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ASSOCIATION OF ENDOTHELIAL INJURY AND SYSTEMIC INFLAMMATION WITH PERIOPERATIVE MYOCARDIAL INFARCTION

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BACKGROUND

Major surgery predisposes to endothelial glycocalyx (EG) injury. EG injury associates with cardiac morbidity, including spontaneous myocardial infarction. (1) In the perioperative setting, EG injury has been shown to associate with both global and regional ischemia and reperfusion. (2) However, the relation of EG injury to development of perioperative myocardial infarction (PMI) is unknown.

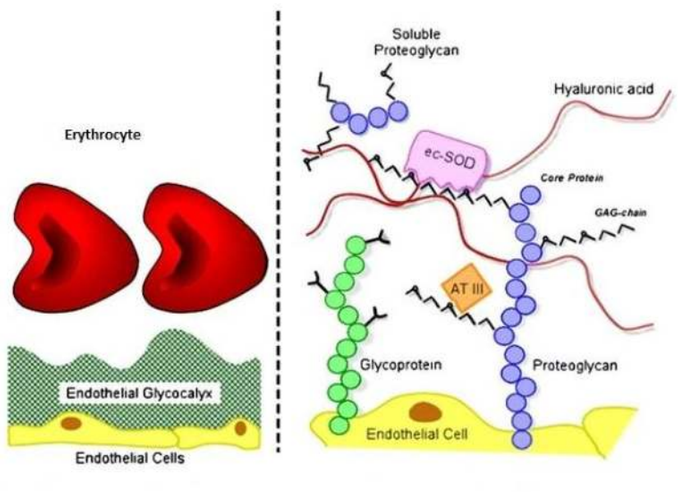

Fig. 1. The basic structure of the endothelial glycocalyx. Modified picture from Pflügers Archiv - European Journal of Physiology June 2007, Volume 454, Issue 3, pp345 - 59, The endothelial glycocalyx: composition, function,and visualization

METHODS

We conducted a laboratory substudy of data published earlier. (3)

- **EG markers**, soluble thrombomodulin (sTM), syndecan-1, vascular adhesion protein 1 (VAP-1), and an inflammatory marker, interleukin-6 (IL-6) measured preoperatively, 6h, and 24h postoperatively.
- **Inclusion**: All PMI patients with available baseline and follow-up blood samples (n=15) and four propensity-matched (age, gender, main medical history, medications, and intraoperative data) controls for each PMI-patients (n=60).
- **Statistics**: Comparisons of continuous variables were made using Mann-Whitney U-test. We calculated the Hodges-Lehmann estimator with 95% CIs to measure the magnitude of differences between PMI and non-PMI patients' values of EG markers and IL-6. The change over time for TnT, EG markers and IL-6 was tested by repeated-measures analysis of variance. We calculated Spearman's correlation, separately for patients with and without PMI, between TnT and each of the EG markers and IL-6 at preoperatively, 6h, and 24h postoperatively.
- **Outcome**: To explore the association of EG injury and systemic inflammation, reflected by IL-6, with TnT release and PMI.

RESULTS

Table 1. The median values of EG markers and IL-6 measured in PMI patients and propensity-matched controls.

	PMI N=15 median [IQR]	**No PMI** N=60 median [IQR]	***p*-value**	**HL** (95% CI)
Preoperative				
sTM	3946 [3131-7020]	4168 [3470-4739]	0.87	-60 (-1014.0, 751.0)
Syndecan-1	64 [49-86]	55 [40-79]	0.17	-9.0 (-23.0, 5.5)
VAP-1	361 [300-507]	357 [304-470]	0.66	-13.5 (-86.0, 56.0)
IL-6	25 [12-92]	7 [3-27]	0.008	-13.3 (-27.3, -3.6)
6h postoperative				
sTM	3500 [2938-5250]	4002 [3388-4693]	0.47	200.0 (-501.0, 846.0)
Syndecan-1	97 [58-119]	66 [44-106]	0.15	-13.4 (-38.3, 7.1)
VAP-1	321 [250-384]	333 [257 [420]	0.57	18.0 (-46.0, 78.0)
IL-6	205 [53-290]	69 [27-122]	0.013	-72.1 (-182.3, -12.2)
24h postoperative				
sTM	4053 [3713-5315]	4303 [3647-5073]	0.94	44.5 (-661.0, 645.0)
Syndecan-1	72 [52-98]	65 [48-85]	0.44	-7.0 (-24.4, 11.2)
VAP-1	298 [259-398]	331 [261-417]	0.53	16.5 (-35.0, 74.0)
IL-6	207 [101-324]	73 [23-154]	0.006	-93.2 (-199.2, -23.1)
Highest				
sTM	4191 [3718-7020]	4373 [3647-5338]	0.87	-76.5 (-920.0, 646.0)
Syndecan-1	111 [64-139]	70 [57-106]	0.12	-19.1 (-48.9, 4.8)
VAP-1	384 [300-513]	374 [297-473]	0.67	-15.5 (-90.0, 57)
IL-6	238 [101-349]	102 [36-191]	0.022	-93.1 (-213.0, -12.0)

IL-6: interleukin-6 (pg/mL); EG: endothelial glycocalyx; PMI: perioperative myocardial infarction; HL: Hodges-Lehman estimator; IQR: interquartile range; CI: confidence interval; sTM: soluble thrombomodulin (pg/mL); Syndecan-1 (ng/mL); VAP-1: vascular adhesion protein 1 (ng/mL).

IL-6 levels of PMI patients were significantly higher across all the time points, p=0.002, p=0.002, and p=0.001, respectively. In PMI patients, a significant postoperative IL-6 rise was observed, p<0.001.

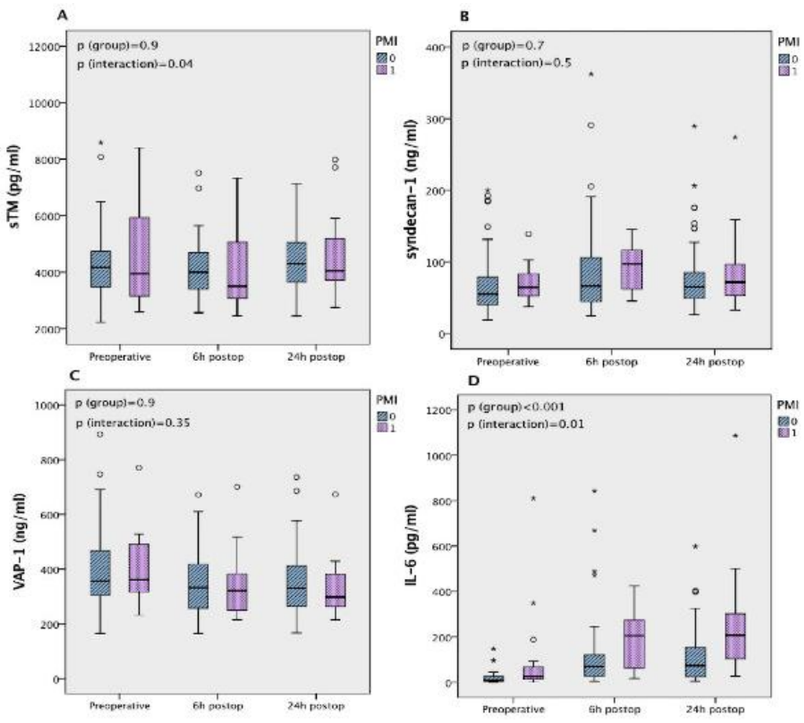

Fig. 2. Fig. 2. Kinetics of endothelial glycocalyx markers and interleukin-6 in PMI and non-PMI patients. PMI: perioperative myocardial infarction; sTM: soluble thrombomodulin; VAP-1: vascular adhesion protein 1; IL-6: interleukin-6.

Preoperative IL-6 correlated positively with preoperative and postoperative TnT values in PMI patients, p=0.05. Further, preoperative IL-6 had a positive correlation with sTM levels in PMI patients, p=0.01. sTM and TnT levels correlated positively pre- and postoperatively in non-PMI patients only, p=0.001.

CONCLUSION

Systemic inflammation, reflected by IL-6, associates with PMI and endothelial injury. sTM correlated positively with TnT release. The findings are preliminary and need to be confirmed or refuted in future larger studies.

References:

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