

Inflection points in urology as witnessed by Mark Soloway

Part 2: Prostate and kidney cancers

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Citation: Soloway MS. Inflection points in urology as witnessed by Mark Soloway. Part 2: Prostate and kidney cancers. Cent European J Urol. 2023; 76: 283-286.

Article history

Submitted: July 16, 2023

Accepted: July 25, 2023

Published online: Nov. 25, 2023

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Key Words: prostate cancer ↔ kidney cancer ↔ renal tumors

Periprostatic nerve block for prostate biopsy

I was fortunate to take a trip to Copenhagen in the 1980s and meet Professors Jens Gammelgaard and Hans Henrik Holm who were among the first to explore the technique of transrectal ultrasound of the prostate (TRUS). They worked with the Bruel and Kjaer company. I was impressed with the instrumentation and purchased a machine for use in my office at The University of Tennessee, Memphis [1]. Once I became adept at visualizing the prostate I went to visit William Cooner, a urologist in Mobile, Alabama, who had experience using TRUS to perform biopsies of the prostate. This was 1989.

During the next decade I would perform hundreds of biopsies without the use of anesthesia. Unless patients had their biopsies performed in an operating room this was the norm for a decade.

A 'Eureka' moment occurred in 1999. I was performing a TRUS biopsy in the office and my urologic oncology fellow, Can Obek, was with me (Figure 1). As usual the patient was moderately uncomfortable during the biopsy procedure and was counting the biopsies and wondering how soon I would be finished.

I mentioned to Can that when a patient goes to a dentist and requires a procedure the dentist injects a local anesthetic before any drilling so that the patient has minimal discomfort. For years urologists have been performing ultrasound-guided prostate biopsies without anesthesia. Can mentioned that a young urologist in Turkey presented a paper at one of their meetings in which he used a long spinal needle alongside the ultrasound probe and injected lidocaine in the region of the neurovascular bundles. I used this technique, and the results were dramatic. After 50 cases I submitted an article describing the periprostatic nerve block to The Journal of Urology. Jay Gillenwater, the editor, was aware of this concept and accepted the paper [2]. We subsequently performed a randomized trial asking patients to complete a pain scale following the TRUS biopsy. Half had a periprostatic nerve block and the others did not have local anesthesia. This confirmed our initial report of its efficacy [3]. Within a couple of years there were several other publications confirming the benefit of the periprostatic nerve block.

As I researched the literature prior to my publication I found a study published in The Journal

of Urology in 1996. Nash et al performed a small trial injecting saline on one side of the prostate and lidocaine on the other and the patients indicated less pain on the side which had lidocaine injected [4]. I had not read this paper and apparently few did as it took four years for me to 'reinvent' the periprostatic nerve block. There are at least 500,000 prostate biopsies performed annually in the US. This change in practice has probably benefited more patients than any other contribution.

Hormonal therapy

As a urologist with a subspecialty interest in urologic oncology at a major medical center I would care for more patients with prostate cancer (PC) than bladder cancer. Early in my career bilateral scrotal orchiectomy or diethylstilbestrol (DES) were the only methods to reduce the testosterone level, i.e., androgen deprivation. When we had patients who were 'hormone resistant' adrenalectomy was occasionally performed. Much has changed. I was an active participant in a large comparative clinical trial which compared the luteinising hormone-releasing hormone (LH-RH) analog buserelin acetate to orchiectomy or DES. The two methods yielded equivalent results [5]. This may seem like the dark ages to contemporary urologists. The next randomized similar trial compared leuprolide to orchiectomy or DES. The demonstration of equivalence led to the approval of leuprolide [6]. Soon thereafter goserelin was compared to the prior standard form of androgen deprivation and led to its approval [7]. Quality of life and patient preference analysis indicated that men preferred to have an injection as compared to orchiectomy and the latter is now obsolete in developed countries [8]. The last large multi institutional trial I was actively involved with was with bicalutamide. One study evaluated this new antiandrogen as monotherapy and another compared flutamide to bicalutamide when used with an LH-RH analog [9].

Neoadjuvant hormonal therapy

Having a short acting reversible method of androgen deprivation, either an LH-RH analog or bicalutamide, led to the consideration of using an LH-RH analog prior to radical prostatectomy for cT2b PC with the hope of improving the cure rate. I had initiated a small study on my own. We compared the pathologic stage for those who received three months of preoperative LH-RH analog to historical controls, and it appeared that the gland was smaller and there were less cases with a positive margin [10, 11]. This led to a pharmaceutical sponsored multi cen-

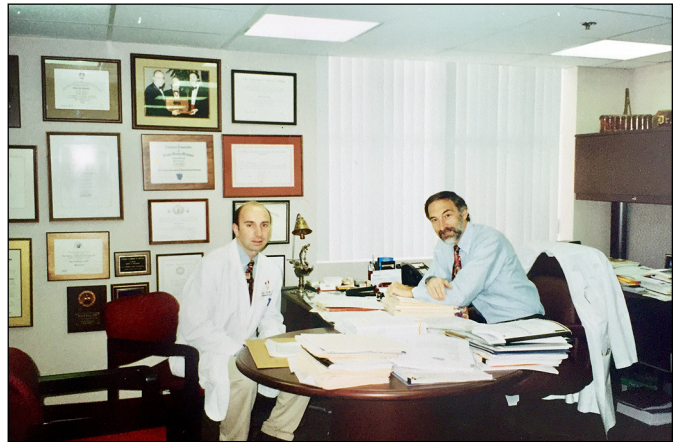


Figure 1. Dr Can Obek with me in my office in 1999.

ter prospective trial in the USA. The initial impression regarding a reduction of positive margins was confirmed; however, the recurrence rate was not improved [12, 13]. A subsequent Canadian trial confirmed this finding and preoperative systemic therapy with androgen deprivation (AD) was abandoned. There is currently a resumption of interest in preoperative AD with the plethora of other agents used for locally advanced and metastatic PC.

It is important to recall that in the 1960s–1990s there was a dramatic change in the stage of presentation for men with PC. Until the introduction of prostate-specific antigen (PSA) and its widespread utilization for early detection of PC most men had locally advanced or metastatic PC at diagnosis. Those diagnosed with low volume, well differentiated PC were thought to be fortunate to have been detected "early" and were offered a radical prostatectomy (RP) or radiation therapy. One of the few in the USA who did not adhere to this approach was Willet Whitmore, Jr. He stated that men with small volume well differentiated PC did not necessarily require treatment (Figure 2). There were a few astute urologists in Europe who also held this view. They were clearly in the minority, however.

Active surveillance

As the new millennium approached, I was influenced by Peter Albertson, Gerry Chodak, and Lorry Klotz who suggested that these patients do not all require have surgery or radiation. I was also influenced by a review we made of the incidence of PC in patients who underwent cystoprostatectomy for bladder cancer [14]. Thirty percent had prostate cancer! Almost none had PC diagnosed prior to their surgery. Most, of course, were well differentiated, i.e., Gleason grade 3. I began to change my thoughts and

published a paper on deferred treatment of PC for the elderly patient with localized PC [15]. I realized that urologists and radiation oncologists were overtreating men with small volume well differentiated, i.e., Gleason score (GS) 6, PC. One major change during these decades was the introduction of TRUS biopsies and PSA. This provided more tissue from the prostate and more precise evaluation of the tumor volume as well more confidence in the tumor grade, i.e., not miss a higher grade cancer.

It took eight years for me to accumulate and follow enough patients on active surveillance (AS) to publish our Miami experience [16]. Our team subsequently published several papers emphasizing the safety and benefits of AS for low-risk PC [17–21]. During the first few years I biopsied these men annually but after I gained confidence that the PSA and digital exam were reliable indicators of progression, I minimized biopsies but see these men every four months and suggest an magnetic resonance imaging or biopsy when there is a significant increase in the PSA. I have entered men as young as 40 years old into the AS protocol and in my patient population the treatment rate is less than 10-15%. Lower than published by others. Very few drop out of AS because of concern of cancer progression. I have followed many of these men for over 15 years and am currently monitoring over 250 men on AS. I do not believe any of those entered on AS died of PC! Increasingly we understand that men with GS 6 PC do not die of PC. Although AS has become widely accepted for men with low-risk PC I recently read that in the USA 40% of men with low-risk GS 6 PC are still being treated with RP or radiation therapy. I have indeed witnessed a dramatic evolution of our management of PC over my 47 year career.

Surgery for renal cancer

One of the more challenging operations performed by urologists is the removal of large renal tumors particularly when the tumor involves the renal vein and vena cava or are very bulky with many parasitic vessels. If the tumor is in the upper pole the surgery can be more difficult because of the proximity of the liver, spleen or even the pancreas. Injury to one of these organs can increase the blood loss and may result in a splenectomy on the left or a liver injury. While I was in Memphis in the 1980s I watched one of the liver transplant surgeons, Santiago Vera, mobilize the liver and realized this maneuver might facilitate removing large retroperitoneal masses, e.g., kidney or adrenal tumors. We began operating together and the improvement in perioperative morbidity and especially minimizing blood loss was apparent. When



Figure 2. Willet Whitmore, Jr., the father of urologic oncology at Memorial Sloan Kettering in NYC, Tadao Nijijima, the chair of Urology, University of Tokyo, and the author.

I moved to Miami, I developed a close relationship with Gaetano Ciancio who was a resident in urology. After completing the urology residency, he took a two year fellowship in kidney and liver transplant at The University of Miami. Recalling my experience in Memphis I collaborated with him on hundreds of complex cases involving a large retroperitoneal mass over a 19 year period. Most were renal cancers with an inferior vena cava thrombus. Gaetano, a brilliant surgeon, has published extensively on the approach of using liver transplant techniques for the improvement of surgical removal of large renal cancers often with IVC thrombus [22–28].

Message

It has been a privilege to have been a participant in the many changes in the way we approach our urologic cancer patients over the past 50 years. As I am still practicing urology full time it seems that the improvements are accelerating. Nonetheless we have much to learn. There remains a great deal of judgement that comes with helping our oncology patients make the best decision for themselves. Many patients still present with locally advanced cancer and a multidisciplinary approach is required for most of these patients. We have a lot of responsibility to keep aware of progress and be mindful that many of our decisions may have a major quality of life impact on our patients. Hopefully this is for an improvement of their longevity with as minimal side effects as possible. This is often a delicate balance and it is our obligation to provide an understanding of the consequences of these management decisions.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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