Prostate Cancer

Prostate cancer is a leading cause of cancer morbidity and mortality in the U.S. Considerable effort has gone into public health programs designed to increase screening by digital rectal exams and prostate specific antigen testing – much to the dismay of men on their 50th birthdays. In fact, the U.S. health care system is good at detecting early prostate cancer in the population, and U.S. five-year prostate cancer survival rates are among the best in the world. There is, however, a dark side to this apparent success story – we are taking biopsies from and subsequently treating lots of men who will never develop clinical disease. This has real consequences for patients and society – these invasive procedures frequently induce considerable morbidity (occasionally mortality) and are costly. Close to home - but for having someone in his family looking over his shoulder, my 70-year-old father would have had a radical prostatectomy three years ago for a "mid-grade" cancer. This would have occurred in a reputable community hospital by a well meaning surgeon following guidelines and convinced he was doing the right thing. Today my father is hale and hearty, and is about to go back to yearly surveillance – without life-altering intervention.

Ideally, prostate cancer screening methods should be developed that have a high sensitivity and specificity for distinguishing prostate cancers that will become symptomatic. Over the last few years, there have been a number of advances to that end. First, genome-wide association studies have identified well over a dozen genetic markers that are associated with prostate cancer risk. At least a few of these markers appear to be associated with more aggressive forms of the disease. This has led to several lines of investigation, including a re-examination of genetic marker associations with biopsy grade of prostate cancer in previously collected patient cohorts. Additionally, studies are getting underway to look at how a combination of genetic markers and clinical risk information might enhance the performance of PSA testing.

Investigation of biomarkers for prostate cancer has also accelerated. Recently, attention has focused on the use of screening panels of metabolic markers, including the molecule sarcosine (a marker that appears to be associated with more advanced disease), to come up with more effective screening for more aggressive disease. Somatic (non-germ line) DNA markers for prostate cancer are also detectable in urine, including the marker PCA-3 – this DNA marker, when elevated, is specific but not highly sensitive for prostate cancer in urine. It seems likely that, over time, a panel of tests will emerge that provide enhanced prostate cancer screening.

In the realm of primary prevention of prostate cancer there has been a recent re-analysis of data from a study that examined prostate cancer chemoprophylaxis using finasteride in in the context of the Prostate Cancer Prevention Trial (PCPT). The initial analysis of this data was disheartening – it appeared that the drug actually increased the risk of more aggressive cancers. Several recent re–analysis of the data, with proper corrections for the study design, suggest that the drug could reduce prostate cancer risk by about 25% - not inconsiderable given that about one in six males is likely to develop the disease (see: http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_052708/page2) .

However, this approach to prostate cancer prevention would be costly if untargeted, both in terms of dollars and side effects.

The next leap in prostate cancer prevention and screening will occur when studies are developed that look at the effectiveness of different strategies for prevention and screening through the lens of individual genomic information. For example, it is plausible that certain screening tests reduce morbidity and mortality most effectively when applied to individuals with a specific genetic risk profile. Likewise, it is reasonable to think that individual genotypes might predict the benefits or side effects of preventive measures like the daily use of finasteride. The cost of genotyping is no longer much of a barrier to studies that can address these issues – which is a great contrast to five years ago.

Returning to my personal anecdote, one might argue that a genomic profile wasn't needed in my father's case– it appears that the right call was made without any hi-tech testing. However, genomic discoveries are being made on a daily that promise to reduce the uncertainty in the decision process, and I for one sleep better for it.