ABSTRAK
INDEKS PLATELET DAN *IMMATURE PLATELET FRACTION* (IPF) PADA PASIEN SINDROMA KORONER AKUT

Latar Belakang :

Sindroma koroner akut (SKA) dibedakan menjadi *ST-elevation myocardial infarction* (STEMI), *non-ST elevation myocardial infarction* (NSTEMI) dan *unstable angina.* Platelet berperan penting dalam patogenesis SKA. Indeks platelet terdiri dari jumlah platelet, *mean platelet volume* (MPV), *platelet distribution width* (PDW), *plateletcrit* (PCT). Indeks platelet dan *immature platelet fraction* (IPF) dapat memperkirakan aktivasi platelet. Tujuan penelitian ini adalah menganalisis perbedaan indeks platelet dan IPF diantara pasien SKA.

Metode :

Penelitian analitik observasional dengan desain *cross sectional*. Subjek terdiri dari 30 pasien STEMI, 25 pasien NSTEMI dan 24 pasien *unstable angina* pada periode Mei-September 2019 di RSUD Dr. Soetomo. Sampel menggunakan sampel darah EDTA. Indeks platelet dan IPF diukur menggunakan Sysmex XN-1000. Perbedaan indeks platelet dan IPF antara pasien STEMI, NSTEMI dan *unstable angina* (UA) dianalisis dengan uji Krusskal-Wallis dan uji lanjutan Mann-Whitney.

Hasil dan Pembahasan :

Perbedaan bermakna MPV, PDW, P-LCR, dan IPF didapatkan diantara ketiga kelompok. Nilai MPV, PDW, dan P-LCR pada STEMI lebih tinggi bermakna dibandingkan UA (p<0,05). Nilai MPV, PDW, dan P-LCR pada NSTEMI lebih tinggi bermakna dibandingkan UA (p<0,05). Nilai IPF berbeda bermakna diantara semua kelompok. Perbedaan bermakna antara STEMI dan NSTEMI terhadap UA disebabkan kondisi trombotik pada STEMI dan NSTEMI yang lebih berat. Perbedaan bermakna antara STEMI dan NSTEMI tidak didapatkan karena kondisi trombotik sebenarnya pada pembuluh darah tidak diketahui.

Simpulan :

Nilai MPV, PDW, P-LCR pada STEMI dan NSTEMI lebih tinggi bermakna dibandingkan UA. Terdapat perbedaan IPF antara STEMI-NSTEMI, STEMI-UA, dan NSTEMI-UA.

Kata Kunci :

Sindroma koroner akut, indeks platelet, IPF, STEMI, NSTEMI, *unstable angina*

ABSTRACT
PLATELET INDICES AND IMMATURE PLATELET FRACTION (IPF) IN ACUTE CORONARY SYNDROME PATIENTS

Background :

Acute coronary syndrome (ACS) includes ST-elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA). Platelet plays important roles in ACS pathogenesis. Platelet indices consist of platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT). Platelet indices and immature platelet fraction (IPF) can predict platelet activations. This study aimed to analyze the differences of platelet indices and IPF among ACS patients.

Method :

This study was an observational analytical cross sectional study conducted in the Dr. Soetomo Hospital during May-September 2019. The subjects consisted of 30-STEMI, 25-NSTEMI and 24-UA patients. The EDTA-samples of each patients was measured for platelet indices and IPF using Sysmex XN-1000. The differences of platelet indices and IPF among STEMI, NSTEMI, and UA patients were analyzed using Kruskall-Wallis and Mann-Whitney test.

Results and Discussion :

The MPV, PDW, and P-LCR were significantly higher in STEMI and NSTEMI compared to UA ($p<0.05$). The IPF was significantly different between STEMI-NSTEMI, STEMI-UA and NSTEMI-UA. The significant differences value between STEMI and NSTEMI toward UA could be caused by the more severe thrombotic conditions in STEMI and NSTEMI compared to UA. The insignificant differences between STEMI and NSTEMI could be caused by the exact thrombotic condition in the body which was unknown.

Conclusion :

The MPV, PDW, and P-LCR were significantly different between STEMI and NSTEMI toward UA patients. The IPF was significantly different between STEMI-NSTEMI, STEMI-UA and NSTEMI-UA patients.

Keywords :

Acute coronary syndrome, platelet indices, IPF, STEMI, NSTEMI, unstable angina

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RINGKASAN

Sindroma koroner akut (SKA) merupakan manifestasi penyakit jantung koroner yang paling sering ditemui. Sindroma koroner akut dibedakan menjadi 3 kondisi, yaitu *ST-elevation myocardial infarction* (STEMI), *non-ST segmen elevation myocardial infarction* (NSTEMI) dan *unstable angina* (UA). Kondisi STEMI dan NSTEMI dikelompokkan sebagai infark miokard akut (IMA) karena pada kedua kondisi ini telah terjadi nekrosis miokard yang mengakibatkan peningkatan penanda kerusakan otot jantung. Nekrosis miokard dan peningkatan kadar penanda jantung tidak didapatkan pada UA (Kumar dan Cannon, 2009).

Platelet berperan penting dalam patogenesis SKA. Platelet berperan dalam pembentukan plak aterosklerosis dan pembentukan trombus setelah ruptur plak aterosklerosis. Konsumsi platelet pada plak aterosklerosis menyebabkan pelepasan platelet oleh sumsum tulang yang berukuran besar. Platelet yang berukuran besar bersifat lebih aktif secara metabolik maupun enzimatik karena mengandung materi protrombotik seper tromboksan A2 lebih banyak dan mengekspresikan glikoprotein IIb/III a yang lebih banyak (Slavka *et al*, 2011; Syahrir *et al,* 2017). Aktivasi dan rekrutmen platelet lebih lanjut terjadi pada proses pembentukan trombus setelah terjadinya erosi atau ruptur plak aterosklerosis (Slavka *et al*, 2011; Syahrir *et al,* 2017; Patil dan Karchi, 2017).

Indeks platelet merupakan parameter platelet yang didapatkan melalui pemeriksaan *complete blood count* (CBC) rutin. Berbagai indeks platelet yang bisa didapatkan yaitu jumlah platelet, *mean platelet volume* (MPV), *platelet distribution width* (PDW), *plateletcrit* (PCT), *platelet-large cell ratio* (P-LCR). *Immature platelet fraction* (IPF) merupakan fraksi atau persentase platelet yang belum matang dibandingkan platelet total. Indeks platelet dan IPF mencerminkan aktivasi dan produksi platelet. Kondisi SKA berhubungan dengan penungkatan aktivasi platelet sehingga memicu penggunaan dan *turn over* platelet (Khalifa *et al,* 2017). Tujuan dari penelitian ini adalah menganalisis perbedaan berbagai indeks platelet dan IPF diantara pasien SKA.

Penelitian ini merupakan penelitian analitik observasional dengan desain *cross sectional*. Pengambilan sampel dilakukan di RSUD Dr. Soetomo selama periode Mei-September 2019. Penelitian ini mendapatkan 30 pasien STEMI, 25 pasien NSTEMI dan 24 pasien UA.

Uji normalitas dengan uji Saphiro-Wilk menunjukkan data tidak

terdistribusi normal. Uji Krusskal-Wallis menunjukkan terdapat perbedaan bermakna nilai MPV, PDW, P-LCR dan IPF diantara ketiga kelompok, namun tidak didapatkan perbedaan bermakna jumlah platelet dan PCT diantara ketiga kelompok. Uji lanjutan Mann-Whitney dilakukan terhadap parameter MPV, PDW, P-LCR dan IPF untuk mengetahui perbedaan lebih lanjut antara 2 kelompok.

Nilai MPV, PDW, P-LCR lebih tinggi pada STEMI dan berbeda bermakna dengan kelompok UA dengan nilai p semua parameter tersebut adalah < 0,001. Nilai MPV, PDW, P-LCR juga lebih tinggi pada NSTEMI dan berbeda bermakna dengan kelompok UA dengan nilai p berturut-turut   0,002; <0,001 dan < 0,001. Perbedaan bermakna nilai IPF didapatkan antara kelompok STEMI dan UA, STEMI dan NSTEMI serta NSTEMI dan UA dengan nilai p berturut-turut <0,001; 0,013 dan 0,004.

Faktor lain diluar jumlah platelet yang lebih berpengaruh terhadap kejadian SKA dibandingkan jumlah platelet dapat menyebabkan jumlah platelet tidak berbeda bermakna. *Plateletcrit* juga tidak berbeda bermakna. *Plateletcrit* merupakan parameter yang didapatkan dari perhitungan antara jumlah platelet dan MPV. Hasil PCT yang tidak berbeda bermakna ini berhubungan dengan hasil jumlah platelet yang tidak berbeda bermakna.

Mean platelet volume, PDW dan P-LCR lebih tinggi bermakna antara pasien STEMI-UA dan NSTEMI UA. Hal ini dapat disebabkan oleh kondisi trombosis pada STEMI dan NSTEMI yang lebih berat daripada UA. Kondisi STEMI dan NSTEMI yang tidak berbeda bermakna dapat berhubungan dengan kondisi trombosis pada pasien yang dapat diketahui dengan *coronary angiography* tidak dilakukan pada penelitian ini.

IPF didapatkan berberda bermakna antara kelompok STEMI-NSTEMI, STEMI-UA dan NSTEMI-UA. Peningkatan IPF berhubungan dengan respon cepat megakariosit terhadap konsumsi atau kehilangan platelet cepat. Spektrum SKA memiliki tingkat keparahan tertinggi pada STEMI, diikuti NSTEMI lalu UA.

Parameter MPV, PDW dan P-LCR dapat digunakan untuk membedakan IMA dan UA dengan penelitian lebih lanjut. Parameter IPF dapat digunakan untuk membedakan STEMI, NSTEMI dan UA dengan penelitian lebih lanjut. Uji diagnostik lanjutan yang meneliti kemungkinan parameter ini digunakan dalam membedakan ketiga kondisi spektrum SKA perlu dilakukan.

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SUMMARY

Acute coronary syndrome (ACS) is the most common coronary heart disease manifestation. Acute coronary syndrome consists of 3 condition, i.e. ST-elevation myocardial infarction (STEMI), non-ST segmen elevation myocardial infarction (NSTEMI) and unstable angina (UA). The STEMI and NSTEMI conditions are separately grouped into acute myocardial infarction (AMI) because of myocardial infarction that increases myocardial damage biomarker has already been found in these two conditions. Conversely, myocardial infarction and myocardial damage biomarker increases are not found in UA (Kumar and Cannon, 2009).

Platelets play important roles in ACS pathogenesis. Platelets play roles in atherosclerosis plaque formation and also thrombus formation after atherosclerosis plaque rupture. Platelets consumption in atherosclerosis plaque formation location can stimulate bone marrow to produce more platelets that tend to be larger in size. Larger platelets metabolically and enzymatically are more active as they contain more prothrombotic material such as A2 thromboxane and express more glycoprotein IIb/IIA (Slavka *et al*, 2011; Syahrir *et al,* 2017). Further platelet recruitment and activation occured in thrombus formation which happened after atherosclerosis plaque rupture (Slavka *et al*, 2011; Syahrir *et al,* 2017; Patil dan Karchi, 2017).

Platelet indices are platelet parameter obtained in routine complete blood count examination. These platelet indices consist of platelet count. mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-large cell ratio (P-LCR). Immature platelet fraction (IPF) is a percentage of immature platelet that sometimes called reticulated platelet as this platelet contain nucleic acid in their cytoplasm. Platelet indices and IPF can reflect paltelet activation and production. Acute coronary syndrome condition correlate with increase in platelet activattion that stimulate platelet production and increase platelet turn over (Khalifa et al, 2017). This study aimed to analyze the differences of platelet indices and IPF value among ACS patients.

This study was an analytical observational study conducted as a cross sectional design. Samples were collected in the Dr. Soetomo Hospital during May-September 2019. This study involved 30 STEMI, 25 NSTEMI and 24 UA patients.

Data normality test conducted using Saphito-Wilk test showed non normal distribution. Krusskal-Wallis test showed significant differences of MPV, PDW, P-LCR and IPF value, but no significant difference of platelet count and PCT value among 3 ACS groups. Advanced differential study using Mann-Whitney was conducted towards MPV, PDW, P-LCR and IPF to know any advance diffences between each 2 groups.

Mann Whitney test showed significant differences of MPV, PDW, P-LCR values between STEMI and UA with p values of all parameters were < 0.001. The significant differences of MPV, PDW, P-LCR were also found between NSTEMI and UA groups with p value of 0.002; <0.001 and < 0.001, respectively. The IPF were significantly different between STEMI-UA groups, STEMI-NSTEMI groups and also NSTEMI-UA groups with p value of <0.001; 0.013 dan 0.004, respectively.

The platelet count was not significantly different among the 3 groups could be caused by another factor beyond platelet count which had more influence toward ACS event compared to platelet count. The plateletcrit was also not significantly different. Plateletcrit is a parameter obtained from calculation involving platelet count and MPV value so that this result could be correlated with insignificant difference of platelet count.

Mean platelet volume, PDW and P-LCR were significantly different between STEMI-UA and NSTEMI-UA groups. These results could be caused by the more severe thrombotic condition in STEMI and NSTEMI compared to UA. However, the values were not significcantly different between STEMI and NSTEMI condition. This result could be influenced by unknown in vivo thrombotic conditio in those patients, that thromobotic condition usually examined using *coronary angiography*.

IPF was significantly different between STEMI-NSTEMI, STEMI-UA and NSTEMI-UA groups. The increase of IPF value was correlated with quick response of megakaryocytes toward platelet consumption. The severity of ACS is the highest in STEMI and the lowest in UA.

The MPV, PDW and P-LCR parameters can be used to differentiate IMA and UA based on this study. Further study about application of those parameter is required. IPF can differentitate STEMI, NSTEMI and UA condition. The application of this parameter in differentiating three 3 ACS conditions requiere further diagnostic study.