A Composite Measure of Gender and Its Association With Risk Factors in Patients With Premature Acute Coronary Syndrome

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ABSTRACT

Objective: To create a gender index by using principal component analyses (PCA) and logistic regression, and to determine the association between gender, sex, and cardiovascular risk factors among patients with premature acute coronary syndrome (ACS).

Methods: GENESIS-PRAXY is a cohort study including ACS patients aged 55 years or below, and with ACS recruited between 2009 and 2013 from 26 centres across Canada, the United States, and Switzerland. A sample of 1075 patients was used for this study. Psychosocial variables assumed to differ between sexes (i.e., gender related) were included in PCA. Variables identified on retained components were included in logistic regressions where coefficient estimates of variables associated with sex were used to calculate a gender score. Cardiovascular risk factors were assessed using self-report and chart review data.

Results: After the inclusion of 26 psychosocial variables in PCA, we identified 17 variables within retained components; 7 of which were associated with sex in logistic regression. The gender distribution revealed that half of women had a more androgyne or masculine gender score, and 16% of men exhibited a more feminine gender score. In univariable analyses, feminine gender scores and female sex were associated with hypertension, diabetes, family history of cardiovascular disease (only gender), and depressive/anxious symptoms. In multivariable models including both gender score and sex, feminine gender score but not female sex was associated with the presence of risk factors.

Conclusions: Sex and gender are distinct constructs, and the derived gender index offers a current and pragmatic option to measure gender within ACS populations. Our results further suggest that traditional sex differences in cardiovascular disease risk factors may be partly explained by patient's gender-related characteristics.

Key words: sex, gender, index, premature acute coronary syndrome, risk factors.

INTRODUCTION

The distinction between sex and gender, which is common in social sciences, has largely been neglected in health sciences. However, gender plays a central role in men's and women's health, and the integration of a gender-based framework in health research is considered to be a much needed/long-awaited development (1,2).

Unlike sex, which is a biologically based construct, gender has a wider scope and incorporates the effects of social norms and expectations for men and women in a given society (1–5). Specifically, gender has previously been referred to as the psychosocial aspects of being a woman or a man (1,3,6). We could therefore qualify gender as the "psychosocial sex," as different from the "biological sex." *Psychosocial* variables that characterize women and men in a given population (i.e., gender-related variables) can help in explaining differences in many aspects of health and disease between and within sexes.

Evidence that gender-related variables may help in explaining health-related sex differences includes the higher prevalence of cardiovascular diseases (CVD) in younger men than women. The reason why men are at an increased risk may partly be explained by their

ACS = acute coronary syndrome, **CVD** = cardiovascular disease, **PCA** = principal component analysis

SDC Supplemental Content

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propensity to engage in risk-taking behaviors such as smoking or excessive alcohol consumption. However, some men and women may report gender-related characteristics traditionally attributed to the opposite sex. As such, the distribution of gender-related characteristics within populations of men and women is likely to influence health differently than biological sex. According to the Global Gender Gap Report of 2012, the level of inequality (e.g., financial, educational, and medical) between men and women in North America and Europe has decreased considerably since 2006 (7). This phenomenon is likely related to the continual improvement in women's economic participation and opportunities, as well as educational attainment. In parallel, most women continue to retain major "feminine" responsibilities (e.g., child care) even when employed outside the home, and men whose wives work are also faced with increased demands to take charge of such responsibilities (8). To assess the impact of gender-related roles and attitudes on women's and men's health, the integration of a gender-based framework is imperative.

Different approaches have been proposed to conceptualize and measure gender since the mid-20th century. Gender was first described as a bipolar one-dimensional personality trait (i.e., ranging from femininity to masculinity), and later, as a concept that distinguished masculinity and femininity as two separate and independent dimensions (9–11). However, two-dimensional approaches do not seem to be more efficient than one-dimensional views of gender in predicting gender-related aspects such as nurturing behaviors, aggressiveness, or specific mathematical skills (5,9–11). Regardless, we consider both approaches defensible and focused instead on identifying their limitations that needed to be addressed. Indeed, one of the major weaknesses of these approaches was the inclusion of specific variables often focused on personality traits in the construction of a survey for any given population. This focus is problematic because gender roles and attitudes are largely dependent on culture, age, and era. Therefore, operationalizing gender solely in terms of personality characteristics like "nurturing" may not be so useful because; for example, men of one generation may be significantly more nurturing than men of another generation, and this variable may not always allow you to identify "feminine-behaving" men. As such, an approach developing a "method" to measure gender in specific populations, rather than a "survey" applicable to all, would likely be more appropriate.

In 1990, Lippa and Connelly (5) presented their gender diagnosticity approach, which refers to "the Bayesian probability that an individual is predicted to be a man or a woman on the basis of some set of gender-related diagnostic indicators." Their method was designed to assess "gender-related individual differences in terms of behaviors that actually discriminate between men and women within a given population rather than in terms of gender stereotypes." Although this approach has considerable advantages, it has been constructed based on men's and women's occupational preferences and hobbies, and has been associated with specific gender-related behaviors (e.g., mathematical and verbal skills), all of which could be updated to better suit health research, especially CVD research.

Our objective was therefore to construct a gender index including a variety of psychosocial gender-related variables, which would allow for discrimination between men and women in our cohort. We also aimed to determine the association between the derived gender score and the presence of CVD risk factors among a cohort of patients with a premature acute coronary syndrome (ACS). To do so, we used an approach similar to that of Lippa's and adapted it to health research by following some propositions from researchers in the field (1,3). These researchers propose to identify specific cohorts, assess health prognosis or specific disease-related risk factors or morbidity, and determine which psychosocial sex-differing aspects are associated with adverse outcomes or morbidity in that cohort (1).

METHODS

Study Design and Procedure

We used data from GENESIS-PRAXY (Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond -Premature Acute Coronary Syndrome), a multicenter, observational study of patients with premature ACS. Participants were recruited between January 2009 and April 2013, from the Coronary Care Unit of 24 centers across Canada, 1 in the United States, and 1 in Switzerland. The detailed methodology of the GENESIS-PRAXY study has been previously published (12).

In Quebec, a multicenter ethics review allowed for the McGill University Heath Centre to act as the central review board and coordinate ethics approval for all centers. All other centers received ethics approval from their respective hospital ethics review board.

Patients who presented to one of the participating hospitals with ACS were eligible for recruitment if they were a) 18 to 55 years of age, b) fluent in English and/or French, c) and able to provide informed consent. Eligible ACS patients were approached by a research nurse in the coronary care unit at the earliest possible time after admission. For the current study, 1075 patients (32% women) with a median age of 48 years were included (Appendix A, Supplemental Digital Content, http://links.lww.com/PSYMED/A209).

After the completion of the consent form at the coronary care unit, participants were asked to complete a self-administered questionnaire that assessed gender-related variables described later. Medical chart reviews were also undertaken by the research nurse to collect participants' CVD risk factors data.

Gender-Related Variables

As part of the GENESIS-PRAXY study, numerous variables relevant to CVD research were measured to cover most of the four gender aspects described by the Women Health Research Network of the Canadian Institute of Health Research (gender roles, gender identity, gender relations, and institutionalized gender; Table 1) (3). These variables were initially selected to be included in the GENESIS-PRAXY study by a subgroup of the study investigators. This group was in charge of identifying most categories of gender-related variables relevant to CVD research, from previous literature, and based on the widely used definition of gender-related variables

TABLE 1. Four Aspects That Represent Gender, According to the Women Health Research Network of the Canadian Institutes of Health Research

Gender roles	Represent the behavioral norms applied to men and women in society, which influence individuals' everyday actions, expectations, and experiences. Gender roles often categorize and control individuals within institutions such as the family, the labor force, or the educational system
Gender identity	Describes how we see ourselves as female or male (or as a third gender), and affects our feelings and behaviors
Gender relations	Refer to how we interact with or are treated by people in the world around us, based on our ascribed gender
Institutionalized gender	Reflects the distribution of power between men and women in the political, educational, and social institutions in society. The institutionalized aspect of gender also shapes social norms that define, reproduce, and often justify different expectations and opportunities for men and women.

Definitions in this table come from Johnson et al. (7).

(i.e., have been historically reported as being different in men and women (1,3,6)). The following variables were therefore measured using a self-administered questionnaire: household's primary earner status (assessed using the question: “Are you the primary earner in your household?” to which participants answered “yes” or “no”); employment status; number of hours of work per week; level of responsibility for caring for children (assessed using the question: “For the children that live with you, to what level are you responsible for caring for them?” to which participants rated their level of responsibility on a scale from 0 to 6); level of responsibility for disciplining the children (using the same question as the previous but replacing “caring for” with “disciplining”); number of hours per week spent doing housework; being the person at home primarily responsible for doing housework; gender-related personality traits assessed using masculinity and femininity scores on the BEM Sex Role Inventory (BSRI) (13); stress level at work, at home, and overall (on a scale from 1 to 10 for the three stress-related variables); level of confidence in stress management abilities (assessed using the question: “How confident do you feel in managing your stress?” to which participants chose between “not confident” (1), “a little confident” (2), “moderately confident”, and (3) “very confident”); social support–related variables, found in the items of the Enhancing Recovery in Coronary Heart Disease Patients Social Support Instrument (14); marital status; personal income; level of education; perceived social standing within patient's community and within Canada, assessed using the MacArthur Perceived Social Standing Scale (15); and job value and job quality deficits-related variables (e.g., advancement opportunities, schedule flexibility, and benefits), assessed using a previously modified (16) version of the Canadian Policy Research Network-Ekos Changing Employment Relationships Survey Questionnaire (16).

Risk Factors for Cardiovascular Diseases

Hypertension, dyslipidemia, diabetes, obesity, family history of CVD, cigarette smoking, and depressive (17) and anxious (18) symptoms were determined using a combination of self-report and medical chart review data. Body mass index was calculated from height and weight, and obesity was defined as a body mass index of 30 kg/m^2 or greater. To assess symptoms of depression and anxiety present before the onset of ACS, the Hospital Anxiety and Depression Scale (19) was used with the following instruction: “Before your heart attack (Please tick the box that most reflect your feelings to the following statements).”

Construction of the Gender Index

To group and reduce the number of gender-related variables to be included in the gender index, we first used principal component analysis (PCA). The principal axis method was used to extract the components, and “one” was used as prior communality estimates (20). A scree test was also used to visually identify a “break” between the components with relatively large eigenvalues and those with small eigenvalues. Only the components that appeared before the break were assumed to be meaningful and were retained for varimax rotation (20,21).

Second, to determine which variables were actually gender related in our cohort of patients, we conducted logistic regressions using sex as the dependent variable. This dependent variable was chosen because gender-related variables have mostly been historically based on social norms and expectation reported for men and women. Thus, we aimed to objectively define the variables that were more associated with the reality of “being a men or a women” in the GENESIS-PRAXY cohort. This approach to determining the gender-related nature of variables has previously been reported (1,4,5) and is justifiable by a common definition of gender-related variables (psychosocial variables that differ between men and women), as well as by the objective pursued by the construction of a gender index (to discriminate between men and women based on a variety of psychosocial variables). For this purpose, a first logistic regression was conducted, including sex as the dependent variable and the variables retained from the PCA as the independent variables. A series of regressions were conducted whereby variables that were not significantly associated with sex ($p > .05$) were removed from the regression model one at a time, in descending order based on their respective p value (22), until all the remaining variables had a p value of <.05.

Coefficient estimates obtained through the final logistic regression were used to calculate a propensity score, which we called the gender score. Such scores are used in observational studies to estimate the conditional probability of a particular exposure (in our case, being a woman) versus another (i.e., being a man), for one person, given observed confounders (all the gender-related variables retained in the model and constituting the gender index). Patients with similar scores share similar characteristics and probability of exposure (23).

Gender Score

The gender score was used to categorize patients according to the masculine and feminine characteristics they present (i.e., according to their gender profile). This score represented the probability between 0% and 100% for each patient of our sample to be a “woman.” The lower the gender score is, the more masculine a patient is and vice versa (i.e., higher gender scores represent patients with higher level of characteristics associated with women in our sample). Therefore, this gender scale is considered as a continuum, ranging from masculine characteristics (gender scores toward zero) to feminine characteristics (gender scores toward one hundred). Middle scores are rather indicative of androgynous types of gender (similar levels of both masculine and feminine characteristics).

Statistical analyses were performed using SAS version. 9.2 (Cary, NC). *p* Values <.05 were considered statistically significant. All statistical models were including two-thirds of the GENESIS-PRAXY cohort, in which a portion of the cohort was selected randomly. The remaining one-third of the sample was used to validate the results obtained with the first sub-sample.

RESULTS

Principal Component Analysis

We first conducted a correlation analysis including all traditionally defined gender-related variables described earlier. For each pair of variables for which the correlation coefficient was equal to or greater than 0.80, one of the two variables was randomly excluded (20). Because job quality-related variables were all strongly correlated between each others, as well as with the variable representing "being employed," we excluded all of the job value and quality deficit variables and included the employment variable only, to reduce as much as possible the number of variables to include in further steps. After this procedure, perceived social standing within Canada, child discipline responsibility level, and job value and job quality deficit–related variables were excluded. The PCA analysis was then conducted using the remaining 26 variables. The first 6 components displayed eigenvalues greater than 1, and the results of the scree test also suggested that only the first six components were meaningful. Therefore, in the present analysis, only the first six components were retained for rotation. Combining components 1 to 6 accounted for 70% of the total variance in our data set. Gender-related variables and corresponding factor loadings are presented in Table 2.

In interpreting the rotated factor pattern, an item was said to load on a given component if the factor loading was 0.40 or greater for that component and was less than 0.40 for the others. Using the previous criteria, a total of 17 gender-related variables were found to load on the six retained components.

TABLE 2. Gender-Related Variables and Their Corresponding Factor Loadings From the Principal Component Analysis

	Component 1	Component 2	Component 3	Component 4	Component 5	Component 6
Primary earner status	−20	−13	3	37	−18	46[a]
Personal income	11	2	1	73[a]	−23	18
Employment status	9	−13	1	60[a]	−12	3
Education level	0	4	5	74[a]	14	−13
Level of responsibility for caring for children (from 0 to 6)	3	9	90[a]	5	−4	5
No. hours per week doing housework	4	7	33	−14	67[a]	−21
Primary responsibility for doing housework	−24	5	−9	−5	79[a]	−10
Level of stress at home (from 1 to 10)	−10	84[a]	18	−5	7	7
Level of stress overall (from 1 to 10)	−7	89[a]	3	4	12	14
Stress management abilities (from 1 to 10)	15	−65[a]	9	14	7	29
BSRI masculinity score	12	5	1	0	−7	80[a]
BSRI femininity score	17	4	−3	−15	55[a]	34
Someone available to listen to you (from 1 to 5)	87[a]	−7	−7	3	10	10
Someone available to give you advice (from 1 to 5)	86[a]	−10	−7	6	9	9
Someone available to give you affection (from 1 to 5)	83[a]	0	6	4	−9	−6
Someone available that you can trust and confide in (from 1 to 5)	82[a]	−11	0	5	0	4
Level of emotional support (from 1 to 5)	92[a]	−11	0	5	0	4

BSRI = Bem sex role inventory.

[a] Refers to items significantly loading on given components, according to the cutoff ≥ 40.

TABLE 3. Variables Associated With Sex in Patients With Premature Acute Coronary Syndrome

	Coefficient Estimate	*p*
Primary earner status	−1.31	<.001
Personal income	−0.31	<.001
No. hours per week doing housework	0.06	<.001
Primary responsibility for doing housework	2.31	<.001
Level of stress at home	0.19	<.001
BSRI masculinity score	−0.37	.019
BSRI femininity score	0.71	<.001

BSRI = Bem sex role inventory.

Logistic Regressions

Of the 17 variables identified through the PCA, 7 variables were found with logistic regression to be associated with sex (Table 3). We quantified the predictive accuracy of the retained gender-related variables by using the *c* statistic (24) to test the hypothesis that these variables were performing significantly better than chance to predict biological sex (indicated by a *c* statistic of 0.5). The final regression model including seven gender-related variables yielded a *c* statistic of 0.9, indicating that our model explained biological sex significantly better than chance.

Gender Scores Distribution in the GENESIS-PRAXY Cohort

We calculated gender scores and computed tertiles for the first two-thirds of our cohort, and in men and women separately. In the first subsample, one-third of patients had a gender score between 0 and 5, another third had scores between 6 and 39, and the last third had gender scores ranging between 39 and 100. Interestingly, when calculating tertiles scores for men and women separately, we observed that for men, gender scores ranged between 0 and 3, 4 and 12, and 13 and 100, for the first, second, and third tertiles, respectively. In comparison, scores for the associated tertiles in women ranged between 0 and 48, 49 and 82, and 83 and 100, respectively. An overlap between a considerable proportion of men and women across the gender score continuum highlights the fact that sex and gender are at least partly independent (Fig. 1).

The coefficient estimates obtained through the final logistic regression of the first two-thirds of the sample were used to calculate the gender score of patients in the remaining one-third of the validation subsample. The results obtained yielded a gender distribution similar to that observed in the first subsample. When men and women were combined, one-third of the patients had a score between 0 and 10, another third had a score between 11 and 39, and the last third of the sample had a score between 40 and 100. In stratified analyses, associated gender scores ranged between 0 and 7, 8 and 25, and 26 and 100 in men, whereas in women, tertile scores ranged between 0 and 42, between 43 and 75, and between 76 and 100.

Associations Between Gender, Sex, and Risk Factors for Cardiovascular Diseases

Patient characteristics are presented in Tables 4 and 5. In univariable models, higher gender scores (toward high level of feminine characteristics) were associated with an

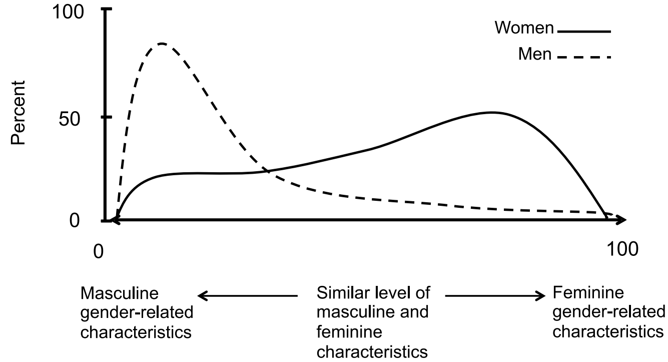

FIGURE 1. Gender distribution in men and women with premature ACS. ACS = acute coronary syndrome.

TABLE 4. Patient Demographic and Clinical Characteristics According to Tertiles of the Gender Score

	Tertile 1 Masculine Characteristics	Tertile 2 Masculine and Feminine Characteristics	Tertile 3 Feminine Characteristics	*p*
Demographic characteristics				
Age, y, median (IQR)	48 (8)	48 (7)	48 (7)	.70
Married or common law	258 (86)	116 (58)	186 (60)	<.001
Women	6 (2)	60 (20)	207 (66)	<.001
Men	294 (98)	240 (80)	102 (34)	<.001
Race, white	267 (89)	266 (85)	272 (88)	.43
Clinical profile				
Hypertension	132 (44)	133 (43)	173 (56)	.004
Dyslipidemia	175 (59)	165 (55)	162 (52)	.32
Diabetes	37 (12)	38 (13)	71 (23)	<.001
Obesity	120 (40)	113 (38)	124 (40)	.77
Family history of CVD	62 (21)	58 (19)	84 (27)	.046
Smoking	111 (37)	121 (40)	133 (43)	.95
Significant depression (score ≥8 on the HADS)	58 (19)	66 (22)	90 (29)	.013
Significant anxiety (score ≥8 on the HADS)	92 (31)	122 (41)	167 (54)	<.001

IQR = interquartile range; CVD = cardiovascular disease; HADS = Hospital Anxiety and Depression Scale.
Data are presented as *n* (%) unless otherwise indicated.

increased risk of hypertension, diabetes, and family history of CVD, as well as with increased levels of depressive and anxious symptoms (Table 6).

Univariable results for sex yielded a similar pattern as female sex was associated with an increased risk of hypertension and diabetes, as well as with increased levels of depressive and anxious symptoms. However, there was no association between sex and family history of CVD.

We further assessed the Spearman correlation between the gender score and sex, for which we obtained a correlation coefficient of 0.62. Given the moderate association between the two variables, we conducted multivariable

TABLE 5. Patient Demographic and Clinical Characteristics According to Sex

	Men	Women	*p*
Demographic characteristics			
Age, y, median (IQR)	48 (8)	48 (7)	.52
Married or common law	490 (66)	203 (61)	.09
Race, white	610 (82)	284 (85)	.27
Clinical profile			
Hypertension	333 (45)	181 (54)	.004
Dyslipidemia	410 (55)	176 (53)	.42
Diabetes	102 (14)	77 (23)	<.001
Obesity	283 (38)	141 (42)	.21
Family history of CVD	144 (19)	81 (24)	.07
Smoking	274 (37)	143 (43)	.07
Significant depression (score ≥8 on the HADS)	147 (20)	95 (28)	.001
Significant anxiety (score ≥8 on the HADS)	260 (35)	173 (52)	<.0001

IQR = interquartile range; CVD = cardiovascular disease; HADS = Hospital Anxiety and Depression Scale.
Data are presented as *n* (%) unless otherwise indicated.

TABLE 6. Coefficient Estimates of the Associations Between the Gender Score, Sex, and Cardiovascular Disease Risk Factors

	Hypertension, OR (95% CI)	Dyslipidemia, OR (95% CI)	Diabetes, OR (95% CI)	Obesity, OR (95% CI)	Family Hx, OR (95% CI)	Smoking, OR (95% CI)	Depressive Sx, β (95% CI)	Anxious Sx, β (95% CI)
Univariable models								
Gender score	2.11 (1.36–3.26)**	0.79 (0.51–1.22)	3.04 (1.74–5.29)***	1.22 (0.79–1.89)	1.94 (1.17–3.19)**	1.48 (0.96–2.29)	3.09 (2.11–4.54)***	4.47 (3.04–6.60)***
Univariable models								
Female sex	1.45 (1.12–1.88)*	0.90 (0.69–1.17)	1.88 (1.35–2.61)**	1.18 (0.91–1.54)	1.33 (0.97–1.81)	1.28 (0.98–1.66)	1.81 (1.44–2.29)***	2.21 (1.75–2.80)***
Multivariable models								
Gender score	1.85 (1.04–3.29)*	0.88 (0.49–1.56)	2.07 (1.00–2.39)*	1.21 (0.68–2.18)	1.93 (1.00–3.78)*	1.14 (0.64–2.04)	2.68 (1.61–4.44)***	3.62 (2.17–6.01)***
Sex	1.14 (0.78–1.67)	0.91 (0.62–1.32)	1.46 (0.89–2.39)	1.00 (0.68–1.48)	1.00 (0.64–1.56)	1.30 (0.89–1.90)	1.16 (0.83–1.61)	1.24 (0.89–1.73)

OR = odds ratio; CI = confidence interval; Hx, history; Sx, symptoms.

* $p < .05$, ** $p < .001$, *** $p < .0001$.

models including both the gender score and sex as the exposure variables. In these analyses, a higher gender score, but not female sex, was associated with an increased risk of hypertension, diabetes, family history of CVD, and increased depressive and anxious symptoms (Table 6).

DISCUSSION

In this study, we report the construction of a composite gender index for measuring gender in patients hospitalized for premature ACS. We initially included gender-related variables that were selected based on traditional assumption of a sex difference and that covered the four aspects of gender as defined by the Women Health Research Network of the Canadian Institutes of Health Research (3): gender roles, gender relations, gender identity, and institutionalized gender. The inclusion of the final seven gender-related variables that discriminated between sexes in our cohort had an excellent predictive accuracy, suggesting that our gender index does include *psychosocial* characteristics mostly associated with the reality of being a man or a woman in our cohort. We further observed that more feminine types of gender, as opposed to more masculine gender scores were associated with a heavier burden of CVD risk factors, independent of female sex.

Although the incidence of ACS has always been higher in men than in women of all ages, it has recently been observed that this incidence is increasing disproportionately among younger women compared with younger men. Thus, stereotypes, or gender-related characteristics traditionally attributed to men and women, may not be representative of the reality of younger men and women experiencing premature ACS and of younger adults at risk for CVD in general. In fact, an important proportion of women in our cohort had a gender score toward a high level of masculine characteristics. In other words, these patients are of female biological sex, but of rather masculine "psychosocial sex." This specific distribution of gender-related roles and traits may help in explaining why these men and women sustained an ACS at such a young age. Further prospective studies are needed to assess whether gender-related roles and traits are associated with the development of CVD in young healthy adults.

Our finding that feminine gender scores are associated with CVD risk factors burden independently of female sex suggests that traditional sex differences in risk factors (25–28) may partly be explained by patients' personality traits, social roles, and life context. For example, men and women who are responsible for the care of children and housework and who have poor stress management abilities and/or face lack of resources may adopt poor health behaviors, be sleep deprived, or develop endocrine imbalances, leading to the development of CVD risk factors. It is noteworthy that being the "primary earner" in the house and being the "primary person responsible" for doing housework were the gender-related variables with the highest weight in the calculation of the gender score, suggesting that financial responsibility and home-related workload play a role that is especially important in the risk factor profile of young adults with ACS.

Results of the present study are consistent with previous results showing an association between family roles and coronary heart disease incidence (29). In one study, Japanese women living with both spouse and children had a 2.1-fold higher risk of coronary heart disease compared with women living with spouse, but not any children. Overall, the finding that our ACS cohort exhibits predominantly masculine characteristics but that more feminine gender characteristics are associated with CVD risk factors is also in line with the pattern of ACS incidence in younger adults (higher in men than in women) and risk factor trends in younger ACS populations (heavier burden of diabetes, hypertension, family history, and depressive and anxious symptoms in women than in men) (30,31). However, our results add to the existing literature by suggesting that traditional sex differences in ACS and risk factors prevalence may be better explained by patients' gender-related characteristics than by biological sex characteristics. This finding suggests that secondary prevention in ACS patients may need to incorporate the consideration of gender-related characteristics and not only sex-specific risks.

Our study is important because in the last decade, literature focusing on the importance of distinguishing gender from sex, as well as the important role gender may play in the incidence of CVD, has multiplied (1–3,32). For example, Ristvedt (2) and Krieger (32) aimed to highlight the differences and connections between gender and sex and to stress the importance of considering both constructs in the context of health research. Both researchers presented some health studies in which gender and sex are relevant as independent or synergistic determinants of studies outcomes, and Krieger stressed that “the relevance of gender relations and sex-linked biology to a given health outcome is an empirical question, not a philosophical principle; depending on the health outcome under study, both, neither, one, or the other may be relevant as sole, independent, or synergistic determinants.”

The need for the construction of a composite gender index is further emphasized by previous reports on the statistical problems associated with the need to deal with multiple variables to assess a single construct (33). Finding a pragmatic way to assess the effects of psychosocial factors has proved to be a challenge. Whitaker et al. (34) used PCA to measure common variance among multiple psychosocial variables (although not representing gender specifically) such as depressive and anxious symptoms. That study aimed to create a composite variable that would explain the presence of CVD risk factors and events among a cohort of women. The authors concluded that composite scores can represent a good summary of multiple psychosocial variables, the latter of which usually need to be entered all together in statistical models.

Our proposed gender index therefore represents a most needed option. Researchers interested in measuring gender could use our gender index within their study samples of patients with premature ACS and use this index in multivariable regression analyses to measure the effect of gender. Furthermore, researchers could follow the methodology presented to construct a gender index suited to their specific populations. In brief, the proposed gender index represents a pragmatic option for health researchers to measure gender.

Our approach considers gender as a bipolar one-dimensional continuum. Because gender-related variables can be present in both men and women, but at different levels, we think that considering “masculine gender” and “feminine gender” as a one-dimensional concept is as defensible as two-dimensional approaches. Moreover, the one-dimensional approach has specific methodological advantages over the two-dimensional ones. For example, only one variable needs to be included in statistical models, as opposed to multiple variables such as femininity, masculinity, and androgyny, which later option may lower statistical power and make the interpretation of the results more complex. The one-dimensional continuous view of gender is also consistent with Lippa's conception of gender and gender diagnosticity approach (5).

The present study should be interpreted in light of some methodological limitations. First, no official definition for gender-related variables currently exists. Therefore, our selection of variables representing the four aspects of gender is arbitrary. However, we believe that defining a gender-related variable as a psychosocial variable that differs between men and women is in keeping with the existing gender literature, which mostly refers to gender using roles, attitudes, opportunities, and expectations for men versus women (1,3,6,32). Second, as no gold standard for gender exists, we elected to use biological sex as a dependent variable in our logistic regression analyses. The Bem Sex Role Inventory could have been used instead of biological sex as the dependent variable. However, this scale solely includes personality traits that are thought to be more representative of a man or a woman and only represents the gender identity aspect of the gender construct. Third, our cohort comprised a majority (68%) of men and because gender and sex are interrelated, the results obtained may have been influenced by this distribution. However, the prevalence by sex in our cohort is representative of what is observed in other ACS cohorts (35,36), and therefore, the gender distribution we observed may be representative. Finally, depressive and anxious symptoms that were present before the index ACS were assessed at the hospital after the ACS. Therefore, we cannot exclude the possibility of a recall bias, which could also be sex specific. However, the proportion of patients in our cohort with significant depression and anxiety (23% and 42%, respectively) is consistent with what has previously been reported in hospitalized myocardial infarction cohorts (26), and as such, it is representative of this population.

In conclusion, our study proposes a simple index to measure gender and calculate gender scores in patients with premature ACS. Our results also highlight that sex and gender are not interchangeable notions and that they are partly independent. Indeed, we further observed that feminine gender scores were associated with a heavier burden of CVD risk factors, independent of biological sex. A measure of gender will lead to a paradigm shift in understanding sex differences in CVD. Future studies in CVD may benefit from using the proposed index to measure gender and/or to validate other propositions of gender indices using a similar approach.

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