

Risk of prostate cancer in ICSI treated men

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Study question:

At what risk for prostate cancer are clinically sub-fertile men who have undergone ICSI as compared to men conceiving naturally?

Summary answer:

Men who had undergone ICSI had a statistically significant increased risk of prostate cancer, in particular, early-onset prostate cancer, compared to men conceiving naturally.

What is known already:

Register-studies have reported lower risk of incident prostate cancer for childless men than biological fathers. Other studies have indicated that men with impaired fertility are at higher risk for prostate cancer than fertile men. The majority of the men undergoing ICSI treatment are subfertile and since they are in contact with the health care system, these men are well suited as target for preventive measures.

Study design, size, duration:

This register-based study sourced data from the Swedish Medical Birth Register, the Swedish Cancer Registry, and the Swedish Quality Register for Assisted Reproduction. All fathers and their first child born 1994-2014 were identified. ICSI fathers were compared to those who had become fathers by natural conception (controls) and IVF fathers regarding incident prostate cancer during a follow up of total 51990101 person-years until 2016. Sensitivity analysis stratified upon age at diagnosis of prostate cancer.

Participants/materials, setting, methods:

Among all fathers (n=1 181 490), 20 618 and 14 882 had undergone IVF and ICSI, respectively; and 3 211 were diagnosed with prostate cancer. Associations between mode of conception (ICSI/IVF/natural) and subsequent prostate cancer were investigated using Cox regression models with their date of birth as start of follow-up and adjusted for education level. Early and late-onset prostate cancer was defined according to age at diagnosis: ≤50 and >50 years.

Main results and the role of chance:

Fathers who had undergone ICSI had a higher risk of prostate cancer (at any age) as compared to controls (HR=1.47, CI 95% 1.15-1.89; p=0.002). Conversely, IVF-men did not have an increase in prostate cancer risk when compared to controls (HR=1.14, CI 95% 0.91-1.43; p=0.25).

When stratified into age groups at cancer, the fathers who had conceived through ICSI had higher risk for early-onset prostate cancer (HR=2.94, 95% CI=1.84 - 4.71; p<0.001) i.e. diagnosed before 50 years of age. However, ICSI-men did not have an increased risk for late-onset prostate cancer

compared to controls. No increased risk of early onset PCa was detected for IVF-fathers (HR=1.06, 95% CI=0.57 - 1.98; p=0.86).

In sensitivity analysis excluding fathers who were diagnosed with cancer prior to their offspring conception date, ICSI-fathers still had a statistically significant increased risk of PCa (HR=1.32, 95% CI=1.01 - 1.72; p=0.045) and of early onset PCa (HR=2.54, 95% CI=1.52 - 4.24; p<0.001).

Limitations, reasons for caution:

Even with a cohort of this size, the prostate cancer cases within the ICSI group were quite limited (n=63). The study design did not allow inclusion of the heterogeneous group men who had never fathered children.

Wider implications of the findings:

The results show immense risk for early-onset prostate cancer, generally considered more aggressive, in men referred for ICSI. These men may already have a latent tumor at the time of ICSI, why the possible benefits of targeted screening could be considered.

Trial registration number:

N/A

Yes

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