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Gender differences in coronary heart disease in elderly populations

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Summary. Coronary heart diseases (CHDs) represent one of the leading causes of death in developed countries, and particularly in elderly populations. There are several gender-specific differences in the risk factors, presentation, management, and prognosis of CHDs in middle-aged and elderly adults. Elderly women, for example, tend to present with these diseases at an older age compared to men and are characterized by a greater number of risk factors and comorbidities at diagnosis. As far as symptomatic acute coronary syndromes are concerned, older women are less likely to report critical arterial obstruction, but seem to be more frequently affected by adverse outcomes and higher mortality. These features, which need to be considered during the management of coronary artery diseases in clinical practice, often lead to a lower rate of diagnostic investigations and less invasive therapeutic strategies for females compared to males. Some have hypothesized that the clinical approach toward CHDs in older women may be affected by a biased view due to the scarcity of literature involving women and elderly patients. The misperception that women have a lower cardiovascular risk compared to men and the fact that fewer older people were enrolled in the first large clinical trials have, in fact, led to under-recognized and under-treated CHDs in these patient groups. As most recent studies have considered middle-aged and elderly adults together, it is hard to know if the variability observed in the CHDs' features is attributable to gender or to advanced age. Gender- and age-related differences in the characteristics and outcomes of CHDs represent therefore a field requiring further investigation to improve the management of such diseases in the elderly population.

Key words: coronary heart diseases, gender differences, elderly.

Differenze di genere nelle coronaropatie in età geriatrica

Riassunto. Le coronaropatie costituiscono una delle principali cause di morte nei Paesi industrializzati, soprattutto per la popolazione in età geriatrica. Negli anziani, come negli adulti, le malattie coronariche si caratterizzano per una molteplicità di differenze di genere che coinvolgono fattori di rischio, modalità di manifestazione e strategie terapeutiche di tali patologie. Rispetto agli uomini, per esempio, l'esordio delle coronaropatie è più tardivo nelle donne anziane, le quali presentano generalmente un più ampio corredo di comorbilità e di fattori di rischio cardiovascolare al momento della loro insorgenza. Le coronaropatie sintomatiche in età geriatrica, inoltre, si associano meno strettamente alla presenza di stenosi arteriose critiche nel sesso femminile, che però risulta essere gravato da prognosi peggiori e maggiore mortalità rispetto al genere maschile. Il riscontro di tali peculiarità ha inevitabilmente influenzato la gestione delle patologie coronariche nella pratica clinica, portando a un minor tasso di indagini diagnostiche e di trattamenti invasivi rivolti a pazienti di sesso femminile. Tale approccio clinico, tuttavia, non si avvale di fondate basi scientifiche, dal momento che non vi sono ancora solide e concordi indicazioni rispetto alla gestione delle patologie coronariche sia in pazienti anziani che di sesso femminile. Alla base della sottostima e del ridotto riconoscimento delle coronaropatie in tali tipologie di pazienti vi sono diversi fattori; tra questi, la convinzione che le donne abbiano un minore rischio cardiovascolare rispetto agli uomini, e la scarsa partecipazione di soggetti anziani nei primi ampi studi sperimentali rappresentano due aspetti di notevole rilevanza. Inoltre, dato che la maggior parte degli studi clinici effettuati negli ultimi anni considera insieme pazienti anziani e adulti, risulta particolarmente arduo valutare se la variabilità nelle caratteristiche e nella prognosi delle coronaropatie sia imputabile al genere o all'età avanzata. L'ambito delle differenze di genere nelle coronaropatie in età geriatrica richiede dunque ulteriori approfondimenti al fine di elaborare nuove indicazioni diagnostico-terapeutiche che tengano in considerazione la variabilità genere- ed età-correlata di tali patologie.

Parole chiave: coronaropatie, differenze di genere, età geriatrica.

Introduction

The increase in life expectancy in developed countries has led to a change in the main causes of death in the general population, formerly linked to acute infectious diseases and now associated with chronic pathologies[1]. Cardiovascular diseases (CVDs), in particular, today constitute the leading cause of death in elderly populations and have a mortality rate that exceeds that of cancer for persons aged 65 and over[2,3]. As far as cardiovascular pathologies are concerned, coronary heart diseases (CHDs) have one of the highest standardized death rates, accounting for 593.7 deaths per 100,000 inhabitants across European countries[2].

In middle-aged and elderly adults, CHDs are characterized by a number of gender differences affecting their epidemiology, presentation and outcomes. Nonetheless, the current literature still shows a gap in the knowledge about gender- and age-specific characteristics of CHDs due to an under-representation of women and of older people in the principal clinical trials that have been carried out[4]. As demonstrated by Lee et al., only 9% of patients older than 75 and 25% of women were included in studies carried out between 1991 and 2000, percentages that are well below the representation of those patients within the entire myocardial infarction (MI) population[4]. Considering that the onset of CHDs is later in women[5,6], it could be hypothesized that part of the current *gender gap* depends on the *age gap* as the under-enrolment of elderly subjects may have limited the knowledge regarding CHDs particularly in older women[4]. These gender- and age-related gaps in the literature could be ascribed to several reasons. As regards advanced age, recruitment difficulties and lower compliance with medical treatments among elderly people can partially explain their low representation in clinical trials[4]. Moreover, the reluctance to expose older subjects to invasive therapies given the presence of multiple comorbidities or simply the preconception that age *per se* represents a factor that increases risk of adverse events also play a part in this bias[4,7,8].

With regard to the gender gap, the belief that the female gender represents an independent factor that lowers the risk of CVDs has led many to underestimate the risk of heart diseases in women[9,10]. One of the most accredited hypotheses underlying this misperception is the belief that endogenous oestrogens have cardioprotective effects on the metabolic, coagulative and inflammatory pathways during fertile age[11,12]. Hormonal changes after menopause do not, however, entirely explain the decrease in the male/female ratio of CHD mortality occurring in advanced ages[13] and the growing rate of women patients that has recently been observed[14]. This tendency was underlined by a large study based on a Finnish population showing that, while in 1980 middle-aged men represented the most dominant CHD group, in 2000 the dominant group was made up of women aged over 75[14].

Gender differences in CHD risk and symptoms in the geriatric population are therefore an important, complex topic that requires further investigation since generalizing results from trials including mostly men and younger persons to female and elderly patients cannot be considered a reliable approach. Moreover, considering that elderly people account for a large proportion of hospitalizations, being able to reliably evaluate CHD in older men and women could aid in identifying coronary pathologies at an early stage or patients at high risk of developing them and improve clinical practice[15].

Given these considerations, this study sets out to examine the current literature regarding gender-specific differences with regard to risk factors, presentation, management and prognosis of coronary heart diseases in elderly populations.

Risk factors for coronary heart diseases in the elderly

The risk patterns for CHDs in older persons are characterized by a multitude of comorbid, behavioural and lifestyle factors accumulated with aging. Women, in particular, who generally develop CHDs approximately 7-10 years later than men, are more likely to present with a large number of cardiovascular risk factors at diagnosis[5,6]. In addition to the different prevalence rates of cardiovascular risk factors in men and women, their relevance in influencing the onset of CHDs shows further gender-related variability that could change between middle-aged and elderly adults.

The impact of excess weight on CHDs, for example, has been widely investigated in large longitudinal studies, and its negative metabolic and inflammatory consequences have been confirmed in both middle-aged and older individuals. However changes in body composition such as the increase and redistribution of fat in the visceral compartment occurring at older ages[16-18] seem to influence this association. According to the study by Rimm et al., while obesity predicts CHD risk independently of fat distribution in men younger than 65, at older ages abdominal adiposity was a stronger predictor of CHD risk than body mass index (BMI)[19]. Similar results have been observed for the female gender in whom the central redistribution and accumulation of adipose tissue in post-menopausal age and the metabolic syndrome were more strongly associated with higher risk of coronary artery diseases than BMI[20,21].

Other components of the metabolic syndrome and particularly lipid metabolism, are influenced by the fall in oestrogen beginning in the perimenopausal period. After menopause, in fact, LDL cholesterol increases in women and tends to exceed the levels found in men[9,22-24], although women demonstrate larger and less atherogenic LDL[25]. Conversely, HDL concentrations fall slightly in women during the post-menopausal period, but they maintain higher levels[22,26] and stronger inverse associations with CHDs and related mortality compared with men[27,28].

The impact of diabetes and hypertension on coronary artery diseases has also been found to be stronger in women than in men. Although previous meta-analyses comparing the impact of diabetes on CHDs produced contrasting results[29-31], Huxley et al. reported a 50% higher risk for fatal CHDs in diabetic women compared

to middle-aged or elderly men[32]. Diabetic women tend, in fact, to have a higher-risk cardiovascular profile than men with worse lipid concentrations and blood pressure values[32]. As regards blood pressure, ageing is characterized by a progressive rise in systolic values in both genders, but after early adulthood this increase is steeper in women. This pattern is probably due to variations in endogenous oestrogen levels[33] leading to higher average blood pressure values in women from the seventh decade of life[34]. Though increasing blood pressure has been associated to higher CHD incidence and mortality in both genders, its impact in older women seems to be greater than in men[35,36]. Conversely, mean diastolic blood pressure tends to gradually fall beginning at 60 in both men and women[34], with the latter generally showing lower values. A consequent higher prevalence of isolated systolic hypertension has, therefore, been reported in elderly women compared with same-aged men and represents an additional factor increasing cardiovascular risk[37].

Lifestyle factors and risk behaviours are other important determinants of cardiovascular risk in older populations. Though smoking is generally more common in men, its impact on the onset of ischemic heart diseases primarily seems to concern women. Compared with non-smokers, in fact, Prescott et al. demonstrated that female smokers had about a 50% higher relative risk of myocardial infarction than men across all age groups[38]. The risk difference between genders seemed to be attenuated in the population aged over 65 years, suggesting that in addition to its pro-inflammatory effect, the interaction between smoking and sex hormones could play a significant role[38]. With regard to dietary style and physical activity, no significant associations were found between dietary fat intake and coronary artery diseases in older persons[39], while a meta-analysis by Sattelmair et al. reported that physical activity has a beneficial effect on CHD risk in both men and women, with stronger results for the latter[40].

Presentation of coronary heart diseases in older men and women

Gender differences have been observed in the diagnosis and presentation of coronary artery diseases in both middle-aged and elderly adults. This variability could be attributable to gender-specific physiological and pathological characteristics of those diseases that may be exacerbated by aging.

From a pathophysiological viewpoint, women have smaller coronary vessels and stiffer aortas, present more often with microvascular dysfunction and poorer vascular reactivity compared to men, determining a lower vasodilator response[41]. The atherosclerotic process in coronary arteries may also differ in the two genders since women with CHD have demonstrated less widespread obstruction and a lower probability of presenting three-vessel coronary diseases or left-main stenosis[6,42] and collateral vessels[43]. Plaque composition is characterized by lower necrotic core content and calcium in women who have a lower probability of plaque rupture[42]. Coronary calcification seems, however, more associated with mortality in women who also have thin-cap fibroatheromas with a higher vulnerability[42]. The characteristics of vessels and atherosclerotic plaques could influence clinical and electrocardiographic signs of CHDs that tend to be poorly correlated with the angiographic report of obstructive coronary disease, especially in women. In a sample of patients with unstable angina and non-Q wave myocardial infarction, Hochman et al. demonstrated that women had a higher probability of non-critical obstructions[44], and this finding has been confirmed for all age groups including for individuals over 80[45]. Similarly, Sharaf et al. found that only 43% of middle aged and elderly women with suspected ischemic chest pain had a stenosis >50% and more than one third had no detectable obstructions[46]. Sex-specific features have also been observed in the non-invasive diagnostic testing of coronary diseases, which is less reliable in women than in men. Factors such as a higher resting heart rate, longer QT intervals and lower exercise capacity could, in fact, affect the overall predictive value of ECG and treadmill testing in women[47,48]. Reliable diagnostic tools for CHDs are particularly relevant in geriatric populations in which acute coronary syndrome (ACS) can show heterogeneous clinical patterns. Hence, the importance of the growing use in clinical practice of more sophisticated diagnostic imaging that has improved the identification of coronary disease in both genders[9,47].

The clinical presentation of CHDs can present some sex-specific differences in elderly population, although older age seems to be a stronger predictor compared to gender of ACS presentation[49,50]. Since women at CHD onset tend to be older than men, they may therefore show different symptomatology for ACS. As regards symptomatic cases of CHDs, despite the fact that the prevalence of angina is higher in women than in men in middle age, after 65 years of age this disparity tends to be attenuated[51]. In particular, the prevalence of typical chest pain, the primary symptom complaint, has been found to be similar in men and women between the ages of 65 and 74, while it seems to be significantly lower in women than in men over 75[52]. As previously mentioned, chest pain in women is less associated with the presence of obstructive coronary artery disease. More than half of symptomatic women without relevant coronary artery diseases nevertheless continue to report symptoms of CHDs[53], and the presence of

chest pain even in women with normal coronary arteries has been associated with a higher risk of death and adverse cardiovascular events compared to asymptomatic women[54]. Moreover, among symptomatic CHDs, women generally report a higher number of symptoms than men, and they are more likely to have atypical vegetative signs such as nausea, vomiting and indigestion[6,52]. Though the prevalence of MI without chest pain and discomfort declines in advanced age, many studies report a higher rate of non-chest pain MI in women than in men, even after adjusting for age[49,55,56]. Patients with non-specific chest pain require particular attention because the pattern has also been associated with a significantly higher risk for nonfatal CHDs, hospitalized angina and new cardiovascular events[55], in particular in women over 65[57,58].

Management of acute coronary syndrome in the elderly

Compared to other older adults admitted to hospital for ACS, women are generally older and present with a higher number of comorbidities, such as diabetes, hypertension and prior congestive heart failure, which increase their mortality risk and may be important for the therapeutic approaches that can be considered[5,6,56,59]. Management of ACS often proves to be more difficult in elderly patients as a result of the delay in accessing the emergency unit since the time between the onset of symptoms is a fundamental prognostic variable for revascularization strategies[60,61]. This refers particularly to female patients who often present with a longer delay from symptom onset to hospital access (median values range from 1.8 to 7.2 hours for women and from 1.4 to 3.5 hours for men)[61–63]. In addition to common atypical presentation of CHDs, prehospital delay in older women could be due to the fact that women tend to underestimate their cardiovascular risk[61,64] and are often unaware of the relevance of key symptoms[65,66]. An interesting study by Mosca et al. confirmed this pattern and found that only 53% of the women interviewed would call the emergency service if they thought they were having symptoms of a heart attack[66].

Gender differences have also been found in the type of CHDs at presentation, with men more commonly presenting with ST-elevation myocardial infarction (STEMI)[5,6] and, among non ST-elevation ACS, a higher rate of non ST-elevation myocardial infarction (NSTEMI) compared to women[5]. The higher prevalence of unstable angina in women instead reflects the angiographic features previously mentioned, namely a lower prevalence of complete coronary occlusion[5,44,67]. A confounding condition that may further prevent recognition of CHD in older persons is Takotsubo cardiomyopathy. This syndrome consists in a transient left ventricular dysfunction triggered by emotional or physical stress, shows a higher prevalence in the elderly and in the female gender and its clinical pattern is similar to that of ACS[68,69]. Since clinical and electrocardiographic characteristics are the most common tools used to evaluate CHDs, age- and gender-related differences in CHD presentation should be taken into consideration when the management of these patients is being evaluated[70,71].

Management of ST-elevation myocardial infarction

Acute revascularization by percutaneous coronary intervention (PCI) or thrombolysis represents the gold standard for the treatment of acute MI and high-risk ACS[72], and better outcomes have been demonstrated for shorter times to reperfusion[62]. Primary coronary angioplasty is, in particular, now considered the first choice for reperfusion in STEMI[73]. However, despite the fact that 51% of those procedures are performed on patients over 65, only one third of annual PCIs in the United States involve female patients[74]. This data has been confirmed by several authors, who have reported that women with MI were half as likely as men to receive invasive revascularization procedures[75–80], in particular for mild disease[6,81]. As was observed by Clarke et al., the "gender bias" regarding admission to coronary care with a confident MI diagnosis has been confirmed across all age groups and is exacerbated in patients older than 75, even after considering the final diagnosis of CHD and Killip classification[81]. Moreover, as regards coronary care, women reported longer door-to-reperfusion time, showing a mean delay of 8.3 minutes compared with men, and therefore a worse time-related prognosis[82-84]. PCI may be less likely performed in older women because of the higher risk of bleeding after revascularization, observed, in particular, when glycoprotein IIb/IIIa inhibitors are used[85,86]. However, as demonstrated by Cho et al., this additional antiplatelet treatment seems in any case to protect both genders from major adverse outcomes and to only slightly increase the risk of minor bleeding in women[86].

As regards thrombolysis, studies on fibrinolytic therapy after MI in older patients have produced contrasting results, especially for patients older than 75 who often showed a survival disadvantage after thrombolytic therapy, probably due to the age-related increased risk of stroke, bleeding, and sudden death due to mechanical rupture[87–89]. A higher bleeding rate has been observed in particular in women[5,85,90], especially in those cases when thrombolysis was associated to heparin therapies[91] which could be attributable to excessive doses of fibrinolytic and antithrombotic drugs that need to be adjusted based on renal function[85].

Management of non ST-elevation myocardial infarction and unstable angina

Special attention should be dedicated to the management of NSTEMI, which largely depends on clinical, electrocardiographic and biochemical factors, in middle-aged and elderly adults[92]. While in some studies women have demonstrated better long-term outcomes than men when NSTEMI was treated with early invasive revascularization[93,94], others reported a higher risk of major adverse cardiac events after PCI for NSTEMI in the female gender[95,96]. Moreover, Alfredsson et al. found better long-term prognoses for women with NSTEMI, in particular for the oldest group[79,97], although they were less likely to be investigated[71,97] and intensively treated[71,76,79,98,99]. The current guidelines, therefore, recommend classifying women according to their low or high risk, on the basis of biomarker values[100]. As confirmed by a recent meta-analysis, despite the fact that early invasive treatment leads to similar benefits for men and high-risk women as far as mortality, myocardial infarction and rehospitalization for ACS are concerned, the current guidelines for low-risk women continue to be a conservative therapy strategy[101].

Medical treatment of acute coronary syndromes

Pharmacological therapy for ACS also seems to be affected by an age- and sex-related variability. Despite the fact that the benefit of aspirin, beta-blocker, statins, and ACE-inhibitors has been proved for both sexes[102], fewer women are prescribed these drugs after ACS[6,78,81,103–109]. A gender-related variability has also been identified for the therapeutic efficacy of some medical treatments. Women, for example, have shown a higher residual platelet activity after dual antiplatelet therapy compared with men, confirming that there is a variable response to therapy[110,111]. In addition to the gender gap in the prescription of therapies for secondary prevention of CHDs, older age could represent another variable that must be considered when prescribing treatments. Pharmacokinetic and pharmacodynamic changes[112], collateral effects and drug interactions due to polypharmacy[113], and concomitant comorbidities (e.g. hypotension, recent bleeding history, arrhythmias, and chronic pulmonary diseases), in fact, all may influence medical prescriptions and need be taken into consideration when preventive therapies are being evaluated for elderly patients.

Gender-differences in mortality from coronary heart diseases in older patients

Mortality linked to CHDs has gradually fallen in Italy over the past forty years in both genders probably because of the reduction in major risk factors and the improvement in therapeutic strategies[114]. This pattern refers, in particular, to elderly populations, with a higher rate of prevented or postponed death observed for men between 65 and 84 and for women older than 75[114]. The relevance of knowledge about the main determinants of mortality for CHDs in older men and women is thus confirmed in this context given its importance in formulating preventive strategies and in improving clinical practice.

Although female gender has long been considered a factor that *per se* increases the overall mortality for CHDs, a prognostic value now seems to be associated to a number of factors with gender-specific features, such as the type and severity of disease, the subjects' characteristics at presentation, and the intensity of CHD management[5,6,44,115].

As far as subjects with STEMI are concerned, many studies have demonstrated a higher in-hospital mortality and short-term rate of ischemic events in women compared to men[5,56,75,82,90,116–121]. A recent study by Raphael et al. reported an increased death rate after STEMI attributable to non-cardiac causes in women and to cardiac causes in men[122]. The rate of post-procedure complications also seems to show some sex-specific differences. While benefits in terms of survival and reduced intracranial bleeding after primary PCI were similar in men and women with acute myocardial infarction (AMI), women more often than men experienced coronary vascular injuries and bleeding complications, irrespective of coronary size and other confounders[123]. Similar results have been reported for fibrinolysis that was associated with a higher incidence but a lower mortality linked to bleeding in women compared to men[124], although the association may have depended on age and comorbidities and does not seem to be confirmed in terms of long-term survival[125,126]. However, the sex-age interaction influencing outcomes after MI seems to be stronger in younger age groups, while gender differences in the elderly population seem to be attenuated[56,127,128]. As regards NSTEMI and unstable angina, similar or better outcomes were found in women compared to their male counterparts[5,44,92,128-130]. However, as for MI, these results were partially minimized when age, comorbidities and disease management were considered[5,6,90,117,127], further confirming that gender *per se* does not represent an independent prognostic factor for CHDs. According to the Thrombolysis in Myocardial Infarction (TIMI) IIIB trial, for example, outcomes including death, nonfatal MI and failure of therapy at 6-weeks in subjects with unstable angina and non-Q wave MI were associated with the severity of the coronary disease and not with gender[44]. A study by Dey et al. confirmed that disease severity is a negative prognostic factor and found a higher overall death rate in women than in men (4.5% vs 2.6%) only for advanced coronary

artery diseases[6]. On the other hand, the risk of new infarction, stroke, and rehospitalization seemed to be increased in women, irrespective of age, cardiac catheterization and the number of diseased vessels[6].

Psychological burden and functional impairment after CHDs in older subjects

Higher risks of depression and anxiety have been demonstrated in patients after CHDs, and an approximate 20% prevalence of major depressive disorder has been observed during the first year after MI[131–134]. The hypothesis that psychological burden after CHDs could have a negative impact on medical prognosis and mortality has been confirmed by several studies[132,134,135], and Feng et al. reported that patients who experienced post-MI anxiety had a 9-fold increased risk of recurrent MI[133]. These findings, therefore, consolidate the importance of identifying and treating depression and anxiety in patients with CHDs. In addition to a history of prior depressive episodes, belonging to the female gender seems to increase the risk of developing depression after AMI[132-134,136,137]. Women, moreover, showed a higher burden and worse quality of life that was associated with the number and severity of angina symptoms, irrespective of the evidence of myocardial ischemia[138]. Similarly, a study by Bjerkeset et al. reported other sex-related differences in psychological distress during a 5-year follow-up[139]. Despite a higher initial risk for anxiety and depression, women and in particular *older* women demonstrated a risk reduction after two years; conversely, the risk for depression in men rose two years after AMI, suggesting that men have less coping resources compared to women aiding them in adapting to the long-term consequences of CHDs[139-141]. Contradicting previous studies, Zaninotto et al. reported similar results in a sample of older men and women and demonstrated that the latter had better quality of life and an improvement in depressive symptoms over time[142–144]. Among the number of factors influencing quality of life after CHDs, physical impairment and limitation in self-sufficiency involve all age groups and have a greater weight for the female gender[145]. Despite the fact that women demonstrated similar benefits from cardiovascular rehabilitation, fewer are admitted to rehabilitative programs than men, probably because they are older and have more comorbidities at presentation[146]. Unless it is prevented, the loss of functional status after CHDs hastens the age-related decline in older patients and increases the risk of developing other comorbidities, cognitive impairment[147,148] and, finally, disability. Elderly patients suffering from CHDs are therefore at higher risk of becoming frail[149], developing a progressive loss of physiological resilience to stressors [150] that can worsen CHD outcomes[151,152] considering that frailty syndrome, which may be a consequence of CHDs, is also associated with a higher risk of developing other CVDs[150,153–155].

Conclusions

Coronary heart diseases are characterized by several gender differences and age-related features. Sex-specific variability in prevalence, risk factors and presentation of CHDs can lead to difficulties and delays in identifying those pathologies, in particular for women. These patterns, together with the complex clinical condition of older patients who are often characterized by a number of comorbidities, need to be taken into consideration when the management of CHDs is being decided for elderly subjects. For the time being, women continue to be under-investigated and under-treated for CHDs thus resulting in a higher risk of negative outcomes that can progressively impair functional status and give rise to conditions such as frailty and disability. Better management of CHDs in older men and women, therefore, could prevent clinical and functional deterioration and delay worsening of quality of life, all aspects linked to a higher burden for our aging society and healthcare system.

Key messages

- Coronary heart diseases are leading causes of death in the elderly population.
- The current literature still shows a gender and age gap regarding the knowledge of coronary heart diseases in patients of the female gender and those with an advanced age.
- Female patients are older and have more comorbidities at presentation of CHDs.
- A lower rate of diagnostic procedures and invasive therapies are reported for elderly women with respect to men, in particular for mild coronary diseases.
- Female gender has been associated with a worse prognosis and higher mortality for ischemic heart diseases also in advanced age, in particular for ST-elevation myocardial infarction; most of these outcomes seem to be affected by the severity and management of these pathologies.

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