Editorial

ICUrology 2016;57:73-74.
http://dx.doi.org/10.4111/icu.2016.57.2.73
pISSN 2466-0493 • eISSN 2466-054X

INVESTIGATIVE AND CLINICAL UROLOGY
ICUROLOGY

Biomarkers for bladder cancer: The search continues!

Cystoscopy has remained the gold standard for the detection of bladder cancer for decades. Although many new fancy molecular markers have been developed and are widely applied in the diagnosis and management of various cancers today, no single marker has dethroned cystoscopy as "the tool" in the detection of bladder cancer. Although advances in technology have provided fluorescence and narrow-band imaging, cystoscopy is still considered an invasive and expensive diagnostic tool by physicians and patients. Through the years, efforts have been made to improve the way we detect bladder cancer. Numerous urine markers have been introduced for the diagnosis of bladder cancer. Several newly developed markers exhibit sensitivity superior to urine cytology. To my knowledge, however, none of these has been included as a standard diagnostic tool in major clinical guidelines.

In this issue of *Investigative and Clinical Urology*, findings are reported from an elegant study by Kim et al. [1] on the value of urinary topoisomerase-II alpha (*TopoIIA*) cell-free DNA for diagnosis of bladder cancer. In this study, Kim et al. [1] observed significantly higher expression of urinary TopoIIA cell-free DNA in bladder cancer patients compared with controls and nonmalignant hematuria patients. Also, expression of urinary *TopoIIA* cell-free DNA was revealed to be significantly higher in patients with muscle-invasive bladder cancer than in those with non–muscle-invasive bladder cancer in this study. *TopoIIA* is a DNA gyrase isoform that plays a significant role in the cell cycle. Previously, the same group reported that increased expression of *TopoIIA* is significantly related to a higher rate of recurrence and progression of non–muscle-invasive bladder cancer [2]. These breakthrough findings suggest *TopoIIA* as a promising marker for the management of bladder cancer.

The current literature offers many markers that are labeled to detect bladder cancer. However, it is still unclear how much they can improve clinical decision-making. Technical innovations have brought us many potential new biomarkers. However, because these innovations can be costly, they are usually evaluated in small-scale studies. Obviously, new markers for bladder cancer detection should be developed for implementation among patients with symptoms or signs of the disease rather than in healthy control subjects. In the actual clinical setting, patients without hematuria, voiding symptoms, or other signs of bladder cancer are not offered any tests to detect bladder cancer. Such an approach is certainly quite different from that for prostate cancer, which is a disease of higher prevalence. Meanwhile, many published studies on potential markers for bladder cancer include normal controls without any hematopyuria or voiding symptoms. Several relevant case-control trials compare artificially composed cohorts [3]. Such problems in the evaluations of new markers for bladder cancer contribute to a false assessment of diagnostic accuracy. Admittedly, screening of a selected population with higher risk of bladder cancer can be pursued. Still researchers should bear in mind the real need in actual clinical practice.

Despite the abundance of new molecular markers being reported, the search for an "ideal" marker for bladder cancer continues. The ultimate goal of finding an ideal marker would be decreasing cost, time, and patient discomfort in the diagnosis of bladder cancer while increasing diagnostic accuracy. Research accomplished so far has taught us that noninvasive urinary markers are not limited to use in bladder cancer detection. Findings from the current study by Kim et al. [1] provide us with hope that discovery of such a marker is nearing. As the effort continues to replace prostate biopsy, which certainly is an uncomfortable experience for many patients, in the diagnosis of prostate cancer, the same should be done to spare patients the agony of cystoscopy.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

Sung Kyu Hong, MD, PhD
Deputy Editor
Department of Urology, Seoul National University Bundang Hospital,
82 Gumi-ro, 173 Beon-gil, Bundang-gu, Seongnam-si, Kyunggi-do, 13620 Korea
E-mail: skhong@snubh.org

REFERENCES

1. Kim YH, Yan C, Lee IS, Piao XM, Byun YJ, Jeong P, et al. Value of urinary topoisomerase-IIA cell-free DNA for diagnosis of bladder cancer. Investig Clin Urol 2016;57:106-12.
2. Kim EJ, Lee YS, Kim YJ, Kim MJ, Ha YS, Jeong P, et al. Clinical implications and prognostic values of topoisomerase-II alpha expression in primary non-muscle-invasive bladder cancer. Urology 2010;75:1516.e9-13.
3. Schmitz-Drager BJ, Droller M, Lokeshwar VB, Lotan Y, Hudson MA, van Rhijn BW, et al. Molecular markers for bladder cancer screening, early diagnosis, and surveillance: the WHO/ICUD consensus. Urol Int 2015;94:1-24.

http://dx.doi.org/10.4111/icu.2016.57.2.73