Prostate cancer screening clinical brief health essay

Health & Medicine

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Background:

Prostate specific antigen (PSA) is a molecule specific to cells found in the male prostate gland. A cancer in the prostate disrupts the cells and results in this antigen being released into the blood <1>. The levels of PSA can be measured by a simple blood test. PSA levels can go up for reasons other than cancer such as an enlarged prostate, which happens as men age, prostatitis or an infection of prostate, a digital rectal exam, urine retention, ejaculation or even bicycle riding <2>. Currently a PSA level at or above 4. 0 ng/mL makes physicians suspicious for prostate cancer <2>. The PSA test was originally developed for men who had been treated for prostate cancer to check for recurrence of prostate cancer <3> and in alleged cases of rape where the presence of PSA was used to prove that insemination had occurred <2>. Another groups of scientist found that a rise in PSA could be used to predict the likelihood of developing prostate cancer. At the same time, prostate cancer incidence and mortality had been going up steadily. The PSA test was approved by the FDA in 1994 to be used as a screening tool to detect prostate cancer in healthy men with no symptoms of prostate

cancer <4>. The large number of PSA screenings in 1990s saw countless men diagnosed with prostate cancer at an earlier stage than ever before and led to improved survival. Most men over the age of 50, in the United States, have had a PSA, despite the absence of evidence of any large randomized trials showing net benefit <5>. A survey shows that a majority of urologists and primary care physicians who were 50 or older have opted for a PSA test themselves <5>. With improved cure rates, the physicians also noticed that some men suffered serious long term side effects including incontinence and sexual dysfunction. This was the start of a prostate cancer screening controversy which refuses to die out <4>. In order to settle this controversy and measure the risk-benefit ratio of prostate cancer screening, two large trials – The Prostrate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Study of Screening for Prostate Cancer (ERSPC) were started. The controversy was only further muddied by the preliminary results from these studies as they failed to provide a clear answer to the burning question; " Does PSA blood test saves life or exposes men to unnecessary anguish?" <6>. In the absence of evidence, it is no surprise that various medical association and government guidelines range from suggesting absolutely no screening to annual screening starting at age 40 <4>. In this clinical update, we try to look into the evidence, debate and controversy surrounding prostate cancer screening.

Why the controversy – PLCO and ERSPC

The preliminary results from the two largest studies, PLCO and ERSPC, were published in the New England Journal of Medicine in 2009 <6>. More than 250, 000 men were randomized in these two trials and form the basis of

prostate cancer screening recommendation. Although the two studies had similar objectives and endpoints, they were in stark contrast in the way they were setup and interpreted (Table 1). The PLCO trial reported no mortality benefit during the 11 year follow up, while the ERSPC trial showed that PSA screening without DRE was associated with a 20% relative risk reduction (7/10, 000 absolute reduction) in mortality at 9 year follow up. The findings from both the trials findings were not definitive, a clear declaration of futility was amiss from PLCO while the net benefit in the ERSPC was ambiguous at best. Both studies are currently ongoing and continue to follow up on patients. Table 1: PLCO vs ERSPC <4> PLCOERSPCOriginUnited StatesEuropePatients76, 693182, 000Age range55-74 years55-69 yearsGroupsAnnual PSA and DRE vs. " usual care" PSA and DRE every 4 years vs. no screening% screened before enrollmentNearly 70%Unknown, likely smallControls screened (contamination)*52%15%Median follow-up7 years9 yearsIncreased change of prostate cancer diagnosis17%39%Risk of over diagnosis23%> 70%Number of prostate cancer deaths174540OutcomeNo significant difference in prostate cancer death20% reduction in prostate cancer death (increasing with time)*Refers to patients who went outside the trial for a screeningAnother significant controversy arises when we look at the number of prostate cancer deaths between 1981 and 2012. The absolute number of prostate cancer deaths in the United States has actually gone up (20, 790 in 1981, 25943 in 1989, and , 28170 in 2012) <7, 8, 9>. Interestingly the number that is actually reported is the rate of prostate cancer deaths which has plummeted. The reason for this discrepancy is simple, PSA test find a large number of cancers which would

not have affected mortality in most patients. For example, before the advent of PSA test 10 men might have died due to their prostate cancer out of a hundred diagnosed cases, giving us a death rate of 10%. Compare this to the post PSA test era where we can have the same number of patients dying but with an increased diagnose rate, example 200, the death rate becomes 5%.

PSA test – more than just a number

Regular PSA screening at best has a modest benefit in terms of mortality in the first decade of follow up and causes over diagnosis and over treatment in patients. Due to the unclear nature of the risk and benefit ratio of PSA screening, most guidelines recommend a shared decision-making approach where the patient is educated to make an informed decision <3>. Another school of thought calls for proper PSA testing. They believe that the problem is the improper interpretation of PSA results ad not the PSA test itself. Most men tested for PSA are never informed or educated about the subtle factor such as ejaculation, DRE or bicycle riding that may falsely elevate their PSA levels <2>. This in turn can account for over diagnosis and over treatment in many cases. Also diurnal variations in PSA levels should be considered and taken into consideration. Lastly they call for better utilization of various PSA derivative tests such as Free PSA percentage test, PCA-3 test, change in PSA values and rate of change over time to add important information to build a complete picture of PSA screening <2>.

Current approach

The current non-targeted approach to prostate cancer screening is probably not optimal and could explain the lack of benefit seen in PLCO and ERSPC

trials. Better approaches to identify patient at the greatest risk for prostate cancer combined with improved strategy for screening would be instrumental in improving the risk benefit ratio of prostate cancer screening <10>. Further evidence from the PLCO and ERSPC trial along with data generated from other trials such as Prostrate Cancer Intervention Versus Observation Trial (PIVOT) and Prostate Testing for Cancer and Treatment (PROTECT) will be useful to come to a clear conclusion regarding PSA screening <5>. In the meantime, an individualized, multifactorial approach to determine whether or not to screen an individual seems to be ideal <11>. This approach can begin at as early as 40 years of age depending on patient’s medical history and medical comorbidities among other factors. The decision to get a PSA test is the one that requires careful consideration and consultation with a family physician. A follow up plan should be discussed with the patient during the initial discussion as the result could have a significant effect on the lifestyle of the patient. Considering that majority of the prostate cancers detected with screening are low risk, an active surveillance approach may help in reducing over treatment and avoiding associated side effects.