Prostate cancer is one of the most common cancers in men, with a high mortality late after middle age. In Japan, it has become clinically very important because of the increasing number of patients. Moreover, a recent study has shown that prostate cancer mortality age-standardized rates have been constantly and dramatically increasing from 1960 to 2000 in Japan, and the differences between these rates in Japan and other countries have recently diminished (Fig 1). Serum prostate-specific antigen (PSA) is the most sensitive biochemical marker for early detection of prostate cancer. Radical prostatectomy and radiation therapy are the common therapies, though androgen deprivation therapy is also considered to be a treatment option because normal prostate growth is dependent on testicular androgens.

The results of the study by Haruta et al published in this Journal indicate the interesting possibility that male patients with Brugada-like ECG have a high risk of prostate cancer. Haruta et al identified 34 Brugada-like ECG cases in 2,681 male atomic bomb survivors from a biennial follow-up conducted by the Radiation Effects Research Foundation since 1958. After adjustment for other risk factors (smoking habit and radiation dose), Brugada-like ECG remained a significant risk factor for prostate cancer (relative risk: 6.47). This finding is valuable for assessment of the risk of prostate cancer based on surface 12-lead electrocardiography. Brugada syndrome is a distinct form of idiopathic ventricular fibrillation characterized by a unique ECG pattern, consisting of ST segment elevation in precordial leads V1–3. Mutation in the cardiac sodium channel, SCN5A, has been reported to be causally linked to familial Brugada syndrome. Therefore, there should be equal inheritance in males and females, but a clear male predominance in phenotype and symptoms has been reported. Although the precise mechanism of this unique ECG pattern is still unknown, many agents and conditions have been reported to, or are expected to, unmask the Brugada ECG phenotype. ST segment elevation

Sex hormone is a candidate for unmasking the Brugada ECG phenotype. Matsuo et al, in the same group of investigators, first reported 2 cases of asymptomatic Brugada syndrome (these patients were included in Haruta’s study) that displayed a typical Brugada phenotype, but in which the typical ECG pattern disappeared following surgical castration for prostate cancer; removal of testes was associated with loss of Brugada-like ECG. In addition, Shimizu et al showed that a higher testosterone level associated with lower percentage of visceral fat may be related to Brugada phenotype and male predominance. The results of the study by Haruta et al would also contribute to an understanding of gender-related phenotype variations in Brugada syndrome.

It has been reported that gender-related differences exist in the human ECG, especially in cardiac repolarization and genesis of arrhythmias, notably in long QT syndrome and Brugada syndrome. The mechanism has not been fully elucidated, but gonadal steroids would be directly involved in gender-related differences. These steroid hormones are lipophilic and readily enter cells by crossing the cell membrane. Binding of the hormone to the receptor protein in the cytosol results in dimerization of the receptor and its translocation to the nucleus, where the activated receptor binds to hormone-receptor-specific response elements on DNA.
and subsequently catalyzes transcription of the target gene. It has been reported that testosterone influences expression of the cardiac L-type $\mathrm{Ca}^{2+}$ channel in male rats. An androgen-responsive element in the human SCN5A gene that encodes the cardiac sodium channel has been identified. It has also recently been reported that testosterone modulates sodium current dispersion in a canine heart model. In addition, there is evidence that steroid hormones have rapid physiological responses through a non-genomic pathway. Consequently, there is probably a complex interplay of gonadal steroids, genetic and ionic influences. Further experimental/clinical studies are needed.

In conclusion, although the number of patients in the study was small and further study is needed to reach a definitive conclusion, Haruta et al have provided important clinical evidence suggesting that some patients with Brugada phenotype have a high risk of prostate cancer.

**References**


Male cases of Brugada-like electrocardiogram have higher risk of prostate cancer. *Circ J* 2009; 73: 63–68.