Adjuvant or early salvage radiotherapy for patients with risk features after radical prostatectomy

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It has been established that adjuvant post-operative radiotherapy (RT) is effective in reducing biochemical relapse in surgically treated prostate cancer patients with existing risk factors such as T3a/T3b, positive section margins, or elevated Gleason score (1-3). However, there was a lack of clarity regarding the ideal timing of this treatment. A delayed treatment would result in rising levels of prostate specific antigen (PSA), which is a risk factor associated with decreased success of salvage treatment (4). On the other hand, delaying treatment could spare a significant group of patients from undergoing radiation treatment and its associated side effects. A recent meta-analysis now provides level I evidence on this question (5). This analysis considered 2153 patients from three recent randomised prospective trials: RADICALS-RT (6), RAVES (7) and GETUG-AFU 17 (8), and compares adjuvant RT with early salvage RT with immediate treatment initiation when PSAs surpass 0.1 or 0.2.

At five years, the analysis showed that adjuvant RT did not improve event-free survival (EFS), a composite endpoint driven by biochemical progression, but also consisting of clinical or radiological progression, initiation of a non-trial treatment and death from prostate cancer. Importantly, the result was consistent over the different subgroups, with no indication that the effect varied, as defined by Gleason score (7 vs >8), margin status (R1 vs R0), seminal vesicle involvement (pos vs neg), presurgical PSA or overall recurrence risk represented by the cancer of the prostate risk assessment (CAPRA-S) score. On the other hand, RT could be omitted in 60.9% of the salvage group patients, resulting in decreased morbidity, notably late genito-urethral toxicity and erectile dysfunction.

A limitation of the meta-analysis is that the endpoint EFS, driven by biochemical disease-free survival (bDFS), is a poor predictor for later but more relevant endpoints like cancer-specific survival and overall survival. However, as the large benefits in terms of biochemical control that are obtained with post-operative RT have failed to translate into consistent and clear survival benefits in the past (1-3), a clinically meaningful benefit of adjuvant RT appearing with more follow-up seems highly unlikely.

Taken together, early salvage RT should be regarded as the standard of care over adjuvant RT in patients with existing risk factors for biochemical relapse following radical prostatectomy, with the exception of node positive patients, which were heavily underrepresented in these studies, therefore prohibiting reliable conclusions.

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