Residual inflammatory risk at 12 months after acute coronary syndromes is associated with cardiovascular outcome

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Background: C-reactive protein measured by high sensitivity assays (hsCRP) is an established biomarker of systemic inflammation and a cut-off at 2 mg/L has been widely studied and proposed to identify patients at residual inflammatory risk (RIR).

Purpose: It remains unclear how many patients remain at residual inflammatory risk (RIR) at 12 months after acute coronary syndromes (ACS) in a contemporary real-world cohort and if RIR is associated with cardiovascular outcome.

Methods: Patients included in the SPUM-ACS cohort (NCT01000701) with a primary diagnosis of ACS referred for coronary angiography between 2009 and 2012 and available hsCRP measurements at baseline and at 1 year follow-up. High RIR was defined as hsCRP $\geq$2mg/L. Patients were divided into four groups: persistently high RIR, increased RIR (first low-, then high hsCRP), attenuated RIR (first high-, then low hsCRP), or persistently low RIR. Adjudicated major adverse cardiac and cerebrovascular events (MACCE) at 365 days were defined as the composite of MI, clinically indicated coronary revascularization or stroke. Logistic regression models were used to evaluate associations between MACCE and RIR groups and continuous long-term GRACE risk score. Adjustment was made for long-term GRACE risk score.

Results: 1209 patients had available serial biomarker measurements (baseline and 12 months) with clinical and demographic data. Among those, 295 (24.4%) patients (UA 3.4%, NSTEMI 47.5%, STEMI 49.2%) fell in the category persistently high RIR (delta hsCRP median (IQR): –2.3 (–9.9; 0.3) (mg/L) and 72 (5.96%) patients (UA 8.3%, NSTEMI 47.2%, STEMI 44.4%) were in category increased RIR (delta hsCRP median (IQR): +2.45 (1.2; 8.35) (mg/L). Conversely, 390 (32.26%) patients (UA 3.3%, NSTEMI 46.9%, STEMI 49.7%) fell in the category attenuated RIR (delta hsCRP median (IQR): –3.55 (–10; –2) (mg/L) and 452 (37.38%) patients (UA 5.5%, NSTEMI 33.2%, STEMI 61.3%) were in category persistently low RIR (delta hsCRP median (IQR): –0.2 (–0.6; 0.1) (mg/L). Of 90 MACCE, 31 (10.5%) were found in the persistently high RIR group yielding a significantly higher event rate (adjusted HR: 1.71, (95% CI 1.08; 2.7), p-value: 0.02) compared with the three other groups combined (increased RIR: 3 (4.2%), attenuated RIR 30 (7.7%), persistent low RIR 26 (5.8%)). Of note, in that group the long-term GRACE risk score was significantly higher compared with the three other groups (adjusted HR: 1.1, (95% CI 1.0; 1.17), p-value: 0.04).

Conclusion: Residual inflammatory risk at 12 months after an ACS is found in nearly a third of patients. Patients with persistently elevated hsCRP throughout the first year post-ACS suffered most adverse events warranting studies of anti-inflammatory drugs in these patients.