

CARDIOVASCULAR DISEASES

All-cause mortality and mortality of myocardial infarction for 989 legally castrated men

Finn Edler von Eyben¹, Christian Graugaard² & Michael Vaeth³

¹Department of Internal Medicine, Herning Central Hospital, Herning; ²Department of Public Health, University of Copenhagen, Copenhagen; ³Department of Biostatistics, University of Aarhus, Aarhus C, Denmark

Accepted in revised form 15 August 2005

Abstract. *Background:* Male gender is an independent coronary risk factor. *Method:* Long-term follow-up of 989 Danish men who underwent legal castration between 1929 and 1968. *Results:* The legally castrated men were unmarried and belonged to social class IV and V more often than were Danish men in general. During the follow-up until 2000, 835 of the 989 (85%) castrated men died, including 148 who died of myocardial infarction. In multiple Poisson regression analyses, the men had a standardized mortality rate (SMR) for all-cause mortality of 1.30 (95% CI: 1.26–1.36) and a SMR for mortality of myocardial infarction of 1.08 (95% CI: 1.04–1.16). Thus, the castrated

men had a lower proportion of deaths of myocardial infarction (148/792, 18.7% (95% CI: 16.0–21.6%)) than was expected based on the mortality rates for the Danish male population (136/608, 22.4%). The castrated men had discordant changes for the SMR for all-cause mortality and mortality of myocardial infarction whereas subgroups of the Danish population previously has been found to have concordant changes for the two SMRs. *Conclusion:* The castrated men had fewer deaths of myocardial infarction than expected, so men may not have increased risk of coronary heart disease from unphysiologically low levels of endogenous androgens.

Key words: All-cause mortality, Castration, Myocardial infarction mortality, Poisson regression

Introduction

Cardiovascular disease is the most frequent cause of death in Western Societies. Male gender is an independent coronary risk factor besides family history, age, smoking, obesity, hypertension, and hypercholesterolemia [1]. For all ages, adult men have higher mortality rates of coronary heart disease than women [2], and the excess mortality of cardiovascular disease contributes to men having shorter median life expectancy than women.

Nevertheless, little is known as to how male gender acts as a coronary risk factor [3–5]. Studies of endogenous androgens have given conflicting findings as to whether androgens contribute to the difference between the two genders in morbidity and mortality of cardiovascular disease. In prospective studies of normal men, physiologic levels of endogenous androgens were not significantly associated with male susceptibility for coronary events whereas some cross-sectional studies showed that coronary heart disease was associated with low levels of endogenous androgens [4, 6]. Studies of surgical castration of men gave conflicting results as to the outcome following the reduction to unphysiologically low levels of androgens. Castration of mentally retarded men decreased the mortality of infectious disease and prolonged survival median 13.6 years but did not reduce the mortality of

heart disease [7]. In contrast, in two randomized studies, castration of men with prostatic carcinoma decreased the cardiovascular mortality [8, 9].

The present study aimed to evaluate 1) whether castration of men changed the risk of all cause mortality in general and cardiovascular mortality in particular, and 2) whether the castration had a dose-response association with the pattern of the two mortalities.

Materials and methods

Study population

In all, 1012 consecutive Caucasian Danish men underwent legal castration between 1929 and 1968. We included 989 (97.8%) men and excluded 23 (2.2%) men due to anonymity, lack of follow-up reports, and treatment with sex hormones or gender-shift surgery after castration, as shown in Figure 1. The number of Danish men recruited for legal castration per year changed markedly during the recruitment period [10].

Our castrated men comprised of three groups. The first and second group had been diagnosed as mentally retarded and psychopaths, respectively, and the third group consisted of the remaining, normal men. A

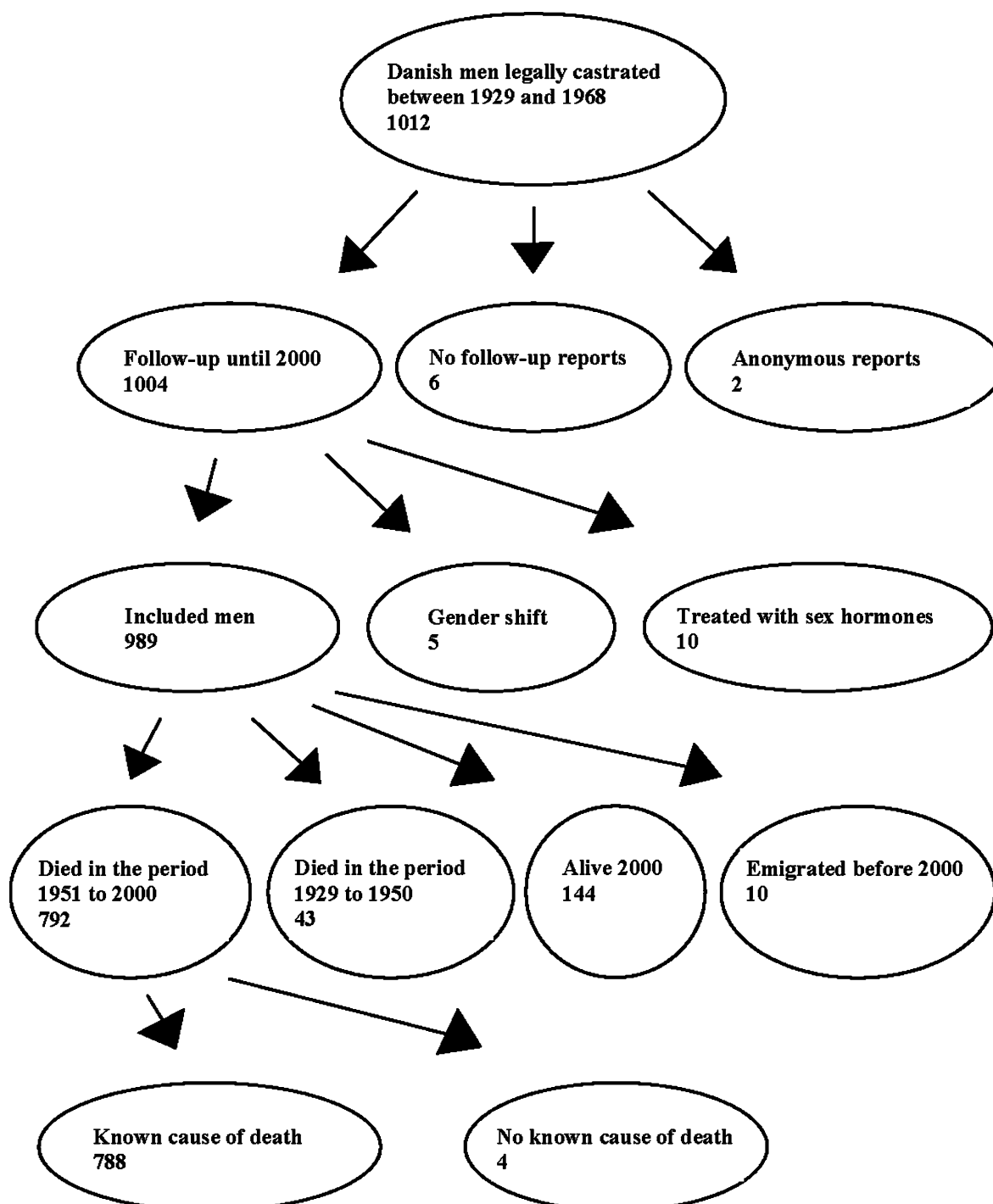


Figure 1. Flow sheet showing the inclusion and exclusion of Danish legally castrated men, and the follow-up as of March 1 2000. The numbers are the numbers of men in the subgroups.

mandatory follow-up examination was carried out within the first year after castration and implied that coronary risk factors like age, social class, obesity, and hypertension were recorded in follow-up forms. As part of our study, one author (FEvE) assessed the social class according to a classification used in previous Danish studies of coronary risk [11]. We calculated the standardized mortality ratio (SMR) using the Danish male population as external reference group.

Follow-up

We set March 1 2000 as census date, calculated the number of person-years at risk from the date of castration to the date of death or the census date, and evaluated two endpoints, all-cause mortality and mortality of myocardial infarction. Ten castrated men emigrated and were included for only the period in Denmark. We used the official Danish coding of