Editorial

Round up

The POUT trial[1] was an open-label, phase 3 randomized multicenter trial to evaluate the benefit of adjuvant chemotherapy for patients with upper tract urothelial cancer (UTUC) after nephroureterectomy with curative intent. UTUC staged pT2–4, pN0–3M0 or pTanyN1–3M0 was randomized to either surveillance or four cycles of chemotherapy (gemcitabine/cisplatin or carboplatin) 90 days after nephroureterectomy. The primary endpoint was disease-free survival. A total of 261 participants were enrolled with 132 patients in the chemotherapy arm. Adjuvant chemotherapy conferred 55% reduction in relative risk (RR) of disease recurrence or death (hazard ratio [HR] 0.45, 95% confidence interval [CI] 0.30–0.68; $P = 0.0001$) at a median follow-up of 30.3 months. Three-year disease-free survival estimates were 71% (95% CI 61–78) in patients allocated chemotherapy and 46% (36–56) in those allocated surveillance, with an estimated absolute difference of 25% (95% CI 11–38). Forty-four percent of the participants had Grade 3 or more adverse events in the chemotherapy arm. Based on this trial, adjuvant platinum-based chemotherapy may be the new standard of care for locally advanced UTUC.

The role of adding external beam radiotherapy (EBRT) to the prostate along with long-term androgen deprivation therapy (ADT) is the accepted treatment option for locally advanced cancer prostate. The long-term outcome of such a treatment strategy was studied in a randomized fashion in a multicenter Phase III trial.[2] Forty-six Gray radiation was given to the pelvis and a boost of 20–28 Gy to the prostate. The primary endpoint was progression-free survival (PFS), while the secondary endpoint was overall survival, disease-specific survival, locoregional PFS, metastasis-free survival, biochemical PFS, and tolerance. After a median follow-up of 7.3 years, 263 patients were included. The 8-year PFS was 48% in EBRT + ADT arm versus 7% in ADT only arm (HR 0.27, 95% CI 0.17–0.39; $P < 0.001$). The cancer-specific mortality was also significantly reduced (HR 0.48, 95% CI 0.25–0.91; $P = 0.02$). However, there was no overall survival difference (57% vs. 65%). The long-term outcomes confirm the benefit of adding EBRT to ADT in the management of locally advanced prostate cancer.

An extended 3-year follow-up of the Randomized Open versus Robotic Cystectomy (RAZOR) trial has been published.[3] Previously, the trial had shown noninferior 2-year PFS for robotic radical cystectomy. Per protocol analysis was done on 302 patients from the RAZOR study. The PFS at 36 months was 68.4% and 65.4% for robotic versus open groups, and the overall survival was 73.9% and 68.5% ($P = 0.334$). Patients older than 70 years, poor performance status, and major complications predicted 36-month PFS. Stage and positive margins were the significant predictors of recurrence, PFS, and overall survival. The surgical approach (open or robotic) did not make a difference with regard to any of the outcomes studied.

Nocturia is a common and difficult to treat a problem in the geriatric population. It not only causes disruption in sleep but also is associated with increased comorbidity and decreased quality of life. A systematic review[4] was done to evaluate the association of nocturia with mortality. From 5230 reports, 11 observational studies were included for this analysis. The definition of nocturia varied from 2 to 3 or more voids per night. Pooled estimates showed a RR of 1.27 (95% CI 1.16–1.40, I^2 48%), with an absolute 1.6% and 4.0% 5-year mortality difference in individuals aged 60 and 75 years, respectively. The RR of mortality due to nocturia did not differ across age, gender, follow-up duration, or nocturia case definition. They concluded that nocturia was associated with a 1.3-fold increased risk of death; however, the quality of evidence for the same was low.

Hypofractionated radiotherapy for localized carcinoma prostate has been attractive for the potential for lower dose, lower side effects, and lower duration of therapy compared to conventional radiotherapy. This single-institution randomized prospective trial[5] presented the updated 10-year disease outcomes using the updated NCCN risk stratification and definition of biochemical failure. Intermediate- and high-risk prostate adenocarcinoma received conventional image-modulated radiotherapy (C-IMRT, 76 Gy in 38 fractions) or hypofractionated image-modulated radiotherapy (H-IMRT, 70.2 Gy in 26 fractions). ADT was given for 24 months in the high-risk group and 4 months in the intermediate-risk group. Lymph nodes were included in radiation field in the high-risk group patients. Three hundred and three men were randomized with a median follow-up of 122.9 months. Ten-year incidence of biochemical and/or clinical disease failure rate was 25.9% in the C-IMRT arm and was 30.6% in the H-IMRT arm (HR 1.31, 95% CI 0.82–2.11). The two treatments had similar biochemical failure rates, prostate cancer-specific mortality, and overall mortality. The 10-year cumulative incidence of distant metastasis was high in the H-IMRT arm. H-IMRT failed

to demonstrate superiority compared to C-IMRT even in long-term disease outcomes.

The role of magnetic resonance imaging (MRI)-targeted biopsy of visible prostate cancer lesions has been more or less established. The omission of conventional 12 core biopsies is still debated. In this study,[6] 2103 patients with a visible lesion on MRI scan underwent biopsy by both methods. Prostatic cancer was diagnosed in 1312 (62.4%) cases by a combined biopsy, of which 404 (19.2%) cases chose to have a radical prostatectomy and were included in the study. Combined biopsy led to cancer diagnosis in more men (9.9%) compared to either method alone and upgrading in 458 (21.8%) men. MRI-targeted biopsy alone would have misclassified 8.8% clinically significant cancer (grade group > 3). Combined biopsy was associated with fewest upgrade to significant cancer (3.5%) on final full-mount histopathological examination after radical prostatectomy compared to MRI-targeted biopsy (8.7%) and systemic biopsy (16.8%). This trial reiterates the role of MRI before biopsy approach and combining targeted biopsy to systematic biopsy in MRI-detected lesions for more accurate diagnosis and preventing misclassification of clinically significant prostate cancer.

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