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Research Article

Co-morbidities in Coronary Artery Disease Post-menopausal Women: Data from Southern Italy

Marco Matteo Ciccone[1], Francesca Cortese[2*], Pietro Scicchitano[3], Annapaola Zito[4], Michele Gesualdo[5], Maria Maiello[6], Pasquale Palmiero[7]

[1-5]Cardiovascular Diseases Section, Department of Emergency and Organ Transplantation (DETO), University of Bari, Bari, Italy

[6, 7]Cardiology Department, ASL BR, Brindisi District, Brindisi, Italy

***Corresponding author**
Dr. Francesca Cortese
Email: francescacortese@hotmail.it

Abstract: The aim of our study was to determine the "real-world" prevalence of co-morbidities in a Southern Italian population of postmenopausal women with or without coronary artery disease (CAD) who come to the emergency department for chest pain and suspicion of coronary involvement. 6535 post-menopausal women (mean age: 64 ± 9 years) were enrolled in the study. On the base of results of coronary angiography we recognized CAD-group and CAD-free group. Congestive heart failure (CHF), stroke and chronic lower respiratory tract diseases (CLRTD), hypertension, diabetes, dizziness or syncope, chronic renal failure, urinary incontinence, >4 medications and/or Warfarin use were detected. Results of our study show that 528 (8.1%) women suffered from CAD. Compared to CAD free group, women with CAD have higher prevalence of CHF (9.1% vs. 1.6%, p=0.02), stroke (6% vs. 0.6%, p<0.01) and CLTRD (6.5% vs. 5.4%, p=0.04). Moreover in CAD population, we found significant higher percentages of patients with low GFR (0.9% vs. 0.6%, p=0.02) and Warfarin use (2.3% vs. 2%, p<0.01) than in CAD-free one. The two group did not differ about hypertension, diabetes mellitus, >4 medications use and urinary incontinence (p=ns). Among postmenopausal women with chest pain and suspicion of coronary involvement, those with CAD showed higher co-morbidities percentage than CAD-free. The overall clinical condition should be considered in order to ameliorate care, improve quality of life, reduce morbidity/mortality.

Keywords: postmenopausal women, Co-morbidities, Coronary artery disease, Prevalence, Quality of life, Morbidity, Mortality.

INTRODUCTION

Over the past two centuries, coronary artery disease (CAD) has become the leading cause of morbidity and death in Western countries [1]. Its prevalence increases with age reaching a value of 37% in men and 26% in women aged > 65 years. It represents the greatest cause of death in aging female population due to the well-known loss in cardiovascular protection linked to reproductive hormones [2-4].

The elderly population is rapidly rising in developed countries, with an associated increase in chronic disease, disability-related dependence and institutionalization. Nevertheless, the health, social and economic burden of these patients suffering from major co-morbidities (at least two chronic diseases) and other significant clinical conditions (hypertension, diabetes, chronic renal failure, etc.) is not well considered [5, 6].

About 79% of elderly women with CAD have at least one additional major chronic disease, which determines an increased risk of hospitalizations and a poor outcomes. Co-morbidities and other significant clinical conditions, moreover, could interfere whit CAD therapy, contraindicating the use of essential drugs and driving physicians' treatment decision [7-12].

These elements should be taken into account during prognostic stratification and risk adjustment although few experiences tried to understand how they may affect health status complexity and clinical decision-making [13, 14].

Moreover co-morbidities are often ignored during development of more relevant international clinical practice guidelines, because the largest trials tend to exclude patients suffering from many diseases in order to reduce bias and made more homogeneous population samples.

Our retrospective observational study aims to determine the "real-world" prevalence of some co-morbidities and clinical coexisting conditions in a Southern Italian population of postmenopausal women suffering from chest pain.

MATERIALS AND METHODS

8555 consecutive women admitted to the Cardiology Department, ASL Brindisi, Brindisi, Italy were investigated. All patients underwent coronary angiography as they presented at admission chest pain and suspicion of coronary involvement (troponine elevation not well explained by any other causes and kinetic abnormalities on echocardiography evaluation with or without electrocardiographic signs of cardiac damage) and/or high CAD risk factors (with positive or equivocal cardiac stress testing) [15].

We considered only postmenopausal women, which constituted 76.4% (6535 women, mean age + SD: 64 +9 years) of the overall sample.

On the basis of angiographic results we divided population in two groups: women with coronary atherosclerosis (CAD-group) and patients without it (CAD- free group). Demographic, anamnestic and clinical data were collected in detail.

To the purpose of our study we identified and analyzed for each patient concomitant major diseases (i.e. major co-morbidities), already proved as leading causes of death and/or morbidity in general population, or able to interact with CAD and its treatment, and coexisting clinical conditions, i.e. every status having a weight in the decision-making process of prescribing drugs, as they may represent absolute or relative contraindications (i.e., dizziness in antihypertensive therapy) or may affect quality of life and adherence to therapy.

The study was approved by local ethics committee and carried out in accordance with the principles of the Helsinki Declaration; all patients gave informed consent before entering the study.

Co-morbidities

Concomitant major diseases were diagnosed through a detailed anamnesis, a careful clinical examination and the evaluation of results of specific laboratory and instrumental exams, we focused our attention on the presence of congestive heart failure (CHF), chronic lower respiratory diseases (CRLTD) and stroke.

We considered the diagnosis of CHF when patients had a documented history of CHF and/ or received a specific treatment with beta-blocker, angiotensin converting enzyme-inhibitors and diuretics. The diagnosis was also confirmed by physical examination with the following signs and symptoms: shortness of breath (dyspnea) in exerting or in lying down, fatigue and weakness, declivious oedema, rapid or irregular heartbeat, reduced ability to exercise, ascites, jugular venous distension, abdomino-jugular reflux, pulmonary rales, third sound [16].

CLRD refers to chronic (ongoing) diseases that affect the lower respiratory tract (including the lungs) which include both chronic obstructive pulmonary disease (emphysema or/and chronic bronchitis) and asthma. The diagnosis of each pulmonary diseases was considered possible when was in line whit American Thoracic Society guidelines [17].

Finally we considered plausible the diagnosis of stroke if patients had a documented history (medical reports, cranial computer tomography and magnetic resonance findings consistent with ischemic or hemorrhagic disorders) and clinical signs and symptoms (paresis or paralysis of face, arm, or leg, especially on one side of the body; aphasia, trouble seeing in one or both eyes; trouble walking, loss of balance or coordination) confirming our opinion [18].

Clinical coexisting conditions

The following clinical coexisting conditions were considered: arterial hypertension, diabetes, dizziness or syncopes, chronic renal failure, urinary incontinence, the use of more than four medications and warfarin use.

The diagnosis of arterial hypertension was done in presence of systolic blood pressure [SBP] > 140 mmHg and/or diastolic blood pressure [DBP] > 90 mmHg, or with the use of antihypertensive drugs; of diabetes when fasting blood glucose was > 126 mg/dl in at least two determinations, or > 200 mg/dl during 75 gr oral glucose tolerance test, or patients took antidiabetic drug(s) [19, 20].

Chronic renal failure was defined by a Glomerular Filtration Rate (GFR) value < 60 ml/min/1.73m2, using the Modification of Diet in Renal Disease (MDRD) equation [21, 22]**.**

Moreover we considered patients suffering from urinary incontinence when they referred involuntary loss of urine at least twice/month and affected by dizziness and syncope when they respectively reported dizziness or vertigo for at least 2 weeks or a transient and abrupt loss of consciousness whit fall in the last year [23].

Finally we identified patients taking home more than four medications/daily (included over-the counter analgesics) and warfarin [24].

Statistical analysis

Continuous variables were expressed a mean ± standard deviation or number and percentage of patients. They were compared with Student's t test for paired samples, and frequencies using the chi-square test. A p value< 0.05 was considered statistically significant. Statistical analyses were performed by using STATISTICA 6.1 software (StatSoft Inc., Tulsa, OK).

RESULTS

Table 1 highlights demographic and clinical characteristics of study population.

Our results showed that among 6535 postmenopausal women, 528 (8.1%, mean age 66 + 5 years) presented an atherosclerotic involvement of coronary arteries (CAD-group), while 6007 (91.8%, mean age 63 + 8 years) had not significant atherosclerotic disease of coronary arteries (CAD-free group). The two group did not differ according to age (p=ns). Furthermore, as regard major co-morbidities, we found a statistically higher percentage of patients affected by CHF (9.1% in CAD-group vs. 1.6% in CAD-free one, p=0.02), CLRTD (6.5% in CAD-group vs. 5.4% in CAD-free, p=0.04) and stroke (6% in CAD-group vs. 0.6% in CAD-free one, p<0.01) in CAD-group compared to CAD-free one.

Moreover our results showed an increased prevalence of chronic renal failure (GFR<60 ml/min/1.73m2) and warfarin use in CAD-group than CAD-free counterpart (0.9% in CAD-group vs. 0.6% in CAD-free one, p=0.004 and 2.3% in CAD-group vs. 2% in CAD-free one, p<0.01, respectively). On the contrary we found statistically higher values of referred dizziness or syncope in CAD-free group then in CAD-group (0.6% in CAD-group vs. 1.6% in CAD-free group, p=0.02).

No statistically significant differences were outlined about arterial hypertension, diabetes mellitus, the daily use of more than four medications and urinary incontinence between the two groups considered.

Table 2 depicts the distribution of co-morbidity among CAD women: CHF, CLRTD and Stroke seemed to be the most common diseases affecting respectively 41 (7.7%), 26 (4.9%) and 32 (6%) of considered subjects, while less frequent appeared the contemporary presence of two major disease in addition to coronary atherosclerosis: CHF + Stroke, CHF + CLRTD and Stroke + CLRTD affected only 6 (1.1%), 1 (0.2%) and 1 (0.2%) of CAD patients.

Finally our analysis showed that the overall number of women whit coronary atherosclerosis suffering from at least one other major diseases was 99 (18.1%).

Table 1: Demographic and clinical characteristics of study population

Demographic variables	**Total**	**CAD-free group**	**CAD-group**	p
Menopausal women (%)	6535 (100)	6007 (91.9)	528(8.1)	
Age (mean age ± SD) years	64±9	63±8	66±5	ns
Co-morbidities				
Congestive heart failure (%)	141 (2.16)	93 (1.6)	48 (9.1)	=0.02
Stroke (%)	68 (1.04)	34 (0.6)	32 (6)	<0.01
CLRTD (%)	299 (4.58)	265 (5.4)	34 (6.5)	=0.04
Clinical Coexisting Conditions				
Arterial Hypertension (%)	3822 (58.49)	3511 (58.4)	311 (58.9)	ns
Diabetes mellitus (%)	1990 (30.4)	819 (14)	171 (32.4)	ns
Dizziness or syncopes (%)	101 (1.55)	98 (1.6)	3 (0.6)	=0.02
GFR <60 ml/min/1.73m^2 (%)	28 (0.43)	23 (0.6)	5 (0.9)	=0.004
> 4 Medications (%)	3178 (48.63)	2790 (46.4)	388 (73.5)	ns
Urinary incontinence (%)	1167 (17.86)	1082 (18)	85 (17)	ns
Warfarin use (%)	130 (1.99)	118 (2)	12 (2.3)	<0.01

Numbers (percentages); CAD: coronary heart disease; CLRTD: Chronic lower respiratory tract disease; GFR: Glomerular filtration rate. p< 0.05

Table 2: Co-morbidity rate in patients with CAD

Co-morbidities	CAD group N (%)
CHF	41 (7.7)
Stroke	26 (4.9)
CLRTD	32 (6)
CHF + Stroke	6 (1.1)
CHF + CLRTD	1 (0.2)
Stroke + CLRTD	1 (0.2)
CHF + Stroke/ CHF + CLRTD/ Stroke + CLRTD	8 (1.5)
All	99 (18.1)

Numbers (percentages); CAD: coronary artery disease CHF: Congestive heart failure; CLRTD: Chronic low respiratory tract diseases

DISCUSSION

Our study showed the great complexity of the clinical condition of postmenopausal women suffering from CAD, suggesting it should be considered in clinical trials, guidelines development and clinical decision-making.

All the tree co-morbidities considered (CHF, CLRTD and stroke,) in addition to chronic renal failure (GRF< 60 ml/min) and warfarin use seemed to be more common in women with CAD respect to women CAD-free ($p< 0.05$). (Table 1).

In particular, 99 (18.8%) postmenopausal women had one major disease in addition to CAD and 8 of them (1.5%) more than one (tables 2). We found an elevated rate of clinical coexisting conditions too (Table 1).

Clinical coexisting conditions and major chronic diseases are often present and strongly associated with repeated hospitalization [5, 6]. These findings suggest to consider targeted interventions in order to reduce this unfavorable phenomenon.

To date, there is no consensus on which measures are most suitable for this kind of patients [25]. The utility of this epidemiological analysis is therefore to lead to a reconsideration of the guidelines planning and development because these are generally based on trials not considering all the aspects of patients' clinical status. Implementation of guidelines on the base of clinical practice is difficult, but could improve quality and efficacy in patients care [26-30]. Since guidelines are generally focused on specific diseases and conditions, their application outside of the provided cases could effectively be ineffective and unjustified [2, 31, 32].

Our data suggested that strict adherence to guidelines in women with CAD and co-morbidities, may be associated to poor outcomes: i.e. the prescription to subjects just taking drugs for their own diseases of recommended medications could result in adverse effects (bleeding with antiplatelets drugs in patients under previous oral anticoagulant therapy) [33].

By providing a framework of the complexity of Italian female population whit CAD, our study provides a limited representation of the actual size of a problem, that of co-morbidity, which may have many consequences especially about clinical decision-making process [2]. This article however does not mandate a specific set of conditions that should be considered in the development of clinical practice guidelines, but suggests the necessity of improving their formulation.

Our results showed the need of an overall evaluation of clinical picture of post-menopausal women as constant part of their management. According to our findings, in fact, one every five women have one or more chronic diseases, more than one half hypertension, more than one third diabetes and three quarters assumes more than four medications.

Further studies are necessary in order to improve our results.

Limitations

Although study results could be extended to all the Italian postmenopausal women, our research did not fully assess all factors adding complexity to CAD women management, including depression and other diagnosed mental illnesses, active cancer, aspirin sensitivity, and many others.

Furthermore, this is a single center, retrospective observational study.

Despite these limitations, our work represents a reliable glimpse of the real clinical complexity of adult women with CAD, affirming its importance, more than has been previously recognized in clinical practice.

CONCLUSION

The description of the clinical complexity of post-menopausal women suffering from CAD represents a first step in development of new guidelines more focused on evidence-based medicine than the former ones. This attention may lead to improve quality of life, health care, safety, morbidity and mortality of the overall population.

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