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INTRODUCTION

EVEN IN the best screening/early diagnosis programmes, 25–35% of the patients treated by radical prostatectomy are discovered to have extracapsular disease (pT3 AB or C) [1] and thus to be exposed to the risk of local/distant failure.

Therefore, it comes as no surprise that the question of adjuvant therapy has been raised, and more specifically the use of adjuvant radiation therapy: as radical prostatectomy is currently used for clinically localised disease, it is arguable that the presence of extracapsular extension, often nowadays limited, due to the current stage migration, may lead more frequently to a local recurrence amenable to a local therapy than to metastatic disease where hormone manipulation remains the only available option.

Considering the fact that modern prostate specific antigen (PSA) assays allow a very early detection of biochemical failure—the current lower limit of detection of 0.05 and 0.1 ng/ml is currently considered to characterise biochemical relapse [2], it is reasonable to assume that candidates for adjuvant radiation therapy can be selected on the basis of the follow-up PSA and pathological features of radical prostatectomy specimens.

Adjuvant radiation therapy should not be applied routinely after surgery on the sole basis of unfavourable pathological features for the following reasons: early adjuvant radiation therapy even using state-of-the-art equipment and techniques has significant side-effects when applied in the early postoperative period and should not be considered at least during the first 3–6 months after surgery, as it exposes patients to the risk of persistent/recurrent incontinence and erectile dysfunction, as well as vesicourethral anastomotic strictures [3]. In addition, early radiation therapy in the presence of persistent detectable levels of serum PSA after surgery is usually doomed to failure as early persistent detectable levels of PSA are in the majority of the cases associated with distant failure such as overlooked or undetected positive lymph nodes [3] or distant metastasis obviously no longer amenable to any form of local treatment. Finally, early adjuvant radiation therapy triggered solely by unfavourable prognostic features at the pathological review of the specimen (extracapsular extension, positive surgical margins, positive seminal vesicles) exposes to overtreatment 50% of the patients in whom the presence of unfavourable prognostic features has no impact on prognosis: it is well known today that surgery alone may indeed cure a significant proportion of these patients, particularly in the presence of low risk factors for biochemical recurrence such as: preprostatectomy PSA $\leq$ 10 ng/ml, prostatectomy Gleason sum $\leq$ 6 and limited capsular perforation [4–6].

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Adjuvant radiation therapy should be applied only in the presence of a documented local failure: documented means that the decision of adjuvant radiation therapy should be made on the basis of a biochemical relapse characterised by a recurrent detectable level of PSA in the serum; local failure implies that the patients who are obviously at risk of distant failure should be spared the side-effects of radiation therapy and it is currently accepted that patients with early and fast rising levels of PSA, massive seminal vesicle invasion and of course positive lymph nodes are at maximum risk of distant failure and should not be offered radiation therapy [6]; therefore, the decision of whether or not to use adjuvant radiation therapy should be based solely on pathological features and on the profile of the PSA recurrence.

Transrectal ultrasound guided biopsies of the vesicourethral anastomosis are of value only when they are positive, and this positivity does not of course, rule out the possibility of associated distant failure [7]. Immunoscintigraphy using specially designed monoclonal antibodies is currently under investigation [8].

Based on all these considerations, it appears that: adjuvant radiation therapy for biochemical failure after radical prostatectomy certainly prolongs disease-free survival, however its impact on overall survival has yet to be determined as PSA is only a surrogate marker of treatment efficacy. In addition, modern era PSA assays usually pick up biochemical relapse very early and it is now well known that the efficacy of radiotherapy is directly related to the low level of PSA at the start of the treatment; and prescribing adjuvant radiation therapy to every patient with unfavourable prognostic features regardless of postoperative PSA probably results in overtreatment [3, 6, 9–17].

CONCLUSION

To learn, when one has done, or been submitted to, a radical prostatectomy for a clinically localised prostate cancer that the pathological features of the specimen are indeed unfavourable and may be associated with a significant risk of ultimate biochemical/clinical failure, is undoubtedly unpleasant. However, this unpleasantness should not lead the urologist and/or the patient to take emotional decisions, and the following facts should be acknowledged: PSA although the best marker, has not been shown to be an absolute surrogate marker of overall survival; no randomised trial has as of today demonstrated the superiority of early (at biochemical relapse) over late (at clinical symptoms) adjuvant therapy in the presence of PSA relapse after radical prostatectomy; and the efficacy of early adjuvant therapy on the sole basis on pathological findings cannot and should not be judged on non-randomised retrospective studies, however large they may be, that are obviously heavily biased by individual urologists' and patients' personal decisions.

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INTRODUCTION

RADICAL PROSTATECTOMY is the accepted standard treatment in the management of localised prostate cancer, clinically classified T1–2 (cT1–2), all the more as individual prostate specific antigen (PSA) screening is gaining in popularity [1]; this procedure was recommended by the National Cancer Institute (NCI) Conference Consensus meeting [2] in men under 75 years of age with a World Health Organisation (WHO) performance status lower than 2, provided pelvic lymphadenectomy made beforehand is negative on frozen sections. Nomograms taking into account clinical tumour stage, Gleason score, and baseline PSA, may assist physicians in predicting organ-confined disease [3]. Since three-dimensional conformal therapy with high-dose and high precision can provide results as good as those given by radical surgery [4] with regard to disease-free survival (biochemically defined) [5], concertation and a multidisciplinary approach between urological surgeons and radiation oncologists has to be reinforced to optimise the therapeutic choice. After radical prostatectomy, pathological analysis of resected tissue reveals that in 30–50%, the tumour has extended beyond the prostate, giving rise to pathological stage T3 (pT3) [6–8]. Capsule perforation, positive surgical margins, and invasion of seminal vesicles, represent criteria of high risk of local relapse either isolated or intercorrelated [9]: the definition of such criteria are linked to the quality assurance of the pathological assessment which improves the accuracy and validity of the pathological diagnosis [10]. pT3 patients have a risk of local relapse associated with significant morbidity and this risk may be the source of distant metastases: external irradiation, effective on infra-clinical disease, has been proposed to reduce this risk. There are two modalities of postoperative external irradiation: adjuvant in case of high risk of local failure or clinical evidence of tumour persistence, and therapeutic in case of documented local recurrence. In the present issue, two outstanding urological surgeons give their opinions on the role of postoperative external irradiation. Boccon-Gibod and colleagues advise irradiation only in the presence of a documented failure, but not immediately after surgery to avoid overtreatment and complications. Van Poppel and associates give updated data and recommend immediate postoperative irradiation as it increases local control. As radiation oncologists, we will try to give our point of

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