

# Activation of coronary venous endothelium as an impulse for myocardial Regeneration

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**Background:** Periodic coronary venous pressure elevation initiates regeneration opening new opportunities in the quest for myocardial recovery<sup>1</sup>.

**Objectives:** We introduce a clinically feasible concept of mechanotransduction using coronary venous hemodynamics as adjunctive therapy in patients undergoing primary revascularization procedures.

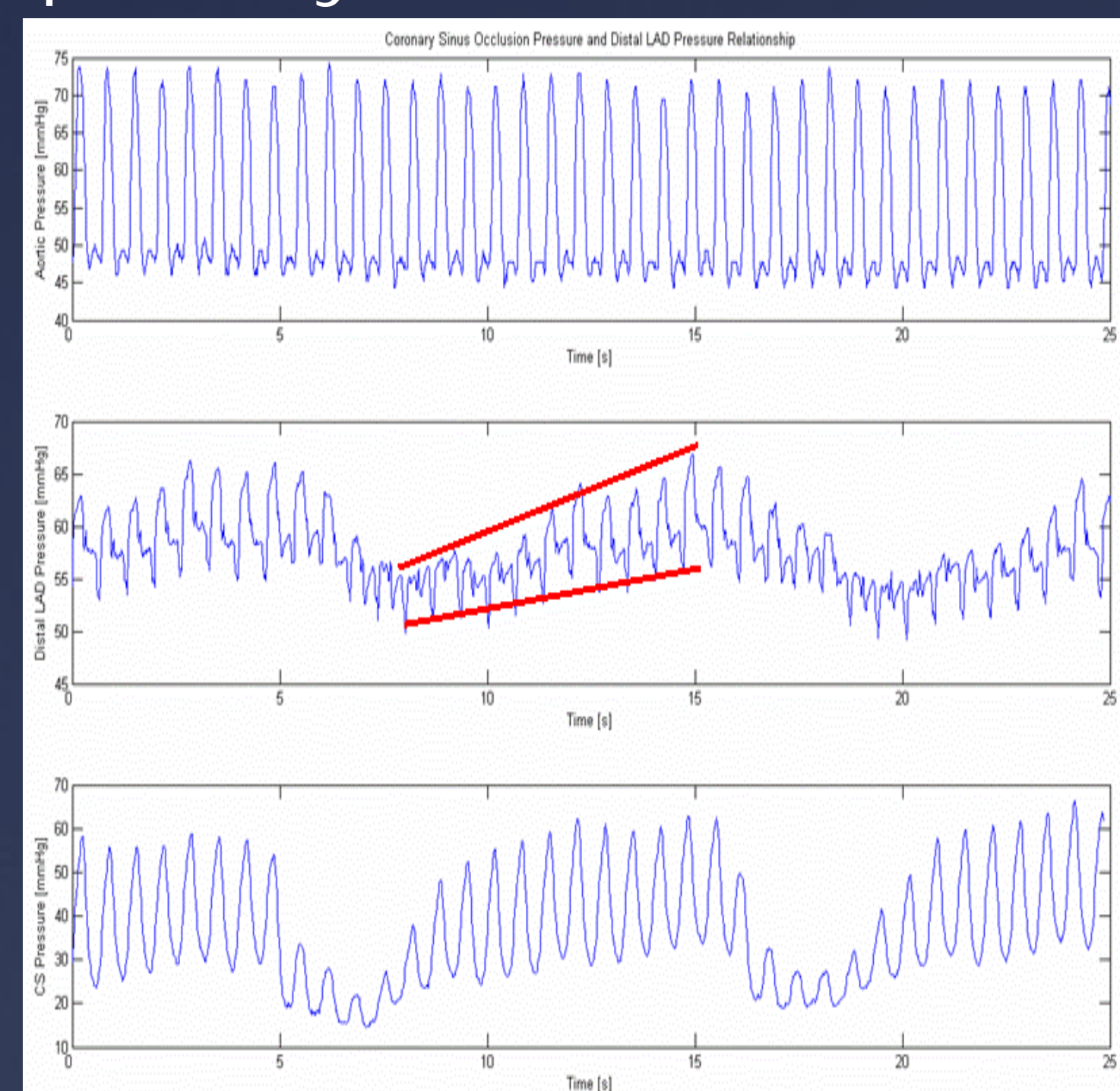
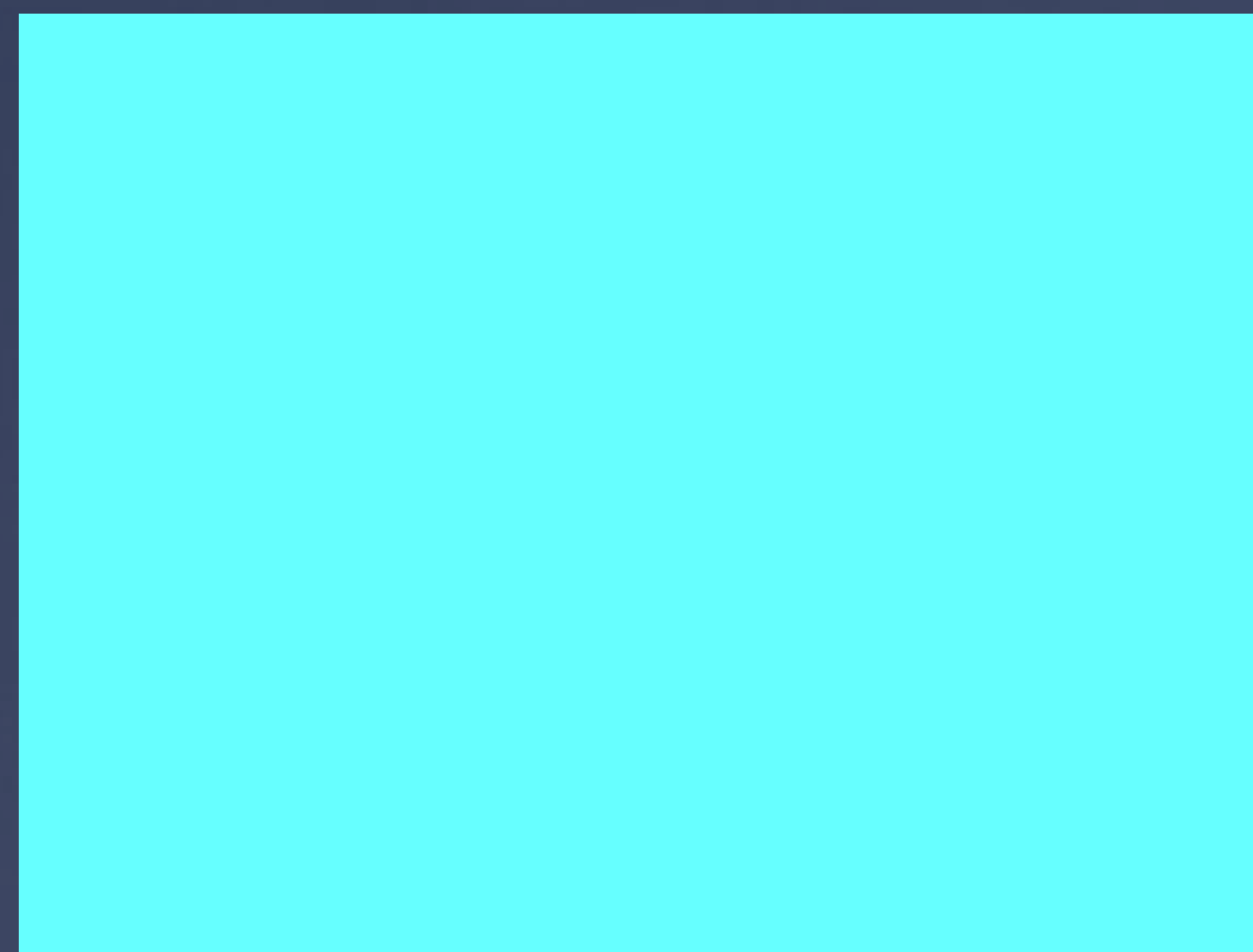


Figure 1 : Concomitant increase in LAD pressure after coronary sinus pressure elevation

**Methods:** We compared experimental and clinical data on pressure controlled intermittent coronary sinus occlusion (PICSO) in order to translate this innovative concept into clinical practice.



**Results:** Meta-analysis (Fig. 2) of the salvage potential of different intermittent coronary sinus occlusion techniques revealed a significant reduction in infarct size of 29.3% in different species during experimental myocardial ischemia ( $p < .001$ )<sup>2</sup>. An inverse relationship between coronary sinus pressure increase and infarct size ( $r = -0.92$ ;  $p < .007$ ) indicates that the hemodynamic force of venous blood and its mechanotransduction results in salvage, cytoprotection and enhanced collateral flow. Subsequent experiments showed changes in gene expression pattern marked by a 4 fold increase of hemoxygenase-1 expression ( $p < .001$ ) (Fig. 3b) in the center of infarction and a 2.5 fold increase of vascular endothelial growth factor (VEGF)(Fig. 3a) ( $p < .002$ ) in border zones in treated animals compared to controls<sup>3</sup>. Hypoxia induced factor (HIF) activity however remained unchanged by PICSO suggesting an independent regenerative stimulus.

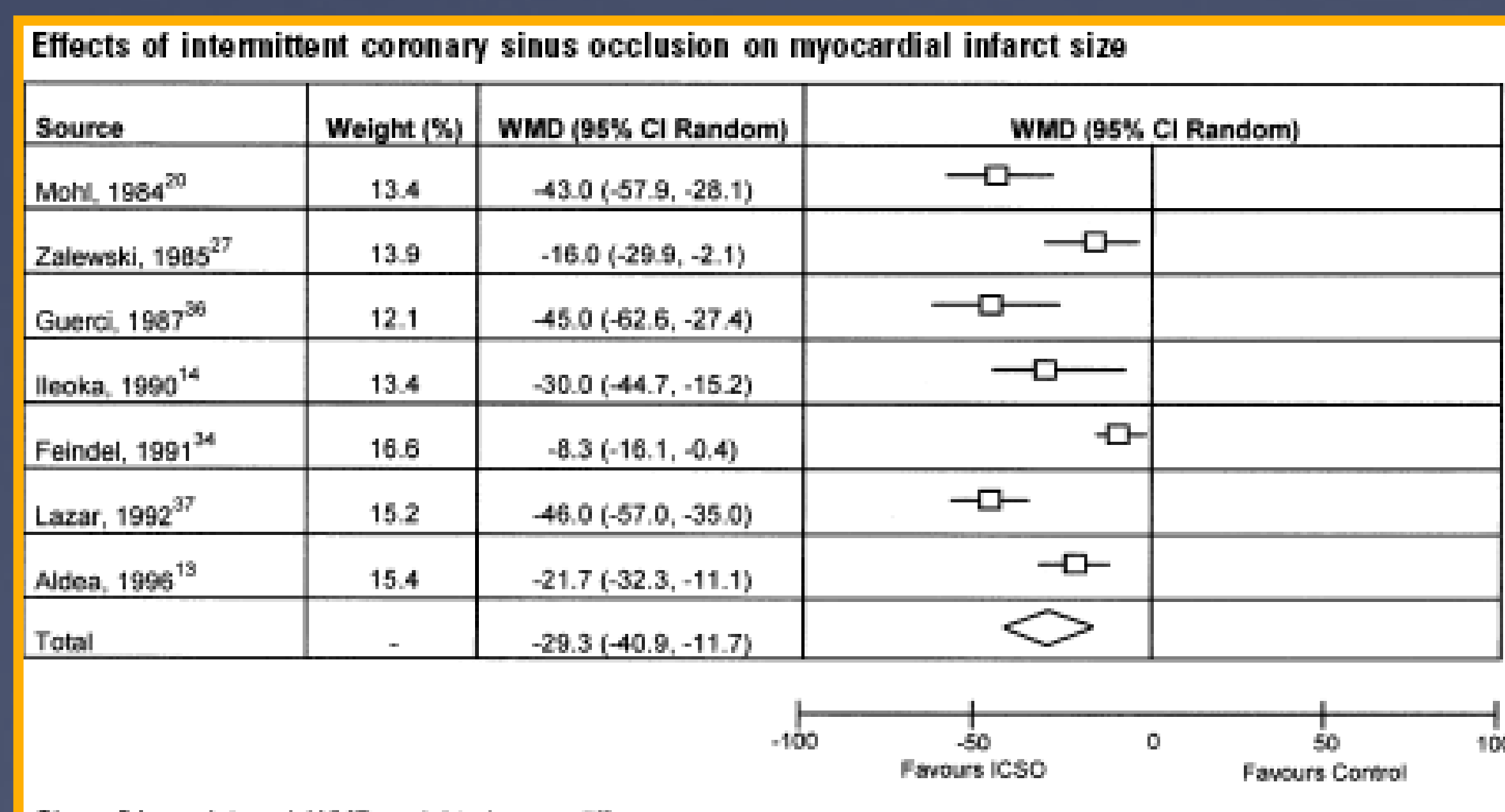


Figure 2 : Intermittent coronary sinus pressure elevation significantly reduces infarct size.

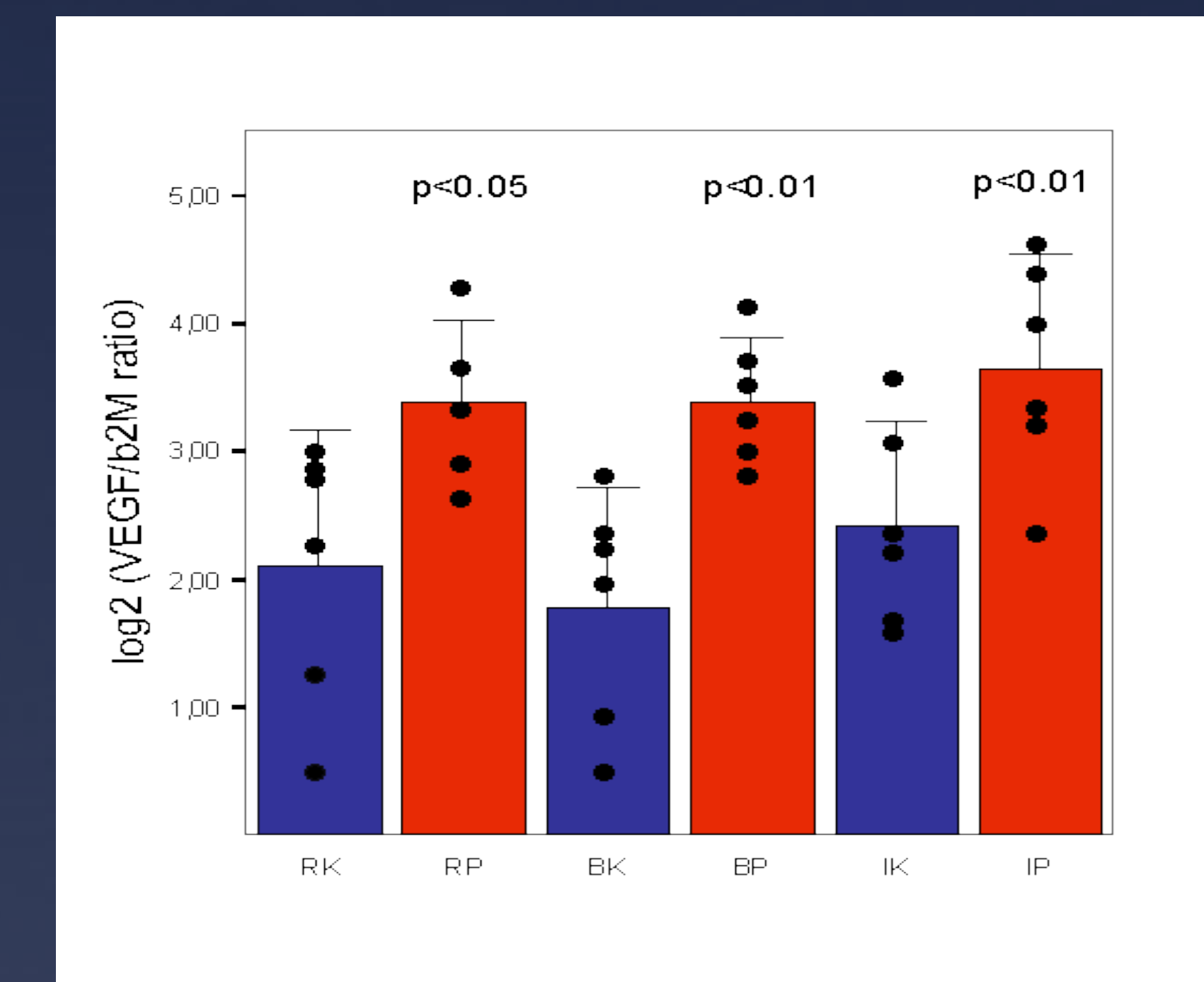


Figure 3a : Augmented VEGF expression as a consequence of an intermittent coronary sinus pressure elevation

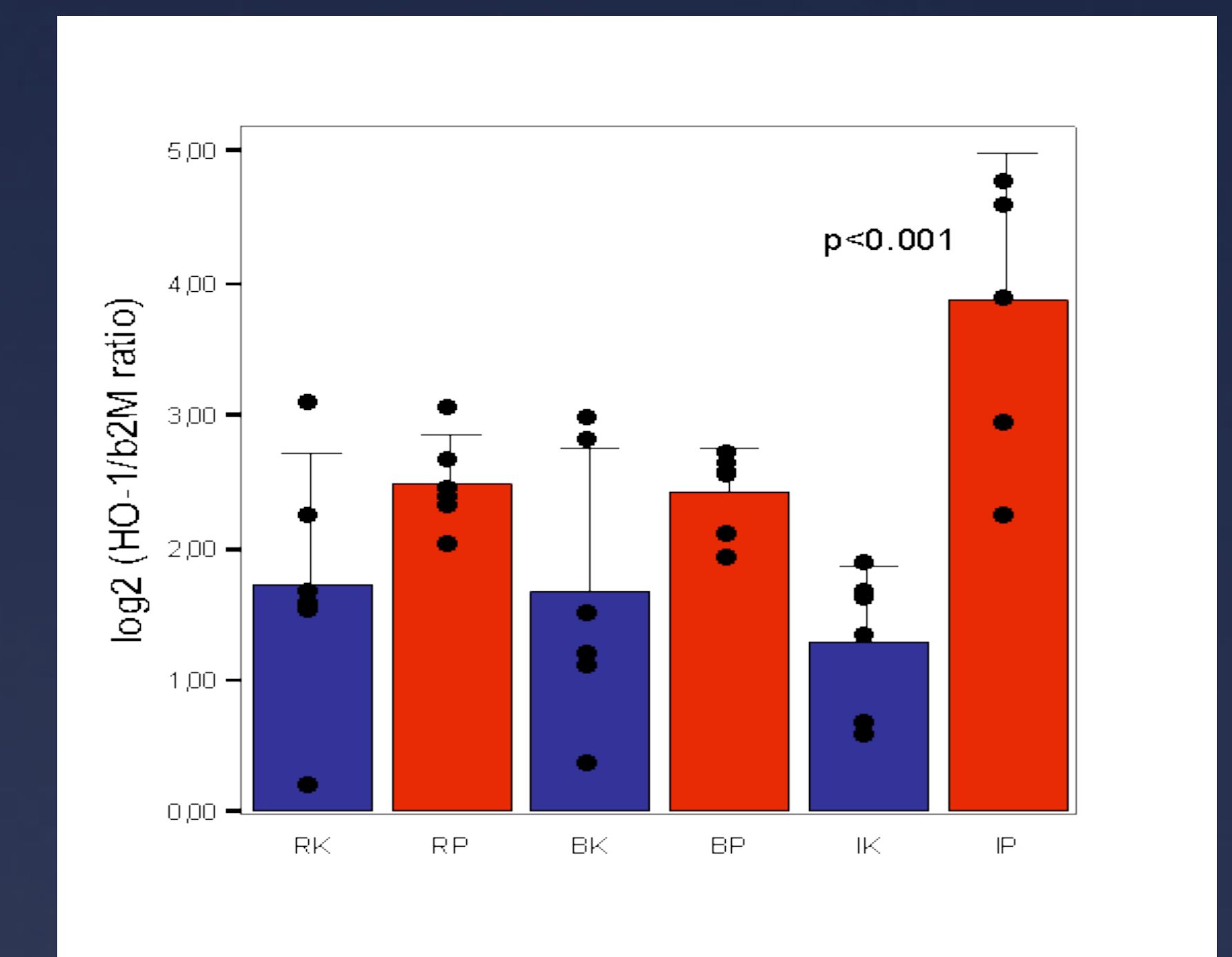


Figure 3b : Enhanced HO-1 expression after intermittent coronary sinus occlusion

**Conclusion:** Our hypothesis emphasizes that activation of pluripotent coronary venous endothelium is the common denominator of the PICSO concept<sup>4</sup>, which is confirmed by event free survival in patients with acute myocardial infarction and PICSO during primary revascularization with thrombolysis (risk reduction for event free survival and reinfarction 60 months after the acute event ( $p < .0001$ )) (Fig. 4a,b) underscoring the clinical potential as adjunctive therapy in primary revascularization procedures<sup>5</sup>.

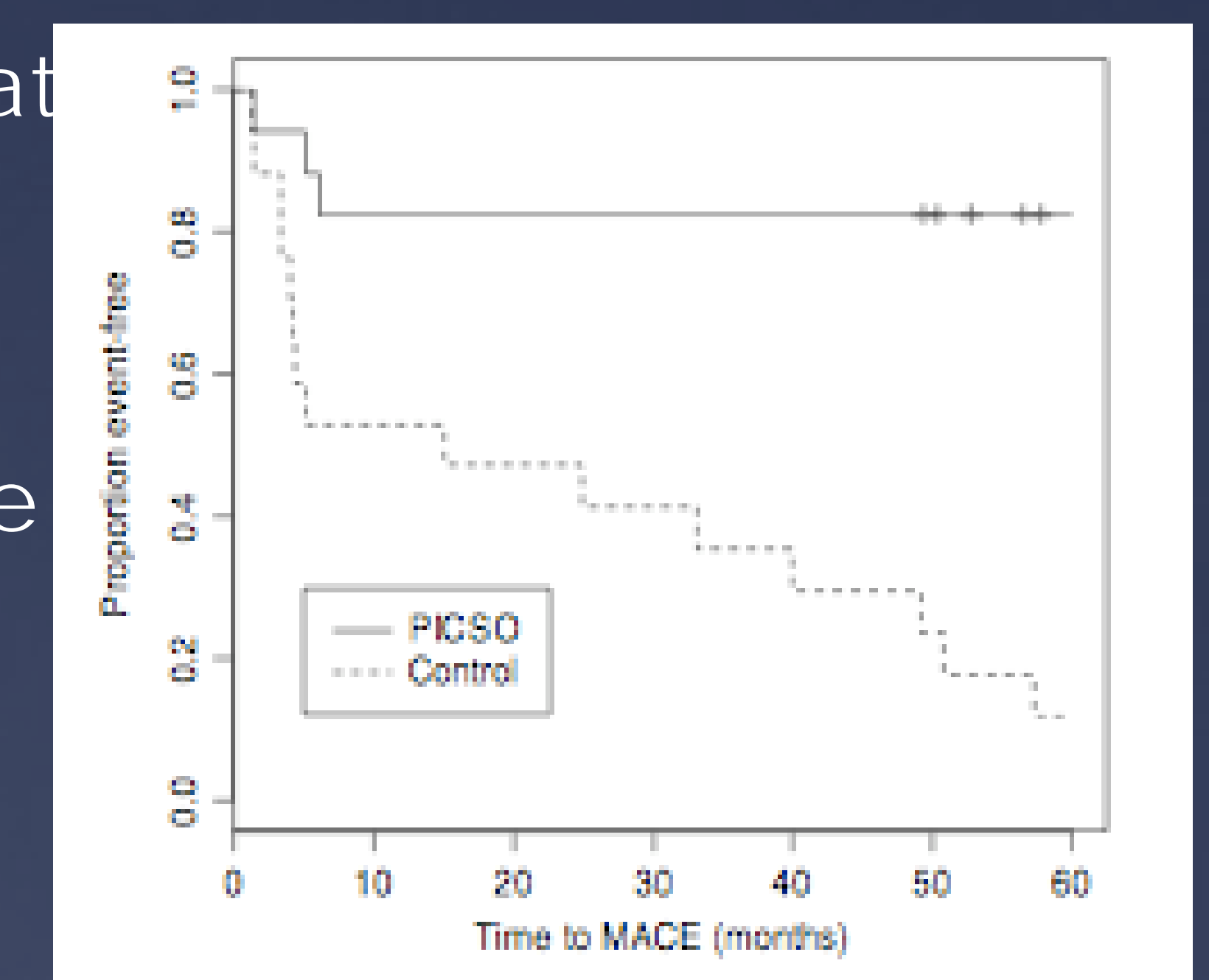


Figure 4a : Significantly lower occurrence of MACE in patients treated with PICSO compared to control group.

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