

CLINICAL AND LABORATORY FEATURES OF LONG-COVID SYNDROME: A CROSS-SECTIONAL STUDY OF 1,337 COVID-19 SURVIVORS.

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Background. The term 'long-Covid' is used to describe in Covid-19 survivors the persistence of symptoms beyond 4 weeks and includes 'ongoing symptomatic' (4-12 weeks) and 'post-Covid-19' syndrome (>12 weeks) phases, based on symptoms' duration.

Aim. To evaluate the contribution of circulating hemostatic biomarker alterations to the diagnosis of long-Covid syndrome.

Methods. A clinical and diagnostic multidisciplinary follow-up of Covid-19 patients discharged from our Institution after the first pandemic wave was implemented (ACCORDI Study, July - November 2020). In 1310 out of 1337 Covid-19 survivors who attended the clinical visit, blood samples were obtained for measurements of blood cell count, liver and renal function tests, LDH, C-reactive protein, fibrinogen, prothrombin fragment 1+2, D-dimer, von Willebrand factor antigen, thrombomodulin (TM), tissue plasminogen activator and its inhibitor PAI-1.

Results. In the 1337 survivor cohort (863M/474F, median age 60 years, median time from Covid-19 onset=127 days), clinical symptoms were: cardiopulmonary in 50% of subjects, flu-like in 35%, respiratory in 27%, and neurological in 11%. The long-Covid syndrome was diagnosed in 655 patients

(375M/280F): 101 classified as 'ongoing symptomatic' and 554 as 'post-Covid'.

Among study population, 56 survivors experienced VTE during the acute phase (43M/13F, median age 62 years). 80% had isolated pulmonary embolism; 16% isolated proximal deep vein thrombosis; 4% deep vein thrombosis and pulmonary embolism. A significant association appeared between VTE during acute phase and development of long-Covid syndrome.

The hemostatic laboratory analysis of 1310 samples showed no significant differences in the biomarkers' levels between long-COVID and symptom-free survivors. However, among subjects assessed within 12 weeks from disease onset, the 'ongoing symptomatic' group showed significantly higher TM levels ($p < 0.05$) compared with the symptom-free group. Further, after logistic regression analysis corrected for age and gender, TM or PAI-1 levels above the 75th percentile were found significantly associated with a diagnosis of long-Covid (OR 2.156; 95% CI:1.24-3.75; $p = 0.007$).

Conclusions. Our study shows the occurrence of an endotheliopathy in ongoing symptomatic long-Covid patients and supports the role of VTE in the long-Covid syndrome appearance.

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