Letters to the Editor

RE: RENAL CELL CARCINOMA: PROGNOSTIC SIGNIFICANCE OF INCIDENTALLY DEFECTED TUMORS

K.-H. Tsui, O. Shevarts, R. B. Smith, R. Figlin, J. B. deKernion and A. Belledge run


To the Editor. I read with interest this report on the followup of a large patient population, confirming lower stage and grade and better patient survival in incidentally detected renal cell carcinoma. In the 95 incidental cases mean age was 62.9 years compared to 59.2 in the 538 symptomatic cases. We found similar results in a study of 1,002 patients with incidental and symptomatic renal cell carci-

oma. The authors “advocate the implementation of some form of screening program,” assuming that symptomatic cases represent the manifest phase of incidental tumors. However, clinical, radiological and autopsy data should be considered.

The lower mean age of symptomatic cases attenuates this point of view. In fact, mean age would be expected to be lower in preclinical, that is incidental, but not symptomatic renal cell carcinoma. Bosniak et al followed 40 less than 3.5 cm. incidentally detected renal parenchymal tumors with computerized tomography for a mean of 3 years. A total of 26 tumors were removed surgically of which all were stage 1, 22 were grade 1 and 4 were grade 2. Metastatic disease did not develop in any patient. The authors recommended watchful waiting for slow growing tumors in the elderly or patients with poor surgical risk. Data from autopsy series show that 67% to 74% of renal cell carcinomas remained undetected until death and that only 8.9% to 20% of patients with unrecognized renal cell carcinoma finally died of the disease. Furthermore, the age at diagnosis was confirmed to be significantly lower in symptomatic than in incidental cases (51 and 62 years, respectively), even in autopsy studies. The concept of incidental tumors as the inevitable preclinical phase of symptomatic tumors and the opportunity to screen and treat these tumors in the same manner as symptomatic renal tumors, particularly in patients with small masses and the elderly, deserve further evaluation.

Respectfully,

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Reply by Authors. Luciani asserts that incidental tumors may not be the precursors to more aggressive, symptomatic renal cell neoplasms and that these tumors may be treated more conservatively than symptomatic counterparts. Indeed, it has been suggested previously that incidentally detected, low stage lesions are slow growing, and rarely metastasize and lead to mortality. A recent study also demonstrated that a majority of these incidentally detected tumors grow at a negligible pace and rarely metastasize (reference 6 in letter). However, that study showed that the incidentally detected tumors in 2 of 13 patients demonstrated rapid growth, progressing to aggressive and symptomatic tumors. This possibility of progression emphasizes the need to surgically treat these lesions if clinically feasible, which is particularly true given the excellent outcomes and low morbidity of radical or partial nephrectomy for low stage renal cell carcinoma.

We agree with Luciani that the concept of incidental tumors as the inevitable preclinical phase of symptomatic tumors needs to be investigated further. The molecular genetic makeup of more aggressive, symptomatic tumors may be different from that of incidental tumors. At our institution we are attempting to determine if this difference exists by compiling tumor micro-arrays to identify molecular tumor markers associated with the more aggressive tumor types. Through the identification of such tumor markers, we could assess more confidently which incidentally detected tumors need to be treated aggressively because of the potential for aggressive growth.


RE: PENILE FRACTURE IN KERMANSHAH, IRAN: REPORT OF 172 CASES

J. Zargoooshi


To the Editor. This article represents one of the larger series of penile fractures in the world literature. All but 2 patients underwent surgical repair using a degloving circumferential incision of the penile skin. From our experience we agree that the diagnosis can be made reliably based on history and physical findings, and ultrasonography and cavernosography with the attendant risks are rarely warranted. The precise location of the tear can also be determined clinically. We use the “rolling sign” to identify the site of the hematoma confined below Buck’s fascia. While the degloving technique will identify a torn urethra, the diagnosis can be made preoperatively when there is blood per urethra and can be confirmed on urethrography. There were no reported complications but the followup procedure seems to be incomplete as the author admits. Review of the literature revealed a relatively high complication rate (14% to 25%) using this technique, including wound infection, access formation and subcoronal skin necrosis. We believe that these complications can be avoided by using a less invasive approach that does not involve degloving the penis. The use of this distal circumferential incision with degloving is an unnecessarily traumatic approach to the pathology site, which is most commonly proximal as reported in this article. When the exact site has been located, simple repair can be performed with the patient under local anesthesia using a small longitudinal incision directly over the fracture site, and the patient can be discharged home on the same day. We have performed 12 of these procedures with no complications. All of our patients have had excellent erectile function and no loss of sensation. This result is expected since the longitudinal incision will produce minimal cutaneous nerve damage. This technique may not be applicable when concomitant urethral injury is present, especially if the tear involves both cavernosa. However, the preoperative diagnosis of concomitant urethral tears can be made clinically and confirmed on retrograde urethrography, allowing the appropriate incision and surgical approach to be used.

Respectfully,

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LETTERS TO THE EDITOR


Reply by Author. In my experience the precise location of the tear can be determined clinically only in cases presenting immediately with small, Buck's fascia contained fractures. Otherwise, the penis is covered entirely by a hematoma that obscures and deform all anatomical landmarks and the fracture site. The results of circumferential incision in our long-term survey, which will be reported in the future, indicate the occurrence of a small but defined number of complications. I believe that this versatile incision provides unrivaled access to all 3 corpora and the benefits clearly outweigh the low rate of complications.

RE: SIMULTANEOUS IRRADIATION FOR PROSTATE CANCER: INTERMEDIATE RESULTS WITH MODERN TECHNIQUES


To the Editor. The authors report the 5-year disease-free status of 689 men with T12NOX prostate cancer treated with a permanent 125I iodine prostate implant and external beam radiation therapy. They define outcome as the achievement and maintenance of a prostate specific antigen (PSA) nadir of 0.2 ng/ml. or less. However, this definition is not considered the standard for reporting radiation treatment results in the urological literature.

Before 1997 many institutions used different definitions of biochemical control, making treatment comparisons difficult. We have shown previously that using different definitions of biochemical control can result in statistically significant differences in outcome that are attributable only to the definition chosen.1 No such ambiguity exists in the urological oncology literature. In an effort to resolve this confusion and develop a unified definition of PSA cure for reporting success or failure after irradiation, the American Society for Therapeutic Radiology and Oncology (ASTRO) convened a panel of prostate cancer experts in 1997 to establish a standard definition of biochemical cure after radiation therapy. The ASTRO definition defines biochemical failure as 3 consecutive increases in posttreatment PSA after achieving a nadir. Biochemical failure was considered the time midway between the nadir and the first increase in PSA.2 The Consensus Panel specifically addressed the issue of posttreatment PSA nadir by stating, "Nadir PSA is a strong prognostic factor but no absolute level is a valid cut point for separating successful and unsuccessful treatment." In addition, the ASTRO definition of biochemical control states that "absolute PSA nadir may differ with different methods of delivering radiation therapy," making this end point unreliable for reporting results.

While treatment results using combined permanent implant with external beam radiation therapy are important, they should be presented in a standard manner that facilitates comparison with results from other radiation and surgical studies. In their reply the authors discount the ASTRO definition in part because of the requirement of 3 consecutive increases before treatment is considered a failure. The consecutive increase rule is necessary precisely because PSA can bounce after treatment. Results from radiation series should be reported in compliance with established uniform treatment end points.

Respectfully,
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Reply by Authors. Horwitz et al should note that it is in our own best interest to calculate prostate cancer cure rates using the ASTRO definition of freedom from disease. In our study 81 men had recurrence using a PSA cutoff point of 0.2 ng/ml to define disease-free status. If we had used the ASTRO definition, 30% (24/81) of these men would be reclassified as disease-free, and our Kaplan-Meier calculated failure rate would decrease from 12% to 8%.

Nonetheless, we calculate our disease-free survival rates using an undetectable PSA nadir (0.2 ng/ml) and not the ASTRO definition because that definition is flawed. Prostate cancer disease-free survival rates calculated using the ASTRO definition are inaccurate and misleading compared to surgical results. This observation is demonstrated dramatically by comparing 10-year disease-free survival rates in men treated with the obsolete retropubic implant to those treated with modern radical prostatectomy performed by Walsh who calculates results using a PSA cutoff point of 0.2 ng/ml. Using the ASTRO definition men treated with retropubic implantation have a slightly better 10-year survival rate than those treated with surgery. On the other hand, when the identical definition of freedom from disease is used for both series, 10-year disease-free survival rates in men treated with retropubic implantation are significantly decreased compared to those who underwent radical prostatectomy. This latter finding is realistic.

Horwitz et al quotes the ASTRO consensus statement, which finds that nadir PSA is not a valid end point to determine treatment success and that the absolute PSA nadir may vary with different methods of irradiation delivery. However, those statements are speculative since no long-term data are presented in the consensus statement to support those observations (reference 2 in letter). In contrast, we analyzed the PSA of men with followup of at least 5 years after simultaneous radiation and documented that disease-free status after irradiation, with rare exceptions, is determined by achievement and maintenance of a PSA nadir of 0.2 ng/ml or less.3 Multivariate analysis of those data documented that PSA nadir is the only factor of significance for determination of disease-free status. Of equal importance, to our knowledge no irradiation study using another technique has refuted these findings. We also report that PSA also raise the issue of PSA bounce. Since the peak time for PSA bounce is 18 months post-implant, the effect of PSA bounce is minimized by evaluating men with followup of at least 3 years.2

Although I am a radiation oncologist, I believe that the gold standard for treatment of prostate cancer is radical prostatectomy performed by highly skilled surgeons. Any challenge to the supremacy of surgery should be made according to the standards set for radical prostatectomy. Horwitz et al suggest that a standard definition of disease-free status, the ASTRO definition, be used for irradiation. However, a different standard, undetectable PSA, is used to determine freedom from disease after radical prostatectomy. I agree with Horwitz et al that a standard definition is needed but it should apply to all prostate cancer treatments. There should not be different definitions of disease-free status for radical prostatectomy and irradiation because inaccurate and misleading observations can be made as illustrated with men treated with retropubic implantation. In other words, a level playing field is needed to compare prostate cancer treatment results. We again challenge all investigators of prostate cancer treatment to calculate disease-free survival rates using a PSA cutoff point of 0.2 ng/ml.