PROSTATE CANCER

The IMPACT of *BRCA2* in prostate cancer

Men with *BRCA2* mutations had a significantly increased cancer incidence rate per 1,000 person years

Men with *BRCA2* mutations are more likely to be diagnosed with clinically significant prostate cancer than those without, according to new data published in *European Urology*. Thus, men with germline pathogenic *BRCA2* mutations might benefit from systematic PSA screening.

The IMPACT study is an international trial involving men at increased risk of developing prostate cancer as they harbour pathogenic mutations in *BRCA1* and *BRCA2*. *BRCA2* mutations in men are known to be associated with an increased risk of early-onset and clinically significant prostate cancer. Furthermore, germline *BRCA2* status is an independent prognostic factor for prostate cancer outcomes. However, the influence of *BRCA1* mutations on prostate cancer is unclear. Participants included in the IMPACT study receive targeted annual PSA screening to determine the prostate cancer incidence in men who have these germline mutations.

The recently reported interim analysis included 2,932 unique individuals, comprising 919 men with *BRCA1* mutations and

709 without; 902 men with *BRCA2* mutations and 497 without — 95 men without *BRCA2* mutations who were sequenced for both *BRCA1* and *BRCA2* mutations were included in both control cohorts.

Overall, 2,932 men had a PSA screening test at baseline. Of these men, 228 (7.7%) had serum PSA levels >3.0 ng/ml and cancer was diagnosed in 69 (2.4%) via biopsy sampling. After four PSA screening tests, PSA levels >3.0 ng/ml were found in 527 men (18%) and prostate cancer was diagnosed in 112 men using biopsy sampling. The overall prostate cancer detection rate was 3.8% (112/2,932) and the rate of prostate cancer incidence per 1,000 person years was 15.

Analysis by cohort showed that, in the *BRCA2* group, prostate cancer was diagnosed in 47 men with mutations and in 15 without. Prostate cancer incidence rate per 1,000 person years was 19 in men with mutations and 12 in those without, which was significantly different ($P=0.031$). Positive predictive value (PPV) of PSA >3 ng/ml was 31% in *BRCA2* mutation carriers versus

18% in noncarriers ($P=0.025$). In comparison, PPV of prostate biopsy was 39% and 28% in mutation carriers and noncarriers, respectively.

In the *BRCA1* group, 31 men with mutations and 19 men without were diagnosed with cancer. The rate of prostate cancer per 1,000 person years was 14 in men with mutations and 11 in those without, which was not significantly different ($P=0.300$). The PPV of PSA >3 ng/ml was 23% and 15% in *BRCA1* mutation carriers and noncarriers, respectively. By contrast, PPV of prostate biopsy was 32% in men with *BRCA1* mutations and 20% in men without.

Prostate cancer was diagnosed at a younger age in men with *BRCA2* mutations (61 years) than in men without (64 years). Furthermore, 37 of 48 *BRCA2* carriers with prostate cancer were diagnosed with intermediate-risk or high-risk disease compared with 6 of 15 noncarriers. Age and risk category at diagnosis did not differ between men with and without mutations in the *BRCA1* cohort.

These interim results show that the trends seen at baseline screening strengthen after 3 years of follow-up monitoring. The role of screening in men with *BRCA1* mutations is still unclear. Men with *BRCA2* mutations had a significantly increased cancer incidence rate per 1,000 person years, are diagnosed at a young age and are likely to have clinically significant disease. Thus, these men might benefit from systematic PSA screening.

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ORIGINAL ARTICLE Page, E. C. et al. Interim results from the IMPACT study: evidence for prostate-specific antigen screening in *BRCA2* mutation carriers. *Eur. Urol.* <https://doi.org/10.1016/j.eururo.2019.08.019> (2019)

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