

New Findings in Prostate Cancer

Highlights from the 23rd Annual Congress of the European Association of Urology, March 26–29, 2008, Milan, Italy

[Rev Urol. 2008;10(4):290-293]

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Key words: Prostate cancer, cT3 • Prognostic factors • Pelvic lymphadenectomy • Dynamic contrast-enhanced magnetic resonance imaging • Quality of life • Radical prostatectomy • Postoperative urinary continence

The 23rd Annual Congress of the European Association of Urology offered an array of more than 1000 posters and 42 videos on several themes. Major topics regarding prostate cancer included basic research, prognostic factors, surgical and functional outcome, and management of postoperative urinary leakage and erectile dysfunction. Important new research was presented on diagnosis, prognostic factors, therapeutic modalities, T3 tumor, and surgical approaches for carcinoma of the prostate.

Diagnosis and Prognostic Factors

An interesting contribution by Herwig and colleagues¹ was the analysis of immunologic reactions of the monocytic

lineage in prostate cancer. Understanding of the immunologic response to tumors, especially with respect to the monocyte/macrophage (CD14+) lineage, is largely speculative. For the first time, an elevation of blood macrophages in prostate cancer patients compared with healthy controls, as well as in accordance with tumor load, could be shown. Similar reactions of these cell populations could be observed in acute sepsis; the elevation of activated cells seems to be the most significant. Further distinction of these cells may lead to a better stratification of patients with prostate cancer.

Anagnostou and coworkers² evaluated the outcome of first repeat biopsy performed with a modified Vienna Nomogram Scheme. Results showed that if the modified Vienna Nomogram Scheme is used in repeat biopsy, cancer is detected at significant rates and is usually of median Gleason sum and located laterally in

the peripheral zone. Repeat biopsy can improve cancer detection if the transition zone and suspicious areas are sampled in addition to the original scheme.

The need for pelvic lymphadenectomy in patients with low-risk prostate cancer undergoing radical prostatectomy is a controversial subject. Heidenreich and associates³ presented a study in which they tried to identify preoperative prognostic risk factors associated with lymph node metastases. A total of 499 men with low-risk prostate cancer according to the D'Amico criteria underwent radical prostatectomy and extended pelvic lymphadenectomy. Number of removed nodes, number of positive lymph nodes, Gleason score of the radical prostatectomy specimen, pathohistologic data, and anatomic distribution of lymph node metastases were determined. A correlation between preoperative serum prostate-specific antigen (PSA) value, biopsy Gleason score, percentage of

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positive biopsy results, and the presence of lymph node metastases was calculated. The investigators concluded that (1) the frequency of lymph node metastases is low in low-risk prostate cancer; (2) if more than 50% of biopsy cores are involved with prostate cancer, the risk of lymph node metastases increases significantly; and (3) if performed, pelvic lymphadenectomy has to be done in an extended variant.

Preoperative serum PSA value, biopsy Gleason score, and PSA density are the best prognostic factors for patients with clinically locally advanced prostate cancer (cT3a). The combination of preoperative PSA value and biopsy Gleason score provides accurate prediction of final histopathology. The aim of the study by Joniau and colleagues⁴ was to determine whether PSA density is a stronger predictive factor than preoperative PSA value for adverse final histopathology (positive section margins, seminal vesical invasion, and positive lymph nodes). The study also analyzed whether PSA density can be used as a prognostic factor for biochemical progression-free survival in patients with cT3a prostate cancer. The study consisted of a cohort of 200 patients with unilateral cT3a prostate cancer, assessed by digital rectal examination. All patients underwent radical prostatectomy and bilateral lymphadenectomy. Multivariate analysis showed that PSA density is an independent prognostic factor and is stronger than PSA value in the prediction of adverse histopathology and biochemical progression-free survival in cT3a prostate cancer. Therefore, PSA density can be used for patient counseling before treatment selection in cases of locally advanced prostate cancer.

Therapeutic Modalities

A very interesting new approach to dealing with prostate cancer is dynamic contrast-enhanced magnetic resonance

imaging (DCE-MRI) after vascular targeted photodynamic therapy (VTP) with padoporfin (Tookad®; Steba Biotech, The Hague, Netherlands).⁵ Tookad is a new photosensitizing drug being evaluated in phase I/II clinical trials. Each patient in the trial had an MRI scan upon enrollment. Tookad was administered intravenously, and light was delivered by cylindrical diffusers in the prostate. Tookad provokes tissue ablation by causing occlusion of the blood vessels in a target tissue. Seven days later MRI was performed again, and subsequent MRI examinations followed at 1 month, 3 months, and 6 months after treatment. Tookad VTP produced lesions that were clearly delineated by DCE-MRI. On the basis of the MRI data it seems likely that the Tookad VTP treatment leads to ablation of target tissue with minimal effects on surrounding tissues (ie, it respects the anatomic and tissue boundaries within the target lesion).

Quality-of-life issues are a major concern for patients seeking therapeutic intervention once they are diagnosed with prostate cancer. Binbay and colleagues⁶ prospectively compared short-term quality-of-life scores of 36 patients who were treated with either laparoscopic radical prostatectomy or open retropubic radical prostatectomy. Different questionnaires were used to assess postoperative quality of life. The study showed that although patients who underwent laparoscopic prostatectomy expressed a more favorable attitude toward surgery in the early period, there was no significant difference in quality of life at 3 months after surgery between the 2 groups.

Djavan and coworkers⁷ presented an update of the European Study on Radical Prostatectomy. The aim of the study was to evaluate the legacy and impact of preservation of the tip of the seminal vesicle during radical

retropubic prostatectomy on potency and continence rates. The investigators concluded that preservation of the tip of the seminal vesicles significantly increased post-radical prostatectomy potency rates without jeopardizing oncologic outcomes.

T3 Prostate Cancer

Prostate cancer patients with locally advanced disease and a PSA value of 20 ng/mL or higher are considered very-high-risk patients. For that reason, most will receive a combination of radiotherapy with hormonal treatment or hormonal therapy alone. Radical prostatectomy is not considered a valuable treatment option in this patient group. A Belgian study⁸ evaluated 133 patients with cT3-4N0-1 prostate cancer and a preoperative PSA value of 20 ng/mL or higher who underwent radical surgery at 4 institutions. The results showed that, in this very select high-risk prostate cancer population, radical prostatectomy with or without adjuvant or salvage treatment provided very good long-term cancer-specific survival. The investigators pointed out that radical surgery should not be ignored as a first step in a multimodality approach for very-high-risk prostate cancer.

Djavan and coworkers⁹ evaluated oncologic outcomes of radical prostatectomy and radiotherapy in men with cT3 prostate cancer. The outcome of the study showed clearly that men with cT3 prostate cancer represent a largely inhomogeneous cohort. Disease-specific survival and cancer-specific survival were significantly lower than with cT2 disease. Furthermore, it was shown that treatment allocation and selection should be made on the basis of Gleason score, PSA value, and age. Age remains an independent and strong predictor of outcome.

Interesting conclusions could be found at 5 and 10 years' follow-up. First, in highly selected men with cT3

prostate cancer, radical prostatectomy offers an effective treatment option. Second, in men with cT3, Gleason score less than 7, and a PSA value of 4 to 10, external beam radiotherapy plus hormonal therapy is equally as effective as radical prostatectomy. Third, in men with cT3, age 60 years or less, a PSA value less than 4 or greater than 10, and Gleason score of 7 or more, radical prostatectomy is superior to external beam radiotherapy plus hormonal therapy in terms of cancer-specific survival.

Postoperative Urinary Continence

Urinary incontinence is one of the major drawbacks after radical prostatectomy. Nevertheless, according to the literature, within 1 year most patients regain continence. However, time to reach full urinary continence is still a matter of debate. Rocco and associates¹⁰ described a new surgical approach to regain urinary continence. The dissection of the prostate is performed according to a technique described by Patel and colleagues.¹¹

Before the anastomosis is done, the posterior portion of the rhabdosphincter is identified and sutured to the residual of the Denonvilliers fascia with a single running suture. After suture tightening, a further stitch is passed 1 to 2 cm cranially and posteriorly to the bladder neck and then finally tightened. Anastomosis is then completed according to the Van Velthoven technique, modified by Patel. The study results confirmed that robot-assisted posterior reconstruction of the rhabdosphincter in radical

additional modifications to regain urinary continence as soon as possible. A total of 205 patients were analyzed with a validated health-related quality-of-life survey administered at 1, 6, 12, 24, and 52 weeks postoperatively. Median time to reach continence was 3 weeks; continence at 1 week was 37%, at 6 weeks was 80%, at 12 weeks was 90%, and at 24 weeks was 96%.

A comparison of continence recovery rates in a prospective, nonrandomized study of patients undergoing

Robot-assisted laparoscopic radical prostatectomy was associated with significantly better results in terms of early urinary continence, time to continence recovery, and overall continence rates.

prostatectomy is a feasible and easy procedure with excellent outcome regarding urinary continence.

Another interesting study that dealt with urinary incontinence came from Jhaveri and associates.¹² A new surgical approach was presented, using the Pagano and Rocco principle with

robot-assisted laparoscopic radical prostatectomy (RALP) or retropubic radical prostatectomy showed that RALP was associated with significantly better results in terms of early urinary continence, time to continence recovery, and overall continence rates at follow-up.¹³

Main Points

- A study of 499 men with low-risk prostate cancer (D'Amico criteria) who underwent radical prostatectomy and extended pelvic lymphadenectomy showed that (1) the frequency of lymph node metastases is low in low-risk prostate cancer; (2) if more than 50% of biopsy cores are involved with prostate cancer, the risk of lymph node metastases increases significantly; and (3) if performed, pelvic lymphadenectomy has to be done in an extended variant.
- Multivariate analysis of a study of 200 patients with unilateral cT3a prostate cancer showed that prostate-specific antigen (PSA) density is an independent prognostic factor and is stronger than PSA value in the prediction of adverse histopathology and biochemical progression-free survival.
- On the basis of the magnetic resonance imaging data it seems likely that vascular targeted photodynamic therapy with padoporfin leads to ablation of target tissue with minimal effects on surrounding tissues (ie, it respects the anatomic and tissue boundaries within the target lesion).
- The European Study on Radical Prostatectomy showed that preservation of the tip of the seminal vesicles significantly increased post-radical prostatectomy potency rates without jeopardizing oncologic outcomes.
- A study of 133 patients with cT3-4N0-1 prostate cancer and a preoperative PSA value of 20 ng/mL or higher who underwent radical surgery showed that, in this very select population, radical prostatectomy with or without adjuvant or salvage treatment provided very good long-term cancer-specific survival.
- Preoperative and postoperative membranous urethral length (MUL) and the MUL loss ratio are related to the recovery time and level of urinary continence after radical prostatectomy; therefore, preservation of urethral length during surgery is recommended.

A very promising contribution by Paparel and colleagues¹⁴ assessed whether recovery of urinary continence after radical prostatectomy is associated with endorectal MRI findings regarding preoperative and postoperative membranous urethral length (MUL), percentage change in MUL, and postoperative urethral and periurethral fibrosis. The conclusion of the study was that preoperative and postoperative MUL and the MUL loss ratio are related to the recovery time and level of urinary continence after radical prostatectomy. Therefore, preservation of urethral length during surgery is recommended. Periurethral fibrosis might impede the recovery of continence after radical prostatectomy by altering the elasticity of the external sphincter.

The 23rd Annual EAU Congress in Milan, Italy, was a great platform for urologists from all around the world to present their recent investigational data. Stunning findings were presented during the 4 days, and it was shown again that research in the

urologic field is still not complete. There is a lot to come and much yet to be discovered. ■

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