EDITORIAL

Renaming Low Risk Prostate Cancer: Proceed Cautiously

The adage that 'men are more likely to die with prostate cancer rather than of prostate cancer' is getting renewed attention today. Numerous contemporary studies and organizations are questioning the validity of the aggressive treatment of all prostate cancers in the PSA era. In a disease accounting for the second leading cause of cancer deaths in men, "over diagnosis" and "over treatment of prostate cancer" is a major concern. Prostate cancer is a lethal disease in men with high risk features and this fact requires our continued attention to reduce mortality from prostate cancer. Where we fall short is recommending active treatment in a man who will never suffer any consequences from prostate cancer. In some series, up to 80%-90% of cancers diagnosed in the modern PSA era will never impact a patient's life and many are considered to be low risk indolent cancers.

When presented with the diagnosis of "cancer" the typical response can be shock, denial, despair and a sense of impending doom. Studies suggest that the mere diagnosis of prostate cancer may increase the short term risk of sudden death and suicide. There is interest in renaming low risk prostate cancer to send a message to the patients that often this "cancer" is not as ominous as the diagnosis may appear. It encourages men with appropriate features to consider "active surveillance" over "active treatment". NCCN guidelines have made a step in this direction by identifying prostate cancer in terms of "low risk" and "very low risk" disease.

The current literature debate involves renaming certain low risk Gleason 6 cancers with a name that does not suggest a malignancy. Gleason score 6 cancers are generally considered to be low risk cancers meaning their potential to metastasize is low and curability is quite high. Pathologically, the diagnosis of Gleason score 5 or less is rare and there is a suggestion that these lesions should not be considered malignant. The vast majority of cancers diagnosed today are Gleason score 6-10.

The robust nature of the Gleason score, PSA and clinical staging in determining those patients who are appropriate for active surveillance are generally accepted. In our quest to appropriately encourage men diagnosed with low risk prostate cancer to take this conservative course, we must be cautious about the presumed benign nature of some Gleason 6 lesions. We currently lack the sophisticated tools to accurately predict the ultimate malignant potential for all prostate cancers regardless of Gleason grade.

The "Epstein criterion" are well accepted in identifying low risk prostate cancer patients who may be candidates for active surveillance: Gleason 6 or less, PSA density of < 0.15, no more than three needle cores positive for cancer and no needle core containing $> 50\%$ cancer. Low clinical stage and a PSA of less than 10 are also included by some groups. Using current active surveillance protocols, a follow up up biopsy is uniformly recommended. Unfortunately, 20%-30% of the time additional areas of higher grade cancers are found, suggesting the need to a change from active surveillance to active treatment.

Another uncertainty is the true biology of Gleason 6 cancers: could they indicate a global prostate genetic instability with the potential for other areas of the prostate to transform into aggressive cancer? Can they suggest the presence of a higher Gleason grade in another region of the prostate? Over time, do these Gleason 6 lesions grow and undergo genetic changes that transform them to higher grade aggressive disease?

Several years ago, the WHO reclassified certain forms of bladder cancer as PUNLMP (papillary urothelial neoplasm of low malignant potential) attesting to their low risk. In breast cancer, DCIS (ductal carcinoma in situ) is considering a name change to minimize the connotation of its malignant potential. Dr. Ian Thompson has suggested the term IDLE (InDolent Lesions of Epithelial origin) to be used in low risk epithelial cancers. The growing theme is to consider reclassify low risk, low stage prostate cancer using a similar terminology.

To paraphrase visionaries such as Drs. Willett Whitmore and Donald Coffey there are "good prostate cancers and bad prostate cancers". Research continues to refine these common sense terms in a better defined scientific basis. The personalized medicine approach to prostate cancer through new molecular or genetic studies may allow us move beyond these broad classifications. Renaming low risk prostate cancer is worthy of discussion but we must move cautiously to avoid a misstep in our treatment recommendations.

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