

TESIS

**HUBUNGAN ANTARA KADAR MARKER KOAGULASI DAN
FIBRINOLISIS PADA PASIEN KANKER PADAT YANG MENGALAMI
COVID-19 DENGAN KEJADIAN KEMATIAN**

(Studi di RSUP Dr. Kariadi Semarang)



**Diajukan untuk memenuhi persyaratan menyelesaikan
Program Pendidikan Dokter Spesialis-1
Program Studi Ilmu Penyakit Dalam**

**Pendy Wastu Haribowo
22040218310011**

Pembimbing:

**Dr. dr. Budi Setiawan, Sp.PD K-HOM
dr. Nur Farhanah Sp.PD KPTI, M.Si. Med**

**PROGRAM STUDI ILMU PENYAKIT DALAM
FAKULTAS KEDOKTERAN UNIVERSITAS DIPONEGORO
RSUP Dr. KARIADI SEMARANG**

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LEMBAR PENGESAHAN

**HUBUNGAN ANTARA KADAR MARKER KOAGULASI DAN
FIBRINOLISIS PASIEN COVID-19 DENGAN KANKER PADAT
TERHADAP KEJADIAN KEMATIAN
(Studi di RSUP Dr. Kariadi Semarang)**

Disusun oleh:

dr. Pedy Wastu Haribowo

22040218310011

Disetujui:

Pembimbing I

Pembimbing II

Dr. dr. Budi Setiawan, Sp.PD, K-HOM

NIP 19730132002121006

dr. Nur Farhanah Sp.PD, K-PTI

NIP 197204072008122001

Kepala Divisi,
Hematologi Onkologi Medik

Ketua Program Studi,
Ilmu Penyakit Dalam

Dr. dr. Damai Santosa, Sp.PD, K-HOM

NIP 19740526200801105

dr. Fathur Nur Kholis, Sp.PD, K-P

NIP 19691012200812002

ABSTRAK

Hubungan antara kadar marker koagulasi dan fibrinolisis pada pasien kanker padat yang mengalami COVID-19 dengan kejadian kematian

Pendy Wastu Haribowo*, Budi Setiawan **, Nur Farhanah ***

*PPDS 1 Fakultas Kedokteran Universitas Diponegoro / RSUP Dr.Kariadi Semarang

** Divisi Hematologi Onkologi Medik, Bagian Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Diponegoro / RSUP Dr.Kariadi Semarang

*** Divisi Tropik Infeksi, Bagian Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Diponegoro / RSUP Dr.Kariadi Semarang

Latar Belakang: Pasien kanker padat memiliki risiko trombosis yang tinggi. Kondisi inflamasi pada kanker akan memproduksi beberapa sitokin pro inflamasi seperti CRP, IL-6, TNF α , IL-1 dan IL-8. Sitokin pro-inflamasi akan menginduksi ekspresi *Tissue Factor* (TF) yang menyebabkan aktifnya kaskade koagulasi untuk membentuk trombus. Infeksi pada COVID-19 dapat memicu terjadinya trombosis. Pasien COVID-19 derajat berat memiliki risiko tinggi emboli paru dengan atau tanpa gejala saat tinggal di rumah sakit. Koagulopati terkait COVID-19 termasuk peningkatan jumlah D-dimer, fibrinogen, dan trombosit, dan pemanjangan waktu protrombin yang menyebabkan aktifnya kaskade koagulasi yang membentuk tromboemboli vena. Mortalitas pasien COVID-19 dengan kanker lebih tinggi daripada penderita COVID-19, atau kanker padat saja tanpa komorbid.

Tujuan : Menganalisis hubungan kadar D-dimer, fibrinogen, ppt, pttk, trombosit pasien COVID-19 dan pasien kanker padat dengan kematian.

Metode : Penelitian ini merupakan penelitian kohort retrospektif pada 30 pasien COVID-19 dengan pasien kanker padat terhadap kejadian meninggal di RSUP dr. Kariadi Semarang selama Maret 2020 hingga bulan Maret 2022.

Hasil : Terdapat hubungan bermakna pasien COVID-19 dan kanker padat terhadap kematian dengan kadar D-dimer ($p < 0,001$), kadar fibrinogen ($p = 0,045$), jumlah trombosit ($p = 0,035$), nilai *prothrombin time* (PT) ($p = 0,001$). Tidak terdapat hubungan pasien COVID-19 dan kanker padat terhadap kematian nilai (*aPTT*) ($p = 0,139$). *Cut off* kadar D-dimer 2215 ng/mL memiliki sensitivitas 95%, spesifisitas 90%, RR=18.0; CI 95% 2.63-122.95. *Cut off* fibrinogen 173,75 ng/mL memiliki sensitivitas 95% dan spesifisitas 20%, RR=2.25; CI 95% 0.83-6.04. *Cut off* jumlah trombosit adalah 141.500 sel/L memiliki sensitivitas 65%, spesifisitas 10%, RR=1.48; CI 95% 0.95-2.28. Nilai *cut off* PT adalah 12,8 detik memiliki sensitivitas 80%, spesifisitas 80%, RR=6.00; CI 95% 1.53-23.5. Nilai *cut off* *aPTT* adalah 28,6 detik memiliki sensitivitas 75%, spesifisitas 60%, RR=2.59; CI 95% 0.93-7.21. Kurva ROC menunjukkan bahwa D-dimer, nilai PT, nilai *aPTT*, kadar fibrinogen dan jumlah trombosit secara berurutan masing-masing sebesar 92,5%; 86%; 68,3%, 28,5% dan 25,8%. Kadar D-dimer merupakan faktor yang berpengaruh paling kuat terhadap kematian pasien COVID-19 dengan kanker padat.

Kesimpulan : Terdapat hubungan bermakna antara kematian dengan nilai PT, kadar D-dimer, kadar fibrinogen dan kadar trombosit pasien COVID-19 disertai kanker padat. Tidak terdapat hubungan bermakna antara kematian dengan nilai *aPTT* pada pasien COVID-19 dengan kanker padat.

Kata Kunci : kanker padat, COVID-19, D-dimer, fibrinogen, ppt, pttk, trombosit, tissue factor

ABSTRACT

Association between coagulation marker levels and fibrinolysis in solid cancer patients who have COVID-19 with mortality

Pendy Wastu Haribowo^{*}, Budi Setiawan^{**}, Nur Farhanah^{***}

^{*}Resident, Internal Medicine Department, Faculty of Medicine Diponegoro University / Dr. Kariadi Hospital Semarang

^{**} Division of Hematology and Medical Oncology, Internal Medicine Department, Faculty of Medicine Diponegoro University / Dr. Kariadi Hospital Semarang

^{***} Division of Infectious and Tropical Diseases, Internal Medicine Department, Faculty of Medicine Diponegoro University / Dr. Kariadi Hospital Semarang

Background: Solid cancer patients have a high risk of thrombosis. Inflammatory conditions in cancer will produce several pro-inflammatory cytokines such as CRP, IL-6, TNF α , IL-1 and IL-8. Pro-inflammatory cytokines will induce the expression of Tissue Factor (TF) which causes the activation of the coagulation cascade to form a thrombus. Infection with COVID-19 can trigger thrombosis. Severe COVID-19 patients have a high risk of pulmonary embolism with or without symptoms while hospitalized. COVID-19-related coagulopathy includes increased amounts of D-dimers, fibrinogens, and platelets, and lengthening of prothrombin time leading to activation of the coagulation cascade that forms venous thromboembolism. The mortality of COVID-19 patients with cancer is higher than that of people with COVID-19, or solid cancer alone without comorbidities.

Objective: Analyze the relationship between D-dimer, fibrinogen, ppt, pttk, platelet levels of COVID-19 patients and solid cancer patients with mortality.

Methods: This study use retrospective cohort study on 30 COVID-19 patients with solid cancer patients on the incidence of death at RSUP dr. Kariadi Semarang during March 2020 to March 2022.

Results: There was significant relationship between COVID-19 and solid cancer patients on mortality with D-dimer levels ($p = <0.001$), fibrinogen levels ($p = 0.045$), platelet count ($p = 0.035$), prothrombin time (PT) values ($p = 0.001$). There was no association between COVID-19 patients and solid cancer to mortality value (aPTT) ($p = 0.139$). Cut off D-dimer levels 2215 ng/mL has 95% sensitivity, 90% specificity, RR=18.0; CI 95% 2.63-122.95. The 173.75 ng/mL fibrinogen cut-off has 95% sensitivity and 20% specificity, RR=2.25; CI 95% 0.83-6.04. The platelet count cut off was 141,500 cells/L having a sensitivity of 65%, specificity of 10%, RR=1.48; CI 95% 0.95-2.28. The PT cut-off value is 12.8 seconds has 80% sensitivity, 80% specificity, RR=6.00; CI 95% 1.53-23.5. The cut off value of aPTT is 28.6 seconds has a sensitivity of 75%, specificity of 60%, RR=2.59; CI 95% 0.93-7.21. The ROC curve shows that D-dimer level, PT value, aPTT value, fibrinogen level and platelet count respectively amounted to 92.5%; 86%; 68.3%, 28.5% and 25.8%. D-dimer levels are the factor that has the strongest influence on the death of COVID-19 patients with solid cancer.

Conclusion: There was a significant relationship between mortality and PT scores, D-dimer levels, fibrinogen levels and platelet levels of COVID-19 patients with solid cancer. There was no significant association between mortality and aPTT values in COVID-19 patients with solid cancer.

Keywords : solid cancer, COVID-19, D-dimer, fibrinogen, ppt, pttk, trombositis, tissue factor