

May 24-25, 2018
London, UK

Branislav Zagrapan et al., J Vasc Endovasc Therapy 2018, Volume 3
DOI: 10.21767/2573-4482-C1-002

AN IMPROVED DIAGNOSTIC SCORE FOR ABDOMINAL AORTIC ANEURYSMS BASED ON A COMPREHENSIVE ANALYSIS OF MYELOID CELL PARAMETERS

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Background: The pathogenesis of abdominal aortic aneurysm (AAA) involves a central component of chronic inflammation which is predominantly mediated by myeloid cells. Both, neutrophils and monocytes are recruited to the AAA wall and intraluminal thrombus and contribute to vessel destruction by the release of proteases and reactive oxygen species.

Purpose: We hypothesized that the local activation of myeloid cells may be reflected in systemic alterations of neutrophil and monocyte populations as well as in associated soluble factors which might serve as biomarkers to diagnose the often-asymptomatic disease.

Methods: The methods of this study were to establish their diagnostic marker potential, neutrophil and monocyte subsets were measured by flow cytometry in peripheral blood samples of 41 AAA patients and 38 healthy controls matched for age, sex, body mass index and smoking habit. Comparably, circulating factors relating to myeloid cell activation and recruitment were assayed in plasma by multicytokine array and ELISA.

Results: Significantly elevated levels of CD16+ monocytes, activated neutrophils and newly released neutrophils were recorded for AAA patients compared to controls. In line, the monocyte chemoattractant protein 1 and myeloperoxidase were significantly increased in patients' plasma. The diagnostic value was highest for myeloperoxidase, a mediator which is released by activated neutrophils as well as CD16+ monocytes. Comparison of the investigated myeloid factors with established AAA parameters by multivariable logistic regression identified myeloperoxidase and D-dimer as highly significant, independent variables. These two biomarkers were combined to yield a potent diagnostic score which was subsequently confirmed in a validation cohort.

Conclusions: Based on a comprehensive comparison of myeloid cell activation parameters, plasma myeloperoxidase

was identified as the most potent AAA biomarker. Since D-dimer and myeloperoxidase represent two sensitive markers of AAA which reflect distinct components of the AAA pathomechanism (thrombus formation and inflammation) they may be combined to yield an improved diagnostic score.

Recent Publications

1. Takagi H, Manabe H, Kawai N, et al. (2009) Plasma fibrinogen and D-dimer concentrations are associated with the presence of abdominal aortic aneurysm: a systematic review and meta-analysis. *European Journal of Vascular and Endovascular Surgery* 38:273-277.
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3. Golledge J, Muller R, Clancy P, et al. (2011) Evaluation of the diagnostic and prognostic value of plasma D-dimer for abdominal aortic aneurysm. *European Heart Journal* 32:354-364.
4. Houard X, Touat Z, Ollivier V, et al. (2009) Mediators of neutrophil recruitment in human abdominal aortic aneurysms. *Cardiovascular Research* 82:532-541.
5. Dale Ma, Ruhlman M K and Baxter B T (2015) Inflammatory Cell Phenotypes in AAAs. *Arteriosclerosis, Thrombosis, and Vascular Biology* 35:1746-1755

Biography

Branislav Zagrapan is pursuing his PhD on the topic of molecular and cellular diagnostic and prognostic markers of abdominal aortic aneurysms. He is a Pathologist in training at the Academic Teaching Hospital Feldkirch, Austria

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