

Testosterone levels: Key to survival after myocardial infarction?

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Existence of relationship between the level of sex-steroids and the risk of cardio-vascular events has been suspected for years. Men experience a gradual decrease in testosterone levels from the age of 30 and onward.

Age and male gender are the strongest independent risk factors for coronary artery disease (CAD). Whilst a wide variation in CAD mortality exists between countries, a male to female ratio of approximately 2:1 is consistently observed. Sex hormones decline with age in both sexes but the relationship of sex hormones to cardiovascular risk is complex. Pre-menopausal women have a lower incidence of CAD, but this rises after menopause so that the risk rapidly approaches that of males. One explanation for this phenomenon is that sex hormones influence the development and progression of coronary artery disease. These observations have led to the assumption that testosterone may exert a damaging influence on the cardiovascular system. Despite this, coronary atherosclerosis increases with age, while a marked fall in serum bioavailable testosterone levels is observed. Low testosterone level promote adverse risk factor profile [1]. It was documented that older men with low testosterone level have higher risk of development impaired glucose tolerance and diabetes in comparison with older men having higher testosterone concentrations [2]. Some studies demonstrated the positive association between levels of testosterone and HDL cholesterol both in male and in female [3]. Other studies show even more univocally results. In Tromso study men with lowest free testosterone levels had increased risk of all-cause mortality [4].

On the other hand it is not obvious if testosterone ‘supplementation’ brings positive effects. The problem in properly caring for ‘low’ testosterone patients is that we do not yet have definition for ‘normal’ testosterone values at different ages, nor have we identified specific signs and symptoms to accurately discriminate between those who need ‘treatment’ and those who do not. Another issue relates to the health outcomes affected by testosterone treatment [5]. If it is decided to correct a man’s testosterone levels, it should be defined what to expect from treatment. A meta-analysis of randomized trials that assessed the effect of testosterone use on cardiovascular events and risk factors in men done by Haddad et al. [6] revealed that currently available evidence weakly supports the conclusion that testosterone use in men is not associated with important cardiovascular effects.

Several previous studies documented that plasma levels of both total and bio-available testosterone fell transiently in the first 24 hours after myocardial infarction [7–9]. In addition the pro-fibrinolytic activity of testosterone was noted and a relation with hemostatic factors confirmed by several subsequent studies of healthy men and subjects with coronary disease risk factors [10, 11].

In this issue of *Cardiology Journal*, Militaru et al. [12] evaluated the association between serum testosterone levels and 30-day mortality in 126 patients with acute myocardial infarction. Testosterone levels were significantly lower in 16 patients who died than in survivors (2.1 ± 0.8 vs 4.3 ± 3.3 ng/mL; $p < 0.001$). The authors demonstrated that patients with lower values of testosterone had higher prevalence of diabetes and obesity, higher levels of total cholesterol and triglycerides but also they had higher level of HDL cholesterol and lower levels

of LDL cholesterol. At the same time, they showed higher level of C-reactive protein (CRP) than patients with higher levels of testosterone. This observation might indicate that higher levels of HDL cholesterol might not be protective in the presence of ongoing inflammatory process, measured by elevated CRP and in the presence of low testosterone levels. The association between less protective effects of HDL cholesterol and testosterone levels requires further investigations. Despite these differences in clinical presentation among patients with different testosterone levels, evaluated by quartiles, the authors found that the risk of death after myocardial infarction was found to be significantly associated with lower levels of testosterone after adjustment for imbalances in clinical covariates. The word of caution has to be expressed regarding a possibility that a presence of prior myocardial infarction and heart failure, factors known to be associated with lower testosterone levels, might have contributed to lower testosterone levels in non-survivors. Nevertheless, since ejection fraction and brain natriuretic peptide levels did not show meaningful differences, one could assume that these factors were of lesser influence in studied population.

These important observations made by Militaru et al. [12], based on relatively small study population, require further proof in larger cohorts. However, these findings are encouraging to further evaluate the role of testosterone levels in the setting of acute coronary syndromes with potential repercussions regarding possible treatment of patients with low testosterone levels.

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