Organ function during porcine haemorrhage and resuscitation with pre-existing atherosclerosis

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Background and Goal of Study: Haemorrhagic shock causes tissue hypoxia, hyper-inflammation and subsequent multi-organ failure (MOF). Pre-existing cardiac comorbidity increases mortality after trauma¹. However, obesity, a risk factor for ischemic heart disease, is associated with reduced ICU mortality². Therefore, we investigated the impact of atherogenic diet-induced coronary artery disease (CAD)³ on MOF during haemorrhage and resuscitation.

Materials and methods: 18 anesthetized and instrumented familial LDL-cholesterol-receptor^{-/-} (FBM) pigs with (CAD, n=9) or without (control, n=9) atherogenic diet underwent 3 hours of haemorrhage (removal of 30 % of the calculated blood volume, mean arterial pressure (MAP) = 44 (42-45) mmHg) followed by 48 h of resuscitation comprising re-transfusion of shed blood, crystalloids and noradrenaline (NA) titrated to maintain MAP at pre-shock levels. Before, at the end of and every 12 hours after haemorrhage we assessed systemic, pulmonary and renal haemodynamics (left ventricular (LV) pressure-conductance and pulmonary artery catheterization; renal artery ultrasound flow probes), gas exchange and organ function. Data are median (range).

Results and Discussion: Survival time (CAD: 48 (26-48) h; control: 38 (24-48) h, p=0.84) and NA requirements needed to reach target haemodynamics (CAD: 1.5 (0.8-3.9) $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; control: 1.1 (0.9-1.7) $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, p=0.39) were comparable. Creatinine clearance was 66 (18-88) ml/min vs. 66 (39-94) ml/min (p=0.60) and 90 (35-105) ml/min vs 70 (28-98) ml/min (p=0.63) in CAD and control groups during 0-24h and 24-48h of resuscitation, respectively. Systemic and pulmonary haemodynamics, gas exchange and LV function ($\text{dp}/\text{dt}_{\text{max}}$ and min , isovolumic relaxation constant τ) did not show significant inter-group differences during 48h of observation either.

Data on hemodynamics, acid base equilibria and gas exchange.

		baseline	shock	12h	24h	36h	48h
Heart rate [1/min]	control	96 (83;113)	176 (134;186)	176 (162;174)	166 (162;181)	161 (137;168)	153 (112;165)
	CAD	92 (85;105)	162 (153;176)	162 (125;171)	176 (168;187)	187 (148;206)	150 (112;172)
MAP [mmHg]	control	103 (101;114)	44 (42;44)	86 (76;104)	76 (67;91)	84 (76;101)	111 (97;118)
	CAD	118 (104;127)	45 (41;46)	100 (88;112)	88 (78;108)	108 (87;117)	116 (102;129)
MPAP [mmHg]	control	30 (28;37)	21 (16;24)	36 (35;44)	44 (34;52)	37 (34;48)	39 (34;49)
	CAD	30 (26;35)	17 (13;23)	42 (30;44)	39 (35;48)	43 (36;53)	39 (31;46)
PAOP [mmHg]	control	10 (8;11)	3 (2;6)	17 (16;20)	19 (18;22)	20 (18;22)	20 (18;22)
	CAD	11 (9;12)	2 (1;6)	16 (16;20)	17 (16;18)	20 (18;21)	19 (17;21)
CO [L/min]	control	6.0 (5.1;7.3)	1.7 (1.4;2.8)	7.3 (3.8;9.0)	7.3 (4.8;7.5)	5.6 (3.8;7.5)	5.3 (4.3;6.9)
	CAD	6.4 (4.6;8.3)	2.0 (1.7;2.5)	5.6 (4.5;7.4)	6.8 (5.8;9.8)	6.9 (6.0;10.9)	6.2 (5.0;6.8)
Arterial pH	control	7.49 (7.47;7.51)	7.33 (7.29;7.42)	7.46 (7.36;7.52)	7.40 (7.22;7.46)	7.41 (7.39;7.45)	7.47 (7.45;7.53)
	CAD	7.50 (7.47;7.51)	7.36 (7.29;7.38)	7.43 (7.26;7.50)	7.40 (7.33;7.50)	7.42 (7.38;7.46)	7.45 (7.36;7.52)
Base excess [mmol/L]	control	4.1 (2.7;5.4)	-3.2 (-6.4;-0.8)	2.1 (-1.7;4.4)	1.0 (-7.5;3.8)	-0.3 (-1.6;4.5)	4.1 (-1.1;7.1)
	CAD	3.5 (2.7;5.2)	-5.3 (-6.0;0.8)	1.7 (-9.1;7.0)	-0.4 (-6.2;6.5)	0.1 (-2.6;3.6)	0.3 (-4.4;6.8)
Lactate [mmol/L]	control	1.6 (1.4;2.4)	5.2 (3.5;7.9)	2.1 (1.8;3.8)	3.1 (2.3;5.3)	2.0 (1.6;3.3)	1.2 (0.7;1.5)
	CAD	2.6 (1.7;2.9)	6.3 (5.2;7.5)	2.3 (1.0;10.6)	2.8 (1.3;5.0)	2.0 (1.4;4.6)	1.0 (0.8;1.3)
Horowitz index [mmHg]	control	372 (338;453)	393 (361;466)	280 (151;382)	302 (53;370)	308 (205;359)	327 (267;381)
	CAD	411 (350;456)	363 (318;411)	353 (196;383)	309 (153;393)	240 (105;360)	333 (179;370)

Conclusion: In our model of resuscitated haemorrhagic shock, pre-existing atherosclerosis neither increased mortality nor aggravated the severity of MOF. Aggressive fluid resuscitation and high-dose NoA may have overcome any impact related to pre-existing chronic cardiovascular disease. In addition, putative protective effects due to the “obesity paradox” may have blunted otherwise detrimental influence of pre-existing atherosclerosis.

References:

1. Ferraris et al: *J Trauma* 2010;69:645
2. Pickkers et al: *Crit Care Med* 2013;41:1878
3. Thim et al: *EuroIntervention* 2010;6:261

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