Can we predict aggressiveness of prostate cancer before surgery with a blood test?

Embargo until: Sat 12 Mar 00.01 (Central European Time, Munich)

Prostate cancer is the most common male cancer, with 400,000 new cases every year in Europe. The success of surgery depends on a variety of factors. Now a new study from scientists in Milan has shown that for local prostate cancers treated with radical prostatectomy, you can preoperatively predict the aggressiveness of the prostatic disease, via a simple blood test.

When describing prostate cancer, urologists normally use the Gleason pattern, where a tissue sample from a biopsy is analysed to show much of the sample has been taken over by tumour cells. Gleason pattern 1 means that the cells in the tissue are normal, whereas Gleason pattern 5 (the highest score) indicates that the tissue is largely taken over by tumour cells. If a patient has Gleason pattern 5, then the predicted outcomes are poor.

Now a group of Italian researchers have been able to show that hypogonadism (which is low levels of the sex hormone testosterone) predicts that the patient will have a high Gleason score – which indicates a poor outcome after treatment.

A group led by Dr Marco Moschini (San Raffaele Hospital, Milan) retrospectively correlated hormone levels and Gleason scores in 1017 patients who underwent radical prostatectomy surgery at the San Raffaele hospital in Milan. 118 of the patients showed Gleason pattern 5. After adjusting for age, they found that the hypogonadism status and levels of sex-hormone-binding globulin (SHBG) was able to predict patients with Gleason pattern 5 (OR 1.79, p=0.025).

According to Dr Marco Moschini:
“*We found that hypogonadism, and the levels of SHBG, were able to predict whether or not patients had Gleason factor 5, which is the worst Gleason score. This association will allow us to predict what the outcome will be before we decide to treat a patient with surgery. Potentially this can be helpful to identify patients with the most aggressive prostate cancer before surgery.*

*There is an urgent need for new research to uncover the role which hormones play in prostate cancer development.*

*What we don’t yet know is if this is an association, or if hypogonadism in some way increases the risk of developing high-grade prostate cancer. If this is the case, then it may be that treating the hypogonadism can lessen this risk, but we need more work before we can be sure of that*”.

Commenting, Professor Alexandre de la Taille (Paris), member of EAU Scientific Congress Committee, said: “*Several reports in the literature mention that low serum testosterone level is associated with prostate cancer aggressiveness. This study highlights the fact that SHBG is also linked to high Gleason score. These cancers, developed in this special hormonal environment, are probably due to different molecular pathways and represent a new field to explore*”. 
Hypogonadism independently predicts pathological Gleason pattern 5 at the time of radical prostatectomy

Moschini M.1, Dell'Oglio P.1, Fossati N.1, Gandaglia G.1, Larcher A.1, Stabile A.1, Saitta G.1, Ventimiglia E.1, Barbagli G.2, Shariat S.3, Bollens R.4, Montorsi F.1, Briganti A.1

1IRCCS Ospedale San Raffaele, Division of Oncology/Unit of Urology; URI, Milan, Italy, 2Centro Chirurgico Toscano, Dept. of Urology, Arezzo, Italy, 3Medical University of Vienna, Dept. of Urology, Vienna, Austria, 4Jules Bordet Institute, Université Libre De Bruxelles, Dept. of Urology, Brussels, Belgium

INTRODUCTION & OBJECTIVES: Pathological Gleason score is a powerful predictor of oncological outcomes in patients diagnosed with prostate cancer (PCa) and treated with radical prostatectomy (RP). Particularly, a pathological Gleason pattern 5 is associated with poor survival outcomes. Similarly, the presence of hypogonadism has been associated with higher rates of biochemical recurrence and more advanced pathological stage. Our study aimed at evaluating the ability of preoperative sex hormones to predict the presence of pathological Gleason pattern 5 in RP specimen, which may explain the unfavorable outcomes of hypogonadal men diagnosed with PCa.

MATERIAL & METHODS: A cohort of 1,071 consecutive Caucasian-European patients who underwent RP at a single institution was analyzed with pre-operative serum hormones values available. None of the patients had taken any hormonal neoadjuvant treatment or other hormonal preparations during the previous 12 months. Serum testosterone (TT), 17β-estradiol (E2) and sex hormone-binding globulin (SHBG) were measured the day before surgery (8-10 AM) in all cases. Hypogonadism was defined as defined as TT<3 ng/ml. Dedicated uropathologists assigned the Gleason score. Univariable and multivariable logistic regression models tested the impact of preoperative circulating sex steroids and presence of both pathological Gleason pattern 5 pattern and pathological Gleason score 8-10 at final pathology. Separated models were created for each single hormone, as well as for the presence of hypogonadism. Covariates consisted of age and D'Amico risk groups.

RESULTS: Mean age was 65 years. Overall, 118 patients (11.0%) harbored a pathological Gleason pattern 5 at RP specimen, 27 (22.9%) as primary and 96 (81.3%) as secondary pattern, of which 5 (4.2%) harbored Gleason 5+5. At univariable analyses, no differences were recorded between patients with or without Gleason pattern 5, regarding TT, E2, age and PSA. Conversely, SHBG (41.8 vs. 37.5 mmol/dL) and the rate of hypogonadism (32.0% vs. 21.4%)
were higher in patients harboring Gleason pattern 5 (all $p<0.007$). At multivariable analyses, TT and E2 were not associated with either pathological Gleason pattern 5 (all $p>0.4$), while SHBG levels (OR: 1.02, $p=0.03$) were able to predict the presence of pathological Gleason pattern 5. After adjusting for age, d’Amico risk groups and SHBG, the presence of hypogonadism (OR 1.79, $p=0.025$) was independently associated with the presence of pathological Gleason pattern 5.

**CONCLUSIONS:** Hypogonadism status and preoperative SHBG levels were independent predictor of pathological Gleason 5 pattern at final pathology. Our results may explain the increased risk of hypogonadal men to harbor unfavorable pathological and long term outcomes in men diagnosed with PCa and treated with RP.