AARHUS UNIVERSITY

Is Oxidative Stress Important in AAA Pathogenesis?

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Introduction

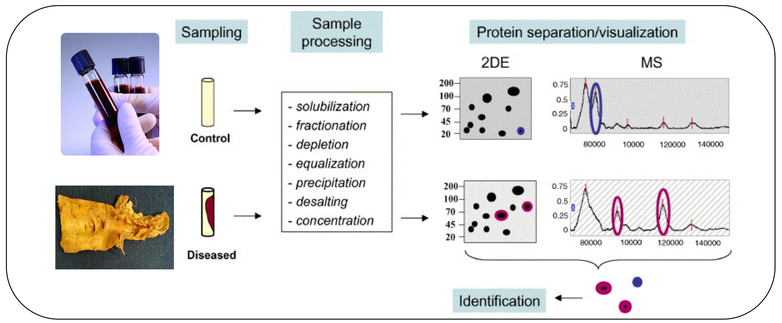
Active investigations continue to identify markers other than size that would predict a risk of AAA rupture. Circulating biomarkers could also indicate optimal intervals between the surveillance intervals. Finally, the identification of biomarkers also may identify potential pathogenic pathways, and thus may open possibilities for pharmacological inhibition of growth. In the search of novel biomarkers of AAA progression, serum and wall material proteins were analyzed by a differential proteomic approach.

Hypothesis

We hypothesized that serum and AAA wall proteins could associate with abdominal aortic aneurysms progression and rupture.

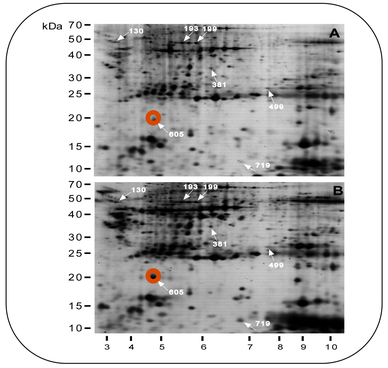
Methods

Same layers of AAA wall from ruptured (rAAA) and non-ruptured AAA were incubated, and the proteins released were analyzed by 2-dimensional difference in-gel electrophoresis. Proteins from serum were analyzed and correlated with AAA size and annual expansion rate. Identified proteins was further validated by Western blot and immunohistochemistry.



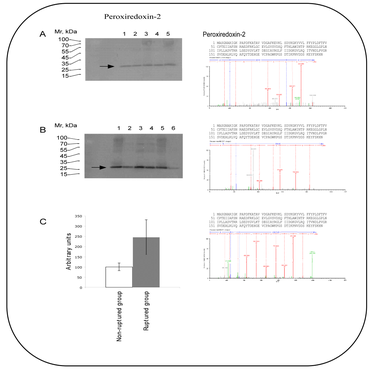
Results

Several differentially expressed proteins involved in main AAA pathological mechanisms (proteolysis, oxidative stress and thrombosis) were identified by mass spectrometry. Among the proteins identified, peroxiredoxin-2 (PRX-2) was more prominent, which was further validated by Western blot and immunohistochemistry. We demonstrated increased PRX-2 serum levels in rAAA patient wall material compared with AAA subjects.



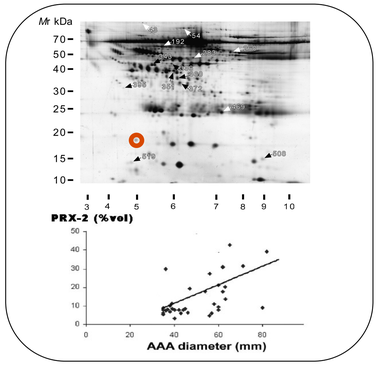
•Proteomic identification of differentially expressed proteins in aortic wall of patients with ruptured and non ruptured abdominal aortic aneurysms.

•PRX-2 marked in red.

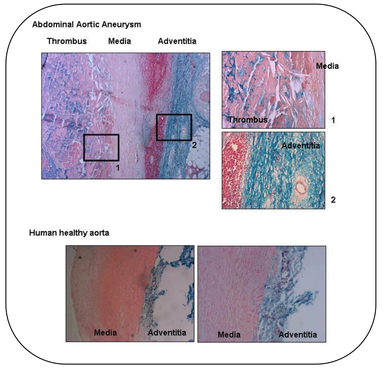


•Western blotting analysis using anti-peroxiredoxin-2 from non-ruptured AAA group (A) from ruptured AAA group (B). The bands indicated with arrows are significantly differentially regulated in the ruptured group.
•Peroxiredoxin-2 is up-regulated in the ruptured group.

We demonstrated positive correlation in serum among PRX-2 and AAA diameter and annual expansion rate also. Immunostaining of PRX-2 showed strong results in AAA wall in comparison to normal aortic wall.



•Proteomic identification of differentially expressed proteins in serum of patients with abdominal aortic aneurysms. PRX-2 marked in red.
•Positive PRX-2 (% vol) correlation with AAA diameter. (ρ=0.52; P<0.05, n=30)
•PRX-2 (% vol) correlates with AAA growth (ρ=0.27; P<0.05, n=15)



•Immunostaining of PRX-2 in AAA. Positive staining appears in green. Upper panel show a strong staining of the adventitia of AAA samples (×10) and inset two (×40).

•Thrombus displays a diffuse staining whereas media was negative. Lower panel: normal aortic wall shows a staining only in the adventitia.

Conclusion

Several proteins associated with AAA pathogenesis have been identified by a proteomic approach. Protein profiles identified in the serum would appear to be a convenient monitoring tool that has the ability to be both sensitive and specific for AAAs. PRX-2 serum levels are increased in rAAA patients and correlate with AAA size and growth rate, suggesting the potential use of PRX-2 as a biomarker for AAA evolution.