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Invited Commentary | Imaging

The Evolving Paradigm of Prostate Cancer Screening

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The 1987 report by Stamey et al[1] showing that prostate-specific antigen (PSA) levels correlate with prostate cancer volume ushered in the modern age of prostate cancer management. Four years later, Catalona et al[2] published results from a large case series analysis showing that men undergoing biopsy as the result of an elevated serum PSA level frequently harbor prostate cancer. Shortly thereafter, screening for prostate cancer with serum PSA level became the standard of care in North America, and the incidence of prostate cancer tripled.[3] Equally important, clinicians during this era considered all cancers identified by PSA testing to be clinically significant; as a consequence, most of the men who received a diagnosis of prostate cancer underwent treatment with surgery or radiation. Unfortunately, many of these men experienced incontinence, impotence, or bowel dysfunction as a result.

Many European countries, especially the United Kingdom, were much more hesitant to adopt PSA screening. Urologists in Scandinavian countries recognized that men with well-differentiated prostate cancer often lived many years with their disease without symptoms. They organized the Scandinavian Prostate Cancer Group 4 trial and the Goteborg Randomized Screening Trial to determine the relative efficacy of screening and treatment.[4] During the 1990s, the Goteborg screening trial joined with several other European screening trials to form the European Randomised Study of Screening for Prostate Cancer,[5] which evaluated whether PSA testing could decrease prostate cancer–associated mortality. Shortly thereafter, 3 clinician researchers in the United Kingdom organized an even more ambitious study, the Prostate Testing for Cancer and Treatment trial,[6] which explored the combined impact of PSA screening and treatment on prostate cancer–associated mortality.

Central to the proliferation of PSA screening in North America and Europe was the development of 2 important tools: the transrectal ultrasonography probe and the spring-loaded biopsy needle. These 2 advances help facilitate the performance of transrectal ultrasonography and prostate biopsy in the office setting. A sextant biopsy technique evolved over the next 2 decades to a 10- to 12-core standard transrectal biopsy template.

The consequences of widespread treatment of screen-detected prostate cancer became increasingly evident about a decade ago. Clinicians and researchers recognized that there are many indolent prostate cancer tumors in older men. Most of these cancers are well differentiated and rarely progress to clinically significant disease. These cancers are often described as Gleason 3 + 3 tumors or Gleason grade group 1 tumors. Less-differentiated cancers, Gleason 3 + 4 and higher tumors (Gleason grade groups 2-5), are less common and are more likely to progress during a patient's lifetime. This is what Elwenspoek et al[7] mean by "clinically significant" prostate cancer. The PSA test is sensitive, and widespread PSA testing has led to the diagnosis of many clinically insignificant prostate cancers. Estimates suggest that more than one-half of the cancers identified by PSA testing are indolent and do not require treatment.[8]

Clinicians and researchers have tackled this public health crisis with 2 important innovations to decrease the likelihood of treating indolent disease.[9] One approach has involved the development of genetic markers that are designed to differentiate patients who have clinically significant disease from those who do not. Validation of these genetic tests has been problematic. Another approach has involved the development of imaging that allows urologists to target prostate abnormalities

rather than randomly obtaining biopsy samples. Multiparametric pelvic magnetic resonance imaging (MRI) has become the preferred modality.

Clinicians in the United Kingdom were some of the first to propose an alternative paradigm to the traditional approach of subjecting men with an elevated PSA level to transrectal ultrasonography and prostate biopsy.[10] They suggested restricting prostate biopsies to only MRI-targeted lesions. They argued that this approach has a higher likelihood of identifying clinically significant lesions while bypassing clinically insignificant disease and, as a consequence, lessening the overdiagnosis of prostate cancer that has been associated with the traditional practice of randomly sampling the entire prostate. Many urologists outside the United Kingdom have been skeptical that MRI could identify all clinically significant lesions, thereby prompting the initiation of several randomized trials.

The article by Elwenspoek et al[7] summarizes the findings of 7 randomized clinical trials evaluating whether the traditional technique of obtaining 10 to 12 biopsy cores distributed within the prostate is superior to a technique that biopsies only lesions seen at MRI. The clinical trials differed in many respects, but the overarching conclusion is that targeted biopsies appear to be much better at identifying clinically significant disease while avoiding clinically insignificant disease than techniques that sample the entire prostate. The concept of obtaining a prostate MRI study after an elevated PSA level but before a biopsy is conducted is well supported by the trials reviewed.

As the prostate cancer screening paradigm shifts, several new issues are raised. First, what is the best MRI sequence and how large a magnet is needed? Does a 1.5-T magnet perform as well as a 3.0-T magnet? Is a multiparametric approach the best, or can MRI be performed without the use of contrast agent, saving patients time and possible complications? Frequently, the T2-weighted and diffusion-weighted images are sufficient to identify clinically significant lesions. What biopsy approach should be taken, transrectal or transperineal? The transrectal approach is simple to perform, but risks include bleeding and sepsis. Furthermore, the anterior and apical portions of the prostate can be difficult to sample. The transperineal approach can access these regions more easily, but often requires more complex equipment and anesthesia. Finally, how should a surgeon merge the images seen at MRI with the ultrasonography image at biopsy? Can this be done cognitively by simply viewing both images at the time of biopsy, or does this require computer-driven fusion software?

The public health crisis of prostate cancer overdiagnosis demands a change in the current PSA screening and biopsy treatment paradigm. The systematic review and meta-analysis by Elwenspoek et al[7] offers strong support for an alternative approach that calls for a prebiopsy MRI. This new approach raises important questions, but overall this analysis provides an excellent summary and discussion of the next step in the continually evolving paradigm of prostate cancer screening.

ARTICLE INFORMATION

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