year[5,6]) or in the primary prevention cohort of Japanese with hyperlipidemia treated with simvastatin in the J-LIT study[7] which was 0.86 per 1,000 patients-year. However, the prevalence rate of IFG, hyperlipidemia and hypertension at the time of registration in this study was approximately 40%, 55% and 58%, respectively, which is approximately double or triple the values in the administrative report. These high incident rates of risk factors and of MI are reasonably attributed to the fact that participants in this study had significant coronary atherosclerosis confirmed with CAG.

The present report addressed the gender difference in many clinical profiles such as age, congestive heart failure, IFG, hyperlipidemia, hypertension and fibrinogen, all of which were more frequent or higher in value in females, whereas height, weight, BMI, smoking, history of coronary heart disease, coronary intervention, uric acid and CRP concentration, all of which were more common or higher in males (**Table 1**). These findings are in agreement partly with observations reported elsewhere, in which women presenting with the first clinical symptom are generally older than men[8–12] and have significant higher rates of diabetes mellitus, hypertension and previous CHF.[13]

Men experience worse outcomes than women, with an increased risk of cardiac events[14] but the incidence of unstable angina in the current study was higher in females than males. Contributing factors for unstable angina in this study are hypertension and number of vessel disease other than gender (**Table 3**). Percentage of hypertension was significantly higher in females (**Table 1**). The higher incidence rate of unstable angina in females is somewhat surprising but similar results were reported in patients of CAVEAT-I study.[15] The reasons are speculative. The variability in results probably reflects the mixed populations studied, with differing percentages of patients with non-Q-wave and Q-wave infarction. A smaller percentage of women than men had infarction with ST elevation.[13] Furthermore, parameters used are varied among the studies, and the weights of parameters are influenced by the covariate used.[16]

Most studies report higher mortality after unstable angina[14] or MI[17–23] in women compared to men. This effect is primarily seen in younger women and progressively declines with age, with equivalent outcomes in the elderly.[19] The worse outcome in women is largely related to increased age and greater comorbidity,[9,18,20,22] such as diabetes mellitus and hypertension,[17,24] comparable with our results. Heart failure is also more common in females than males.[25,26] This seems to be due at least in part to a greater frequency of diastolic dysfunction,[26] which might relate with hypertension. Another risk factor for heart failure in women is diabetes mellitus.[27] However, women were less likely to have clinically significant coronary artery stenosis. The latter finding might explain a similar[28] or better outcome than men,[13,14,29] and after multivariate analysis, women had a trend toward a lower risk of death. A later analysis from Finland suggested that the prognosis might not be different in women.[30] The outcome of JCAD study showed lower all-cause mortality in females than males, and cerebro/cardiovascular death accounted for more than a half of deaths in both sexes.

Current reports provide important insight into our understanding of the impact of gender on the natural history of atherosclerosis, but it remains uncertain whether the pathophysiology of CAD differs in women.[25,31,32] The traditional view has proposed that clinical events typically begin later in life in women, which is attributed to the protective influence of endogenous estrogen. Other explanations about differences between the sexes might relate to differences in thrombotic and fibrinolytic activity[33–36] or differences in the extent of collateral blood flow.[37–39] Reduced collateral blood flow in women might account for the higher rate of complications when total coronary occlusion (infarction with ST elevation) occurs.[39] Alternative mechanisms underlying gene by sex interaction has been suggested to be considered.[40]

Finally, we have to keep in mind that women are typically under-represented in clinical trials and less likely to be investigated, and are not referred as often as men for appropriate diagnostic and/or therapeutic procedures, despite similar clinical conditions.[41,42]

Study Limitations

This study is quite unique in that it enrolled a large number of patients with angiographically-confirmed coronary atherosclerosis. However, this is a subanalysis of the JCAD study, and further studies are necessary to determine which factors account for the significant differences in outcome between both genders.

In the current study of subjects with angiographically evident CAD, women had less coronary atheroma. It remains to be established whether there are any gender-specific differences in the pathophysiology of atherosclerosis and which factors account for the significant differences in outcome.

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