Sessler DI, Devereaux PJ: Perioperative Troponin Screening. *Anesth Analg* 2016; 123: 359-60
5. Lange RA: Coronary angiography is not picture perfect for determining perioperative MI pathophysiology. *Catheter Cardiovasc Interv* 2012; 80: 777-8
6. van Waes JA, Grobbee RB, Nathoe HM, Kemperman H, de Borst GJ, Peelen LM, van Klei WA, Cardiac Health After Surgery I: One-Year Mortality, Causes of Death, and Cardiac Interventions in Patients with Postoperative Myocardial Injury. *Anesth Analg* 2016; 123: 29-37
7. Redfern G, Rodseth RN, Biccard BM: Outcomes in vascular surgical patients with isolated postoperative troponin leak: a meta-analysis. *Anaesthesia* 2011; 66: 604-10
8. Levy M, Heels-Ansdell D, Hiralal R, Bhandari M, Guyatt G, Yusuf S, Cook D, Villar JC, McQueen M, McFalls E, Filipovic M, Schunemann H, Sear J, Foex P, Lim W, Landesberg G, Godet G, Poldermans D, Bursi F, Kertai MD, Bhatnagar N, Devereaux PJ: Prognostic value of troponin and creatine kinase muscle and brain isoenzyme measurement after noncardiac surgery: a systematic review and meta-analysis. *Anesthesiology* 2011; 114: 796-806
9. Beattie WS, Karkouti K, Tait G, Steel A, Yip P, McCluskey S, Farkouh M, Wijeyesundera DN: Use of clinically based troponin underestimates the cardiac injury in non-cardiac surgery: a single-centre cohort study in 51,701 consecutive patients. *Can J Anaesth* 2012; 59: 1013-22
10. van Waes JA, Nathoe HM, de Graaff JC, Kemperman H, de Borst GJ, Peelen LM, van Klei WA, Cardiac Health After Surgery I: Myocardial injury after noncardiac surgery and its association with short-term mortality. *Circulation* 2013; 127: 2264-71
11. Botto F, Alonso-Coello P, Chan MT, Villar JC, Xavier D, Srinathan S, Guyatt G, Cruz P, Graham M, Wang CY, Berwanger O, Pearse RM, Biccard BM, Abraham V, Malaga G, Hillis GS, Rodseth RN, Cook D, Polanczyk CA, Szczeklik W, Sessler DI, Sheth T, Ackland GL, Leuwer M, Garg AX, Lemanach Y, Pettit S, Heels-Ansdell D, Luratibuse G, Walsh M, Sapsford R, Schunemann HJ, Kurz A, Thomas S, Mrkobrada M, Thabane L, Gerstein H, Paniagua P, Nagele P, Raina P, Yusuf S, Devereaux PJ, Devereaux PJ, Sessler DI, Walsh M, Guyatt G, McQueen MJ, Bhandari M, Cook D, Bosch J, Buckley N, Yusuf S, Chow CK, Hillis GS, Halliwell R, Li S, Lee VW, Mooney J, Polanczyk CA, Furtado MV, Berwanger O, Suzumura E, Santucci E, Leite K, Santo JA,

Jardim CA, Cavalcanti AB, Guimaraes HP, Jacka MJ, Graham M, McAlister F, McMurtry S, Townsend D, Pannu N, Bagshaw S, Bessissow A, Bhandari M, Duceppe E, Eikelboom J, Ganame J, Hankinson J, Hill S, Jolly S, Lamy A, Ling E, Magloire P, Pare G, Reddy D, Szalay D, Tittley J, Weitz J, Whitlock R, Darvish-Kazim S, Debeer J, Kavsak P, Kearon C, Mizera R, O'Donnell M, McQueen M, Pinthus J, et al.: Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology* 2014; 120: 564-78

12. Biccari BM: Postoperative Troponin Elevation, Myocardial Injury, and Pulmonary Embolism. *Anesth Analg* 2018; 126: 1435-1437

13. Gillmann HJ, Meinders A, Grohennig A, Larmann J, Bunte C, Calmer S, Sahlmann B, Rustum S, Aper T, Lichtinghagen R, Koch A, Teebken OE, Theilmeier G: Perioperative levels and changes of high-sensitivity troponin T are associated with cardiovascular events in vascular surgery patients. *Crit Care Med* 2014; 42: 1498-506

14. Writing Committee for the VSI, Devereaux PJ, Biccari BM, Sigamani A, Xavier D, Chan MTV, Srinathan SK, Walsh M, Abraham V, Pearse R, Wang CY, Sessler DI, Kurz A, Szczeklik W, Berwanger O, Villar JC, Malaga G, Garg AX, Chow CK, Ackland G, Patel A, Borges FK, Belley-Cote EP, Duceppe E, Spence J, Tandon V, Williams C, Sapsford RJ, Polanczyk CA, Tiboni M, Alonso-Coello P, Faruqi A, Heels-Ansdell D, Lamy A, Whitlock R, LeManach Y, Roshanov PS, McGillion M, Kavsak P, McQueen MJ, Thabane L, Rodseth RN, Buse GAL, Bhandari M, Garutti I, Jacka MJ, Schunemann HJ, Cortes OL, Coriat P, Dvirnik N, Botto F, Pettit S, Jaffe AS, Guyatt GH: Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA* 2017; 317: 1642-1651

15. Nagele P, Brown F, Gage BF, Gibson DW, Miller JP, Jaffe AS, Apple FS, Scott MG: High-sensitivity cardiac troponin T in prediction and diagnosis of myocardial infarction and long-term mortality after noncardiac surgery. *Am Heart J* 2013; 166: 325-332 e1

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