



Physician connect

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you '**Physician connect**' which contains latest and interesting news in the field of Medicine.

This issue contains

- Can there be an association with Acute Pulmonary Embolism and COVID-19 Pneumonia?
- Ticagrelor With or Without Aspirin in Acute Coronary Syndrome After PCI: TICO Study
- Comparison of IL-6, CRP, and LDL-C as biomarkers of residual risk in contemporary practice: CIRT trial

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Can there be an association with Acute Pulmonary Embolism and COVID-19 Pneumonia?

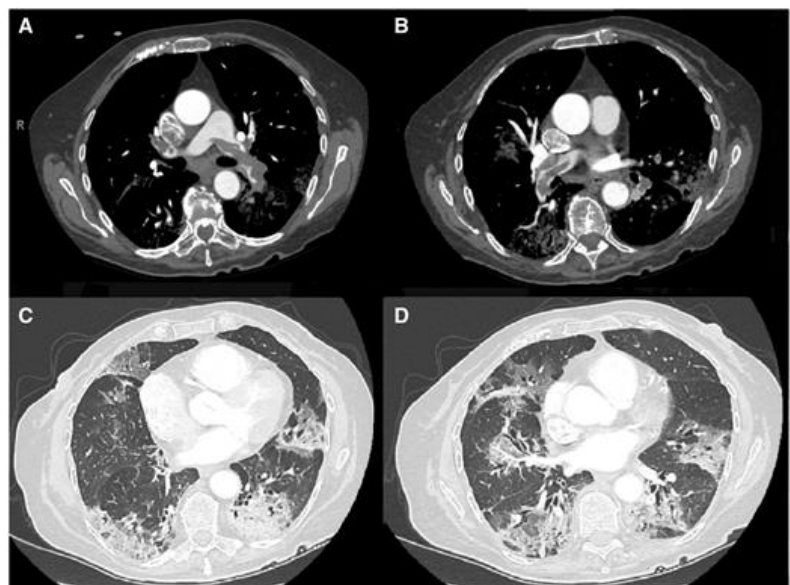
Acute infections are associated with a transient increased risk of venous thrombo-embolic events.

A 77-year-old man, with 10-day history of fever and a recent onset of dyspnoea was found to be COVID-19-positive. The patient had severe bilateral pneumonia and concomitant acute pulmonary embolism, was hospitalized after.

The patient was haemodynamically stable and without strong predisposing risk factors for venous thrombo-embolism. The ECG at baseline was also normal. There was a modest leucocytosis was present ($11.360/\text{mm}^2$) with increased values of C-reactive protein (180 mg/L), troponin I (3240.4 ng/mL), and D-dimer (21 $\mu\text{g/mL}$). While on oxygen, arterial blood gas revealed a PaO_2 of 78.0 mmHg with a PcO_2 of 25.1 mmHg and an sO_2 of 95.6%.

A right basal infiltrate was evident at the chest X-ray, while echocardiographic evaluation showed a dilated and severely hypokinetic right ventricle with a mean derived pulmonary arterial pressure of 60 mmHg.

CT scan documented the presence of a bilateral filling defect diagnostic for pulmonary embolism (Panels 1A and B), associated with extensive ground-glass opacifications involving both the lung parenchymas with predominant consolidation in the posterior basal segment of the left lower lobe (Panels 1C and D). Lower-limb compression ultrasonography was negative.



Based on these findings, treatment with low molecular weight heparin, lopinavir/ritonavir, and hydroxychloroquine was started.

The absence of major predisposing factors in this case of diffuse bilateral COVID-19 pneumonia seems to confirm the role of severe infections as a precipitant factor for acute venous thrombo-embolism and the causal relationship.

Source: Danzi GB et al. Eur Heart J. 2020 March [online ahead of print]. doi.org/10.1093/eurheartj/ehaa254

Ticagrelor With or Without Aspirin in Acute Coronary Syndrome After PCI: TICO Study

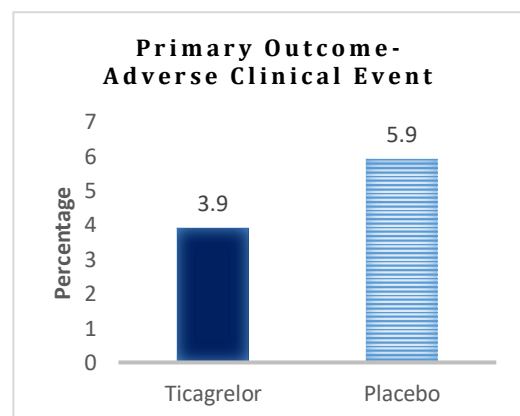
This study was conducted to assess the efficacy and safety profile of ticagrelor monotherapy for patients with ACS undergoing PCI. TICO study was as a randomized, parallel, open-label trial in a population of 3056 patients. Patients included in the trial received ticagrelor dual antiplatelet therapy with aspirin for 3 months before being randomized to ticagrelor plus placebo or ticagrelor plus aspirin for 9 months.

In patients with ACS who are treated with stents, Ticagrelor monotherapy could be an optimal strategy

Of the 3056 included in the study, 1527 patients were assigned to ticagrelor plus placebo and 1529 patients were randomized to ticagrelor-based dual antiplatelet therapy with aspirin, which is the current standard therapy. The mean age of study participants was 61 years, 21% were female, and 27% had diabetes.

Inclusion criteria for the study included ACS treated with ultrathin bioresorbable polymer sirolimus-eluting stent and being at least 19 years of age. Exclusion criteria for TICO included being older than 80 years of age as well as having an increased risk of bleeding, need for oral anticoagulation therapy, current or potential pregnancy, bradycardia, and hepatic dysfunction.

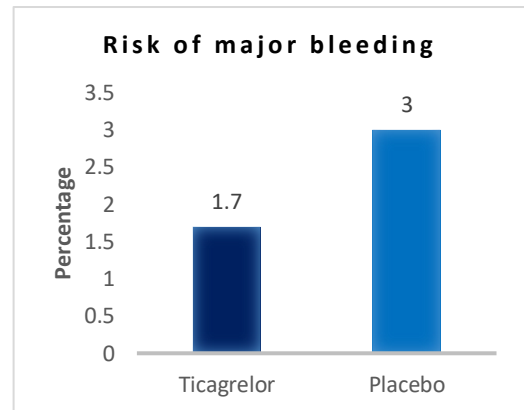
The primary outcome measure of the study was net adverse clinical event (NACE) at 12 months. Investigators defined NACE as a composite of TIMI-major bleeding and major adverse cardiac and cerebrovascular, which included all-cause death, MI, stent thrombosis, stroke, or target vessel revascularization.



Upon analysis, results indicated the primary outcome had occurred in 3.9% (n=59) of patients receiving ticagrelor plus placebo compared to 5.9% (n=89) of patients in the ticagrelor plus aspirin (HR, 0.66; 95% CI, 0.48-0.92; P=.01). Investigators pointed out the difference was primarily driven by a lower risk of major bleeding observed with use of ticagrelor plus placebo (1.7% vs. 3.0%;

HR=0.56; 95% CI, 0.34-0.91; P=.019). Of note, major adverse cardiac and cerebrovascular events occurred similarly between the 2 treatment arms (HR, 0.69; 95% CI, 0.45-1.06; P=.09).

The Ticagrelor with or Without Aspirin in Acute Coronary Syndrome After PCI (TICO) study shows very similar results as the TWILIGHT trial reported last year. But whereas TWILIGHT enrolled a more general PCI population, TICO only included patients with acute coronary syndrome (ACS). In patients with ACS who are treated with stents, ticagrelor monotherapy could be an optimal strategy for reducing bleeding risk without increasing the risk for adverse events caused by arterial blockages.



Source: Jang et al. Ticagrelor with Or Without Aspirin In Acute Coronary Syndrome After Percutaneous Coronary Intervention: Randomized Evaluation Of Ticagrelor Monotherapy After 3-month Dual-antiplatelet Therapy In Acute Coronary Syndrome. ACC 2020

Comparison of IL-6, CRP, and LDL-C as biomarkers of residual risk in contemporary practice: CIRT trial

In epidemiologic cohorts initiated >30 years ago, inflammatory biomarkers, such as interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hsCRP) were shown to independently predict future cardiovascular events with a magnitude of effect comparable to that of low-density lipoprotein cholesterol (LDLC). Whether aggressive contemporary therapy for atherosclerosis has altered these relationships is unknown yet has major implications for future drug development.

Atherosclerosis may require a combination of inflammation inhibition and additional cholesterol reduction.

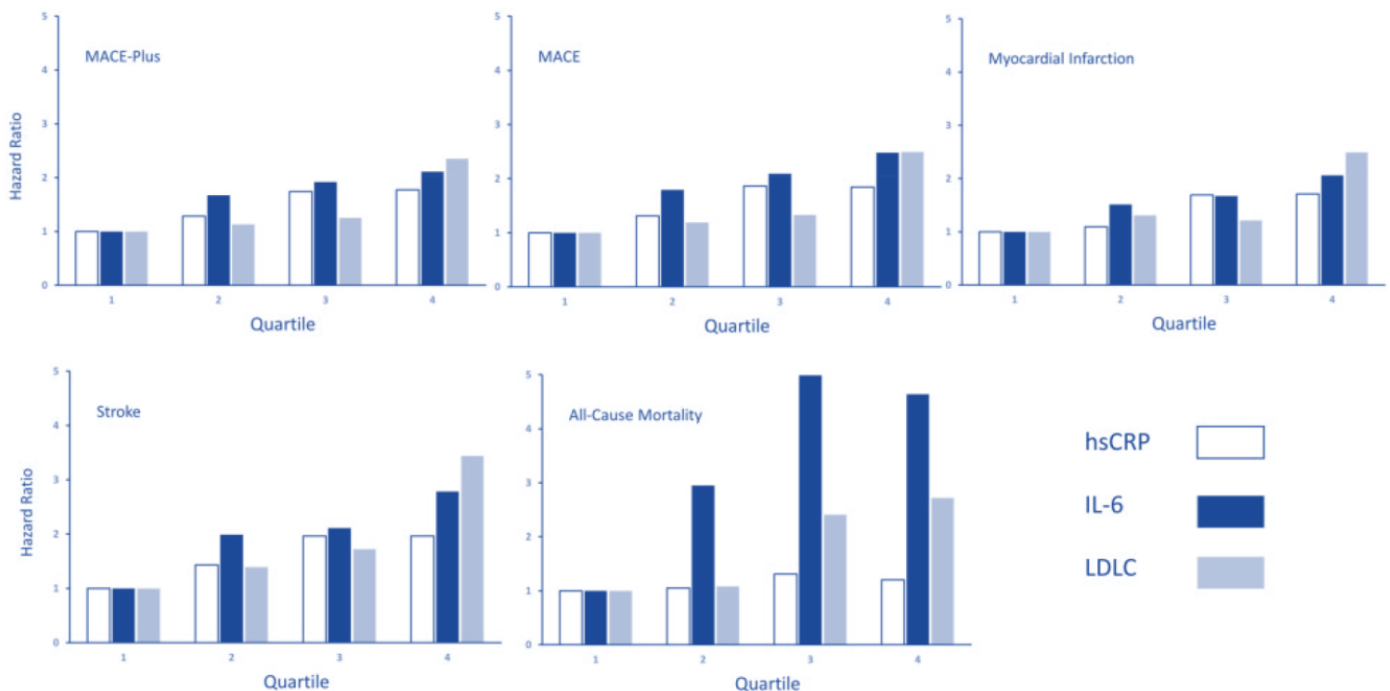
Interleukin-6, hsCRP, and LDLC were measured at baseline in up to 4168 North American patients enrolled in the contemporary Cardiovascular Inflammation Reduction Trial with prior myocardial infarction or multivessel coronary disease who additionally had diabetes or metabolic syndrome and were followed for a period of up to 5 years for incident major recurrent cardiovascular events and all-cause mortality. Three-quarters of the cohort were previously revascularized and the great majority was taking statins, angiotensin blocking agents, beta-blockers, and antithrombotic agents.

Participants were randomly allocated to low-dose methotrexate 15 mg weekly or to placebo. Randomized use of methotrexate had no effect on event rates nor

plasma levels of IL-6, hsCRP, or LDL over time. Yet, baseline levels of IL-6, hsCRP, and LDLC were all predictors of major recurrent cardiovascular events; adjusted hazard ratios [HR; 95% confidence interval (CI)] for the lowest to highest baseline quartiles of IL-6 were 1.0 (referent), 1.66 (1.18–2.35), 1.92 (1.36–2.70), and 2.11 (1.49–2.99; $P < 0.0001$), while adjusted HRs for increasing quartiles of hsCRP were 1.0 (referent), 1.28 (0.92–1.79), 1.73 (1.25–2.38), and 1.79 (1.28–2.50; $P < 0.0001$) and adjusted HRs for increasing quartiles of LDLC were 1.0 (referent), 1.12 (0.78–1.62), 1.25 (0.87–1.79), and 2.38 (1.72–3.30; $P < 0.0001$). Effect estimates were not statistically different in these analyses for comparisons between IL-6, hsCRP, or LDLC, although IL-6 was the strongest predictor of all-cause mortality. The highest absolute risks were observed among those with elevated levels of both cholesterol and inflammation [HR 6.4 (95% CI 2.9–14.1) for those in the top quartiles of baseline IL-6 and LDLC, HR 4.9 (95% CI 2.6–9.4) for those in the top quartiles of baseline hsCRP and LDLC, both $P < 0.0001$].

Despite aggressive contemporary secondary prevention efforts, the relationships between inflammation, cholesterol, and cardiovascular risk are largely unchanged from those described two decades ago. These data are consistent with the hypothesis that future treatments for atherosclerosis may require a combination of inflammation inhibition and additional cholesterol reduction.

Table: Adjusted hazard ratios for major adverse cardiovascular events-plus, major adverse cardiovascular events, myocardial infarction, stroke, and all-cause mortality according to baseline quartiles of interleukin-6, high-sensitivity C-reactive protein, and low-density lipoprotein cholesterol



Source: Ridker PM et al. Comparison of interleukin-6, C-reactive protein, and low-density lipoprotein cholesterol as biomarkers of residual risk in contemporary practice: secondary analyses from the Cardiovascular Inflammation Reduction Trial. ACC 2020.



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