Važnost funkcije trombocita u sekundarnoj plućnoj hipertenziji uzrokovanoj kroničnim sistoličkim popuštanjem srca

Significance of platelet function in pulmonary hypertension secondary to chronic systolic heart failure

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Uvod: Trombociti (Trc) su posrednici u svim procesima ključnim za promjene cirkulacije u plućnoj hipertenziji (PH): vazokonstrikciji, upali, zgrušavanju i remodeliranju krvožilja. Niz istraživanja je potvrdio važnost uloge Trc u patogenezi primarne PH.[1-3] Međutim, iako je riječ o mnogo učestalijoj dijagnozi, patogeneza sekundarne PH posljedične bolestima srca je nedovoljno istražena. Cilj ovog istraživanja je ukazati na važnost Trc u nastanku PH uzrokovane kroničnim sistoličkim popuštanjem srca (CSHF).

Bolesnici i metode: Aktivnost Trc je mjerena u 160 bolesnika (57±10 godina; 65% muškaraca) s CSHF, hospitaliziranim u Kliničkom bolničkom centru Zagreb od listopada 2011. do listopada 2016. godine. Svi bolesnici su bili kandidati za napredne metode liječenja, zbog čega im je učinjena desnostrana kateterizacija srca. Po završetku invazivnog mjerenja hemodinamskih parametara

Background: Role of platelets in the pathogenesis of primary pulmonary hypertension is well established. Platelets act as mediators of vasoconstriction, inflammation, coagulation and vascular remodeling, all of which result in changes to the pulmonary circulation.[1-3] Although being a more common entity, data on pathogenesis of pulmonary hypertension (PH) secondary to heart disease remain scarce. The aim of this study was to shed light on the importance platelets have in the pathogenesis of PH secondary to chronic systolic heart failure (CSHF).

Patients and Methods: Measurement of platelet function was performed on 160 patients (57±10 years; 65% male) with CSHF admitted to University Hospital Centre Zagreb from October 2011 till October 2016. All patients were candidates for advanced treatment modalities and underwent right heart catheterization. Following the invasive

TABLE 1. Baseline hemodynamic parameters and aggregation tests.

	Mean ± Standard Deviation
CVP	11.4 ± 5.8 mmHg
Mean PAP	34.9 ± 10.9 mmHg
PCWP	24.2 ± 8.4 mm Hg
CI	1.8 ± 0.5 L/min/m^2
TPG	10.8 ± 5.3 mmHg
PVR	3.4 ± 2.0 Wood Units
ASPI	49.7 ± 33.4 U
ADP	51.7 ± 26.6 U
COL	42.9 ± 24.5 U
TRAP	73.7 ± 37.7 U

CVP – central venous pressure; PAP – pulmonary artery pressure; PCWP – pulmonary capillary wedge pressure; CI – cardiac index; TPG – transpulmonary pressure gradient; PVR – pulmonary vascular resistance; ASPI – acetylsalicylic acid induced aggregation test; ADP – ADP induced aggregation test; COL – collagen induced aggregation test; TRAP – thrombin receptor activating peptide-6 aggregation test

TABLE 2. Changes in hemodynamic parameters and aggregation tests following vasoreactivity testing with alprostadil.

	Mean ± Standard Deviation
ΔMean PAP	-8.8 ± 6.1 mmHg
ΔPCWP	-6.3 ± 4.9 mm Hg
ΔCI	+0.6 ± 0.8 L/min/m^2
ΔTPG	-2.9 ± 3.7 mmHg
ΔPVR	-1.7 ± 1.5 Wood Units
ΔASPI	-6.4 ± 17.1 U
ΔADP	-10.7 ± 22.1 U
ΔCOL	-6.7 ± 15.7 U
ΔTRAP	-7.5 ± 19.4 U
TRAP	73.7 ± 37.7 U

CVP – central venous pressure; PAP – pulmonary artery pressure; PCWP – pulmonary capillary wedge pressure; CI – cardiac index; TPG – transpulmonary pressure gradient; PVR – pulmonary vascular resistance; ASPI – acetylsalicylic acid induced aggregation test; ADP – ADP induced aggregation test; COL – collagen induced aggregation test; TRAP – thrombin receptor activating peptide-6 aggregation test

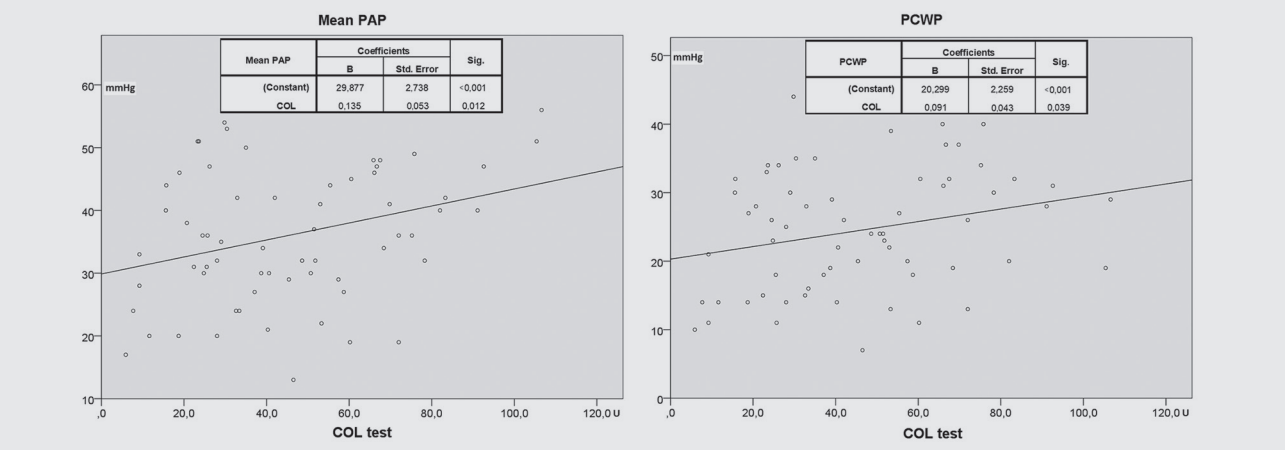

FIGURE 1. Regression plots showing linear interrelation between collagen induced aggregation (COL) and mean pulmonary artery pressure (PAP), i.e. left ventricular filling pressure (PCWP).

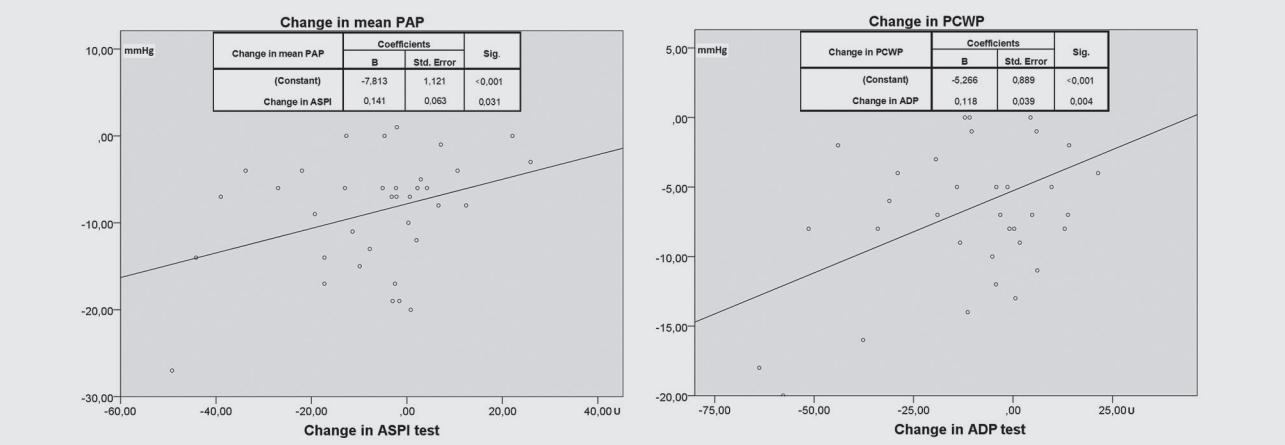

FIGURE 2. Regression plots showing linear interrelation between changes in acetylsalicylic acid induced aggregation (ASPI) and in mean pulmonary artery pressure (PAP), i.e. changes in ADP induced aggregation (ADP) and in left ventricular filling pressure (PCWP), following vasoreactivity testing with alprostadil.

(uključujući tlak u plućnoj arteriji-PAP i test vazoreaktivnosti alprostadilom), uzimao se manji uzorak krvi iz plućne arterije. Multiplate uređajem se odredila agregabilnost Trc inducirana acetil-salicilnom kiselinom (ASPI), adenozin difosfatom (ADP), kolagenom (COL) ili trombin receptor aktivirajućim peptidom-6 (TRAP).

Rezultati: Ishemijska (ICMP) i dilatacijska (DCMP) kardiomiopatija su bile najčešći uzroci CSHF (45% vs 43%). Očekivano, svim bolesnicima je izmjeren snižen srčani indeks te je ustanovljena PH uzrokovana povišenim tlakom punjenja lijeve klijetke (PCWP) (**tablica 1**). Bazične vrijednosti testova agregacije su pokazale reduciranu aktivnost Trc, uz značajno niži ASPI u bolesnika s ICMP ($p < 0,001$, zbog liječenja acetilsalicilatnom kiselinom). Vrijednosti COL testa su značajno korelirale s PAP i PCWP (**slika 1**). Test vazoreaktivnosti je učinjen u 26% bolesnika te je bio pozitivan u 53% slučajeva (**tablica 2**). Promjene u PAP i PCWP su značajno korelirale s promjenama u ASPI i ADP testovima (**slika 2**).

ZAKLJUČAK: Uloga Trc se doima važnom u patogenezi sekundarne PH uzrokovane CSHF. Nužno je daljnje proučavanje mehanizama i potencijalnog kliničkog značaja ovog međuodnosa.

measurement of hemodynamic parameters (including pulmonary artery pressure-PAP and vasoreactivity testing using alprostadil), blood samples were obtained from the pulmonary artery. Platelet aggregation induced by acetylsalicylic acid (ASPI), adenosine diphosphate (ADP), collagen (COL) or thrombin receptor activating peptide-6 (TRAP), was measured using Multiplate Analyzer.

Results: Most common causes of CSHF were ischemic and dilated cardiomyopathy (ICMP 45% vs DCMP 43%). As expected, all patients presented with decreased cardiac index and PH due to elevated left ventricular filling pressure (PCWP) (**Table 1**). Baseline aggregation tests showed reduced platelet activity, with ASPI being lower in patients with ICMP ($p < 0.001$, due to acetylsalicylic acid therapy). COL test values were found to correlate significantly with PAP and PCWP (**Figure 1**). Vasoreactivity testing was performed in 26% of patients, and positive in 53% of cases (**Table 2**). Changes in PAP and PCWP correlated significantly with changes in ASPI and ADP tests (**Figure 2**).

Conclusion: Platelets seems to play an important role in pathogenesis of PH secondary to CSHF. Further research on mechanisms and potential clinical significance of this interaction is warranted.

LITERATURE

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