Variation in the Definition of Biochemical Recurrence in Patients Treated for Localized Prostate Cancer: The American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel Report and Recommendations for a Standard in the Reporting of Surgical Outcomes

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Purpose: The American Urological Association Prostate Guideline Update Panel was charged with updating the Guidelines for Clinically Localized Prostate Cancer. In assessing outcomes with treatment, it became apparent that a highly variable number of definitions exist with respect to biochemical recurrence. Herein, we review the variability in published definitions of biochemical recurrence and make recommendations directed toward improving this terminology by recommending a standard definition in patients treated with radical prostatectomy.

Materials and Methods: Four PubMed® literature searches were performed between May 2001 and April, 2004 and covered articles published from 1991 through early 2004. The search terms included the MeSH® major headings of prostate cancer and prostatic neoplasm. All potentially relevant articles were retrieved and a more detailed screen for relevance was performed. An article was considered relevant if it reported treatment outcomes of patients with clinical T1 or T2N0M0 prostate cancer. Data extractors recorded the definition of biochemical recurrence and definitions were then collapsed into categories representing the same criteria. The results of biochemical failure were subcategorized by initial treatment.

Results: Of 13,800 citations, a total of 436 articles were selected. Among these, a total of 145 articles contained 53 different definitions of biochemical recurrence for those treated with radical prostatectomy. Of these, the most common definition (35) was a prostate specific antigen of >0.2 ng/mL or a slight variation thereof. In addition, a total of 208 articles reported 99 different definitions of biochemical failure among those treated with radiation therapy. Of these, the American Society for Therapeutic Radiology and Oncology definition (70) and/or a variation thereof was the most commonly reported. In total, 166 different definitions of biochemical failure were identified. Following radical prostatectomy, the Panel recommends defining biochemical recurrence as an initial serum prostate specific antigen of ≥ 0.2 ng/mL, with a second confirmatory level of prostate specific antigen of >0.2 ng/mL. The Panel recommends the use of the American Society for Therapeutic Radiology and Oncology criteria for patients treated with radiation therapy and acknowledges that these criteria will soon be updated although not yet published.

Conclusions: A high degree of variability in the definition of biochemical recurrence exists following treatment for localized prostate cancer. Strict definitions for biochemical recurrence are necessary to identify men at risk for disease progression and to allow meaningful comparisons among patients treated similarly. The Panel acknowledges the American Society for Therapeutic Radiology and Oncology criteria and future modifications thereof for those receiving radiation therapy and recommends the newly developed American Urological Association criteria for those treated with radical prostatectomy. The purpose for the establishment of this standard is for data reporting purposes and for comparison of similarly treated patients. It is not intended to represent a threshold value for which to initiate treatment. The Panel acknowledges that the clinical decision to initiate treatment will be dependent on multiple factors including patient and physician interaction rather than a specific prostate specific antigen threshold value.

Key Words: prostate, prostatic neoplasms, prostate-specific antigen, practice guidelines

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For another article on a related topic see page 757.

While cancer specific mortality remains the ultimate measure of efficacy of treatment among patients with solid tumor malignancies, prostate cancer presents a special circumstance in which clinicians have the unique ability to monitor treatment response with a serologic marker that indicates treatment failure up to a decade before clinical failure.[1] Among patients with localized prostate cancer, the use of PSA to monitor for disease recurrence after treatment and to evaluate the effectiveness of definitive local therapies has become widely accepted.[2,3] A detectable serum PSA after radical prostatectomy or a rising PSA following RT has been termed "biochemical," and is generally accepted as evidence of cancer recurrence.[4,5]

Unfortunately, defining biochemical failure following treatment for localized prostate cancer is problematic. Depending on the type of therapy, the level of PSA which would be defined as indicating disease varies. Following radical prostatectomy, the serum PSA level should become undetectable within 6 weeks of surgery as its source of production has been removed. Thus, a detectable PSA following radical prostatectomy implies residual prostate tissue and most likely residual or recurrent prostate cancer.[6] There is no PSA level for which there is consensus that disease recurrence is present after radical prostatectomy.[7]

As radiation therapy does not consistently eliminate all prostatic epithelium, PSA levels may not decrease to an undetectable level and may take as long as 2 to 3 years to reach the posttreatment nadir. Accordingly, because of the potential for residual functioning epithelium and its ability to produce PSA, there is significant debate with regards to the timing and level of serum PSA that constitutes treatment failure following radiation therapy.[8,9] A definition for PSA failure after radiation therapy, developed by ASTRO, defines biochemical failure as 3 consecutive PSA increases, with the date of failure defined to be the midpoint between the PSA nadir and the first of the 3 consecutive increases.[4] Despite the attempt to standardize the definition of biochemical recurrence among patients treated with radiation therapy, the ASTRO criterion has been the subject of debate.[10–13]

The varying definitions of biochemical failure makes the use of this end point challenging when comparing within and among treatments for localized prostate cancer. Nonetheless, patient decision-making for treatment is often based on this end point. In 1995, the AUA Prostate Guideline Update Panel published Guidelines for Clinically Localized Prostate Cancer.[14] The resulting publication currently serves as a reference for clinicians and patients seeking objective evidence based outcomes with respect to treatment options for localized cancer of the prostate. In updating these Guidelines, an assessment of recently published literature was performed. In assessing outcomes for localized prostate cancer, it became apparent that an extraordinary number of definitions exist with respect to biochemical recurrence for both radical prostatectomy and radiation therapy. It is the goal of this manuscript to describe the variability in reporting of biochemical recurrence in the literature as it relates to outcomes for patients with localized prostate cancer and to make recommendations for standardizing these definitions.

MATERIALS AND METHODS

The AUA Prostate Guideline Update Panel was charged with updating the Guidelines for Clinically Localized Prostate Cancer released in 1995.[14] These guidelines were restricted to the treatment of clinical stage T1-T2N0M0 prostate cancer. A series of 4 literature searches were performed between May 2001 and April 2004. These searches were conducted using PubMed and covered articles published from 1991 through early 2004. The search terms included the MeSH major headings of prostate cancer and prostatic neoplasm and were limited to human subjects and English language. The citations and abstracts were reviewed for relevance. All potentially relevant articles were retrieved and a more detailed screen for relevance was performed using the actual articles. An article was considered relevant if it reported outcomes (either efficacy or side effects) of the treatment of prostate cancer in patients with T1 or T2 disease. If higher stage patients were included and the outcome results were not stratified to allow an analysis of T1-T2 patients, the articles were rejected.

A data extraction form was developed for patient characteristics, treatments and outcomes data, including the definition of biochemical progression used in the study. The extracted data were then entered into a Microsoft® Access™ database. During the extraction process, articles were again reviewed for relevance and articles were rejected if outcomes were not reported or not stratified for early stage patients. From the articles deemed acceptable for inclusion, relevant data were extracted and entered into the database. This database served as the basis for the results of the current report.

The focus of this report is to highlight the variability of reported definitions of biochemical recurrence as related to outcomes for patients with localized prostate cancer. Data extractors recorded the definition of biochemical recurrence or no evidence of biochemical recurrence using the author's definition. As a result, many definitions were only slightly different from others. The list of definitions was reviewed and collapsed to categories that represented the same criteria. In some cases, the original article was rechecked to resolve uncertainty. The results of biochemical failure were subcategorized by initial treatment (ie watchful waiting, radical prostatectomy or radiation therapy, including external beam and interstitial brachytherapy).

RESULTS

A total of 13,800 citations resulted from literature searches. Of these, after review of abstracts, 592 articles were selected for further evaluation. During the data extraction process, an additional 156 were rejected, leaving a total of 436 articles. Of these, a total of 319 included various definitions of biochemical recurrence (tables 1 to 4). A summary of the results of the various definitions of biochemical recurrence by treatment type are displayed in table 1. Of note, some

TABLE 1. *Biochemical recurrence definitions by treatment*

Treatment	No. Articles	No. Definitions
Radical prostatectomy	145	53
RT	208	99
Other	14	14

TABLE 2. *Biochemical recurrence definitions for patients treated with radical prostatectomy*

Descriptor	Incidence
2 Consecutive PSA values >=0.1 ng/mL	2
2 Consecutive PSA increases >0.1 ng/mL	3
2 Consecutive PSA increases >0.1 ng/mL following undetectable	1
2 Consecutive PSA increases >0.2 ng/mL	2
2 Consecutive PSA increases >0.3 ng/mL	1
2 Consecutive PSA increases 3 months apart	1
2 Consecutive PSA values >0.1 ng/mL	4
2 Consecutive PSA values >0.1 ng/mL following undetectable	4
2 Consecutive PSA values >0.2 ng/mL	6
2 Consecutive PSA values >0.2 ng/mL following undetectable	1
2 Consecutive PSA values >0.4 ng/mL	3
2 Consecutive PSA values >=0.1 ng/mL	1
2 Consecutive PSA values >=0.4 ng/mL	1
2 Consecutive PSA values >=1.0 ng/mL	1
2 Consecutive PSA values (>0.2) or >0.1	1
2 PSA values >0.15 ng/mL 6 mos apart	1
2 PSA values >0.2 ng/mL following undetectable	1
2 PSA values >1 ng/mL	2
2 PSA values >0.4 ng/mL	1
2 Rising PSA values >0.4 ng/mL	1
3 Rising PSA values >0.4 ng/mL	1
Return to measurable PSA levels or PSA level that continues to rise	1
Detectable PSA post-prostatectomy or rise in PSA levels >0.2 ng/mL for radical prostatectomy pts + 2 consecutive rising PSA levels after nadir for RT pts	1
ASTRO	8
ASTRO-PSA >0.2 ng/mL	1
Detectable PSA based on stage according to 1992 American Joint Committee on Cancer	1
Elevated prostatic acid phosphatase >2 μL	1
Failure to reach undetectable PSA	1
No definition provided	2
No PSA relapse or PSA relapse in >=4 yrs	1
Undetectable PSA (<0.2 ng/mL) at 1 yr	1
Detectable PSA (>0.2 ng/mL) after surgery	14
PSA >0.1–0.4 and rising	1
PSA >0.2 ng/mL	35
PSA >0.3 ng/mL	6
PSA >0.4 ng/mL	14
PSA >0.5 ng/mL	2
PSA >0.6 ng/mL	3
PSA >0.7 ng/mL	1
PSA >1.5 ng/mL	1
PSA >2.0 ng/mL	1
PSA >=0.1 ng/mL	5
PSA >=1 ng/mL above nadir or detectable PSA after surgery	1
PSA >=1.4 ng/mL	1
PSA doubling <10 mos	1
PSA nadir >0.5 ng/mL or rise above level	3
Rising PSA >0.1 ng/mL	1
Rising PSA >0.2 ng/mL	3
Rising PSA >0.4 ng/mL	3
Rising PSA >=0.4 ng/mL	1
Rising PSA >=0.7 ng/mL	2
Rising PSA >=4 ng/mL	1
Single PSA >0.2 ng/mL or 2 PSA values = 0.2 ng/mL	1

articles used multiple definitions of biochemical recurrence and some definition groups were used for multiple treatments. In total, 166 different definitions of biochemical recurrence were reported for the treatments assessed. Table 2 displays the various definitions for patients treated with radical prostatectomy. Of these, a PSA cutpoint of >0.2 ng/mL was the most commonly used definition (35) following radical prostatectomy. Table 3 displays the various definitions for patients treated with radiation therapy. Of these, the ASTRO definition (70) and/or a variation thereof was the most commonly used definition. Table 4 demonstrates the definitions for treatments other than radical prostatectomy or radiation therapy.

DISCUSSION

The importance of defining biochemical recurrence and properly identifying patients with early treatment failure using a consistent terminology and definition cannot be understated. First, an accurate marker of early treatment failure allows clinicians and newly diagnosed patients to select therapies that are most likely to result in durable cancer control rather than waiting to base decisions on survival data that may be determined more than a decade after treatment is completed. Secondly, patients with biochemical failure may be candidates for early salvage therapy and thus correctly identifying patients who relapse prior to clinical progression may allow for application of effective therapy to alter the natural history of recurrent cancer. Finally, only by using standardized definitions of biochemical relapse can reliable comparisons be made among series of patients receiving a given therapy. It is often desirable to compare different treatments using a PSA surrogate end point but at this time, there are no methods to accomplish this reliably. Furthermore, given the high degree of variability in reporting of the definitions of biochemical failure along with the treatment-related differences in PSA kinetics, caution should be exercised in any attempts to draw comparisons between series using different treatment modalities, and this is particularly true when attempting to compare surgery and radiation therapy.

This report is a sobering observation regarding the lack of standardization of the definitions of biochemical recurrence based on a prospective, comprehensive evaluation of literature related to treatment outcomes for T1-T2N0M0 prostate cancer. Based on this analysis, it is clear that there is no standard definition for PSA recurrence following radical prostatectomy. In our review, we found 53 different variations in the definition of PSA progression or non-progression. These definitions range from any detectable PSA following surgery to a varying set of PSA levels to changes in PSA. When studying the same patient population, slight changes in this definition can result in significant changes in biochemical disease-free survival. For example, Amling et al found that by raising the PSA threshold from 0.2 to 0.5 ng/mL, the difference in biochemical outcome ranged from 16% at 5 years to 18% at 10 years.[7] Not only is the optimal level of PSA not established following surgery, but the timing and need for confirmatory PSA levels is debated. Using the same patient series, by simply requiring 2 values of 0.4 ng/mL, as compared to a single 0.4 ng/mL and a second value greater than 0.4 ng/mL, the difference in outcomes varied from 7% to 18% at 5 and 10 years, respectively.

There are, however, certain trends that can be drawn from the existing data with respect to defining PSA recurrence following radical prostatectomy. First, a washout period following radical prostatectomy of at least 6 weeks should be used before obtaining the first postoperative PSA value. Second, any detectable PSA following radical prostatectomy should be repeated for confirmation and to eliminate laboratory error. Third, a cutpoint of between 0.2 and 0.4 ng/mL appears to be the most accurate for defining biochemical recurrence which will ultimately translate into clinical failure following radical prostatectomy. The selection of lower values increases the sensitivity of the marker for correlation with ultimate disease recurrence while higher values improve specificity.

TABLE 3. *Biochemical recurrence definitions for patients treated with RT*

Descriptor	Incidence
2 Consecutive adjusted PSA rises >=10% + final PSA >1.5 ng/mL	1
2 Consecutive elevations above nadir or nadir >1 ng/mL	1
2 Consecutive elevations from nadir; + failure to attain PSA of 1.0 or 0.5 ng/mL at last followup	1
2 Consecutive PSA increases	15
2 Consecutive PSA increases >=1.5 ng/mL	4
2 Consecutive PSA increases >=1.5 ng/mL above nadir or nadir >=4.0 ng/mL	1
2 Consecutive PSA increases 3 mos apart	2
2 Consecutive PSA increases 3 mos apart and PSA nadir >1.0 ng/mL	1
2 Consecutive PSA increases with nadir <=1.5 ng/mL	1
2 Consecutive PSA values >0.1 ng/mL	1
2 Consecutive PSA values >0.1 ng/mL following undetectable	1
2 Consecutive PSA values >0.4 ng/mL	1
2 Consecutive PSA values >1.0 ng/mL	1
2 Consecutive PSA values >4 ng/mL	1
2 Consecutive PSA values >0.4 ng/mL	1
2 Consecutive PSA rises >2 ng/mL or commencement of androgen deprivation	1
2 Consecutive PSA rises or nadir >1.0 ng/mL	1
2 Consecutive rising PSA >=1 ng/mL over nadir	1
2 Elevations in PSA or PSA >1 ng/mL	1
2 Increases above nadir (<1 ng/mL) in 1 yr	1
2 Increases above nadir (<1 ng/mL) in 1 yr; 2 increases above nadir (<1 ng/mL) in 1 yr; PSA nadir <4 ng/mL, no time limit	1
2 Increases above nadir (<1.5 ng/mL) in 1 yr	1
2 or More consecutive values were increasing or 2 most recent value exceeded its predecessor by 1 ng/mL	1
2 PSA values >0.2 ng/mL	1
2 Rising PSA >1.5 ng/mL	2
2 Rising PSA values	2
2 Rising PSA values >0.5 ng/mL	1
2 Sequential rises in serum PSA; or PSA >1 ng/mL, 2 or more years after radiation; or PSA >4 ng/mL 2 or more years after radiation	1
3 Consecutive PSA increases	9
3 Consecutive PSA increases >0.2 ng/mL	1
3 Consecutive PSA increases >0.5 ng/mL	1
3 Consecutive PSA increases >1.0 ng/mL	2
3 Consecutive PSA increases or pos biopsy	1
3 Consecutive PSA increases with back dating	1
3 Consecutive PSA increases >10% or single dramatic rise	3
3 Consecutive PSA increases or any rise great enough to provoke androgen suppression	1
3 Consecutive rising PSA values of at least 10% of prior reading	2
3 Rising PSA values	1
Rise in PSA levels >0.2 ng/mL for radical retropubic prostatectomy pts + 2 consecutive rising PSA levels after nadir for RT pts. Detectable PSA levels immediately after RT	1
Any consecutive PSA readings progressively higher than lowest reading	1
Any 3 of: 2 consecutive increasing values; PSA >4 ng/mL with preimplant >4 ng/mL; preimplant with normal value	1
Any rise of 2 ng/mL > current nadir or ASTRO (mos ending in 0.1)	1
Any rise of 2 ng/mL > current nadir or ASTRO (mos ending in 0.1) or modified ASTRO: censored half way between last non-rising PSA + first rise (mos ending in 0.2)	1
ASTRO	70
ASTRO PSA >0.2 ng/mL	1
ASTRO or PSA >1 ng/mL	2
ASTRO with back dating	5
ASTRO with modifications	5
Change in tumor; tumor progression	1
Elevated prostatic acid phosphatase >2 μL	1
If nadir PSA <2 ng/mL, 2 consecutive rises >2.0 ng/mL; if nadir >2 ng/mL, 2 consecutive rises above nadir; initiation of hormone therapy after RT	1
Increase in PSA >1.0 ng/mL for those receiving hormone therapy; ASTRO for non-hormone therapy	1
No change in tumor; tumor progression	1
No clinical evidence of recurrence + PSA <=1.5 ng/mL + not rising	1
No definition provided	4
Normal PSA baseline, which at best doubled during followup to >4 ng/mL; or above normal baseline not less than 50% rise to >4 ng/mL after nadir	1
PSA <1.0 ng/mL	1
PSA <=0.2 ng/mL	1
PSA <=0.5 ng/mL	1
PSA <=1.5 ng/mL	1
PSA >0.1 ng/mL	2
PSA >0.2 ng/mL	7
PSA >0.2 ng/mL following undetectable	1
PSA >0.2 ng/mL for radical prostatectomy, ASTRO for all others	1
PSA >0.3 ng/mL	3
PSA >0.4 ng/mL	4
PSA >0.5 ng/mL	5
PSA >1.0 ng/mL	4
PSA >1.0 ng/mL over nadir	1
PSA >1.5 ng/mL	3
PSA >2.0 ng/mL + >1 ng/mL over nadir	1
PSA >2.0 ng/mL	2
PSA >2.0 ng/mL over nadir	1
PSA >4.0 ng/mL	1
PSA >4.0 ng/mL or rising PSA	1
PSA > pretreatment PSA	1
PSA >=1 ng/mL	1
PSA >=1 ng/mL above nadir	1
PSA >=1 ng/mL above nadir or detectable PSA after surgery	1
PSA doubling <10 mos	1
PSA nadir >0.5 ng/mL or rise above level	1
PSA not maintained at <=1 ng/mL or increase of >=0.5 ng/mL in 1 yr	1
PSA of >=4.0 ng/mL or >=1.5 ng/mL	1
PSA plateaued at value of >1 ng/mL	1
PSA value of >=1 ng/mL or PSA value that rose >=0.5 ng/mL in <=1 yr posttreatment on 2 consecutive measurements, with rise defined at time of failure	1
Rise in PSA >0.2 ng/mL after radical prostatectomy + 3 consecutive increasing PSA level above nadir following external beam RT	1
Rising PSA	2
Rising PSA >0.1 ng/mL	1
Rising PSA >0.2 ng/mL	1
Rising PSA >1.0 ng/mL	1
Rising PSA >1.5 ng/mL	3
Rising PSA >4.0 ng/mL	1
Rising PSA >1.0 ng/mL for 2 or more consecutive values or clinician initiation of hormone therapy for 1 rise of PSA from nadir	1
Rising PSA >=1.5 ng/mL	1
Rising PSA >=4.0 ng/mL	1
Rising PSA or >4.0 ng/mL	1
RT subjects ASTRO definition: 3 consecutive rising PSA levels after nadir, time to failure: midway between time of nadir + first PSA increase. Radical prostatectomy subjects: 2 consecutive detectable PSA levels (>0.2 ng/mL), time to failure: time of initial detection	1
Serial evaluation of PSA	1
Single PSA >0.2 ng/mL or 2 PSA values = 0.2 ng/mL	1

The definition of PSA recurrence after radiation therapy has also been debated. Currently, although not without controversy, the most commonly used definition was developed by the ASTRO Consensus Panel.[4] This definition requires 3 consecutive increases in PSA after nadir has been reached, with the date of failure being the midpoint between the nadir and the first of 3 consecutive rises. A challenging feature of this definition was that the time interval between the consecutive increases in PSA was not specified, and although the level of PSA nadir was recognized as a risk factor, it was not identified as an indicator of treatment

TABLE 4. *Definitions of biochemical treatment other than radical prostatectomy or RT*

Descriptor	Incidence
2 Consecutive rises >0.2 ng/mL or commencement of androgen deprivation	1
2 or More consecutive values rising above nadir if it was higher than its predecessor by 1 ng/mL or by factor of 1.5	1
ASTRO	1
ASTRO with back dating	1
Evidence of disease progression based on biopsy at 6 months: PSA nadir <4 ng/mL beyond 6 mos; PSA nadir <0.5 ng/mL beyond 7 mos	1
Multiple rising PSA	1
PSA >0.1 ng/mL	1
PSA >0.2 ng/mL	1
PSA >0.4 ng/mL	1
PSA >4.0 ng/mL	1
PSA doubling time <2 yrs; final PSA >8 ng/mL, <0.5 ng/mL on regression analysis of initial PSA on time	1
PSA doubling time of <2 yrs	1
PSA level increased by 25%–50%/yr	1
Rising PSA >=1.5 ng/mL	1

success or failure. This criterion of PSA recurrence has been the subject of some criticism.[12] Shortcomings of the definition include failure to use PSA nadir as a risk factor since it is closely related to the development of progression, the need for backdating the time of failure which leads to potentially artificially higher success rates and the failure to more carefully define the intervals at which PSA determinations should be made. Some have suggested improvements for this definition.[15]

The findings of such a high degree of variability in definitions of PSA relapse also challenges comparisons of patients treated with different forms of local therapy. Nonetheless, comparisons of treatment modalities for localized disease are made based on these definitions of biochemical relapse. In 1 such study, outcomes based on risk stratification using ASTRO criteria for both surgery and radiation therapy treated patients found similar outcomes for intermediate-risk and high-risk patients with high volume cancers as determined by biopsy.[16–18] Caution must be exercised when using biochemical control (PSA-free survival) as a surrogate for other disease end points such as metastasis-free, disease specific or overall survival. By illustration of these challenges, if the ASTRO criterion is used for surgical patients, a significant artificial improvement in the rate of biochemical disease-free recurrence from 68% to 90% results.[10]

Given the high degree of variability that exists in the prostate cancer literature with regard to biochemical recurrence, the Prostate Cancer Guidelines Update Panel has recommended a standard definition for biochemical recurrence after radical prostatectomy. It is recommended that biochemical (PSA) recurrence following radical prostatectomy be defined as a serum PSA of 0.2 ng/mL or greater, with a second confirmatory level of PSA of >0.2 ng/mL. The first postoperative PSA should be obtained between 6 weeks and 3 months following therapy. The date of failure should be defined as the date of the first detectable PSA level once this value has been confirmed. The Panel recognizes that higher levels of PSA have a greater specificity for disease recurrence and progression but felt that this value provided high sensitivity for recurrence as well as the greatest generalizability, not relying on ultrasensitive PSA assays. The Panel also believes that it is appropriate to report biochemical outcomes using additional PSA thresholds, but strongly encourages the use of a 0.2 ng/mL standard for which future comparisons can be made.

It is important to bear in mind that this is only a definition of biochemical failure following surgery and in no way is proposed as a threshold value suggestive of initiation of salvage therapy. Importantly, the use of adjuvant or salvage therapies should be individualized based on overall patient risk factors with a thorough patient and physician discussion regarding risks and benefits. Furthermore, this proposed definition should not be misinterpreted as a predictor of death from prostate cancer. In fact, the Panel acknowledges the limitation of any single definition of PSA recurrence and recommends the use of other prognostic tools such as nomograms which consider tumor Gleason grade, pathological stage and PSA kinetics.[19,20]

For patients treated with radiation therapy, it is recommended that the ASTRO criterion be used as a reference. Despite its criticisms and shortcomings, the ASTRO criterion allows comparisons among similarly treated patients. For both the AUA and ASTRO criteria, the Panel realizes that definitions are subject to modifications as more data become available and the use of these standard references will at the least allow for direct comparisons among similarly treated men. In fact, it is anticipated that a modification of the ASTRO definition of PSA failure will be forthcoming in the very near future having recently convened a second consensus conference, and we believe that such refinements are achievable only through the establishment of set criteria for comparison.

Limitations of this study include the retrospective nature of the review, the lack of a formal statistical analysis of the results and methodology of the literature search which focused primarily on outcomes of therapy for clinically localized prostate cancer rather than definitions of PSA recurrence. The Panel's selection of a value of PSA for defining recurrence was based on its clinical utility as a sensitive and portable marker for disease recurrence.

CONCLUSIONS

The AUA Prostate Cancer Guidelines Panel found a high level of variability in the definitions of biochemical failure after both radical prostatectomy and radiation therapy. This high degree of variability in defining treatment failure among patients with localized prostate cancer significantly affects reported success rates of these localized treatments. Given the protracted natural history of treated and untreated clinically localized prostate cancer, the importance of this end point in predicting outcomes related to the various treatment modalities cannot be understated. Accordingly, standardization of these treatment specific definitions should strengthen the validity of any future comparisons. The purpose for the establishment of this standard is for data reporting purposes and for comparison of similarly treated patients. It is not intended to represent a threshold value for which to initiate treatment. The Panel acknowledges that the clinical decision to initiate treatment will be dependent on multiple factors including patient and physician interaction rather than a specific PSA threshold value. The use of a standardized definition of biochemical failure following radical prostatectomy will permit periodic refinements based on similarly defined outcomes.

APPENDIX

Prostate Cancer Clinical Guidelines Update Panel

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Abbreviations and Acronyms

ASTRO	=	American Society for Therapeutic Radiology and Oncology
AUA	=	American Urological Association
PSA	=	prostate specific antigen
RT	=	radiation therapy

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