PROSTATE CANCER

Proponents of PSA screening boosted by new study

Over the past several months the issue of whether or not to continue PSA screening has been discussed by the world's leading urologists. The latest debate was prompted by the release of the US Preventive Services Task Force (USPSTF) guideline that recommended against screening. The guideline, which we reported on previously (New PSA screening guideline faces widespread opposition. *Nat. Rev. Urol.* 9, 351; 2012), was motivated by analyses of two clinical trials that weighed the mortality benefits of screening against the adverse effects associated with prostate cancer treatment. A new registry-based study by Edward Messing *et al.* has provided additional evidence in support of PSA screening.

The study sought to determine whether the number of patients diagnosed with metastatic prostate cancer has been affected by PSA screening. Using the Surveillance, Epidemiology, and End Results (SEER) database, they extrapolated the diagnoses in the immediate pre-PSA era (1983–1985) to the US population of the latest SEER data (2008). In doing so, the influence of PSA testing on diagnosis could be estimated. “We used metastatic prostate cancer because it is

an invariably fatal, highly symptomatic, costly to treat condition that, if untreated, rapidly becomes symptomatic,” Messing explained. “Such a condition would be very unlikely to have been overlooked in the pre-PSA era, or today.”

According to the SEER data, ~8,000 men were diagnosed with metastatic prostate cancer in 2008. This number pales in comparison with Messing's estimate if PSA screening was not used: ~25,000 men. The more than threefold difference is in agreement with the results of the European Randomized Study of Prostate Cancer Screening, in which the control group of men who did not undergo screening had three times the number of cancer diagnoses of the group that was screened. “We concluded that PSA can effect a significant shift to an earlier stage at diagnosis, which is all one can expect a screening test to do,” finished Messing.

The challenge now is to understand if and how this estimate can inform clinical practice. Most physicians would argue that many of the treatments for prostate cancer are aggressive and, in light of the results of the PIVOT study, perhaps unnecessary for most men with a prostate cancer diagnosis. Indeed, a new study of the Swedish and US

cancer registries has determined that men with prostate cancer are less likely to die from their cancer than other causes. “The majority of men diagnosed with prostate cancer by PSA screening are diagnosed with localized, low-risk disease that is not life-threatening,” commented lead author Mara Epstein. Despite this, many patients choose to undergo aggressive treatments, which are detrimental to their health and do not provide a significant survival benefit. This paradoxical situation, where treatment makes the patient worse off, is one reason opponents of PSA screening take their position.

But is this a sufficient reason to stop screening? A PSA-based diagnosis of prostate cancer can be a springboard for patients to make significant lifestyle changes that will reduce their risk of competing causes of death, such as diabetes mellitus. “Encouraging healthy lifestyle modifications at diagnosis will improve the overall health of men with prostate cancer, increasing both their duration and quality of life beyond that achieved with aggressive cancer treatment alone,” commented Epstein. Without even the option of the PSA test, men lose the opportunity to be diagnosed early, receive appropriate management and be cured. Director of the Vanguard Urologic Institute in Houston, TX, USA, Kevin Slawin, who was not associated with either study, agrees. “A strategy that reduces the complications of treatment for more clinically significant disease, as well as improves the overall health of patients, might be a more effective strategy for capturing the benefits and limiting the harms of PSA-based screening.”

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Original articles Scosyrev, E. *et al.* Prostate-specific antigen screening for prostate cancer and the risk of overt metastatic disease at presentation. *Cancer* doi:10.1002/cncr.27503 | Epstein, M. M. *et al.* Temporal trends in cause of death among Swedish and US men with prostate cancer. *J. Natl Cancer Inst.* doi:10.1093/jnci/djs299

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