## **EDITORIAL VIEW**



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# Cardiac protection: a fact or myth?

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## ABSTRACT

A high rate of peri-operative mortality has been noted in patients with coronary artery disease, which warrants specific measures to prevent cardiac deaths in these patients. Perioperative cardiac protection can be achieved through either revascularization (CABG/PCI) or by pharmacologic means. While the first is only justified by medical reasons, the success of different drugs has proven less than desired. A plan is suggested to manage the unexpected rise of troponin in the postoperative period.

**Key words:** Cardiac protection; Perioperative; Coronary revascularization; Beta blockers; Troponin

**Abbreviations:** CAD (coronary artery disease); ACC/AHA (American College of Cardiology and the American Heart Association; CARP (Coronary Artery Revascularization Prophylaxis)

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The POISE 1 study have shown that 6.9% of patients at risk of, or with known coronary artery disease (CAD) suffer from cardiac death or nonfatal myocardial infarction (MI) within 30 days of non-cardiac surgery.<sup>1</sup> Another 3.5% suffer from other cardiovascular complication e.g. stroke, new AF or cardiac failure.

Cardiac protection options include coronary revascularization and pharmacological measures. In the 2014 ACC/AHA guidelines, revascularization before non-cardiac surgery is recommended, "if it is justified by medical reasons irrespective of the planned surgery".<sup>2</sup> Both the Coronary Artery Revascularization Prophylaxis (CARP) and the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) studies concluded that "in stable CAD, a strategy of revascularization before elective vascular surgery cannot be recommended".<sup>3,4</sup>

Guidelines remain vague about the superiority of either Coronary Artery Bypass Grafting (CABG) or stenting if revascularization was chosen. Coronary Artery Bypass Grafting (CABG) conveys improved survival when done for medical reasons and thus may be the better option. If for whatever reason stenting was chosen, drug-eluting stents should be avoided for the mandatory 12 months use of dual antiplatelet therapy. A bare metal (requiring only 6 weeks) may be better. Effectiveness of either type for perioperative cardiac protection is doubtful.<sup>5</sup>

Pharmacologic protection could be achieved by drugs reducing heart rate and preventing hypertension, anti-inflammatory drugs (aspirin/statins) or by preconditioning.

Both Perioperative Ischemic Evaluation and a recent meta-analysis of RCTs<sup>6</sup> have shown that beta blockers ( $\beta$ -b) reduce the risk of perioperative MI on the expense of increasing all-cause mortality and strokes. Both the American and European current guidelines agreed that "continuation of chronic  $\beta$ -b therapy" is the only indication that achieves class I recommendation. Its initiation "may be useful" (Class IIa) in high risk patients for high risk surgery with 2 conditions: earlier start and titration to a heart rate of 60-65/min. Even with such approach,  $\beta$ -b do not seem to improve outcome.<sup>7</sup>

In Perioperative Ischemic Evaluation 2, alpha2adrenoceptor agonists (clonidine) did not confer cardiac protection,<sup>8</sup> but hypotension and bradycardia were significant. Ivabradine, acting on pacemaker cells responsible for its spontaneous depolarization (funny channels) will reduce the heart rate without hypotension. However, there is only very limited data in the perioperative setting.<sup>9,10</sup>

Inflammatory mediators due to surgery can disrupt atheromatous plaques precipitating acute cardiac events. Aspirin in POISE 2 failed to protect the myocardium. It also increased bleeding risk. Current guidelines recommend against its initiation and only continued in either carotid/cardiac surgery or if indicated after stenting.<sup>2,3</sup>

Statins decrease progression of atheromatous lesions and have a pleiotropic (anti-inflammatory) effect. These are indicated for both primary and secondary prevention of cardiac disease,<sup>11</sup> the risk of developing diabetes is outweighed by averting vascular events.<sup>12</sup> Multiple observational studies<sup>13</sup> in addition to a recent meta-analysis<sup>14</sup> showed statins to decrease mortality, MI, new AF as well as reducing length of hospital stay. Most of these studies are in cardiac surgery, but POISE 3 will address it in non-cardiac surgery.<sup>15</sup> Statins should be continued perioperatively as their withdrawal increases postoperative cardiac events.<sup>16</sup> Initiation is recommended few weeks before vascular surgery as well as for patients with at least one clinical risk factor for elevated risk procedures.<sup>2</sup>

Tranexamic acid has anti-plasminogen effect, which decreases bleeding and reduces the risk of arterial thrombosis including coronary thrombosis in major trauma patients.16 POISE 3 will investigate its cardiovascular protective potential in non-cardiac surgery.<sup>15</sup>

Myocardial preconditioning: Damage by prolonged ischemia can be prevented by a preceding short period of ischemia or by pharmacological agents (e.g. volatile anesthetics). Despite repeated laboratory demonstrations and better outcome when volatiles are used,<sup>18</sup> clinical success is inconsistent.<sup>19</sup> As perioperative pharmacologic protection, with the exception of statins, is proving more elusive, an alternative approach is to monitor high risk patients by serial troponin assays. This is recommended in both the AHA/ACC, ESA/ESC guidelines as well as in a 2017 Canadian guidelines.<sup>20</sup> Recent evidence shows that even a modest elevation of postoperative troponin is associated with increased mortality and other major adverse cardiac events.<sup>21</sup> On the other hand, intensified treatment in response to such elevations greatly enhances event-free survival in vascular surgical patients.<sup>22</sup> In absence of clear guidelines, treatment of such cases should follow the same approach to treating acute phase MI outside the surgical setting, e.g. statins, ACE inhibitors, titrated β-b and anti-platelets.<sup>23</sup>

### CONCLUSION

Preoperative coronary revascularization is only indicated if it is justified by medical reasons irrespective of impending surgery. A surgical approach is likely (but not certain) to offer better protection than stenting. However, the risk of surgical revascularization must then be taken into consideration.

Pharmacologic protection is more elusive than previously thought. It is recommended to continue both  $\beta$ -b and statins for those patients on chronic treatment. Initiating  $\beta$ -b may be useful for high risk patients going for high risk surgery on two conditions: starting early and titrating carefully. It makes sense to start statins in high risk patients going for high risk surgery as such patients should be on long term statins therapy.

How to manage raised troponin postoperatively is not clear, but it may be that initiating statins, aspirin, an ACE inhibitor and a  $\beta$ -b under strict supervision would reduce the risk of further cardiac episodes.

Conflict of interest: Nil declared by the authors

#### REFERENCES

- POISE Study Group, Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial) – Lancet. 2008 May 31;371:1839-1847. [PubMed] [Free full text] DOI: 10.1016/S0140-6736(08)60601-7
- Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al. 2014 ACC/AHA Guidelines on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery" A report by the American college of cardiology/American heart association task force on practice guidelines. J Am Coll Cardiol. 2014 Dec 9;46(22):e77-e137. [PubMed] [Free full text] DOI: 10.1161/CIR.000000000000105
- McFalls E, Ward H, Moritz T, Apple FS, Goldman S, Pierpont G, et al. Predictors and outcome of a perioperative myocardial infarction following elective vascular surgery in patients with documented coronary artery disease: results of the Coronary Artery Revascularization Prophylaxis (CARP) trial. Eur Heart J. 2008;29:394-401 [PubMed] [Free full text] DOI: 10.1093/eurheartj/ehm620
- Kerati MD, Boersma E, Bax JJ, Heijenbrok-Kal MH, Hunink MG, L'talien GJ, et al. A meta-analysis comparing the prognostic accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery. Heart. 2003;89:1327-34. [PubMed] [Free full text]
- Albaladejo P, Morrel E, Samama CM, Collet JP, Abhay K, Loutrel O, et al. Non-cardiac surgery in patients with coronary stents: the RECO study. Heart. 2011 Oct;97(19):1566-1572. [PubMed] DOI: <u>10.1136/</u> hrt.2011.224519
- Bouri S, Shun-Shin MJ, Cole GD, Mayet J, Francis DP. Meta-analysis of secure randomized controlled trials of beta blockers to prevent perioperative deaths in non-cardiac surgery. Heart. 2014;100(6):456-464. [PubMed] [Free full text] DOI: 10.1136/ heartinl-2013-304262
- Hajibandeh S, Hajibandeh S, Antoniou SA, Torella F, Antoniou GA. Effect of beta blockers on perioperative out-

comes in vascular and endovascular surgery: a systematic review and meta-analysis. Br J Anaesth. 2017 Jan;118(1):11-21. [PubMed] [Free full text] DOI: 10.1093/bja/aew380

- Bevereaux PJ, Sessler DI, Leslie K, Kurz A, Mrkobrada M, Alonso-Coello P, et al. Clonidine in patients undergoing surgery. N Engl J Med 2014;370(16):1504-13. [PubMed] [Free full text] DOI: <u>10.1056/NEJ-Moa1401106</u>
- Vitale D, DeSantis V, Guarracino F, Fontana A, Pellegrini F, Tritapepe L. Use of Ivabradine in catecholamineinduced tachycardia after high risk cardiac surgery. Clin Res Cardiol. 2010;99(12):853-55. [PubMed] DOI: 10.1007/s00392-010-0208-9
- LoSapio P, Gensini GF, Bevilacqua S, Chiti E, Paperetti L, Pratesi C, et al. The role of Ivabradine in the incidence of perioperative coronary complications in patients undergoing vascular surgery. Int J Cardiol. Oct 9. 2013: 168(4): 4352-53. [PubMed] DOI: 10.1016/j.ijcard.2013.05.072
- 11. Taylor FC, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev 2013;31(1):CD004816. [PubMed] [Free full text] DOI: 10.1002/14651858.CD004816.pub5
- Sattar N, Preiss D, Murray HN, Welsh P, Buckley BM, de Craen AJ, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomized statin trials. Lancet. 2010 Feb 27;375(9716):735-42. [PubMed] DOI: 10.1016/S0140-6736(09)61965-6
- LeManach Y, Ibanez Esteves C, Bertrand M, Goarin JP, Fléron MH, Coriat P, et al. Impact of preoperative statin therapy on adverse postoperative outcomes in patients undergoing vascular surgery. Anesthesiology. 2011;114(1):98-104. [PubMed] [Free full text] DOI: 10.1097/ ALN.0b013e31820254a6
- de Waal BA, Buise MP, van Zundert AA. Perioperative statin therapy in patients at high risk for cardiovascular morbidity undergoing surgery. A review. Br J Anaesth. 2015 Jan;114(1):44-52. [PubMed] [Free full text] DOI: 10.1093/bja/aeu295
- 15. Devereaux PJ. Perioperative Isch-

emic Evaluation – 3 Trial: a pilot study (POISE 3). 2015; <u>https://clinicaltrials.</u> <u>gov/ct2/show/NCT02546648</u>. Accessed 18/03/2017.

- Roberts I, Perel P, Prito-Merino D, Shakur H, Coats T, Hunt BJ, et al. Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomized controlled trials. BMJ. 2012;345:e5839. [PubMed] [Free full text] DOI: 10.1136/bmj.e5839.
- Roberts I. Scientific letter: could tranexamic acid use in surgery reduce perioperative myocardial infarction? Heart. 2013 Dec;99(23):1785. [PubMed] DOI: <u>10.1136/ heartinl-</u>2013-<u>304292</u>
- Landoni G, Greco T, Biondi-Zoccai G, Nigro Neto C, Febres D, Pintaudi M, et al. Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery. Br J Anaesth. 2013 Dec;111(6):886-96. [PubMed] [Free full text] DOI: 10.1093/bja/aet231
- Kunst G, Klein AA. Perioperative anaesthetic myocardial preconditioning and protection-cellular mechanism and clinical relevance in cardiac anaesthesia. Anaesthesia. 2015 Apr;70(4):467-82. [PubMed] [Free full text] DOI: 10.1111/ anae.12975
- Deceppe E, Parlow J, MacDonald P, Lyons K, McMullen M, Srinathan S, et al. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for patients who undergo non-cardiac surgery. Can J Cardiol. Jan 2017; 33(1): 17-32. [PubMed] [Free full text] DOI: <u>10.1016/j.cjca.2016.09.008</u>
- Devereaux PJ, Chan MT, Allonso-Coello P, Walsh M, Berwanger O, Villar JC, et al. Association between postoperative Troponin levels and 30-day mortality among patients undergoing non-cardiac surgery. JAMA. 2012 Jun 6;307(21):2295-2304. [PubMed] [Free full text] DOI: 10.1001/ jama.2012.5502
- Foucrier A, Rodseth R, Aissaoui M, Ibanes C, Goarin JP, Landais P, et al. The long-term impact of early cardiovascular therapy intensification for postoperative Troponin elevation after major vascular surgery. Anesth Analg. 2014 Nov;119(5):1053-

63. [PubMed] DOI: <u>10.1213/</u> ANE.00000000000302

23. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA Guidelines for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/ American College of Cardiology. J Am Coll Cardiol. 2013 Jan 29;61(4):e78e140. [PubMed] [Free full text] DOI: 10.1016/j.jacc.2012.11.019

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