

## A study on prothrombogenic and antithrombogenic biomarkers in deep vein thrombosis following meta-epiphyseal cancellous bone traumatization in major orthopedic surgeries

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### Abstrak

Latar belakang: Penelitian ini bertujuan untuk menunjukkan perbedaan rerata nilai rasio Kolagen I (Kol I)/Nitric Oxide(NO), Kolagen IV (Kol IV)/NO, Tissue Factor (TF)/NO, P-selectin (P-sel)/NO antara pasien dengan trombosis vena dalam (TVD) positif dan TVD negatif, pasca traumatisasi spongiosa meta-epifisis sendi panggul dan lutut pada operasi besar ortopedi.

Metode: Studi observasional kohort prospektif kasus operasi ortopedi tanpa tromboprolifaksis pada 69 pasien berumur > 50 tahun. Pemeriksaan kadar serum biomarker Kol I, Kol IV, TF, P-sel, dan NO dilakukan tiga kali yaitu sebelum operasi, 72 jam sesudah operasi, dan 144 jam sesudah operasi, masing-masing untuk melihat perbedaan rerata kadar biomarker dan rerata nilai rasio protrombogenik/ antitrombogenik (Kol I/NO, Kol IV/NO, TF/NO dan P-sel/NO) pada 72 jam dan 144 jam sesudah operasi antara pasien TVD positif dan TVD negatif. Kejadian TVD dikonfirmasi pada 144 jam sesudah operasi dengan venografi (kecuali pada 8 kasus yang dikonfirmasi dengan USG color Doppler karena kontra indikasi zat warna).

Hasil: Kejadian TVD positif didapatkan pada 18 pasien (26,1%). Perbedaan rerata kadar antara TVD positif dan TVD negatif ditemukan pada Kol IV sebelum operasi ( $p = 0,022$ ) dan pada NO 72 jam sesudah operasi ( $p = 0,014$ ). Perbedaan rerata nilai rasio protrombogenik/ antitrombogenik antara TVD positif dan TVD negatif ditemukan pada rasio Kol IV/NO, TF/NO, dan P-sel/NO pada 72 jam sesudah operasi ( $p = 0,007$ ;  $p = 0,028$ ;  $p = 0,049$ ), dengan median yang lebih rendah pada pasien dengan TVD positif. Sedangkan pada 144 jam sesudah operasi, perbedaan rerata nilai rasio hanya ditemukan pada rasio Kol IV/NO ( $p = 0,014$ ) dengan nilai median yang lebih tinggi dari median pada 72 jam sesudah operasi.

Kesimpulan: Kejadian TVD pada traumatisasi spongiosa meta-epifisis pasca operasi besar ortopedi sendi panggul dan lutut dipengaruhi oleh keseimbangan protrombogenik dan antitrombogenik yang ditunjukkan dengan adanya perbedaan rasio Kol IV/NO, TF/NO dan Psel/NO pada 72 jam dan rasio Kol IV/NO pada 144 jam sesudah operasi antara TVD positif dan TVD negatif.

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<b>Abstract</b><br>

Background: This study was aimed to show differences in the mean values of Collagen I (Col I)/Nitric Oxide (NO), Collagen IV (Col IV)/NO, Tissue Factor (TF)/NO, and P-selectin (P-sel)/NO ratios between patients with DVT and those without DVT, following hip and knee meta-epiphyseal cancellous bone traumatization in major orthopedic surgeries.

Methods: This is an observational prospective cohort study on 69 patients aged > 50 years, who had orthopedic surgery without thromboprophylaxis. Examination of serum Col I, Col IV, TF, P-sel, and NO biomarker levels were performed three times, i.e. before surgery, 72 hours and 144 hours after surgery. We looked for the differences in mean levels of biomarkers, and mean ratio values of the prothrombogenic/ antithrombogenic (Col I/NO, Col IV/NO, TF/NO, P-sel/NO) at 72 hours and 144 hours post surgery between patients with DVT and those without. DVT events, which were confirmed at 144 hours post

surgery by venography (with the exception of 8 cases where color Doppler ultrasound was done due to contrast usage contraindications).

Results: DVTs were identified in 18 patients (26.1%). There were significant differences of mean levels in pre-surgical Col IV ( $p = 0.022$ ) and 72 hours NO ( $p = 0.014$ ) between patients with and without DVT. In addition, between the same two patient groups, significant differences were found in the mean values of the prothrombogenic/antithrombogenic ratios, i.e. Col IV/NO, TF/NO, and P-sel/NO at 72 hours post-surgery ( $p = 0.007$ ,  $p = 0.028$ , and  $p = 0.049$  respectively), with lower median values that were found in subjects with DVT. At 144-hours post surgery, the only significant ratio difference between the two groups was the mean values of Col IV/NO ratio ( $p = 0.014$ ) with the median values that were higher than the median values at 72-hours post surgery .

Conclusion: The incidence of DVT following traumatization of the meta-epiphyseal cancellous bone after major orthopedic surgeries in hip and knee is influenced by the balance of prothrombogenic and antithrombogenic factors as shown by the significant differences in Col IV/NO, TF/NO and P-sel/NO ratios at 72-hours and Col IV/NO ratio at 144 hours after surgery between DVT positive and DVT negative patients.