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Prostate cancer recurrence – new prognostic factors are needed

Zew Wajzman

University of Florida, Department of Urology, USA

Cancer remains a major health problem the world over. Approximately fifteen million people are predicted to be affected by malignancy in 2020, and 10 million will die of cancer each year according to WHO estimates. Prostate cancer is among the leading causes of cancer deaths in American men, with approximately two hundred and forty thousand men in the United States diagnosed each year.

In the current issue of the Central European Journal of Urology, Takehiro, Sejima, and others [1], present their experience with the prediction of biochemical recurrence of prostate cancer in their patient population.

Predicting the outcome of prostate cancer remains a critical issue. While it is well known that prostate cancer is frequently a deadly disease, it is also known to be over diagnosed and over treated in many patients, causing unnecessary morbidity and even mortality. Biochemical recurrence (BCR) while not predictive of imminent death from cancer remains a strong surrogate for poor prognosis. The outcomes confirm the observations of the authors and, high preoperative PSA, high Gleason scores of preoperative and surgical specimens, positive surgical margins, seminal vesicle invasion and finally lymph node metastases – all represent extremely poor diagnostic factors.

The rather new observations reported in this paper; in that low preoperative levels of serum albumin predict lymph node metastases, correlates surprisingly well with BCR. This rather unexpected finding is of clinical importance since this low level of albumin was found in patients otherwise considered good candidates for major surgery, and who therefore must have been in good general health and have clinically localized disease.

The predicted value of albumin levels in other malignancies has been reported in recent literature. Higher serum albumin levels were associated with better survival in gastrointestinal cancer and in potentially curable lung cancer; while among other factors associated with poor survival were a serum albumin level below 3.5.

A study of colorectal cancer has shown that preoperative CEA, as well as a preoperative level of albumin below 3.5 G/DL, predicts poor survival. While all of these aforementioned studies address the predictive value regarding survival, the current study in this Journal emphasizes the fact that low albumin levels can predict BCR and, indirectly, also predict poor final outcomes. The information provided by the authors considers a cutoff level of low albumin as 4.0 in G/DL, significantly higher than the 3.5 level used in other studies.

It's believed that hypoalbuminemia is a rather late phenomenon with cancer progression, usually associated with an inflammatory response with the release of IL-6, Cytokines, and other factors which affect albumin levels in advanced stages.

Finding low level albumin in the authors study increases our ability to better predict a poor outcome in high risk patients. I would argue, however, with the authors' final conclusion that "delayed diagnostic and therapeutic procedures in patients with low serum albumin levels may lead to PCA". I believe the conclusion should be to the contrary. It appears, in this study, that when an otherwise healthy patient presents with low stage prostate cancer, without obvious high risk factors, and is found to have low albumin level – the necessary time should be spent to discover the cause of this finding. If an advanced disease is detected because of this low albumin level, then the patient will be spared unnecessary surgery. On the other hand, a low protein level may indicate other non-malignant disease(s) and the consequent diagnosis and treatment of such, prior to a definitive treatment of prostate cancer, will prevent unnecessary morbidity. Time should not be an issue since it is unlikely that low stage prostate cancer will progress in the few weeks needed to discover the cause of the low albumin level.

However, when a surgical candidate presents with other high risk factors such as a high PSA or high Gleason score on biopsy specimen, and a low albumin level is detected; a careful metastatic workup is indicated and time should be spent to rule out lymph node metastases.

In any case a patient with other bad prognostic factors, in the presence of hypoalbuminemia, may be considered for less invasive treatment and perhaps be a candidate for treatment with other modalities, especially when so many are available to us today.

This study should stimulate more research regarding low level albumin occurring in GU malignancies, with special attention to the pathophysiology of low albumin levels in patients with clinically localized disease.

References

1. Sejjima T, Iwamoto H, Masago T, Morizane S, Isoyama T, Kadowaki H, Takenaka A. Low pre-operative levels of serum albumin predict lymph node metastases and ultimately correlate with a biochemical recurrence of prostate cancer in radical prostatectomy patients. *Cent Eur J Urol*. 2013; 66: 126–132 ■

Correspondence

Prof. Zev Wajzman
zewwajzman@yahoo.com