

18.1.7 - Reperfusion and Reperfusion Injury

Effects of hyperoxia and cardiovascular risk factors on myocardial ischemia reperfusion injury: a randomized, sham and placebo controlled parallel study

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Recent studies on O₂ supplementation in acute coronary syndrome patients are equivocal. We tested the hypothesis that oxidative stress (OS) is increased in rodents with cardiovascular risk factors and enhances ischemia reperfusion injury in the presence of hyperoxia.

Forty-three Wistar rats (WR), 30 spontaneous hypertensive rats (SHR) and 33 obese Zucker rats (ZR) were randomized in a sham procedure (1/3rd) or a left anterior descending ligation for 60 minutes (2/3rd). This was followed by 3 hours of reperfusion while animals were randomised either in a hyperoxic (HR) or a normoxic reperfusion group (NR). Baseline troponin (cTnT) was larger in SHR and ZR than WR (both $p < 0.001$). HR was associated with a lesser troponin rise in SHR and ZR than in NR (both $p < 0.001$); while the reverse occurred in WR ($p < 0.001$). In SHR, HR limited total MPO (myeloperoxidase) increase as compared to NR ($p = 0.0056$) to the contrary of total MPO in WR ($p = 0.013$). NR was associated with a drastic reduction of total thiols as compared to HR both in SHR and in ZR (both $p < 0.001$).

Despite a heightened baseline OS, HR rather restrained myocardial necrosis and anti/pro-oxidant imbalance in SHR and ZR, to the reverse of healthy WR.

Baseline characteristics of the 3 strain

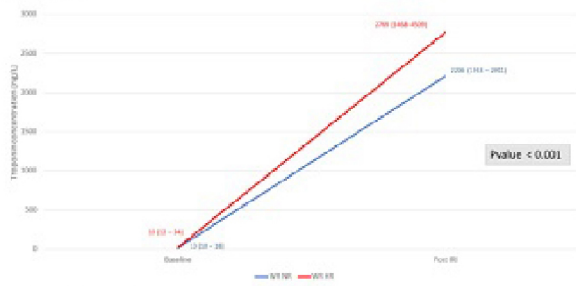
	WR ¹ ; (n = 41)	SHR ² ; (n = 29)	ZR ³ ; (n = 33)
Age (months)	9.0 (7.0 - 10.0)	6.0 (6.0 - 8.3) ^{1 vs 2}	7.0 (6.0 - 8.0) ^{1 vs 3, 2 vs 3}
Weight (mg)	590 (553 - 646)	436 (419 - 485) ^{1 vs 2}	670 (622 - 716) ^{2 vs 3}
Systolic arterial pressure (mmHg)	146 (120 - 174)	165 (120 - 197)	188 (169 - 215) ^{1 vs 3}
Heart rate (beat/minute)	284 (268 - 310) ^{1 vs 2}	244 (216 - 270)	254 (230 - 288) ^{1 vs 3}
Troponin T (ng/l)	13 (9 - 20)	42 (33 - 60) ^{1 vs 2}	33 (23 - 53) ^{2 vs 3}
Triglyceride (mg/dl)	/	87 (64 - 110)	1062 (683 - 2459) ^{2 vs 3}
MDA (nmoles)	0.10 (0.04)	0.09 (0.06)	0.14 (0.10) ^{2 vs 3}
Total MPO (ng/ml)	2889.7 (932.1)	2684.0 (681.7)	4479.7 (728.0) ^{1 vs 3, 2 vs 3}
Free total thiols (μM)	222.6 (213.9 - 240.5)	40.2 (5.3 - 60.2) ^{1 vs 2}	82.3 (17.5 - 235.7) ^{2 vs 3}

Abbreviations: WR: Wistar rats. SHR: Spontaneous Hypertensive rats. ZR Zucker rats. Both paired t-test and Wilcoxon signed rank test were used. Variables are shown in means with standard deviation (mean (SD)) or in median (interquartile range. IQR). Pairwise test – $p < 0.05$; 1vs2: WR vs SHR. 1vs3: WR vs ZR. 2vs3: SHR vs ZR. WR were older than the SHR and ZR. ZR were older than SHR. The ZRs were more obese than SHR and more hypertensive than WR. Baseline Troponin T was larger in SHR than ZR and WR. ZR had higher level of triglyceride than SHR. Total MPO was more elevated in ZR than SHR and WR. Oxidative stress was enhanced in ZR than SHR (higher MDA. more elevated total MPO) and total thiols were the lowest in the SHR.

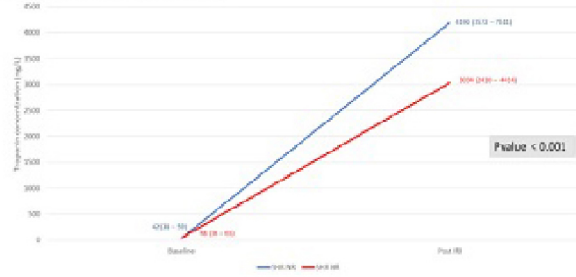
Abstract Figure. Troponin T concentration evolution slope

Troponin T concentration evolution slopes

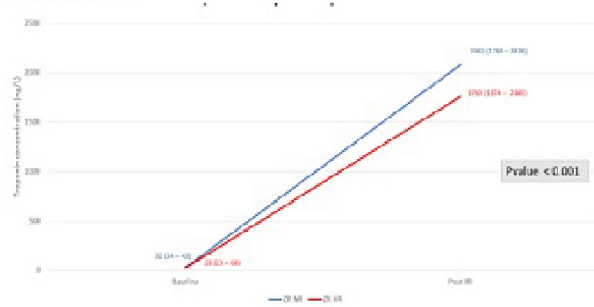
Wistar rats



Spontaneous Hypertensive rats



Obese Zucker rats



Legends: NR: normoxic reperfusion. HR: hyperoxic reperfusion. WR: Wistar rat; SHR: spontaneous hypertensive rat. ZR: Zucker rat.

Linear regression (time as the independent variable and Troponin T as the dependent variable) and pairwise comparisons of Troponin T-time coefficient of regression (slopes) using a Student t-test. Myocardial infarct size assessed by the rise in Troponin T was greater in NR than HR in the animals with cardiovascular risk factors in contrast to Wistar rats.