A gene mutation can radically alter the chances of survival for men with prostate cancer, new research has found.

Men who carry a mutated form of the BRCA2 gene seem to succumb to this type of cancer a decade earlier than those with a most common version of the gene.

Experts say that screening for the BRCA2 gene mutation – which is better known for raising the risk of breast cancer – could improve the outcome of prostate tumour treatment.

Our knowledge of BRCA2 dates back to 1995, when researchers first identified this gene and began to understand its effect on breast cancer. Women with mutations in either BRCA2 or the related BRCA1 gene face up to a seven-fold increase in the risk of breast cancer.

In recent years, scientists have started to piece together how BRCA2 mutations also influence men’s health.

Doubled risk

Studies have found that men who carry certain variants of BRCA2 face a doubled risk of prostate cancer, and are six times more likely to develop pancreatic cancers than people with a normal version of the gene.

Laufey Tryggvadottir at the Icelandic Cancer Registry in Reykjavik and her colleagues decided to see if the BRCA2 mutation had any impact on the progression of prostate cancer once it developed.

According to the Prostate Cancer Foundation, prostate cancer strikes one in six men in the US. And Tryggvadottir says that when doctors conduct autopsies of elderly men who have died from a wide range of causes, including traffic accidents, they find cancerous prostate cells in two-thirds of these men.

But she stresses that only a fraction of men die as a result of prostate tumours: "The big challenge today is how to distinguish between a lethal cancer and a harmless one."

Howard Soule of the Prostate Cancer Foundation in Santa Monica, California echoes this view: "It would be helpful to know whose prostate cancer is aggressive and whose cancer is non-lethal."

Radically shorter

To help address this challenge, Tryggvadottir and colleagues retrieved prostate cancer biopsies that had been taken from 527 patients and deposited in their registry over the past few decades.

Researchers analysed the DNA in these samples and found that 30 of the men tested positive for a BRCA2 mutation, known as 999del5. Men with this mutation had an average survival time of 2.1 years following their cancer diagnosis – a decade shorter than patients with the normal gene, who lived 12.4 years on average.

"That's radically different," says Soule, who adds that patients would likely want to know which of these dramatically different prognoses applies to them.

Moreover, the new study revealed that carriers of the inherited gene mutation received their cancer diagnosis at an average age of 69 – five years earlier than those free of the mutation.

This indicates that the cancer developed earlier, so Tryggvadottir suggests that men with a history of BRCA2-related breast cancer in their family begin prostate screening at age 45, a few years before the generally recommended age of 50.

Watchful waiting
She adds that having a faulty version of the \textit{BRCA2} gene makes cancer more likely because the gene encodes for a protein involved in DNA repair.

Typically, if a man has high levels of prostate-specific antigen (PSA), doctors will conduct a biopsy of the organ. If the cells' DNA looks relatively normal, physicians recommend a period of "watchful waiting", because removal of the prostate can lead to unwanted side effects, including impotence and urinary incontinence.

Soule says that the new findings represent a step towards that goal of having "a test to know who should have their prostate removed today and receive aggressive therapy, and who should have watchful waiting". Immediate surgery and chemotherapy can prevent the tumour from spreading through the body.

Researchers estimate that 0.5\% of men in Iceland carry the 999del5 \textit{BRCA2} mutation, and that a similar proportion of men through the world carry this or other \textit{BRCA2} mutations.

While the overall percentage of men who have the mutation is small, Tryggvadottir says these men likely represent a large number of those with lethal prostate cancer. Each year 28,000 men die of prostate cancer in the US alone, according to Soule.

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