The association between local atherosclerosis and prostate cancer

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OBJECTIVE
To morphometrically compare local atherosclerotic changes in cancerous prostate with those in noncancerous prostate specimens, as epidemiological studies report a positive association between the prevalence of general atherosclerosis and prostate cancer.

MATERIALS AND METHODS
The intima-to-media-ratio (IMR) of 538 prostate capsular tissue arteries was measured in 50 prostate cancer-positive and 29 prostate cancer-negative specimens (including 26 with benign prostatic hyperplasia and three with normal prostatic tissue).

RESULTS
An IMR of >1 was significantly associated with prostate cancer and a greater risk of prostate cancer (odds ratio 2.28). The IMR was >1 in cancer-positive specimens about twice as often as in cancer-negative tissue.

CONCLUSION
Local atherosclerosis (measured by the IMR) was more pronounced in prostate cancer-positive than in prostate cancer-negative specimens. The results support the view that men with local atherosclerotic lesions are at higher risk of prostate cancer.

KEYWORDS
local atherosclerosis, prostate cancer, BPH, intima-to-media-ratio
positive specimens as in negative specimens. Previous reports showed a positive correlation between local atherosclerosis and various types of cancer (e.g., brain, lung, kidney) [7,12–15] but also between general atherosclerosis and pre-cancerous lesions (e.g., adenomatous colonic polyps) [16,17]. However, the role of atherosclerosis in the pathogenesis of prostate cancer is controversial. Some reports suggest no significant association of atherosclerosis to prostate cancer [7], while others report a positive association between prostate cancer and coronary artery disease [3,4,6]. Nevertheless, it was proposed that atherosclerosis might increase the risk of developing cancer [9,10,13]. Atherosclerosis potentially causes insufficient tissue blood supply, resulting in local hypoxia. Consequently, hypoxia-inducible factor-1 increases and induces changes in reactive oxygen species, and hence oxidative DNA damage. Unrepaired or misrepaired damage leads to mutations, and if these involve critical genes such as oncogenes or tumour suppressor genes, cancer initiation and/or progression might result [9,10]. Thus, atherosclerosis in prostate tissue might increase the risk of cancer. The present study aimed to evaluate the prevalence of local atherosclerosis in prostate cancer-positive and -negative specimens. The degree of atherosclerosis was quantified by calculating the IMR, which is the most sensitive marker of atherosclerosis [11]. BPH and prostate cancer arise in different areas of the prostate (inner zone and peripheral zone), but the prostatic branches from the vesical inferior artery are responsible for the blood supply of the whole organ and so we evaluated IMR in the prostatic branches in the capsule of the prostate [18,19].

In cancer-positive specimens, the IMR was significantly greater than in -negative specimens. Similarly, the IMR was greater in BPH than in NPT, but only 11 arteries in NPT were investigated. Although the degree of atherosclerosis in BPH specimens was less than in cancer-positive ones, the association between atherosclerosis and these two entities could indicate pathogenetic similarities. In this context, Harvey [20] reported atherosclerosis of capsular arterial branches to be a major pathogenetic factor for the development of BPH. BPH in turn causes atrophy, which decreases local and general growth inhibitors, resulting in prostatic intraepithelial neoplasia and prostate cancer [20]. Whether prostatic atrophy is a pre-cancerous lesion is controversial [21–26], and until this issue is settled atherosclerosis must be deemed to be only a similarity in the pathogenesis of BPH and of prostate cancer, meaning that additional factors are required in the presence of atherosclerosis to cause prostatic atrophy or carcinogenesis. Also Weisman et al. [19] reported a higher frequency of general atherosclerosis in men with BPH than in men with no BPH.

The IMR of normal arteries can vary from 0.1 to ≥1 [27]. If a much larger IMR (e.g., >1) were more common in tumour-positive specimens, it could probably be deemed support for the above hypothesis. Prostate cancer-positive specimens had an IMR of >1 about twice as often as negative specimens, and there was a significant association between an IMR of >1 and cancer, with a greater risk of prostate cancer (OR 2.28). These findings are consistent with previous reports of a positive association between coronary artery disease and prostate cancer [3,4,6] but conflict with reports refuting an association of atherosclerosis to prostate cancer [7]. However, no previous study has investigated atherosclerosis in the prostatic arteries.

As the prevalence of atherosclerosis increases with age [28], the mean patient age in each group was calculated and the correlation between age, prostate cancer and BPH analysed. The mean patient age in cancer-positive (56 years) and negative (60 years) cases was greater than in NPT cases (29 years), but there was no correlation between the IMR and age in any of the groups.

In conclusion, the IMR in prostate cancer was greater than that of BPH specimens, indicating more pronounced local atherosclerosis. Furthermore, the IMR was >1 in cancer-positive specimens about twice as often as in BPH specimens, and was significantly associated with prostate cancer.

**REFERENCES**


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Abbreviations: IMR, intima-to-media ratio; OR, odds ratio; NPT, normal prostatic tissue.