

## Effects of anti-inflammatory treatment and surgical intervention on endothelial glyco-lyx, peripheral and coronary microcirculation and myocardial deformation in inflammatory bowel disease patients

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**Introduction:** IBD alter gastrointestinal physiology and mucosal immunity through a complex inflammatory process which leads to significant arterial endothelial dysfunction and modification of cardiac structure and function. This study is performed to test the hypothesis that treatment with TNF- $\alpha$  inhibitor or surgical intervention improves cardiovascular function through anti-inflammatory mechanisms.

**Methods:** 57 IBD patients (45 CD and 12 UC, 40  $\pm$  8 years, 57% male) were examined at baseline and 4 months after pharmaceutical (anti-TNF- $\alpha$ ) or surgical intervention. Subjects with a history of established cardiovascular risk factors were excluded.

We measured a) carotid-femoral pulse wave velocity (PWV - Complior SP ALAM) and augmentation index (AI), b) flow mediated dilatation (FMD) of the brachial artery, c) perfused boundary region (PBR) of the sublingual arterial microvessels, d) LV longitudinal strain (GLS) and (PWV/GLS) as a marker of ventricular-arterial coupling, e) peak LV twisting, peak twisting velocity (pTwVel) and peak untwisting velocity (pUtwVel) using speckle tracking echocardiography, f) mitral annulus velocities by tissue doppler imaging (S' and E') and mitral inflow velocity (E), g) coronary flow reserve (CFR) by Doppler echocardiography, h) C-reactive protein (CRP), white blood cells (WBC).

IBD severity was quantified using Mayo score and Harvey-Bradshaw Index (HBI) for UC and CD respectively.

**Results:** At baseline, the disease severity score and the WBC values were significantly correlated with peripheral PWV ( $r = 0.3$ ,  $p < 0.05$  and  $r = 0.364$ ,  $p < 0.05$ ), while central arterial AI was associated with median arterial pressure ( $r = 0.479$ ,  $p < 0.05$ ), lateral and septal mitral E' velocity ( $r = -0.651$ ,  $p < 0.05$  and  $r = -0.587$ ,  $p < 0.05$ ). Four months after treatment, there was a reduction of CRP ( $13 \pm 2.8$  mg/L vs  $3.9 \pm 1.2$  mg/L,  $p < 0.05$ ), CFR ( $2.5 \pm 0.08$  vs  $3.1 \pm 0.11$ ,  $p < 0.05$ ) and PBR5-25 ( $2.27 \pm 0.06$  vs  $2.09 \pm 0.05$   $\mu$ m,  $p < 0.05$ ) more significantly in pharmaceutical group ( $p < 0.05$  vs  $p = 0.23$ ). Moreover, there was an improvement of GLS ( $-18.6 \pm 0.37$  vs  $-20 \pm 0.34$ ,  $p < 0.05$ ), LS-4ch ( $-18.3 \pm 0.47$  vs  $-19.3 \pm 0.41$ ,  $p < 0.05$ ), GcircS ( $-18.1 \pm 0.7$  vs  $-20.1 \pm 0.9$ ,  $p < 0.05$ ) and FMD ( $7.2\% \pm 0.6$  vs  $11.8\% \pm 1.4$ ,  $p < 0.05$ ). Moreover, there was an overall improvement of PWV/GLS ( $-0.49 \pm 0.02$  vs  $-0.43 \pm 0.02$ ,  $p < 0.05$ ). It was greater after with anti-TNF $\alpha$  therapy compared to surgery ( $p < 0.05$  vs  $p = 0.1$ ) and particular for the GLS component ( $p < 0.05$  vs  $p = 0.07$ ). The difference in PBR5-25 was significantly correlated with the difference in GLS ( $r = -0.403$ ,  $p < 0.05$ ) and PWV/GLS ( $r = 0.421$ ,  $p < 0.05$ ).

**Conclusion:** IBD severity is associated with vascular and diastolic dysfunction, with significant improvement after anti-inflammatory treatment. Systemic anti-TNF $\alpha$  inhibition leads to significant improvement in myocardial deformation, endothelial and coronary microcirculatory function compared with local intestinal surgical intervention, possibly through a systemic reduction of excess inflammatory burden.