

ASTRO definition of biochemical failure is outperformed by alternatives

Various definitions of biochemical failure are used to assess prostate cancer recurrence after radiotherapy. Debate continues over which definitions provide optimal reproducibility and correlate best with clinical outcomes; Fitch and colleagues, therefore, retrospectively analyzed data from 2,376 patients with localized, T1–3N0M0 prostate cancer treated at a single center, to determine an optimal definition for biochemical failure.

In total, 1,201 men received conventional-dose (median 66.6 Gy) external-beam radiotherapy (EBRT), 465 received high-dose (median 75.6 Gy) adaptive EBRT, 416 received EBRT and brachytherapy, and 294 received brachytherapy only. Overall, 21% (496 men) also received neoadjuvant androgen deprivation. Patients were followed up 1 month after radiotherapy and every 3–6 months thereafter (median 4.5 years).

The authors assessed multiple definitions of biochemical failure for their positive and negative predictive values and sensitivity and specificity, in predicting local or distant metastasis and survival. Most definitions outperformed the American Society for Therapeutic Radiation and Oncology criteria for biochemical failure (three consecutive PSA rises); however, those that performed best were a PSA threshold of ≥ 3 ng/ml at or after nadir—which appeared to be optimal—and a PSA rise of ≥ 2 ng/ml above nadir. The authors call for further studies to confirm their results.

Surprisingly, all definitions performed better in brachytherapy-treated patients than in those treated with EBRT only. The authors attribute this finding to the particularly low PSA nadir values of brachytherapy-treated patients.

Original article Fitch DL *et al.* (2006) Unification of a common biochemical failure definition for prostate cancer treated with brachytherapy or external beam radiotherapy with or without androgen deprivation. *Int J Radiat Oncol Biol Phys* 66: 1430–1439

Potential new treatment for overactive bladder shows promise

Tachykinins such as substance P (an agonist of NK-1, neurokinin receptor 1) are neurotransmitters involved in the micturition reflex, which suggests that NK-1 antagonists might be an effective

treatment for urge incontinence. Aprepitant (currently used to treat chemotherapy-induced nausea and vomiting) is a potent NK-1 antagonist that acts in the central nervous system.

Green and colleagues' double-blind, randomized, placebo-controlled pilot study (in 26 US centers) evaluated 125 postmenopausal women (mean age 64.8 years) with overactive bladder syndrome and urge incontinence. After a 1-week run-in period on placebo, patients were randomly allocated to receive either 160 mg aprepitant ($n=61$) or placebo ($n=64$) as a once-daily tablet for 8 weeks. Patients recorded their symptoms in a validated voiding diary, and were followed up 1, 2, 4 and 8 weeks after randomization. Compared with placebo, aprepitant markedly reduced the mean number of daily micturitions from baseline (by 6.8%) and incidence of urgency episodes (by 13.2%) over the 8-week study. The magnitude of these effects was similar to that previously reported for antimuscarinic agents—the preferred treatment for overactive bladder syndrome. Aprepitant also consistently improved patients' perceived leakage and the bother of their symptoms, and was generally well tolerated; dry mouth occurred in only four aprepitant-treated patients.

The authors speculate that aprepitant acts at the spinal cord to inhibit bladder sensorial input and raise the signal threshold necessary to initiate micturition. This mechanism of action differs from that of antimuscarinic or antispasmodic medications.

Original article Green SA *et al.* (2006) Efficacy and safety of a neurokinin-1 receptor antagonist in postmenopausal women with overactive bladder with urge urinary incontinence. *J Urol* 176: 2535–2540

Age >30 years reduces the success of testicular sperm extraction in azoospermic men

About 15% of men with nonobstructive azoospermia have Klinefelter syndrome. The testes of men with the nonmosaic (47,XXY) form of this condition show only rare, focal areas of spermatogenesis, and sperm are absent from the ejaculate. In these men, testicular sperm extraction performed with intraoperative microscopy (microTESE) is only successful in about half of cases; Bakircioglu and colleagues, therefore, investigated which factors predicted the success of microTESE.