Abdominal Aortic Aneurysm (AAA) Disease: Mechanism, Stratification, and Treatment

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This Specialized Centers for Clinically Oriented Research (SCCOR) P50 Program will identify novel biomarkers to monitor small AAA disease and test the ability of exercise therapy to modify disease progression.

SIGNATURE PROTEIN PROFILES TO IDENTIFY AAs (Project II)

Background: Serum protein profiling may enable early diagnosis of AAs, predict expansion, and monitor response to novel medical therapies. In this Project, transcriptional profiling of human AAA tissue, database mining for patterns of protein expression, and serum biomarker assessment of experimental models will be used to develop proteomic profiles of AAA disease.

Figure 1. Heatmap of relative serum protein levels that coincide with progression of experimental atherosclerosis. Realtime PCR confirms vascular production of many of these markers (red indicates increased expression).

REST AND EXERCISE HEMODYNAMICS IN AAA PROGRESSION (Project III)

Background: Hemodynamic conditions in the infrarenal aorta play an important role in the pathophysiology of AAA disease. Our goal is to quantify abdominal aortic blood flow at rest and during dynamic exercise, and develop and validate computational methods to model blood flow, pressure, and wall motion in patient-specific reproductions of the abdominal aorta using magnetic resonance angiography (MRA).

Figure 2. Apoprotein E deficient mouse model of AAA disease: Suprarenal AAA present after 28 day infusion with Angiotensin II (1000ng/kg/min) via an osmotic pump (left, arrow), compared to control mouse aorta (right) after normal saline infusion.

Figure 3. MR imaging of the aorta during exercise.

Figure 4. An MR angiogram (left) of a patient with a small AAA is used to construct a solid model of the lumen (right) for analyses.

Figure 5. Mean wall Shear Stress over the flow domain for small AAA subject 1 at rest (A) and exercise (B), and small AAA subject 2 at rest (C) and exercise (D).

EVALUATION OF EXERCISE THERAPY FOR SMALL AAA (Project IV)

Background: Substantial evidence links sedentary existence and resulting pro-inflammatory aortic conditions to the pathogenesis of AAA disease. Our goal is to test the ability of lower extremity exercise to reduce AAA risk, limit small aneurysm progression, and modify biologic markers of disease.

Figure 6. Apoprotein E deficient mouse model of AAA disease: Suprarenal AAA present after 28 day infusion with Angiotensin II (1000ng/kg/min) via an osmotic pump (left, arrow), compared to control mouse aorta (right) after normal saline infusion.

Figure 7. Apoprotein E deficient mouse model of AAA disease: Suprarenal AAA present after 28 day infusion with Angiotensin II (1000ng/kg/min) via an osmotic pump (left, arrow), compared to control mouse aorta (right) after normal saline infusion.

Recruitment Goals:
- 1,400 small AAA patients will complete exercise history and health history questionnaires, and undergo a blood draw and abdominal ultrasound to correlate risk factors with AAA disease status.
- 1,000 patients with previously defined exercise capacity will undergo aortic imaging to correlate fitness status and exercise capacity with aortic diameter.
- 340 patients with small AAAs will be randomized to exercise or usual activity, and followed over three years with serial imaging to test the ability of exercise therapy to modify disease progression and candidate biomarkers of AAA disease.

Recruitment Locations:
- Stanford University Medical Center
- Palo Alto Veteran’s Administration Health Care System
- Kaiser Permanente of Northern California

SUPPORTING INVESTIGATORS
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FUNDING SOURCE
This work was funded by the National Heart, Lung, and Blood Institute grant number P50 HL083800.