

Re: Association of Androgen Deprivation Therapy with Cardiovascular Death in Patients with Prostate Cancer: A Meta-Analysis of Randomized Trials

Nguyen P, Je Y, Schutz FAB, et al

JAMA 2011;306:2359–66

Experts' summary:

Androgen deprivation as a treatment for prostate cancer has been found to be associated with increased cardiovascular morbidity and mortality resulting in a US Food and Drug Administration safety warning in 2010 [1] and similar statements from several scientific associations [2]. In a meta-analysis of eight randomised trials enrolling 4141 patients with poor risk nonmetastatic prostate cancer, Nguyen and coworkers found no association between antiandrogen deprivation and cardiovascular mortality in any subgroup [3].

Experts' comments:

This meta-analysis [3] contributes important evidence to the body of knowledge on the cardiovascular side effects of hormonal treatment in men with poor risk nonmetastatic prostate cancer. Most patients considering such treatment may be counselled that they will not be at an increased risk of dying of competing causes due to androgen deprivation. It remains unclear, however, whether this is also valid for those with serious preexisting cardiovascular comorbidity. The trials included in this meta-analysis [3] were not stratified by the presence of cardiovascular comorbidity. With this limitation, it is questionable whether pooled analyses of randomised trials are able to determine the cardiovascular risk of androgen deprivation conclusively [4].

Patients with preexisting cardiovascular diseases are less likely to be encountered in randomised trials than in daily practice [3]. Therefore, the findings of this meta-analysis [3] should only be applied cautiously to this subgroup. In one randomised trial showing increased survival after adding 6 mo of androgen deprivation to radiotherapy for poor risk localised prostate cancer and stratifying by comorbidity, patients with moderate or severe comorbidity did not benefit from the study treatment possibly due to an interaction between their comorbid diseases and androgen deprivation [5]. Further points worth considering are that the studies evaluated in this meta-analysis [3] were not designed to reveal a relationship between androgen deprivation and cardiovascular morbidity

and mortality and that with only 11%, the overall incidence of competing cardiovascular mortality was relatively low. In patients with poor risk nonmetastatic prostate cancer, there is often rather a comparison between immediate and deferred treatment. Therefore, both arms were exposed to the potential risk factor to some degree. All these points may render the demonstration of small effects difficult.

This meta-analysis [3] demonstrated that early androgen deprivation for otherwise healthy poor risk nonmetastatic prostate cancer is safe and offers survival benefits. However, it is not appropriate to reassure patients with preexisting cardiovascular comorbidity.

Conflicts of interest: The authors have nothing to disclose.

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Michael Froehner, Manfred P. Wirth*
 Department of Urology, University Hospital "Carl Gustav Carus,"
 Technical University of Dresden, Dresden, Germany

*Corresponding author.

E-mail address: Manfred.Wirth@uniklinikum-dresden.de (M.P. Wirth).

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Re: Prostatic Urethral Lift: Two-year Results After Treatment for Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia

Chin PT, Bolton DM, Jack G, et al

Urology 2012;79:5–11

Experts' summary:

The authors prospectively evaluated the safety and effectiveness of the transurethral delivery of the intraprostatic implant UroLift in 64 patients with symptomatic benign prostatic

hyperplasia. The effectiveness on lower urinary tract symptoms (LUTS) and sexual outcomes was assessed at up to 24 mo. The procedures were performed under local anaesthesia in 26 patients, and a mean of four implants were delivered per patient. Approximately half of the patients did not receive a postoperative catheter, and 75% of these were removed the day after the procedure. The only direct adverse events reported were urinary tract infection requiring antibiotics in seven patients. In addition, one patient with a history of heart disease had a myocardial infarction after anticoagulation withdrawal. The reported International Prostate Symptom Score

was reduced to 42% at 2 wk, 49% at 6 mo, and 42% at 2 yr. The peak flow rate was improved by 30% at all intervals. No compromise in erectile or ejaculatory function was observed.

Experts' comments:

The procedure tested in this study is new, is minimally invasive, and is based solely on a mechanical compression of prostate lobes, relieving urethral obstruction without any tissue ablation. It seems to be well tolerated, is effective on LUTS, and is even feasible in the office for selected patients. Would it be too good to be true? None of the previous and so-called mini-invasive procedures proposed as alternatives to medical therapy have achieved such results in terms of feasibility and tolerance. Ablative procedures such as transurethral microwave thermotherapy or transurethral needle ablation are no longer considered, as such, and urethral stents have been all but abandoned because of their reported morbidity. This first study on midterm results, together with a recent report focusing on sexual outcomes [1], is encouraging and anticipates nice perspectives. The single-blinded comparative LIFT study, aiming to determine the safety and effectiveness of the procedure versus placebo, has completed its enrolment and is now in the follow-up phase [2]. Further studies will be needed to compare UroLift with medical therapy, to identify

predictive factors of effectiveness, and to better select potential candidates.

Conflicts of interest: The authors have nothing to disclose.

References

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Nicolas Barry Delongchamps, Marc Zerbib*
Urology Department, Cochin Hospital,
Paris Descartes University, Paris, France

*Corresponding author. Hôpital Cochin,
27 Fg St Jacques, 75014 Paris, France.

E-mail address: marc.zerbib@cch.aphp.fr (M. Zerbib).

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Re: Development of Bladder Outlet Obstruction After a Single Treatment of Prostate Cancer with High-intensity Focused Ultrasound: Experience with 226 Patients

Netsch C, Pfeiff D, Gross AJ

J Endourol 2010;24:1399–403

Expert's summary:

To investigate the occurrence of bladder outlet obstruction (BOO) after a single treatment of high-intensity focused ultrasound (HIFU), the authors followed 226 patients for 2 yr and observed that BOO developed commonly, particularly affecting the bladder neck. Patients' prostate sizes as assessed by transrectal ultrasound were 9–95 cm³ (median: 29 cm³). The authors also investigated the benefit of pre-HIFU transurethral resection of the prostate (TURP). The median tissue removed by TURP was 23 cm³ (range: 14–68 cm³). The authors concluded that combining HIFU with TURP decreases the post-HIFU urinary retention time; however, the combination could not prevent delayed development of BOO, mainly in the form of bladder neck stenoses in 25.66% of the patients.

Expert's comments:

Minimally invasive treatments (MITs) for organ-confined prostate cancer such as HIFU, brachytherapy, or cryotherapy are attractive alternatives to radical prostatectomy (RP). None is complication free, and the most frequently seen complication is prolonged urinary retention or voiding difficulties [1,2]. MIT usually involves thermal or radioactive damage to tissues, which are left behind; the resulting edema subsides, followed by nature taking care of the dead tissue and reshaping the organ, which is unpredictable.

Centers with much experience with HIFU recommend performing TURP before HIFU to reduce the possibility of

urinary retention or severe voiding difficulties [3,4]. The rationale for performing a pre-HIFU TURP is downsizing of the prostate glands, to remove the endovesical midlobe and to reduce the anterior-posterior diameter for complete treatment of the peripheral zone during a single HIFU session [3] as well as to remove the microcalcifications and microabscesses in the prostate. Despite this approach, the combination of an almost century-old procedure (TURP) with a high-tech procedure (HIFU) could not prevent the unwanted complication of bladder neck stenosis, as observed by the authors (25.66%). This complication rate is very high by any standard.

Downsizing large prostatic volume and removing a midlobe are logical for allowing good access to the entire gland for HIFU. Performing TURP on small glands just to prevent urinary retention adds a surgical procedure for these patients as well as additional significant cost. The issue of cost-effectiveness of a procedure includes not only the direct costs of a surgical procedure but also the cost of working days lost for the patient and treatment of complications. We provide care in an era in which cost containment is taking on more and more importance in health care economics, even for wealthy nations.

When easily insertable and removable temporary prostatic stents are available, it is a bit astonishing that prostatic stents were not combined with any of the MITs for localized prostate cancer. They can be inserted immediately after any MIT procedure.

If the total cost of MIT plus stent is less than or equal to the cost of RP (of any form) and the outcome is not less than eradication of the cancer, this combination is a logical alternative to be proposed to the patient. This approach may allow immediate urination by preventing edema-caused