



Supplemental Figure 4: Forest plot of clinical studies on pharmacological conditioning, on cardioprotection in patients undergoing cardiovascular surgery and with biomarker release as end-point to estimate ischaemia/reperfusion injury. The zero represents the mean value, and the gray bars represent the standard error of the mean for the placebo group. Closed squares represent significantly reduced infarct size ($\bar{x} \pm \text{SEM}$), open squares represent non-significant changes. The star on the midline is used when no information was given to the standard error of the mean. BNP = brain natriuretic peptide; CK-MB = creatine kinase (muscle-brain); GIK = glucose-insulin-potassium; GR79236X = adenosine receptor agonist; (hs)Tn(I/T) = (high sensitive) troponin (I/T); n = no propofol anaesthesia; n.s. = not significant; PLA = placebo group; y = yes, propofol anaesthesia; ? = no information was given to the use of propofol

References

- Ahmad, S., Ahmad, R.A., Qureshi, B.A., & Baig, M.A.R. (2017). Myocardial protection with Glucose-Insulin-Potassium infusion during adult cardiac surgery. *Pakistan Journal of Medical Sciences*, 33, 325-329. <https://doi.org/10.12669/pjms.332.12414>

Alam, S.R., Lewis, S.C., Zamvar, V., Pessotto, R., Dweck, M.R., Krishan, A., et al. (2015). Perioperative elafin for ischaemia-reperfusion injury during coronary artery bypass graft surgery: a randomised-controlled trial. Heart, 101, 1639-1645. <https://doi.org/10.1136/heartjnl-2015-307745>

Ammar, A.S., Mahmoud, K.M., Kasemy, Z.A., & Helwa, M.A. (2016). Cardiac and renal protective effects of dexmedetomidine in cardiac surgeries: A randomized controlled trial. Saudi Journal of Anaesthesia, 10, 395-401. <https://doi.org/10.4103/1658-354X.177340>

Belhomme, D., Peynet, J., Florens, E., Tibourtine, O., Kitakaze, M., & Menasche, P. (2000). Is adenosine preconditioning truly cardioprotective in coronary artery bypass surgery ? The Annals of Thoracic Surgery, 70, 590-594. [https://doi.org/10.1016/S0003-4975\(00\)01502-2](https://doi.org/10.1016/S0003-4975(00)01502-2)

Benedetto, U., Melina, G., Capuano, F., Comito, C., Bianchini, R., Simon, C., et al. (2008). Preoperative angiotensin-converting enzyme inhibitors protect myocardium from ischemia during coronary artery bypass graft surgery. Journal of Cardiovascular Medicine (Hagerstown), 9, 1098-1103. <https://doi.org/10.2459/JCM.0b013e32830a6daf>

Besch, G., Perrotti, A., Salomon du Mont, L., Puyraveau, M., Ben-Said, X., Baltres, M., et al. (2018). Impact of intravenous exenatide infusion for perioperative blood glucose control on myocardial ischemia-reperfusion injuries after coronary artery bypass graft surgery: sub study of the phase II/III ExSTRESS randomized trial. Cardiovascular Diabetology, 17, 140. <https://doi.org/10.1186/s12933-018-0784-y>

Billings, F.T. 4th, Hendricks, P.A., Schildcrout, J.S., Shi, Y., Petracek, M.R., Byrne, J.G., et al. (2016). High-dose perioperative atorvastatin and acute kidney injury following cardiac surgery: A randomized clinical trial. Journal of the American Medical Association, 315, 877-888. <https://doi.org/10.1001/jama.2016.0548>

Boldt, J., Rothe, G., Schindler, E., Döll, C., Görlach, G., & Hempelmann, G. (1996). Can clonidine, enoximone, and enalaprilat help to protect the myocardium against ischaemia in cardiac surgery? Heart, 76, 207-213.

Carrascal, Y., Arnold, R.J., De la Fuente, L., Revilla, A., Sevilla, T., Arce, N., et al. (2016). Efficacy of atorvastatin in prevention of atrial fibrillation after heart valve surgery in the PROFACE trial (PROphylaxis of postoperative atrial Fibrillation After Cardiac surgEry). Journal of Arrhythmia, 32, 191-197. <https://doi.org/10.1016/j.joa.2016.01.010>

Chen, S., Hua, F., Lu, J., Jiang, Y., Tang, Y., Tao, L., et al. (2015). Effect of dexmedetomidine on myocardial ischemia-reperfusion injury. International Journal of Clinical and Experimental Medicine,

8, 21166-21172.

Dwaich, K.H., Al-Amran, F.G., Al-Sheibani, B.I., & Al-Aubaidy, H.A. (2016). Melatonin effects on myocardial ischemia-reperfusion injury: Impact on the outcome in patients undergoing coronary artery bypass grafting surgery. International Journal of Cardiology, 221, 977-986. <https://doi.org/10.1016/j.ijcard.2016.07.108>

El Messaoudi, S., Wouters, C.W., van Swieten, H.A., Pickkers, P., Noyez, L., Kievit, P.C., et al. (2016). Effect of dipyridamole on myocardial reperfusion injury: A double-blind randomized controlled trial in patients undergoing elective coronary artery bypass surgery. Clinical Pharmacology and Therapeutics, 99, 381-389. <https://doi.org/10.1002/cpt.106>

Forouzannia, S.K., Abdollahi, M.H., Mirhosseini, S.J., Hadadzadeh, M., Zarepur, R., Zarepur, E., et al. (2013). Adenosine preconditioning versus ischemic preconditioning in patients undergoing off-pump coronary artery bypass (OPCAB). The Journal of Tehran Heart Center, 8, 127-131.

Giannopoulos, G., Angelidis, C., Kouritas, V.K., Dedeiliás, P., Filippatos, G., Cleman, M.W., et al. (2015). Usefulness of colchicine to reduce perioperative myocardial damage in patients who underwent on-pump coronary artery bypass grafting. The American Journal of Cardiology, 115, 1376-1381. <https://doi.org/10.1016/j.amjcard.2015.02.036>

Jakobsen, O., Naesheim, T., Aas, K.N., Sorlie, D., & Steensrud, T. (2013). Adenosine instead of supranormal potassium in cardioplegia: it is safe, efficient, and reduces the incidence of postoperative atrial fibrillation. A randomized clinical trial. The Journal of Thoracic and Cardiovascular Surgery, 145, 812-818. <https://doi.org/10.1016/j.jtcvs.2012.07.058>

Jin, Z.X., Zhou, J.J., Xin, M., Peng, D.R., Wang, X.M., Bi, S.H., et al. (2007). Postconditioning the human heart with adenosine in heart valve replacement surgery. Annals of Thoracic Surgery 83, 2066-2072. <https://doi.org/10.1016/j.athoracsur.2006.12.031>

Le, S., Xiao, J., Li, W., Wang, J., Wang, Q., Xi, W., et al. (2017). Continuous administration of recombinant human B-type natriuretic peptide can improve heart and renal function in patients after cardiopulmonary bypass surgery. Journal of Thoracic Disease, 9, 692-701. <https://doi.org/10.21037/jtd.2017.03.20>

Moludi, J., Keshavarz, S., Tabaee, A.S., Safiri, S., & Pakzad, R. (2016). Q10 supplementation effects on cardiac enzyme CK-MB and troponin in patients undergoing coronary artery bypass graft: a randomized, double-blinded, placebo-controlled clinical trial. *Journal of Cardiovascular and Thoracic Research*, 8, 1-7. <https://doi.org/10.15171/jcvtr.2016.01>

Rinne, T., Laurikka, J., Penttila, I., & Kaukinen, S. (2000). Adenosine with cold blood cardioplegia during coronary revascularization. *Journal of Cardiothoracic and Vascular Anesthesia*, 14, 18-20. [https://doi.org/10.1016/S1053-0770\(00\)90049-1](https://doi.org/10.1016/S1053-0770(00)90049-1)

Teoh, L.K.K., Grant, R., Hulf, J.A., Pugsley, W.B., & Yellon, D.M. (2002). The effect of preconditioning (ischemic and pharmacological) on myocardial necrosis following coronary artery bypass graft surgery. *Cardiovascular Research*, 53, 175-180. [https://doi.org/10.1016/S0008-6363\(01\)00435-7](https://doi.org/10.1016/S0008-6363(01)00435-7)

Walter, D.H., Fichtlscherer, S., Britten, M.B., Rosin, P., Auch-Schweik, W., Schächinger, V., et al. (2001). Statin therapy, inflammation and recurrent coronary events in patients following coronary stent implantation. *Journal of the American College of Cardiology*, 38, 2006-2012.

Wang, X., Wei, M., Kuukasjarvi, P., Laurikka, J., Rinne, T., Moilanen, E., et al. (2009). The anti-inflammatory effect of bradykinin preconditioning in coronary artery bypass grafting (bradykinin and preconditioning). *Scandinavian Cardiovascular Journal*, 43, 72-79. <https://doi.org/10.1080/14017430802180449>

Wei, M., Wang, X., Kuukasjarvi, P., Laurikka, J., Rinne, T., Honkonen, E.L., et al. (2004). Bradykinin preconditioning in coronary artery bypass grafting. *Annals of Thoracic Surgery* 78, 492-497. <https://doi.org/10.1016/j.athoracsur.2003.11.039>

Wei, Q.B., Xie, F., Wang, S.L., & Li, G. (2017). Effect of thyroid hormone on myocardial and cerebral ischemia reperfusion injury in valve replacement under cardiopulmonary bypass. *Journal of Hainan Medical University*, 23, 79-82.

Wong, G.T., Huang, Z., Ji, S., & Irwin, M.G. (2010). Remifentanil reduces the release of biochemical markers of myocardial damage after coronary artery bypass surgery: a randomized trial. *Journal of Cardiothoracic and Vascular Anesthesia*, 24, 790-796. <https://doi.org/10.1053/j.jvca.2009.09.012>

Zheng, Z., Jayaram, R., Jiang, L., Emberson, J., Zhao, Y., Li, Q., et al. (2016). Perioperative rosuvastatin in cardiac surgery. *The New England Journal of Medicine*, 374, 1744-1753. <https://doi.org/10.1056/NEJMoa1507750>

Zhou, R.H., Yu, H., Yin, X.R., Li, Q., Yu, H., Yu, H., et al. (2017). Effect of intralipid postconditioning on myocardial injury in patients undergoing valve replacement surgery: a randomised controlled trial. *Heart*, 103, 1122-1127. <https://doi.org/10.1136/heartjnl-2016-310758>