

#10 NITRIC OXIDE SYNTHASES AND CASPASE 3 MODULATE SIGNALING CASCADES IN THE PATHOGENESIS OF PERIPHERAL ARTERY ANEURYSMS

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Introduction: This investigation examines the expression of nitric oxide synthases and cell death-promoting molecule, caspase-3, in a series of normal arteries and peripheral artery aneurysms.

Methods: Twenty-six popliteal artery aneurysms, 15 iliac artery aneurysms, 6 femoral artery aneurysms and 2 carotid artery aneurysms specimens were obtained from patients undergoing elective repair. All were males with ages ranging from 48 to 81 years old (mean 65 years). Controls were normal arteries (n=12). Expression eNOS, iNOS, CPP-32, and vascular smooth muscle cell (VSMC) actin was obtained by Western blot analysis and localized by immunohistochemistry. Statistical analyzes were by Chi-square, Student & Fisher's Exact t-test.

Results: Not only was a significantly high expression of iNOS noted in the aneurysm tissues ($p < 0.001$), but also a differential expression of it was observed in the regions with inflammatory infiltrate. The expression of eNOS was not significantly altered in the aneurysms. As compared to normal artery tissues, the aneurysms demonstrated large number of cells immunopositive for CPP-32 (56.55 \pm 5.33 %) $p < 0.05$. There was significantly predominant expression of CPP-32 in the inflammatory infiltrate of the aneurysm walls ($p < 0.01$).

Conclusions: The data confirm that the inflammatory infiltrate in the aneurysm tissues have a significant role in its molecular pathogenesis. Cells expressing death-promoting molecules are present in large numbers and are predominantly T-lymphocytes. iNOS was differentially upregulated and might contribute to the modulation of the local inflammatory response as well as affect cell death pattern in aneurysms. Differential expression of caspase 3 within the aneurysm wall suggests a role for this downstream executioner of programmed cell death in the regulation of cellular signals that promote aneurysm development.