Development of a Proteomic Biomarker Signature for Identifying Intracranial Aneurysms

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Abstract

Introduction Intracranial aneurysms occur in approximately 1–2% of the general population and are the leading cause for subarachnoid hemorrhage (SAH). Recent studies have shown the utility of using multiplex immunoassays in biomarker discovery for a variety of diseases. Although a number of biomarkers have been identified to be related to intracranial aneurysms, a proteomic signature has not been defined to predict the presence of an intracranial aneurysm. In this study, we utilized proteomic data from patients with known intracranial aneurysms and healthy controls to identify a proteomic signature in the serum to predict the presence of an aneurysm.

Methods Fifty-six patients were prospectively enrolled in this study, 28 of which with unruptured intracranial aneurysms and 28 sex, age, and comorbidity matched healthy controls. Serum was collected from each patient. Protein expression levels were determined using the Proseek multiplex immunoassay (http://www.olenlk.com/), which included 92 known inflammatory markers. Univariate and multivariate logistic regression models were constructed and systematically assessed using statistical and biological inferences to identify phenotypic and proteomic variables that significantly predicted presence of an aneurysm.

Results Of the 28 patients with intracranial aneurysms, 82.1% (n=23) were female, 46.4% (n=13) were never smokers, 35.7% (n=10) were former smokers, and 17.9% (n=5) were current smokers. Healthy controls were matched on a 1:1 basis, with age ± 5 years. In the patient cohort the mean aneurysm size was 8.9 mm with the most common location being anterior communicating artery (35.7%, n=10). Upon univariate analysis, increased expression of 10 analytes were found to be independent predictors of the presence of an intracranial aneurysm. At the univariate level, IL17 (OR=12.01; 95% CI 4.16 – 53.17; p<0.00001) and CD244 (OR=34.19; 95% CI 6.14 – 344.81; p=0.000531) were found to be the most predictive.

Conclusion This study leveraged individualized data from patients with intracranial aneurysms to determine which proteomic variables predict the presence of an intracranial aneurysm while controlling for essential clinical covariates. Larger multi-omic studies are warranted to develop a more comprehensive biomarker signature for intracranial aneurysms.