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OBSERVATION

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Prostate-specific antigen kallikrein and the heart

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Abstract

Currently, there is growing interest regarding prostate-specific antigen (PSA) and the cardiovascular system. Increased PSA serum levels have been reported after prolonged cardiopulmonary resuscitation, cardiac surgery, extracorporeal cardiopulmonary bypass, acute myocardial infarction (AMI) and coronary artery stenting. The possible role of PSA in cardiac events has been questioned due to the finding of PSA decrease during AMI and by the correlation of variation in PSA levels with coronary lesions and occurrence of major adverse cardiac events. Complexed PSA forms and uncomplexed PSA forms are observed in the bloodstream but the increasing formation of irreversible bound PSA seems to be a crucial finding during AMI. Large studies need to be carried out to confirm these preliminary results and to *elucidate unclear* aspects. These findings present many potential directions for future research including the role of uncomplexed forms of PSA, the possible distribution of PSA in the heart, the relative expression levels in heart disease states, the mode of expression regulation and other potential specific substrates. The journey of PSA investigation could be longer than initially expected.

Currently, a growing interest has been directed towards prostate-specific antigen kallikrein (PSA) and the cardiovascular system[1]. Increased PSA serum levels have been demonstrated after prolonged cardiopulmonary resuscitation[2,3], cardiac surgery[4], extracorporeal cardiopulmonary bypass[5-8], acute myocardial infarction (AMI)[9-15] and coronary artery stenting[16]. However, the possible role of PSA in cardiac events has been questioned due to the finding of PSA decrease during AMI and by the correlation of variation in PSA levels with coronary lesions and occurrence of major adverse cardiac events[17,18]. Recently, a decrease in PSA was also reported in a patient with coronary spasm and without significant coronary stenoses[19]. PSA is a 33 kDa single chain glycoprotein that was first identified in seminal plasma[20] and was subsequently isolated from prostate tissue[21,22]. It has been identified as a member of the human kallikrein family (hK3) of serine proteases[1,23-26] and was initially considered only as a marker for the detection of prostate cancer[27]. Other malignant and non-malignant, non-prostatic and non-cardiovascular diseases[27-32] are also associated with increased PSA serum levels and the PSA unspecificity to prostate, semen, and gender has been demonstrated[1,33-35]. Recently, attention

has been focused on PSA as a ubiquitous protein by the finding of PSA in neuronal cells[35].

The inactive precursor form of PSA, proPSA, is converted rapidly to active PSA by hK2 and other proteases also seem to have a role in the formation of active PSA[1,36]. PSA expression has been shown to be primarily regulated by steroid hormones through androgen receptor-mediated transcription[27,35,37-42]. Two forms of PSA are observed in the bloodstream: complexed PSA forms and uncomplexed (free) PSA forms. Irreversible PSA complexes are formed with serum protease inhibitors and other acute-phase proteins[43-48]. Measurements of PSA levels are more reliable if interpreted in combination with information about C-reactive protein (CRP)[4]. The levels of increased bound PSA seem to have a significant correlation with high-sensitivity CRP and to a 14-d follow-up, with the occurrence of heart failure[48].

A higher occurrence of major adverse cardiac events after AMI and the finding of more frequent and more severe coronary lesions have been reported with elevation of PSA during AMI[1,15,17,48]. PSA in serum has been considered to be a biologically active factor[1,49], but the increasing formation of irreversible bound PSA seems to be a crucial finding during AMI[48]. Large studies need to be carried out to confirm these preliminary results and to elucidate unclear aspects. These findings present many potential directions for future research including the role of uncomplexed forms of PSA, the possible distribution of PSA in the heart, the relative expression levels in heart disease states, the mode of expression regulation and other potential specific substrates. The journey of PSA investigation could be longer than expected[1].

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