

## Clinical Research

# Sex- and Gender-Related Risk Factor Burden in Patients With Premature Acute Coronary Syndrome

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*See editorial by Shaw, pages 12-13 of this issue.*

## ABSTRACT

**Background:** Few contemporary data exist on traditional (TRF) and non-TRF (NTRF) burden in patients with premature acute coronary syndrome (ACS).

**Methods:** Prevalence of TRFs and NTRFs were measured in 1015 young (55 years old or younger) ACS patients recruited from 26 centres in Canada, the United States, and Switzerland. Risk factors were compared across sex and family history categories, and against a sample of the general Canadian population based on the 2000-2001 Canadian Community Health Survey. The 10- and 30-year risks of cardiovascular disease (CVD) were estimated using Framingham Risk Scores.

**Results:** Risk factors were more prevalent in premature ACS patients compared with the general population. Young women with a family history of coronary artery disease showed the greatest risk factor burden including TRFs of hypertension (67%), dyslipidemia (67%), obesity (53%), smoking (42%), and diabetes (33%), and NTRFs of anxiety (55%), low household income (44%), and depression (37%). The estimated median 10-year risk of CVD was 7% (interquartile range [IQR], 3%-9%) in women and 13% (IQR, 7%-17%) in men, whereas the

## RÉSUMÉ

**Introduction :** Peu de données récentes existent sur le fardeau traditionnel (TRF) et le non TRF (NTRF) chez les patients ayant un syndrome coronarien aigu (SCA) prématuré.

**Méthodes :** La prévalence des TRF et des NTRF a été mesurée chez 1015 jeunes patients (55 ans ou moins) ayant un SCA qui ont été recrutés dans 26 centres au Canada, aux États-Unis et en Suisse. Les facteurs de risque ont été comparés entre les catégories de sexe et d'antécédents familiaux, et par rapport à un échantillon de la population canadienne générale tiré de l'Enquête sur la santé dans les collectivités canadiennes de 2000-2001. Les risques à 10 et à 30 ans de maladie cardiovasculaire (MCV) ont été estimés en utilisant les scores de risque de Framingham.

**Résultats :** Les facteurs de risque ont été plus répandus chez les patients ayant un SCA prématuré comparativement à la population générale. Les jeunes femmes ayant des antécédents familiaux de coronaropathie ont montré le plus grand fardeau de facteur de risque incluant les TRF d'hypertension (67 %), de dyslipidémie (67 %), d'obésité (53 %), de tabagisme (42 %) et de diabète (33 %), et les NTRF d'anxiété (55 %), de ménages à faible revenu (44 %) et de

The growing prevalence of risk factors for cardiovascular disease (CVD) in younger adults has contributed to recent increases in the incidence of CVD.<sup>1,2</sup> Today, adults younger than the age of 55 account for nearly a quarter of all patients with acute coronary syndrome (ACS).<sup>3,4</sup> These young patients are thought to exhibit a unique risk factor profile, because the prevalence of smoking,<sup>3-5</sup> obesity,<sup>4</sup> and family history of

coronary artery disease (CAD)<sup>4,5</sup> have been found to be higher than those of older ACS patients. Despite the serious public health and economic burden posed by the premature occurrence of ACS (equal to or younger than the age of 55), traditional (TRF) and non-TRF (NTRF) profiles of these young patients have been poorly described. Most importantly, few studies have examined potential sex differences in the risk factor profiles of premature ACS patients, although ACS has been found to affect men and women differently.<sup>6</sup> Furthermore, individuals with a family history might not share a family risk factor burden compared with patients without a family history.

In this study, we compared the prevalence of TRFs and NTRFs between ACS patients and the general Canadian

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See page 116 for disclosure information.

30-year risk of CVD was 36% (IQR, 22%-49%) in women and 44% (IQR, 31%-57%) in men.

**Conclusions:** Patients with premature ACS, especially women with a positive family history, are characterized by a very high risk factor burden that is poorly captured by 10-year risk estimates but better captured by 30-year estimates. Consideration of NTRFs and use of 30-year risk estimates might better estimate risk in young individuals and improve the prevention of premature ACS.

population, and between men and women with premature ACS. Specifically, we investigated whether the presence of a family history of CAD modifies the risk factor profile in men and women. In addition, we estimated the 10- and 30-year risk of developing CVD among men and women suffering from premature ACS.

## Methods

### Study design and population

We used data from **Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome (GENESIS-PRAXY)**, an ongoing, multicentre prospective cohort study of young adults hospitalized for ACS. A full description of the design and methods of GENESIS-PRAXY has been described previously.<sup>7</sup>

Eligible patients were adults aged between 18 and 55 years, fluent in English or French, able to provide informed consent, and admitted to the hospital with a confirmed diagnosis of ACS. All eligible, consecutive, ACS cases were approached by the research nurse in the coronary care unit at the earliest possible time after admission. Since 2009, 1015 patients have been enrolled across 24 centres in Canada, 1 in the United States, and 1 in Switzerland.

### Data collection

Data were collected in baseline questionnaires completed by patients during hospitalization and in medical chart reviews completed by trained research nurses.

TRFs of diabetes, dyslipidemia, hypertension, smoking, family history of CAD, and obesity were determined using a combination of baseline questionnaire and chart review data. Diabetes, dyslipidemia, and hypertension were determined from chart reviews indicating previous diagnosis, disease-specific medication use, or from the patient's self-reported diagnosis in baseline questionnaires. Current and previous smoking status was determined from the patient's self-reported current and previous use of cigarettes, respectively, in baseline questionnaires. Current smoking was used to represent smoking as a TRF in all analyses. A positive family history was defined as having at least 1 first-degree male relative who experienced ACS before 45 years of age or at least 1 first-degree female relative who experienced ACS

dépression (37 %). Le risque estimé median à 10 ans de la MCV a été de 7 % (écart interquartile (ÉIQ), 3 %-9 %) chez les femmes et de 13 % (ÉIQ, 7 %-17 %) chez les hommes, tandis que le risque à 30 ans de MCV a été de 36 % (ÉIQ, 22 %-49 %) chez les femmes et de 44 % (ÉIQ, 31 %-57 %) chez les hommes.

**Conclusions :** Les patients ayant un SCA prématuré, particulièrement les femmes ayant des antécédents familiaux positifs, sont caractérisés par un fardeau de facteur de risque très élevé qui est médiocrement saisi par les estimations du risque à 10 ans, mais mieux saisi par les estimations à 30 ans. La considération des NTRF et l'utilisation des estimations du risque à 30 ans pourraient mieux estimer le risque chez les jeunes individus et améliorer la prévention du SCA prématuré.

before 55 years of age. Obesity, defined as having a body mass index  $\geq 30$ , was determined by research nurses according to height and weight measurements recorded in patient charts.

NTRFs were determined using the baseline questionnaire, chart reviews, or a combination of these resources. Specifically, "ethnicity" information was collected using the baseline questionnaire in which patients were asked to identify themselves as 1 of black, Caucasian (white), or other. "Marital status" of living alone was defined in patients reporting to be widowed, separated, divorced, or single/never married. "Limited formal education" was defined as having no educational degree, certificate, or diploma. "Low household income" was defined as having an annual family income  $< \$50,000$  CDN. "Unemployment" was determined in patients who reported a current work status of unemployed and looking for work. Screening for stress and adaptation to stress have been recognized as important preventive measures in reducing cardiovascular risk.<sup>8</sup> "High stress" at home and at work were defined using a cutoff score of  $\geq 6$  on a scale ranging from 1 (no stress) to 10 (most stress). "Low stress management" abilities were defined in patients reporting "not confident" to the question, "How confident do you feel in managing your stress" from the choices of "not," "a little," "moderately," and "very" confident. The circumstance of "living with a child" was assessed through baseline questionnaire, and "low social support" was defined using a cutoff score of  $\leq 18$  on the ENRICH Social Support Instrument (ESSI) (including items 1, 2, 3, 5, and 6).<sup>9</sup> "Physical activity" was assessed using the Godin Leisure-Time Exercise questionnaire,<sup>10</sup> in which patients were asked to report the weekly frequency of strenuous, moderate, and mild physical activities. Physical activity scores for each patient were determined using the prespecified formula, physical activity score =  $(9 \times \text{weekly frequency of strenuous activities}) + (5 \times \text{weekly frequency of moderate activities})$ , and used to determine the status of insufficient physical activity (score  $< 14$ ).<sup>11</sup> "Excessive alcohol consumption" was determined as consuming at least 2 alcoholic beverages per day. "Cocaine use" and "recreational drug use" were identified from the self-reported baseline questionnaire. "Anxiety" and "depression" were assessed using the Hospital Anxiety and Depression Scale (HADS),<sup>12</sup> in which patients were asked 7 questions for each of anxiety and depression using a 4-point response category (0-3). With the score scale ranging from 0 to 21, patients with a score of  $\geq 8$

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