Gender Differences in the Management and Clinical Outcome of Stable Angina

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Background—We sought to examine the impact of gender on the investigation and subsequent management of stable angina and to assess gender differences in clinical outcome at 1 year.

Methods and Results—The Euro Heart Survey of Stable Angina enrolled patients with a clinical diagnosis of stable angina on initial assessment by a cardiologist. Baseline clinical details and cardiac investigations planned or performed within a 4-week period of the assessment were recorded, and follow-up data were collected at 1 year. A total of 3779 patients were included in the survey; 42% were female. Women were less likely to undergo an exercise ECG (odds ratio, 0.81; 95% CI, 0.69 to 0.95) and less likely to be referred for coronary angiography (odds ratio, 0.59; 95% CI, 0.48 to 0.72). Antiplatelet and statin therapies were used significantly less in women than in men, both at initial assessment and at 1 year, even in those in whom coronary disease had been confirmed. Women with confirmed coronary disease were less likely to be revascularized than their male counterparts and were twice as likely to suffer death or nonfatal myocardial infarction during the 1-year follow-up period (hazard ratio, 2.09; 95% CI, 1.13 to 3.85), even after multivariable adjustment for age, abnormal ventricular function, severity of coronary disease, and diabetes.

Conclusions—Significant gender bias has been identified in the use of investigations and evidence-based medical therapy in stable angina. Women were also less likely to be revascularized. The observed bias is of particular concern in light of the adverse prognosis observed among women with stable angina and confirmed coronary disease. (Circulation. 2006;113:490-498.)

Key Words: angina ■ epidemiology ■ sex ■ prognosis ■ revascularization

Stable angina is the most prevalent manifestation of coronary artery disease (CAD). Its prevalence increases with age, and despite a higher overall incidence and prevalence of coronary disease in men than in women, stable angina is more common as an initial presentation of coronary disease in women. In fact, many population-based surveys using the Rose questionnaire or similar chest pain evaluation methodology from the United States and Northern and Southern Europe report higher prevalence rates for angina in women than in men.

From the perspective of acute coronary disease, numerous studies have explored the existence of different management practices in women and men in the setting of acute coronary syndromes or in procedure-based registries, with some showing that women are investigated and treated less aggressively than men.

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However, despite the relatively higher prevalence in women, there is comparatively little data on the investigation and treatment of stable angina in this population. Contemporary information about prognosis in stable angina is similarly scarce and is primarily based on male or predominantly male populations. Therefore, we sought to explore the effects of gender on the management, both investigative and therapeutic, of stable angina as it presents for the first time to cardiologists in Europe and also to examine the effect of gender on clinical outcome.
Methods

Population

The methods of data collection have previously been published. Briefly, consecutive patients attending cardiology services with a new presentation of stable angina were considered for enrollment. Eligible patients were those in whom the cardiologist made a clinical diagnosis of stable angina caused by myocardial ischaemia due to coronary disease. A new presentation was defined as a first-ever presentation to a cardiologist or new referral or re-referral, after a period of at least 1 year of not attending (consulting) a cardiologist. Patients were not obliged to have documented evidence of ischaemia to be included, but they did have to have stable angina due to coronary disease in the opinion of the physician investigator. Exclusion criteria included unstable angina, hospitalization within 24 hours of assessment (because of the likelihood of an unstable syndrome), myocardial infarction (MI) during the previous year, prior revascularization, or an etiologic cause for angina other than coronary disease such as aortic stenosis or hypertrophic cardiomyopathy. Consent to be included in the survey was obtained from each patient in the manner deemed appropriate by the local regulatory authorities.

Data Collection

Patients were enrolled from 197 centers across Europe. The attending physician, or a data collection officer in consultation with the attending physician, completed the electronic case report forms, detailing demographic and clinical details of the patients, referral pathway, investigations planned, investigations already performed, treatment recommended, and follow-up procedure observed. Follow-up was conducted by clinical review or telephone as closely as possible to 1 year from initial assessment. When it was not possible to make contact with the patients, data were collected from hospital or clinic records. Details of clinical events were confirmed, and data about these events or the results of investigations were collected from the patient’s records.

The use of investigations in the first 4 weeks was recorded in the baseline data collection. Results of investigations, coronary disease status at follow-up, revascularizations performed, and clinical outcome are reported from the population with completed follow-up.

Definitions

Angina severity was assessed with the use of the Canadian Cardiovascular Society (CCS) classification, and symptoms of heart failure were assessed according to the New York Heart Association (NYHA) classification. Conventional cardiovascular risk factors and comorbid conditions are defined in Appendix B in the online-only Data Supplement. The category of “investigations performed or planned” refers to investigations that were performed in preparation for assessment by the cardiologist or planned by the cardiologist after initial assessment. The primary outcome of interest was the occurrence of death or MI, and the occurrence of all cardiovascular events was also investigated. The category of “all cardiovascular events” refers to the occurrence of at least 1 of the following: cardiovascular death, MI, hospitalization for unstable angina or heart failure, cerebrovascular accident, or emergency revascularization.

Statistical Analysis

Descriptive statistics were used to estimate the prevalence within the sample of risk factors, baseline clinical characteristics, and treatment at presentation. The Student t test was used to test for statistically significant differences in quantitative measures (age in years, body mass index, and blood pressure), and the χ² test was used to test for statistically significant differences in proportions. Distributional assumptions were checked for all continuous response variables before these tests were conducted.

Logistic regression was used to determine the factors associated with the use of investigations. Variables included in univariate analysis of predictors of the use of exercise testing included age (≥70 versus <70 years), sex, employment status, level of education, type of center (invasive facilities available or not), comorbidity, symptom severity (CCS class), duration of symptoms (≥6 versus <6 months), and antiangial drug therapy before assessment (≥1 versus ≤1 antiangial drug). Further variables assessed in analysis of stress echocardiography, myocardial perfusion scanning, and coronary angiography as outcomes included the performance of exercise testing (yes/no), the result of exercise testing (positive versus negative or inconclusive), and the result of stress imaging (positive versus negative or inconclusive). Multivariable models were then developed with the use of prespecified predictors potentially associated with the outcome, with variables progressing to the final model that were significant at P<0.05. Stepwise procedures were not used for the analyses reported. The final model for the use of stress imaging used the performance of exercise ECG rather than the result of exercise ECG, and the final model for the use of coronary angiography used the result of exercise ECG rather than the result of stress imaging to maximize the size of the final populations. Age was retained in all models; and, in the case of noninvasive imaging, gender was forced into the model to allow presentation of an estimate of the effect of gender adjusted for the relevant predictors.

Logistic regression was also used to determine the effect of gender on the use of revascularization in the population with confirmed coronary disease who had completed 1-year follow-up. A multivariable model including factors predictive of the use of revascularization in univariate analysis was then constructed to determine the independence of the association between gender and the use of revascularization.

Survival analysis was performed with the use of Cox regression modeling with the primary outcome of interest being the time to occurrence of death or nonfatal MI. Differences between groups in the cumulative probability of death and MI or of all cardiovascular events were assessed with the log-rank test. Analyses were performed with the use of Stata version 8 statistical software.

Results

A total of 3779 patients enrolled between March and December 2002 were included in the survey. Follow-up data suitable for survival analysis, ie, vital status, information about the occurrence or nonoccurrence of nonfatal MI, and the timing of these events, were returned for 3031 patients (80%). The median duration of follow-up was 13 months (interquartile range, 12 to 15 months). Baseline clinical characteristics of men and women included in the initial study are presented in Table 1. Differences in baseline characteristics between patients with and without completed follow-up were observed for the prevalence of hyperlipidemia (62% versus 57%; P=0.017) and clinical signs of heart failure (10% versus 7%; P=0.013) among those without follow-up.

The mean (SD) age of the population surveyed was 61 (11) years. Women represented 42% of the population overall and were only marginally older than the men. Women were significantly more likely to be hypertensive but less likely to have previous MI or cerebrovascular disease than men. The majority of subjects (88%) had mild to moderate angina (CCS classes I or II). Women had proportionately more class II symptoms and fewer class I symptoms than men (P<0.001).

Medical Therapy and Investigations After Initial Cardiology Consultation

After initial assessment by a cardiologist, men were prescribed aspirin or statin therapy significantly more frequently than women, although there was no difference in the use of β-blockers (Table 2).

An exercise ECG was performed or planned as part of initial assessment in 78% of men and 73% of women...
(P<0.0001), a stress echocardiogram in 4% of men and 4% of women, stress perfusion imaging in 13% of men and 15% of women (P=0.041), and coronary angiography in 49% of men compared with 31% of women (P<0.001). The odds ratios (ORs) for the use of investigations in women compared with men were adjusted for age and other factors that were predictive of the use of each investigation in univariate analysis. For noninvasive testing (exercise ECG and stress imaging), this included comorbidity, symptom severity, symptom duration, and number of antianginal drugs. The performance of exercise testing (yes/no) was further included in the final model assessing the effect of gender on the use of stress imaging, and the results of exercise ECG were included in the multivariable adjustment of effect of gender on the use of angiography. Patients who had not had an exercise test were not included in this final model, but the magnitude and significance of the effect of gender were consistent in the larger population or in the restricted population with exercise testing results available. Women were significantly less likely to undergo exercise ECG and coronary angiography.

Table 1 shows the baseline clinical characteristics of patients included in the initial survey of the Euro Heart Survey of Stable Angina according to gender. The table includes variables such as age, symptom severity, duration of angina symptoms, signs of heart failure, prior MI, prior CVA or TIA, peripheral vascular disease, diabetes, hypertension, smoking, and hyperlipidemia. The table also shows the frequency of use of evidence-based medical therapy in agreement with existing guidelines after presentation to a cardiologist, from the Euro Heart Survey of Stable Angina, according to gender. The table includes medications such as antiplatelet, aspirin, lipid-lowering drug, statin, and β-blocker, along with the number of antianginal drugs.
angiography. A coronary angiogram was performed and results were reported in 47% of all men and 34% of all women with completed follow-up. In all, 79% of patients had significant coronary disease (defined as stenosis of ≥50% affecting 1 or more epicardial vessels) (63% of women and 87% of men; P<0.001). Among patients with obstructive disease, there was a significant gender difference in the severity of coronary disease. Women had more single-vessel disease (46% compared with 30%), and men had more 2- and 3-vessel disease (32% and 38%, respectively, compared with 22% and 32% in women) (P<0.001 for difference in the distributions).

The population was classified into 4 subgroups according to the confirmation of coronary disease and investigational status at the end of the 1-year follow-up period. The confirmed CAD subgroup required a recorded result of coronary disease on angiography. The other subgroups were those with negative investigations (either invasive or noninvasive if angiography was not performed), those with a positive noninvasive test without coronary angiography, and those who had either no investigation performed or inconclusive noninvasive investigation without any further noninvasive or invasive tests.

Revascularization During Follow-up

Revascularization, either percutaneous coronary intervention or surgery, was performed on 511 men (29%) and 170 women (13%) who completed follow-up. In the overall population, without taking account of angiographic findings, women were less likely to receive a revascularization procedure during the course of the survey (unadjusted OR, 0.38; 95% CI, 0.31 to 0.46; P<0.001). Among patients with proven CAD, women remained significantly less likely to have a revascularization procedure (OR, 0.70; 95% CI, 0.52 to 0.94; P=0.019 after adjustment for age and clinical factors predictive of revascularization at univariate level [the presence of diabetes and symptom severity according to CCS class]). Further adjustment for the severity of coronary disease (2- or 3-vessel disease compared with single-vessel disease) and abnormal left ventricular function attenuated the effect of gender so that there was only a trend toward statistical significance (OR, 0.71; 95% CI, 0.48 to 1.04; P=0.08), but the effect was similar.

Pharmacological Treatment at 1 Year in Those With Proven Coronary Disease

At 1-year follow-up, antiplatelet therapy was prescribed in 95% of men and 93% of women in whom coronary disease had been confirmed during the year after initial assessment (P=0.23). In this subgroup, lipid-lowering therapy was prescribed in 81% of men and 76% of women (P=0.05). Optimal secondary prevention, ie, the combination of antiplatelet and lipid-lowering therapy, was prescribed in 71% of women compared with 79% of men (P=0.01). The mean (SD) number of antianginal drugs was 1.5 (0.8) in women and 1.6 (0.8) in men (P=0.02).

Clinical Outcome According to Gender

At the end of follow-up, 25 men (1.4%) and 25 women (2.0%) had died. The numbers of men and women who
experienced death or major cardiovascular events during follow-up in the whole population and in the subgroup with confirmed coronary disease are shown in Table 3. In the overall population, men and women were equally likely to complain of angina at 1-year follow-up (49% of men and 51% of women), and gender was not a significant univariate predictor of death or MI.

However, women with confirmed CAD were less likely to have completely successful treatment of angina, with 43% reporting no angina at follow-up compared with 53% of men (P=0.007). Among this population, women were also significantly more likely than men to suffer death or MI during the follow-up period (Table 3, Figure 2). In a multivariable model adjusted for age, abnormal left ventricular function, the presence of diabetes, and the severity of CAD defined as 1-, 2-, or 3-vessel disease, female gender remained significantly predictive of death or MI, with women remaining more than twice as likely to suffer death or MI during follow-up. The association between gender and outcome was significant when adjusted for each factor individually and together. The effect of gender was not significantly modified by confirmed CAD status (P=0.21 for test of unequal hazard ratio).

In this analysis women remained at increased risk of death or MI after adjustment for the differences in revascularization or the use of evidence-based pharmacological treatment directed at improving prognosis (aspirin, lipid-lowering drugs, and β-blockers) at initial assessment (Table 4).

Regional and Center-Specific Trends in Gender Bias
All patients included in the survey were assessed by a cardiologist and therefore had obtained access to specialist cardiology services. Overall, ~70% had been referred by a primary care physician, and 10% were self-referrals. (The remainder were referred by noncardiology specialists, and <5% were referred for follow-up after presentation to an emergency department.) There were significant regional differences in the distribution of referral sources (P<0.001). In Northern Europe, the majority of patients had been referred by their primary care physician (85%), with 0.2% self-referrals, whereas in Central and Mediterranean Europe, the proportions of self-referrals were 15% and 17%, respectively.

Women represented 40% of the population in Northern Europe, 49% in Western Europe, 42% in Central Europe, and 37% in Mediterranean Europe.

Trends toward less use of exercise testing in women were evident in all regions, although differences did not always achieve statistical significance, particularly in Northern Europe, where the smallest number of patients was enrolled. Gender differences in the use of exercise testing were least apparent in centers where only noninvasive facilities were available (Table 5). Coronary angiography was used less frequently in women in all regions and all types of centers. There were regional variations in the differences observed between men and women in the use of secondary preventative therapy; in particular, less frequent use of statins in women compared with men was significant only in Western Europe, and gender bias in the use of secondary preventative therapy was evident to a greater rather than to a lesser extent in centers with invasive facilities on site (Table 5). Revascularization was performed less frequently in women than in men.

<table>
<thead>
<tr>
<th>TABLE 3. Incidence of Major Clinical Events Occurring During 1-Year Follow-up in the Euro Heart Survey of Stable Angina in All Patients With Stable Angina and in the Subgroup With Confirmed Coronary Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Event</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Noncardiovascular death</td>
</tr>
<tr>
<td>Nonfatal MI</td>
</tr>
<tr>
<td>CVA</td>
</tr>
<tr>
<td>Heart failure*</td>
</tr>
<tr>
<td>Unstable angina*</td>
</tr>
<tr>
<td>Emergency revascularization</td>
</tr>
</tbody>
</table>

Values are number (%).
*Heart failure and unstable angina refer to admission to hospital for heart failure or admission to hospital for unstable angina, respectively.
with confirmed coronary disease in Northern Europe (OR, 0.30; 95% CI, 0.14 to 0.63; \( P < 0.001 \)), but significant gender differences in the use of revascularization were not apparent in other regions.

**Discussion**

The objective of the survey was to evaluate differences in management and in clinical outcome of stable angina between men and women. It can be expected that a substantial proportion of male and female patients with symptoms of angina will not have obstructive coronary disease at cardiac catheterization.\(^{22}\) However, the management of angina in clinical practice, even among cardiologists, is not restricted to only those patients who have documented coronary disease at coronary angiography. The extent to which these patients are investigated noninvasively and treated pharmacologically is a public health and economic issue of at least equal magnitude to the investigation and treatment of patients with proven coronary disease, and therefore the care of both populations has been assessed in this survey. Previous registry data have shown mixed results in terms of gender bias. Relatively recent publications report no evidence for the Yentl syndrome,\(^{22}\) but these assertions are based on angiography registry data, and from this study it is clear that significant selection bias is evident at multiple levels in the assessment of cardiac symptoms, including important effects before invasive assessment.

**Noninvasive Investigation**

Exercise ECG testing is the most frequently employed noninvasive investigation in this population, and female gender has been identified as an important predictor of less frequent use of the investigation despite adjustment for clinical factors such as age, comorbidity, and symptom severity. This is in agreement with previous population-based studies that have documented a significantly lower rate of use of exercise testing in women with a rate ratio for men over women of 2.7, despite equal rates of coronary heart disease mortality.\(^{26}\) A primary care–based study has also reported a \( > 2 \)-fold difference in the performance of exercise ECG between men and women.\(^{27}\) It may be argued that women are not referred for stress testing because of the high rate of false-positives, but in this survey only a quarter who did not receive an exercise ECG went on to have an alternative stress imaging technique. Additionally, the combination of multiple parameters such as exercise capacity in evaluation of stress test positivity can considerably improve diagnostic accuracy in women.\(^{28–30}\) This and the excellent negative predictive power of exercise testing prognostically support stable angina guideline recommendations that, when possible, exercise testing should re-

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**TABLE 4. Hazard of Death or MI Associated With Female Gender in Individuals With Proven Coronary Disease From the Euro Heart Survey of Stable Angina**

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>2.07</td>
<td>1.16–3.72</td>
<td>0.01</td>
</tr>
<tr>
<td>Death or MI, adjusted for age, diabetes, LV function, and severity of coronary disease</td>
<td>2.09</td>
<td>1.14–3.85</td>
<td>0.02</td>
</tr>
<tr>
<td>Death or MI, adjusted for age and use of statin and antiplatelet therapy</td>
<td>2.07</td>
<td>1.14–3.74</td>
<td>0.02</td>
</tr>
<tr>
<td>Death or MI, adjusted for age and revascularization</td>
<td>2.20</td>
<td>1.22–3.98</td>
<td>0.009</td>
</tr>
</tbody>
</table>

LV indicates left ventricular.

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**TABLE 5. Unadjusted Gender OR (Female vs Male) for the Use of Exercise Testing, Coronary Angiography, and Secondary Preventative Medication According to Region and Type of Center**

<table>
<thead>
<tr>
<th>Exercise ECG</th>
<th>Angiography</th>
<th>Aspirin</th>
<th>Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>95% CI</td>
<td>( P )</td>
<td>OR</td>
</tr>
<tr>
<td>-----</td>
<td>-------------</td>
<td>--------</td>
<td>-----</td>
</tr>
<tr>
<td>Total</td>
<td>0.77</td>
<td>0.66–0.90</td>
<td>0.001</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North</td>
<td>0.72</td>
<td>0.46–1.13</td>
<td>0.16</td>
</tr>
<tr>
<td>West</td>
<td>0.64</td>
<td>0.46–0.89</td>
<td>0.008</td>
</tr>
<tr>
<td>Central</td>
<td>0.81</td>
<td>0.64–1.03</td>
<td>0.09</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>0.76</td>
<td>0.57–1.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Center type*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninvasive</td>
<td>0.90</td>
<td>0.68–1.19</td>
<td>0.46</td>
</tr>
<tr>
<td>Catheterization laboratory</td>
<td>0.61</td>
<td>0.45–0.83</td>
<td>0.002</td>
</tr>
<tr>
<td>Cardiac surgery</td>
<td>0.77</td>
<td>0.61–0.97</td>
<td>0.027</td>
</tr>
</tbody>
</table>

*Center type was defined according to facilities available: noninvasive = noninvasive diagnostic facilities only, without catheterization laboratory or cardiac surgery; catheterization laboratory = noninvasive and catheterization facilities without on-site cardiac surgery; and cardiac surgery = full complement of noninvasive and invasive facilities including cardiac surgery.
main the first investigation for angina in women as well as in men.31–33

That these women are not referred for alternative tests but receive a diagnosis of angina without further investigation has far-reaching implications on both patient and population levels. At the individual patient level, there are implications for lifelong secondary preventative therapy, future health insurance or life insurance, and self-imposed lifestyle restrictions. At the population level, there is a need to correctly identify those patients at significantly increased risk of future cardiovascular events to optimize their treatment and to limit unnecessary long-term health resource utilization by patients who have been misclassified.

Invasive Procedures and Revascularization

In agreement with previous findings in the setting of acute coronary syndromes or suspected coronary disease,12,13,15,16,18,34 gender was a significant predictor of the use of coronary angiography as part of the initial investigation of stable angina. Women were 40% to 50% less likely to have an angiogram than men even after adjustment for multiple clinical factors, including the results of exercise testing. Previous studies vary considerably in the reported effects of gender on revascularization.12–16,19–24,35–37 The retrospective analysis of Ayanian and Epstein14 of hospitalizations for coronary heart disease reported a 3-fold increase in revascularization procedures in men with stable angina compared with women, similar to that reported by Tobin et al12 in a much smaller population, whereas other studies have identified a significant difference in rates of coronary artery bypass graft but not percutaneous intervention.

Multiple reasons have been proposed to explain why revascularization may be less frequently utilized in women than men. Women have less obstructive coronary disease for the same degree of symptomatology as men.22,38 One previous study35 has identified gender as a predictor of revascularization after adjustment for clinical variables with the exception of extent of coronary disease and ventricular function but not when the extents of coronary disease and ventricular function are included. In the present study, even in the presence of confirmed coronary disease, women remained significantly less likely to have a revascularization procedure after adjustment for age, diabetes, and symptom severity. Further adjustment for the extent of coronary disease and ventricular function rendered the effect of gender just less than statistically significant but did not materially alter the magnitude of the OR.

Further reasons proposed for lower rates of revascularization in women include relatively poorer outcome and higher rates of complications in women undergoing either coronary bypass graft surgery or percutaneous revascularization.39–41 Finally, it has been suggested that women may be less willing to undergo invasive procedures or surgery. The opposite has been shown in at least 1 study that reported men to be 7 times more likely than women to refuse invasive investigation.42 However, there are undoubtedly differences in the physician-patient interaction, related to factors such as physician prejudices43 and gender-specific description and perception of symptoms,44 that may affect referral for invasive investigation and revascularization.

Pharmacological Therapy in Angina

A striking observation from the study was that women are significantly less likely to receive evidence-based secondary preventative therapy, not just at initial clinical assessment but even after a diagnosis of coronary disease has been confirmed angiographically. It is true that the majority of studies of secondary preventative therapy have been conducted in predominantly male populations. However, at least 1 large-scale antiplatelet study, which has influenced existing guidelines for the management of angina, deliberately recruited 50% female patients and showed significant benefit of aspirin in this population.45 In trials of statin therapy that have included women, there has been no firm evidence to suggest that women obtain less benefit from these medications, and both European and American guidelines advocate the use of secondary prevention in men and women equally.31–33 A recent publication on gender disparity in the application of prevention guidelines in the United States points toward lower perceived risk in women as a cause for differences in the use of appropriate preventative measures.46 Physician awareness and improved education are necessary to redress the balance.

Adverse Outcome in Women With Coronary Disease

The adverse outcome observed in women with confirmed coronary disease is a striking finding of the study. Although women received less aggressive pharmacological therapy and less revascularization, these factors do not completely account for the differences observed in statistical terms. The increased risk was apparent after adjustment for the use of secondary preventative medication and after adjustment for the use of revascularization. Adjustment for baseline characteristics such as diabetes and abnormalities of left ventricular function similarly did not fully explain the increased risk observed in women. There are 2 additional potential reasons for the disparity, which are not mutually exclusive. First, because female gender was not a significant predictor of adverse outcome in the overall population with angina but only in those women with coronary disease, the reason may be related to the highly selected nature of the population, given the observed bias against the use of invasive investigation in women. Second, the underlying pathophysiological substrate may respond differently to therapy in women presenting with angina compared with men, so that beneficial treatments (proven in men) may be less effective in women or counteracted by greater adverse effects.

Limitations of the Study

Because participation in the survey was on a voluntary basis, the survey may be biased with regard to center selection, with more university and teaching centers included than are truly representative. However, through the national coordinators at the national level, every effort was made to maintain a mix of centers that was representative of the practice in each country. In-depth exploration of regional variations and differences
between centers with and without invasive facilities is not possible within the confines of the data available, but our unexpected observation that gender bias was evident to a greater rather than to a lesser extent in centers with invasive facilities on site warrants further study to identify the factors that influence variations in gender bias.

Enrollment was based on the diagnosis of angina by the attending physician and is thus open to interpretation bias. However, because the purpose of the survey was to evaluate patient management, and patient management was based on the working diagnosis of angina, our analysis is suitable for evaluation of clinical practice. Finally, follow-up was complete and suitable for survival analysis in 80% of the original population, but there were no significant differences with regard to the gender distribution between the original and follow-up populations, nor were there differences in the effects of gender on either the use or results of investigation or treatment.

Conclusions

In this large European population, female patients presenting with stable angina to a cardiologist are referred less often for investigation and undertreatment of stable angina. This project forms part of the European Society of Cardiology systematic underinvestigation and undertreatment of stable angina demonstrated at multiple levels in the investigation and optimal secondary preventive medication even in the presence of confirmed coronary disease. The gender differences demonstrated at multiple levels in the investigation and management of stable angina raise serious concerns about systematic underinvestigation and undertreatment of stable angina in women. This trend is all the more worrying when viewed in the context of a significantly worse prognosis for women with angina who have confirmed coronary disease.

Acknowledgments

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Disclosures

None.

References

Gender differences in the clinical outcome of acute myocardial infarction and rates of revascularization have previously been described. Although many population-based studies report the prevalence of stable angina to be at least as high in women as in men, previous investigation into the impact of gender on the diagnostic approach and treatment of stable angina has been limited. In this contemporary European survey of patients presenting de novo to cardiologists with stable angina, the diagnosis of chronic stable angina was more likely to be confirmed after functional testing for ischemia, in particular for exercise testing, less likely to receive angiography even after adjustment for the results of noninvasive tests, and were less likely to be referred for revascularization. Women were also less likely to receive secondary preventative therapies at initial assessment. Among patients with angiographic confirmation of coronary disease during follow-up, women remained less likely than men to receive optimal secondary preventative therapy at 1 year. In the subgroup with confirmed coronary disease, female sex was strongly associated with increased risk of death and myocardial infarction, independent of age and other predictors of adverse outcome. These data provide evidence that women with stable angina are both under-investigated and undertreated in contemporary practice, strengthening the argument that gender bias exists and must be challenged. Further research is needed to elucidate the reasons for the adverse prognosis observed in women with stable angina and proven coronary disease.
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