Tool Estimates Absolute Risk of Prostate Cancer

BY BRUCE JANCIN

DENVER — A man's absolute risk of developing prostate cancer over a 20-year period can be estimated by determining the number of risk alleles present on a simple genetic test and then taking into account the presence or absence of a family history.

It's known that an average 55-year-old man has a 13% risk of developing prostate cancer during the next 20 years. But by adding up how many of 14 known risk alleles the man has on single-nucleotide polymorphisms, his risk can be defined far more accurately.

For example, a man with seven or fewer of the risk alleles plus a negative family history has only an 8% absolute risk of being diagnosed with prostate cancer at age 55-74. The risk shoots up to 52% in a man with 14 risk alleles and a positive family history, Dr. Jianfeng Xu explained at the annual meeting of the American Association for Cancer Research.

By adding up how many of 14 known risk alleles a man has, his risk can be defined far more accurately.

DR. XU

This latter highest-risk group includes 8% of the general adult male population, noted Dr. Xu, professor of epidemiology and cancer biology at Wake Forest University, Winston-Salem, N.C.

He and his coworkers developed their risk model by studying 2,893 men with prostate cancer and 1,781 without the disease who had previously participated in a Swedish case-control study. The investigators demonstrated that while each of the risk alleles contributed a relatively small increase in prostate cancer risk, the risk was additive.

Moreover, the risk was further enhanced in a predictable way by the presence of a positive family history. For example, the 20-year absolute risk in a man with seven or fewer risk alleles and a negative family history is a mere 8%, but it rises to 17% with a positive family history. At the other extreme, a man possessing 14 risk alleles but a negative family history has a 24% risk of being diagnosed with prostate cancer at age 55-74; having a positive family history increases that risk to 52%.

The investigators subsequently confirmed their findings in a retrospective analysis of data from the large Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

Dr. Xu conceded that the current risk model has a major limitation: It doesn't distinguish between indolent and aggressive forms of prostate cancer. Thus, using the model would likely result in overtreatment of many men identified as being at high absolute risk, but who have indolent disease. The investigators have identified several candidate single-nucleotide polymorphisms that do appear to distinguish between nonaggressive and lethal prostate cancer, however, and are now undergoing confirmatory testing.

Even if these new candidate risk alleles don't pan out, Dr. Xu said he sees the current version of the absolute risk assessment as having potential utility. For example, men identified as high risk might elect to embark on a program of risk reduction through diet and lifestyle modification along with chemoprevention using finasteride, which has been shown to reduce prostate cancer risk by about 25%.

For men at average risk—that is, those with 11 risk alleles and no family history of the disease—finasteride could reduce their 20-year absolute risk from 13% to 10% at the cost of roughly $1.6 million per life-year gained. But for men at very high risk, the absolute risk reduction conferred by finasteride would be substantially greater and, as a result, the cost per life-year gained, lower, Dr. Xu noted.

"Even if it were not possible to separate the indolent from lethal disease, the fact that you're preventing those people from getting prostate cancer means they can avoid making difficult decisions about whether to biopsy, whether to remove the prostate," he said. ■