AUTHOR'S REPLY

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The initial purpose of our study was to discover preoperative non-tumor related biomarkers which can easily be obtained by routine laboratory examination. Detailed analyses of relationships between various kinds of laboratory examinations, such as C-reacted protein, hemoglobin, albumin, and others were performed. As a result, only albumin remained a significant biomarker for predicting biochemical recurrence (BCR). Albumin, a readily available and inexpensive laboratory test that is frequently part of a standard preoperative evaluation, is proven to be valuable in predicting survival in such cancers as rectal cancer [1], colon cancer [2], hepatocellular carcinoma [3], renal cell carcinoma [4], and in many types of solid malignancies. However, the role of pre-operative hypoalbuminemia as a biomarker for predicting BCR should not be discussed in the same manner as the aforementioned malignancies because predicting end points are different between prostate cancer (PCa) and other types of malignancies. First, BCR is a surrogate marker for PCa-specific mortality, and does not necessarily correlate patient survival. Second, patient backgrounds for curative surgery may be different between PCa and other types of malignancies. It seems that comorbidities are less prevalent in patients with PCa treated by radical prostatectomy than in patients with other types of malignancies treated by curative surgery. It is unclear why pre-operative hypoalbuminemia is correlated with BCR. The rationale of the phenomenon seems to be different from common reasons such as malnutrition status, influence by inflammatory mediators, or decreased production in liver. Our cut off value of 4.0 g dL was slightly higher than the value of prognostic indicators in other types of malignancies, and slightly lower than the value of the healthy age-matched male population in our country. This delicate cut off value can discriminate patients with comorbidities who are tolerable for radical prostatectomy from patients with no comorbidity. Delayed diagnostic procedure rather than delayed therapeutic procedure might be responsible for micro metastases progression of PCa with high malignant potential such as high Gleason grade. Physicians tend to be afraid of complications related to diagnostic examination rather than those related to therapeutic procedures. The increased possibility of critical complications such as sepsis in patients with comorbidities and hypoalbuminemia compared with those in patients with no comorbidity and normal albumin level might break down the active intention of physicians in charge of our study. Other than that, the possibility of increased serum active testosterone level in hypoalbuminemia should be discussed [5]. PCa is known to be hormonally sensitive to testosterone, but only the free, unbound testosterone has an impact on hormonally sensitive PCa. This is substantial rationale for correlating hypoalbuminemia with BCR; however, no study on this topic has been performed. Therefore, our next research goal is to investigate the androgen receptor concentration in surgical resected tissues from BCR patients with pre-operative hypoalbuminemia.

## References

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