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Obesity and prostate cancer research

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The authors of the manuscript entitled "Obesity, diabetes and aggressive prostate cancer hormone–naïve at initial diagnosis" published in this issue performed a retrospective analysis of 266 patients who underwent prostate biopsies for suspected prostate cancer (PCa). Their results suggest that obesity and diabetes mellitus type II (DMII) are associated with more aggressive PCa (defined as higher biopsy Gleason score), which could have an impact on patients' outcome.

These results are relevant, since they discuss the association of two major public health concerns for middle–aged and older men. Obesity is a growing epidemic, especially in industrialized countries, which is generally accepted to be correlated with cardiovascular disease, diabetes mellitus type II and other diseases. In 2003, it has already been shown that body weight was associated with increased overall cancer and PCa–specific death rates [2]. In light of this, it has already been suggested that lifestyle and diet could play an important role in the development of PCa, which is based on the observation that Caucasians have much higher rates of PCa when compared to Asians. Higher rates of PCa have been found in Asians who have migrated to the USA in comparison to their home–land counterparts, which could partially be explained by diet and lifestyle adjustments [3].

Since then, there has been an increasing interest in understanding the role of obesity in the development and outcome of PCa. Indeed, several studies have shown an association between BMI (kg/m^2) and more lethal disease, with a meta–analysis by Cao et al. showing a 15–21% increased risk of fatal PCa or biochemical recurrence in obese PCa patients [4]. Despite of being interesting, these results only show that there is an association between obesity and PCa and do not provide a causal relationship for this association. There could be multiple explanations for these observations. It could be speculated that PCa diagnosis is delayed in obese patients because digital rectal examination is less sensitive and patients get less PSA testing, since their primary health care is focused on their weight problems and associated (cardiovascular) diseases. Furthermore, there is an inverse relation between PSA levels and BMI, which is suggested to be caused by hemodilution [5]. When diagnosed, curative treatment could be less efficient in obese patients as well. During surgery, abundant subcutaneous and visceral fat could hinder careful dissection, possibly leading to higher rates of positive surgical margins [6].

As the authors of this paper suggest, this association could also be attributed to higher rates of high–grade disease in obese patients. Indeed, this has already been suggested before by Ma J et al., who prospectively showed a clear association between obesity and PCa–specific mortality. After correcting for Gleason score and clinical stage, the size of the association was attenuated, but obesity remained a statistically significant risk factor [7]. This strongly suggests we are still missing the knowledge regarding the mechanisms of action of adipose tissue in PCa development and progression.

Despite the relevance of the article, the authors' data do not add new insights to what is already known on the topic. Future research concerning obesity and PCa outcome should rather focus on unraveling mechanisms behind what makes obese patients more prone to worse outcome. Indeed, the traditional view of adipose tissue as a passive reservoir for energy storage has long been abandoned; current evidence shows that adipose tissue is an organ with multiple endocrine functions [8]. Furthermore, it has been shown that obesity leads to dysregulation of pathways which could in turn influence disease outcomes, as suggested by the authors as well. Regarding this issue, Hursting SD et al. have published a review on the role of multiple hormones, growth factors, cytokines and other mediators in the development of cancer, which represent promising targets for future research. This is a promising research field, since dysregulation of multiple hormonal systems has already been described in obese patients, although

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only a limited number of studies have correlated this with PCa outcome [9, 10]. Moreover Petterson et al. found an association between ERG–positive tumors and lethal PCa in obese patients, suggesting the possible interplay between altered metabolic signaling pathways and other molecular alterations associated with PCa [11]. Therefore, it is mandatory that future research is focused on further unraveling the role of this endocrine organ on PCa–related pathways, which could eventually play an important role in prevention and early intervention of PCa. Considering many arguments supporting a higher PCa mortality risk in obese patients, however, increased awareness within the urological community is warranted. In parallel, obese patients should be properly informed as well and –even though reversibility of this risk is not proven– should be motivated to lose weight.

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