

Biomarkers And Screening Tests For Abdominal Aortic Aneurysm: A Brief Review

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Abstract

BACKGROUND: Abdominal aortic aneurysm (AAA) is a deadly disease and hence various modalities to be used to diagnose at an earlier stage. **OBJECTIVE:** To find out the usefulness and limitations of various biomarkers in diagnosing AAA and drug to prevent/treat it. **MATERIAL AND METHODS:** Published data were collected from web using keywords biomarkers, clinical methods, screening tests and abdominal aortic aneurysm. **RESULTS:** Biomarkers identified for AAA are osteopontin (OPN), osteoprotegerin (OPG), Matrix metalloproteinase-9 (MMP-9), circulating levels of tumor necrosis factor- α , interleukin-1 α , interleukin-6, interferon- γ , amino terminal propeptide of type 3 collagen, C-reactive protein (CRP), fibrinogen, total WBC count, albumin and ultrasonogram of abdomen. Co-existing illnesses influence inflammatory biomarkers. Promising biomarker is osteopontin which is useful to assess status and progression of AAA. The drug, Irbesartan (angiotensin II blocker) has been shown to reduce the size of aneurysm by dwindled the secretion of osteoprotegerin. **CONCLUSIONS:** Primary focus should be on early detection and management. To achieve this goal, orientation of primary care professionals towards symptoms and signs of AAA, surgeons to look for during abdominal surgeries and radiologists to observe during USG/ CT scan of abdomen.

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INTRODUCTION

Biomarker is used to indicate or measure biological processes (for instance, levels of a specific protein in body fluid, genetic mutations or brain abnormalities observed in a PET scan or other imaging test). Detecting biomarker specific to a disease can aid in the identification, diagnosis, treatment and follow up of affected individuals and people who may be at risk but do not exhibit symptoms. Abdominal aortic aneurysm (AAA) is often asymptomatic¹ and causes considerable mortality and morbidity^{1,2}. Risk factors for AAA include increasing age, male gender, smoking, coronary heart disease, hypertension, dyslipidemia, positive family history^{3,4,5} and prolonged steroid intake⁶. Various modalities such as physical examination^{7,8}, biomarkers^{9,10,11,12} and imaging studies^{7,8} can be used to diagnose at earlier stages. Physical examination is inexpensive; it lacks sensitivity and specificity^{7,13}; accuracy largely depends on skill of the examiner and the aneurysm size⁷. Imaging

studies such as CT scan and MRI have high yield in its diagnosis but cost limits its use^{7,8}. Hence, a brief review was made to find out the usefulness and limitations of various biomarkers in diagnosing AAA and pharmacological agent which could treat/prevent aneurysms.

MATERIAL AND METHODS

This study was carried out in Madras Medical College, Chennai, India during the period of May 2007 to August 2007. We have collected published literature on AAA from the year 1995 to 2007 through the web by using keywords biomarkers, clinical methods, screening tests and abdominal aortic aneurysm.

RESULTS AND DISCUSSION

Biomarkers identified for AAA are osteopontin (OPN)¹⁴, osteoprotegerin (OPG)¹¹, Matrix metalloproteinase-9 (MMP-9)¹⁵⁻¹⁹, circulating levels of tumor necrosis factor- α , interleukin-1 α , interleukin-6, interferon- γ , amino terminal propeptide of type 3 collagen²⁰⁻²³, C-reactive protein (CRP), fibrinogen, total WBC count, albumin¹² and ultrasonogram of abdomen^{7,8}.

Osteopontin is a phosphorylated acidic glycoprotein of

molecular mass 44 kDa and molecular weight of 35422 with 314 residues. It is involved in physiological and pathological processes and has a role in promoting inflammation, proteolysis and atherosclerosis, which are all integral processes in AAA. These are induced by a number of mechanisms including supporting macrophages, T cell chemotaxis and adhesion, prolonging lymphocyte survival, enhancing cell mediated immunity and activation of proteolytic pathways. Serum OPN level was significantly elevated in patients with AAA independent of other risk factors. It is also useful to assess status and progression of AAA¹⁴.

Osteoprotegerin, a member of tumor necrosis factor receptor family of member 11b; belongs to functional category of cytokine with Tnfrsf11b as a symbol. Its properties includes molecular weight of 45923, isoelectric point of 8.68, extinction coefficient of

$48660\text{M}^{-1}\text{cm}^{-1}$, absorption coefficient of 1.06 and aliphatic index of 79.93. It is involved in pathogenesis of AAA and atherosclerosis. Serum concentration of OPG was weakly

correlated with aneurysm size and its secretion was abrogated by angiotensin II blocker. Hence, Irbesartan (angiotensin II blocker) has potential benefit in slowing aneurysm expansion¹¹. Since irbesartan has been shown to revert AAA to some extent, it is likely that the early use of irbesartan in susceptible population may avert the onset of development of AAA as well as aneurysm elsewhere in the arterial tree. However, the action of drug in the process of reversal or prevention is yet to be identified.

MMP-9 is the most abundant elastolytic proteinase secreted by human AAA tissues where it plays a key role in connective tissue destruction and actively produced by aneurysm infiltrating macrophages at the site of tissue damage^{17,18}. MMP-9 expression appears to correlate with increasing aneurysm diameter¹⁹ and its plasma level is elevated in patients with AAA^{15,16}. According to Hovsepian¹⁵ et al., plasma level of MMP-9 decreased substantially after aneurysm repair.

Several other biomarkers such as circulating levels of tumor necrosis factor- α , interleukin-1 α , interleukin-6, interferon- γ and amino terminal propeptide of type 3 collagen have been explored²⁰⁻²³. Because many of these proteins are found in higher plasma concentrations in patients with atherosclerotic vascular disease and chronic inflammatory conditions, they have all proved to be nonspecific for aortic aneurysm.

Other biomarkers such as CRP, total WBC count, fibrinogen and albumin are used to distinguish asymptomatic and symptomatic, intact and rupture AAA¹². Abdominal

ultrasound scanning is the best recommended screening test for AAA in our hospital and elsewhere^{7,8}. Screening of AAA reduces overall medical costs^{24,25} and mortality^{7,25}. There was a significant difference observed in cost effectiveness and mortality benefit between elective and emergency surgical repair of AAA²⁶.

Lot of variation was observed in screening protocols. According to MASS²⁷, men of age 65 to 74 years should be screened quarterly if size of AAA is 4.5 to 5.4 cm and annually if size is 3 to 4.4 cm. Frame et al²⁸., suggested to have one follow up at every 5 years for men aged between 60 and 80 years. One time quick screen by ultrasonography of abdomen for men aged 70 was recommended by Lee et al²⁹.

Look and search for AAA in elderly and risky population by ultrasonogram. Our primary focus should be on early detection and management. To achieve this goal, Primary care professionals during regular check-ups and surgeons while doing abdominal surgeries³⁰, should look for AAA. In more than 50% of cases, femoral and popliteal aneurysms are associated with AAA³¹ and hence, radiologist must undertake abdominal scanning if they evaluate peripheral artery aneurysms in lower extremities³². Further research could be needed to assess usefulness of ACE inhibitors/other angiotensin II blocker drugs for prevention/treatment of aneurysm.

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