New Findings in Prostate Cancer, Benign Prostatic Hyperplasia, and Sexual Dysfunction

Highlights from the XVIII Congress of the European Association of Urology, March 12-15, 2003, Madrid, Spain

[*Rev Urol.* 2004;6(1):19-28]

Key words: Prostate cancer • Prostate-specific antigen • Nomogram • Radical prostatectomy • Benign prostatic hyperplasia • Sexual dysfunction • Lower urinary tract symptoms • Erectile dysfunction

The XVIII Congress of the European Association of Urology (EAU), held in Madrid, March 12-15, 2003, gathered together researchers and clinicians to present the latest clinical and scientific developments in the field of urology. Prostate cancer, benign prostatic hyperplasia (BPH), and sexual dysfunction were among the many topics covered.

Prostate Cancer: Epidemiology and Nomograms

Many studies have shown that, compared with a sextant core biopsy, an increase in the number of cores biopsied improves the detection of prostate cancer and that prostate volume has a major impact on the cancer detection rate. Nevertheless, it is unclear how many cores should be taken. To address this issue, Djavan and colleagues[1] conducted a study that included 394 patients with prostate-specific antigen (PSA) levels of 4 ng/mL to 10 ng/mL to validate the Vienna nomogram (Table 1). This nomogram was constructed on the basis of the results of the European Prostate Cancer Detection (EPCD) study. The Vienna nomogram is used to determine the "optimal" number of cores based on a patient's age and total prostate volume. The prostate cancer detection rate in this validation study was 38.7%, compared with 29.9% (22.8% on the initial biopsy plus 7.1% on a repeat biopsy) in the EPCD study.

Another nomogram, which includes a digital-rectal examination and measurements of total PSA (tPSA), free PSA (fPSA), and prostate volume, was constructed by Finne and colleagues[2] for a screening population of patients with PSA levels from 4 ng/mL to 10 ng/mL. This nomogram outperformed the proportion of fPSA (78.3% vs 71.3% area under the curve, respectively).

Prostate cancer can be classified as hereditary in 5% of patients. However, pedigree criteria have a low sensitivity in detecting families with hereditary susceptibility to prostate cancer, and the true proportion of hereditary cancers is unknown. The risk of developing prostate cancer is approxi-

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Table 1
Vienna Nomogram: Optimal Number of Cores on TRUS-Guided Prostate Biopsy Dependent on Prostate Volume

Prostate Volume on TRUS, mL	Patient Age, y			
	<50	50-60	60-70	>70
20-29	8	8	8	6
30-39	12	10	8	6
40-49	14	12	10	8
50-59	16	14	12	10
60-69	–	16	14	12
≥70	–	18	16	14

TRUS, transrectal ultrasonography.
Data from Djavan B et al. *Eur Urol Suppl.* 2003;2(1):6.[1]

mately doubled for brothers and sons of men with prostate cancer compared with those who have no family history of the condition. The risk is substantially higher for brothers and sons of men with early-onset prostate cancer and for those who have more than one affected relative.

In a German study, Herkommer and colleagues[3] evaluated 149 prostate cancer patients who had a positive familial history and 296 patients who had sporadic prostate cancer. The investigators compared the number of screening tests before diagnosis, age, PSA level at diagnosis, stage, lymph-node status, and percentage of Gleason scores less than 7 and found no significant differences between the populations. These results are in contrast to those of trials in US populations.

Foley and colleagues[4] compared the pathologic characteristics of radical prostatectomy specimens of young patients (≤50 years; n = 41) with those of older patients (>50 years; n = 993). The outcomes for younger patients who develop prostate cancer have improved with the use of PSA testing, as prostate cancer can now be detected in asymptomatic patients at younger ages. Results of this study showed no significant differences between the 2 groups with regard to tumor volume, Gleason sum, tumor stage, lymph-node status, vascular invasion, seminal vesicle (SV) invasion, and number of positive prostate biopsies. Nevertheless, 28% of subjects in the younger group had a PSA level less than 4 ng/mL, compared with 9% of those in the older group (P = .001). The authors concluded that these results have implications for the success of prostate cancer screening in patients aged 50 years or younger.

The risk of developing prostate cancer is approximately doubled for brothers and sons of men with prostate cancer compared with those who have no family history of the condition.

Prostate Biopsy

Schöler and colleagues[5] showed that the impairment of sexual function in patients who underwent a transrectal ultrasonography (TRUS) prostate biopsy is transient. Djavan and colleagues,[6] of the Vienna group, reported that, based on the results of the EPCD study, prostate cancer was more dorsoapical and dorsolateral at repeat biopsy. This new repeat prostate biopsy technique, which targets the dorsolateral and dorsoapical regions of the peripheric zone and 2 cores from the transition zone, increased the detection rate 87.0%, from 10.0% to 18.7%, in a systematic repeat biopsy 6 weeks after a negative initial prostate biopsy, without increasing morbidity. Ravery and colleagues[7] showed that prostate cancer detected with repeat biopsy is most often significant cancer and, therefore, early and systematic repeat biopsy is justified.

Addressing the issue of "significant" prostate cancer, Dumonceau and colleagues[8] found that 38 (8.5%) of 445 patients had, in a set of 6- or 10-core TRUS biopsies, one single focus of prostate cancer less than 3 mm and with a Gleason score less than 6. The median PSA level of these patients was 8.5 ng/mL (range, 1.1-35.0 ng/mL). Radical prostatectomy specimens were evaluated according to the Stanford protocol. The mean tumor volume was 0.89 mL (range, 0.003-4.68 mL). Twenty-five patients had a Gleason score of 7 or higher; 33 patients had multifocal disease; and 4 patients had stage pT3 disease. The authors concluded that it is currently not possible to rely on PSA level and biopsy features to predict "insignificant" prostate cancer on radical prostatectomy.

Hammerer and colleagues[9] analyzed 2392 men who underwent radical prostatectomy from 1992 to 2002. The investigators reported that impalpable prostate cancer with normal findings on TRUS significantly differed favorably from abnormal findings, both preoperatively and postoperatively, in Gleason score,

pathologic stage, and cancer volume of the radical prostatectomy specimen. Therefore, TRUS is a valuable tool in refining the staging of impalpable prostate cancer.

Castagnetti and colleagues,[10] in a study from Modena, Italy, reported that all patients (N = 14) who had "only" atypical small acinar proliferation (ASAP) on TRUS biopsy (8-12 cores) and underwent radical prostatectomy had prostate cancer in the final specimen (pT2a [n = 8], pT2b [n = 4], pT3a [n = 1], pT4a [n = 1]). The authors concluded that radical prostatectomy may be a treatment option for young patients with ASAP.

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Prostate Cancer: Prostate-Specific Antigen

Djavan and colleagues[11] demonstrated the use of complexed PSA (cPSA) in prostate cancer staging. Using multivariate analysis, cPSA (cutoff, 6.5 ng/mL), complexed to total PSA ratio (c/t PSA) (cutoff, 92%), and Gleason score on biopsy were found to be the most significant predictors of extracapsular extension in 121 men undergoing radical prostatectomy. Data from another multicenter trial, presented by Bartsch and colleagues,[12] demonstrated that cPSA may be useful as a first-line test for detection of prostate cancer on repeat biopsy and that c/t PSA outperformed the free to total PSA ratio (f/t PSA). In another study, Bartsch and colleagues[13] showed that cPSA findings follow the same trend as PSA level for age-related cutoffs.

Prostate Cancer: Treatment Options

Watchful waiting is a well-known therapeutic strategy for patients with prostate cancer. In a US study, Wu and colleagues[14] showed that, from 1992 to 2002, 1158 of 8390 prostate cancer patients had watchful waiting as their first treatment option. The patients who underwent watchful waiting were significantly older and had lower PSA levels and lower Gleason scores at biopsy compared with those who received active treatment (radical prostatectomy, external beam radiation, brachytherapy). Of the 1158 subjects who underwent watchful waiting, 453 (39.1%) received secondary therapy. A multivariate Cox proportional hazards regression analysis was performed to identify risk factors for secondary therapy: relative risk = exp(–0.034 • diagnosis age + 0.284 • log[PSA] + 0.271 • clinical stage T2 + 0.264 • clinical stage T3). Based on this analysis, 3 groups at risk for secondary treatment after watchful waiting were stratified by patient age, PSA level at diagnosis, and clinical stage.

Radical prostatectomy as a treatment option for prostate cancer is generally recommended for younger (<75 years), healthy patients who have a life expectancy of over 10 years. Two abstracts examined the outcomes of this treatment option in patients aged 75 years or older. Brausi and colleagues[15] reported results of radical prostatectomy in 47 patients with a mean age of 76.3 years, in good general health, with clinical stage T1 or T2 disease, and with a Gleason score of 5 or higher. Of these patients, 51% and 49% had stages pT2 and pT3 disease, respectively; 9 patients had positive lymph nodes. Perfect continence (no pads), mild to moderate incontinence (1-3 pads/d), and severe incontinence (≥3 pads/d) were reported in 76%, 13%, and 6% of patients, respectively. The potency rate after radical prostatectomy was 0%, compared with 23% before the procedure. The 9-year, disease-specific survival rate was 82%; the PSA progression–free survival rate was 68%. Hanschmann and colleagues[16] reported the results of 106 patients who underwent radical prostatectomy at an average age of 76.5 years. Of these patients, 15% had grade 2 stress incontinence. Both of these studies concluded that, in general, radical prostatectomy should not be ruled out based on patient age. Nevertheless, older patients should be informed that the risk of incontinence is higher than for younger patients.

Because SV-sparing radical prostatectomy may have benefits regarding continence and potency, a multicenter study from Brussels, Paris, and Vienna, presented by Zlotta and colleagues,[17] investigated whether SV ablation is mandatory for all patients undergoing radical prostatectomy. Overall, SV involvement was found in 59 (10.98%) of 537 patients. In patients with PSA levels less than 10 ng/mL, 10 ng/mL to 20 ng/mL, and greater than 20 ng/mL, SV involvement was found in 4.79%, 14.00%, and 31.08%, respectively. Multivariate analysis showed the percentage of positive biopsies and Gleason score to be significant predictors of SV involvement. The authors concluded that SV resection is not necessary in

In general, radical prostatectomy should not be ruled out based on patient age.

patients who have a PSA level less than 10 ng/mL, except when the Gleason score is 7 or higher or the Gleason score is 6 and more than half of the prostate biopsy cores show prostate cancer.

Technical modifications to laparoscopic, nerve-sparing, and bladder neck–sparing radical prostatectomy have to be proved efficacious in clinical, prospective studies. As is the case with laparoscopic extraperitoneal radical prostatectomy, when an anterograde radical prostatectomy is performed, it is important to know the long-term results of open surgery. Carini and colleagues[18] reported their experience with anterograde radical prostatectomy from 1989 to 2002 in 632 patients with clinically localized prostate cancer; 49.7%, 26.4%, 18.5%, 5.2%, and 13.7% of the patients had pT2, pT3a, pT3b, pT4, and N1 status, respectively. Ten-year progression-free survival rates were 71.4% overall and 87.8%, 71.3%, 47.5%, and 35.9%, respectively, for organ-confined, extracapsular, SV invasion, and N1 disease. Positive margins were reported in 14.1% of subjects. Nerve-sparing radical prostatectomy, saving both bundles, was performed in 38.9% of subjects. Of these patients, 57.3% were classified as potent. The authors concluded that anterograde radical prostatectomy is an easy and safe procedure, with good oncologic outcomes and accurate control of nerve bundles. Nevertheless, this method allows a low incidence of positive surgical margins.

Binder and colleagues,[19] from Frankfurt, reported results of robotic laparoscopic radical prostatectomy using the da Vinci® Surgical System (Intuitive Surgical, Sunnyvale, Calif) in 90 patients. The median operating time was 290 minutes, which decreased significantly after the first 30 operations. The positive margin rate was 28.9% overall and 12.1% in patients with stage pT2 disease.

The value of imaging modalities to detect prostate cancer is under discussion, and the use of these techniques in this setting is still limited. To address this issue, Khan and colleagues[20] staged 100 patients suitable for radical prostatectomy with the use of whole-body magnetic resonance imaging (MRI) and compared the results to those of the radical prostatectomy specimens. The sensitivity and specificity, respectively, for extracapsular extension were 15% and 91%, for SV invasion were 0% and 98%, and for lymph node metastases were 0% and 91%. The authors concluded that whole-body MRI has a limited role in detecting SV invasion.

The authors concluded that the sensitivity of endorectal MRI for the detection of extracapsular extension is poor.

Palascak and colleagues[21] evaluated the use of endorectal MRI for the detection of extracapsular extension before prostate biopsy and radical prostatectomy. The sensitivity, specificity, accuracy, and positive and negative predictive values of the procedure were 46.1%, 90.5%, 81.8%, 54.5%, and 87.5%, respectively. The authors concluded that the sensitivity of endorectal MRI for the detection of extracapsular extension is poor. The high accuracy and specificity, however, allow for a better selection of patients for curative treatment.

Sauvain and colleagues[22] investigated the value of transrectal power Doppler ultrasound (PDU) for the detection of prostate cancer in 323 men. Three types of blood supply were defined: regular avascular, irregular avascular, and vessels crossing the capsule. The PDU results were compared with histopathologic findings of 282 sextant biopsies and 63 radical prostatectomy specimens. The overall rate of cancer detection was 55.7%. The sensitivities of PDU and B-scan TRUS were 92.4% and 87.9%, respectively; specificities were 72.0% and 57.6%, respectively. The negative predictive value of PDU was elevated to 80.6% ($P < .0001$). The authors concluded that PDU improves the reliability of TRUS and that biopsies of the suspected areas in isoechoic tumors improve diagnostic accuracy.

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Prostate Cancer: PSA Relapse After Curative Treatment

We know from the literature that biochemical failure after radical prostatectomy is a common finding, occurring in 30% to 50% of patients 8 years after the procedure. It is also well known that biochemical failure can result from local recurrence or metastases. However, clinical evaluation, including imaging techniques, shows pathologic findings in only one third of these patients, because of a lead time in biochemical failure and clinical progression. Several abstracts presented at the EAU Congress addressed the issue of improving this detection rate.

Remzi and colleagues[23] showed that PDU of the anastomotic region increased the predictive accuracy of PSA doubling time (cutoff, >10 months) and time-to-recurrence (cut-

off, >18 months) from 65% to 77%. A pilot study by Alavi and colleagues,[24] from Vienna, showed that carbon-11 acetate positron-emission tomography is a promising new imaging modality for patients with biochemical failure following radical prostatectomy. A pathology was found in 33 (76%) of 45 cases; 7 patients were positive with the carbon-11 acetate scan only and negative with all other imaging modalities performed (computed tomography, whole-body MRI, bone scan, and TRUS). Anagnostou and colleagues[25] showed that magnetic resonance, body-coil, enhanced spin-echo sequence imaging is also an appropriate follow-up method for patients with biochemical failure after radical prostatectomy: 24 of 36 patients yielded abnormal findings.

Scattoni and colleagues[26] showed that biopsy results were positive for local recurrence in more than 60% of cases in which hypoechoic lesions were present at the vesicourethral anastomosis region following biochemical failure after radical prostatectomy. In addition, the investigators concluded that, in patients with a PSA level greater than 2 ng/mL and no hypoechoic lesion in the TRUS, biopsy can be avoided, because the negative predictive value is 100%. Anagnostou and colleagues[27,28] confirmed that benign margins can be the reason for a PSA relapse following radical prostatectomy.

In the era of PSA testing, localized prostate cancer is being identified more often and, as alternative treatment options like external beam radiation therapy and brachytherapy become more efficient, it is necessary to improve radical prostatectomy and reduce its associated morbidity. To address this issue, Palisaar and colleagues,[29] of the Hamburg Eppendorf group, conducted a study evaluating 620 consecutive patients who underwent non–nerve-sparing radical prostatectomy and 723 patients who underwent nerve-sparing radical prostatectomy. For each prostate lobe, the positive margin rates for pT2 cancers were 6.0% and 5.1% for the nerve-sparing and non–nerve-sparing radical prostatectomy groups, respectively; for pT3a cancers, the positive margin rates were 10.3% and 17.3%, respectively. The 3- and 5-year recurrence-free survival rates for patients with pT2, pT3a, and pT3b cancers treated with nerve-sparing prostatectomy were 96.1% and 67%, 94.9% and 46%, and 72.5% and 29%, respectively; for cancers treated with non–nerve-sparing radical prostatectomy, the corresponding rates were 94.9% and 54%, 90.8% and 38%, and 71.1% and 25%, respectively (Table 2). The authors concluded that nerve-sparing radical prostatectomy is a safe procedure and that neither the positive-margin rate nor the recurrence-free survival rate was adversely affected by nerve sparing.

Table 2
3- and 5-Year Recurrence-Free Survival Rates After Nerve-Sparing or Non–Nerve-Sparing Radical Prostatectomy

Year	Radical Prostatectomy	Survival, %		
		pT2	pT3a	pT3b
3	Nerve-sparing	96.1	94.9	72.5
	Non–nerve-sparing	94.9	90.8	71.1
5	Nerve-sparing	67	46	29
	Non–nerve-sparing	54	38	25

Data from Palisaar R et al. *Eur Urol Suppl.* 2003;2(1):24.[29]

Metastatic Prostate Cancer

Currently, there is no standard of treatment for patients with hormone-refractory prostate cancer (HRPC) and a rising PSA level. Several abstracts addressing this issue were presented at the EAU Congress. Kramer and colleagues[30] presented results of a study in which patients received 300 mg of intravenous estramustine for 3 days, nothing for 1 day and, on the fifth day, 30 mg/m^2 of vinorelbine to synchronize the cells. Of 22 men, 14 who had no previous chemotherapy received second-line treatment, whereas 8 men received third-line treatment. Median PSA levels were 41 ng/mL in the second-line treatment group and 122 ng/mL in the third-line treatment group; PSA decreases in the second-line and third-line therapy groups were 79% and 25%, respectively.

Kübler and colleagues[31] reported partial remission in 13 of 19 patients and stable disease in 3 of 19 patients who received docetaxel monotherapy, 75 mg/m^2 every 21 days, for a maximum of 20 cycles. The median PSA decrease was 65%; pain was reduced in 13 patients. No patient showed major hematologic (grade 3 or 4) toxicity. Side effects were moderate and reversible and included alopecia (17/19), brownish fingernails (11/19), and neuropathy (10/19). Ferrero and colleagues,[32] from France, reported the results of a study in which 74 patients with HRPC received docetaxel, 40 mg/m^2, 4 times weekly with a 2-week pause for a total of 3 cycles. A PSA decrease of more than 50% was reported in 68.3% of the subjects. The median time to progression was 29 weeks. Grade 3 or 4 hematologic toxicities included anemia (9.7%) and neutropenia (9.7%). Other toxici-

ties included alopecia (12.9%), asthenia (14.5%), diarrhea (8.5%), and nail changes (20.9%). The authors concluded that the regimen showed significant activity with a good safety profile.

Benign Prostatic Hyperplasia

Basic Research

It has been demonstrated that T-cell–derived cytokines induce hyperproliferation of BPH-derived stromal cells. Kramer and colleagues[33] showed that type 2 T-cell cytokines can be found in up to 35% of BPH tissue, compared with less than 5% of normal tissue. A similar pattern of cytokines has been demonstrated for autoimmune and chronic inflammatory diseases.

Habib and Ross,[34] from Edinburgh, investigated why *Serenoa repens* (Permixon®) does not diminish serum PSA, as does finasteride, while it inhibits 5-α-reductase type 2 in the human prostate. Androgen-sensitive LNCaP cells and simian kidney COS cells were purchased from the American Type Culture Collection (Manassas, Va) and propagated according to the instructions of the supplier. COS cells transfected with the 5-α-reductase type 2 gene demonstrated substantial inhibitory activity (70%) following treatment with either finasteride (5 nM) or Permixon (10 µg/mL).

To investigate the impact of the 5-α-reductase inhibitors on the hormone-induced activity of the PSA gene, COS cells were transiently transfected with the PSA-61-Luc construct and cotransfected with the human androgen-receptor expression plasmid. The androgen-induced activity of the constructs was 9-fold more active in the presence of 10 nM dihydrotestosterone than in its absence. In the presence of Permixon (10 µg/mL), the activity remained essentially the same as in controls. However, following treatment with finasteride (5 nM), the activity of the luciferase reporter gene construct was significantly (80%) reduced.

These results are essentially identical to those obtained with the LNCaP cells following exposure to Permixon and finasteride. The secretion of PSA was unaffected by the treatment of the cells with Permixon, whereas the production of PSA was significantly (70%) reduced in the presence of finasteride. This differential response stems from the decrease in the level of androgen receptors following treatment of the cells with finasteride, thus triggering the downregulation of PSA expression. No such change in androgen receptor levels was detected following treatment with Permixon.

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Epidemiology and Evaluation

Dobrovits and colleagues,[35] from Vienna, examined the natural history of lower urinary tract symptoms (LUTS) suggestive of BPH in patients with an International Prostate Symptom Score (IPSS) of 8 or less. The prospective, longitudinal study investigated the outcome of watchful waiting and identified progression parameters over a 4-year follow-up period in 1208 patients who presented to 5 European university clinics with LUTS resulting from bladder outlet obstruction. All patients were followed for up to 4 years at 3-month intervals. The following measured parameters were recorded for each patient: age, PSA level, IPSS, total obstructive symptom score (OSS), irritative symptom score, quality-of-life (QOL) score, maximum flow rate (Q_{max}), mean flow rate, total prostate volume, and transition zone volume. The artificial neural network (ANN) used in the analysis was an advanced multiplayer perceptron. Progression was defined as a change from the mild IPSS group into the moderate (IPSS, 9-18) or severe (IPSS >18) groups or an increase in the IPSS score of more than 3 points. The occurrence of urinary retention or need for surgery (transurethral resection of prostate [TURP]) also qualified as disease progression. QOL scores were recorded separately and cross-analyzed.

Of 1208 men evaluated, 446 had mild symptoms of bladder outlet obstruction (IPSS ≤8). Cumulative progression rates were 6%, 13%, 15%, 24%, 28%, and 31% at 6, 12, 18, 24, 36, and 48 months, respectively (Figure 1). The overall accuracy of the ANN was 79% for predicting disease progression and 82% for predicting the need for surgery. The variables of importance for disease progression in the ANN analysis were, in order of significance, PSA level, OSS, age, and transition zone volume. The combination of age-correlated PSA level and OSS offered 88% accuracy. IPSS, irritative symptom score, QOL score, Q_{max}, and mean flow rate, as well as postvoid residual urine volume (PVR), were not found to add significant predictive value.[35]

Overall accuracy was best in patients who had a PSA level greater than 1.5 ng/mL. At 12, 24, 36, and 48 months, respectively, 66%, 60%, 73%, and 71% of patients deteriorated without shifting to the next higher IPSS category. Of interest, improvement in symptoms was observed in 20%, 17%, 8%, and 3% of patients at 12, 24, 36, and 48 months, respectively, whereas 8%, 10%, 4%, and

2%, respectively, had stable disease. Progression to higher IPSS categories (8-18 and 19-35) occurred in 13%, 24%, 28%, and 31% of the patients at 12, 24, 36, and 48 months, respectively. In those who did not shift into a higher IPSS category, 70% progressed by at least 1 point. Improvement was observed in 20% of subjects at 1 year and decreased to 3% at 4 years, suggesting that serum PSA, OSS, and age were strongly correlated with disease progression, overall symptomatic progression, rate of urinary retention, and need for surgery. Using the ANN presented in this report, based on clinical and biochemical parameters, disease progression can be predicted and treatment initiated for patients at risk.[35]

Scattoni and colleagues[36] investigated 105 patients who presented with a median tPSA of 7.5 ng/mL (range, 6.2-8.2 ng/mL), a cPSA of 5.7 ng/mL (range, 4.4-6.6 ng/mL), and an average total prostate volume of 61.5 mL (range, 54.0-71.0 mL) for correlations of f/t PSA and c/t PSA with prostate volume and inflammation of the prostate found on biopsy specimens. The authors found that f/t PSA showed a significant correlation with the degree of activity of inflammation, whereas no correlations were found between tPSA, cPSA, and c/t PSA and the histologic patterns of prostatitis of any degree. Although the variability of f/t PSA seemed to be influenced by both prostatic volume and the degree of inflammatory infiltrate, c/t PSA appeared to be independent of prostatic weight and activity and the extension of histologic inflammation. c/t PSA may be more specific than f/t PSA in differentiating between prostatic carcinoma and large BPH with histologic inflammation.

Treatment

Graber and colleagues,[37] from Switzerland, conducted a study to compare the efficacy and safety of ProstaLund Feedback Treatment (PLFT) with TURP. Sixty-two patients were randomized to PLFT or TURP in a 2:1 ratio. At 12-month follow-up, IPSS, Q_{max}, PVR, and detrusor pressure were comparable in the PLFT and TURP groups (baseline vs 12-month PLFT [TURP], respectively: IPSS, 20.0 [19.2] vs 4.3 [7.4]; Q_{max}, 7.0 mL/s [6.8 mL/s] vs 19.9 mL/s [25.2 mL/s]; PVR, 101 mL [117 mL] vs 27 mL [40 mL]; detrusor pressure, 80.9 cm H_2O [79.8 cm H_2O] vs 46.7 cm H_2O [42.3 cm H_2O]. The authors concluded that PLFT challenged TURP after 12 months.

Roehrborn and colleagues,[38] for the Proscar Long-Term Efficacy and Safety Study Group, showed that finasteride treatment resulted in a modest but significant increase in serum testosterone in men with BPH, especially those with low baseline testosterone levels. Boyle and colleagues[39] reported data from a prospective, randomized, double-blind, placebo-controlled study that included 1223 men with prostate volumes between 30 mL and 40 mL and 3084 men with prostate volumes greater than 40 mL. The investigators found that dutasteride improved IPSS, Q_{max}, PVR, and the risk of complications, such as acute urinary retention and BPH-related surgery, in men with prostate volumes of 30 mL to 40 mL, as well as in those with prostate volumes greater than 40 mL.

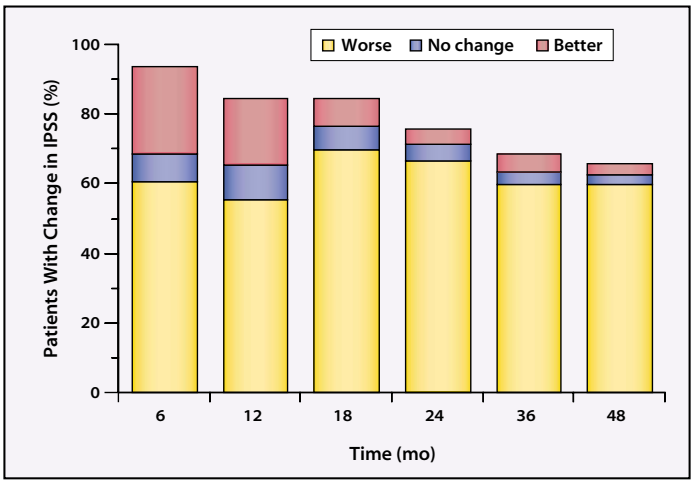

Figure 1. *Variations in International Prostate Symptom Score (IPSS) in a group of subjects with an IPSS of 8 or less. Data from Dobrovits M et al.* Eur Urol Suppl. *2003; 2(1):26.*[35]

Sexual Dysfunction

Alamanis and colleagues[40] investigated penile vascular findings (peak systolic velocity and end-diastolic velocity) in 119 patients with end-stage renal failure. Patients were classified into 3 groups: group A (n = 35) had chronic renal failure, group B (n = 40) had hemodialysis for at least 2 years, and group C (n = 44) had a renal transplantation at least 6 months before the investigation. A power Doppler ultrasound of the penile vessels was performed after an intracavernosal injection of 10 µg of alprostadil. According to the International Index of Erectile Function (IIEF), 36.0%, 37.5%, and 54.5% of patients in groups A, B, and C, respectively, had normal erections ($P < .05$). Patients with severe erectile dysfunction had maximum peak systolic velocities of 17.4 cm/s, 18.7 cm/s, and 22.1 cm/s in groups A, B, and C, respectively.

Results of the Multinational Survey of the Aging Male (MSAM-7), reported by Rosen and colleagues,[41] showed a strong correlation between the severity of LUTS, as determined by IPSS, and erectile dysfunction. Of 12,815

patients surveyed, 90% reported LUTS (severe, 6%; moderate, 25%; mild, 59%). Sexual activity was reported by 83% of subjects, with 71% reporting at least 1 episode of sexual intercourse in the previous 4 weeks. Sexual disorders were strongly correlated with the severity of LUTS. Overall, 49% of subjects had erection difficulties, 46% had ejaculatory disturbance, and 7% had pain during sex.

Moncada and colleagues[42] showed that sildenafil was effective in 40 responders for up to 12 hours after intake, regardless of whether the men tried to achieve an erection 1 hour after intake. Montorsi and colleagues[43] reported long-term data from an open-label study of tadalafil (N = 1173). All patients started therapy with tadalafil, 10 mg; tadalafil was titrated up to 20 mg in 82.7% of the subjects (n = 970). The most frequent adverse events reported were headache (15.3%), dyspepsia (11.0%), infection (10.1%), back pain (7.3%), rhinitis (6.5%), flu syndrome (6.2%), pain (6.1%), and surgical procedure (6%). Overall, 5.4% of subjects discontinued tadalafil therapy because of these adverse events. Of the 3 deaths that occurred during the study, none was judged by the investigators to be related to the treatment.

In a study by Potempa and colleagues,[44] vardenafil, 10 mg, was initiated in 390 of 423 enrolled men. Overall, 91.8% of subjects reported improved erections. Those who remained on vardenafil, 10 mg, for the duration of the study showed the greatest response rates (an increase in the IIEF erectile function domain score of 15.3 at baseline to 28.2 at 6 weeks). The most frequent adverse events were headache (6%), flushing (6%), dyspepsia (2%), and rhinitis (2%). Hatzichristou and colleagues[45] demonstrated the efficacy of vardenafil (86%) versus placebo (36%) in a flexible-dose regimen. Subjects who chose to continue taking vardenafil, 10 mg, had a 92% success rate with the therapy.

Gingell and colleagues[46] presented data from the Global Study of Sexual Attitudes and Behaviors for 27,500 respondents (13,618 men and 13,882 women). Overall, 84% of men and 75% of women reported that they had engaged in sexual intercourse within the previous 12 months (ages 40 to 49 years, 93% of men and 88% of women; ages 50 to 59 years, 89% of men and 74% of women; ages 60 to 69 years, 79% of men and 50% of women; ages 70 to 80 years, 53% of men and 21% of women). Among the sexually active subjects, a substantial proportion of men (45%) and women (38%) engaged in sexual intercourse regularly (≥5 times per month). The most common sexual dysfunction was a lack of interest in sex, which was reported by 31% of women and 18% of men. Other frequently reported dysfunctions among women were the inability to reach climax (21%) and

Main Points

- The Vienna nomogram is used to determine the "optimal" number of cores to biopsy based on a patient's age and total prostate volume.
- In one study, comparisons between younger (≤50 years) and older (>50 years) patients with prostate cancer showed no significant differences between the 2 groups with regard to tumor volume, Gleason sum, tumor stage, lymph-node status, vascular invasion, seminal vesicle invasion, and number of positive prostate biopsies.
- Using multivariate analysis, complexed prostate-specific antigen (PSA) (cutoff, 6.5 ng/mL), complexed to total PSA ratio (c/t PSA) (cutoff, 92%), and Gleason score on biopsy were found to be the most significant predictors of extracapsular extension in 121 men undergoing radical prostatectomy.
- In general, radical prostatectomy should not be ruled out based on a patient's age; however, older patients need to be informed of their increased risk of incontinence.
- One study suggested that c/t PSA may be more specific than the free to total PSA ratio in differentiating between prostatic carcinoma and large benign prostatic hyperplasia with histologic inflammation.
- Results of the Multinational Survey of the Aging Male showed a strong correlation between the severity of lower urinary tract symptoms, as determined by the International Prostate Symptom Score, and erectile dysfunction.
- Several studies showed the efficacy of sildenafil, tadalafil, and vardenafil in improving erections. A range of data on sexual activity and dysfunction from the Global Study of Sexual Attitudes and Behaviors was reported.
- A study from Germany demonstrated for the first time that cyclic adenosine monophosphate and cyclic guanine monophosphate phosphodiesterases can be found in the clitoris. These data may provide a further rationale for the use of phosphodiesterase-5 inhibitors as pharmacotherapy for female sexual dysfunction.

difficulty becoming adequately lubricated (20%); among men, frequently reported dysfunctions included reaching climax too quickly (23%) and erectile dysfunction (17%). Approximately one third of men (31%) and women (38%) reported that they had avoided sex because of their problems.

Ückert and colleagues,[47] from Hannover, Germany, demonstrated for the first time that cyclic adenosine monophosphate and cyclic guanine monophosphate phosphodiesterases can be found in the clitoris. These data may provide a further rationale for the use of phosphodiesterase-5 inhibitors as pharmacotherapy for female sexual dysfunction. ■

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