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

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Abstract

Background: Abdominal aortic aneurysm (AAA), though it is a deadly disease, it remains silent invariably. Hence, one has to suspect and evaluate AAA at least in a susceptible group at an earlier stage to reduce the morbidity and mortality.
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), osetoprotegrin (OPG), Matrix metalloproteinase-9 (MMP-9), circulating levels of tumor necrosis factor-, interleukin-1, interleukin -6, interferon-, 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. The promising biomarker is Osteopontin and this is useful to assess the status and progression of AAA. The drug, Irbesartan (angiotensin II blocker) has been shown to reduce the size of aneurysm by dwindling the secretion of osteoprotegrin.
Conclusions: Primary focus should be on early detection and management. To achieve this goal, orientation of primary health care professionals towards symptoms and signs of AAA, surgeons to look for the same during abdominal surgeries and radiologists to search for it during USG/ CT scan of abdomen.

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INTRODUCTION

Biomarkers are used to indicate or measure biological processes. An example of this is, levels of a specific protein in body fluid, genetic mutations or brain abnormalities observed in a PET scan or other imaging tests. Detecting biomarkers 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 asymptomatic [1] 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 intake [6] . 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, but lacks sensitivity and specificity [7,13] and accuracy largely depends on skill of the examiner and the aneurysm size [7] . 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] , osetoprotegrin (OPG) [11] , Matrix metalloproteinase-9

(MMP-9) [15,16,17,18,19] , circulating levels of tumor necrosis factor-, interleukin-1, interleukin -6, interferon-, amino terminal propeptide of type 3 collagen [20,21,22,23] , C-reactive protein (CRP), fibrinogen, total WBC count, albumin [12] and ultrasonogram of the abdomen [7,8] .

Osteopontin is a phosphorylated acidic glycoprotein of molecular mass 44 kDa and has a role in promoting inflammation, proteolysis and atherosclerosis, which are all integral processes in AAA. The process is 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 AAA [14] .

Osteoprotegrin, 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 48660M $^{-1}$ 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 expansion [11] . 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 vital 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 diameter [19] and its plasma level is elevated in patients with AAA [15,16] . According to Hovsepian [15] et al., plasma level of MMP-9 decreased substantially after aneurysm repair.

Several other biomarkers such as circulating levels of tumor necrosis factor-, interleukin-1, interleukin -6, interferon- and amino terminal propeptide of type 3 collagen have been explored [20,21,22,23] . 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 AAA [12] . 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 AAA [26] .

Numerous variations were observed in screening protocols. According to MASS [27] , men of age 65 to 74 years should be screened quarterly if the size of the AAA is 4.5 to 5.4 cm and annually if the size is 3 to 4.4 cm. Frame et al [28] ., 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 al [29] .

Our primary focus should be on early detection and management. To achieve this goal, primary health care professionals should be trained to search for symptoms and signs of AAA during regular check-ups and surgeons be motivated to look for the same while doing abdominal surgeries [30] , should look for AAA. In more than 50% of cases, femoral and popliteal aneurysms are associated with AAA [31] and hence, radiologist must undertake abdominal scanning to identify peripheral artery aneurysms in lower extremities [32] . Further research is needed to assess the usefulness of ACE inhibitors/other angiotensin II blocker drugs for prevention/treatment of aneurysm.

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