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Sex Differences in Clinical and Angiographic Characteristics in Acute Coronary Syndrome Patients in Dakar, Senegal

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Abstract

Background: Coronary artery disease (CAD) is in relentless progression, along with the adoption of western lifestyle in sub-Saharan Africa. In Senegal, the incidence of acute coronary syndrome (ACS) rose from 5% to 12% in Dakar during the last 20 years. That increase was observed in both women and men, and according to current data, the former paid the heaviest price in terms of mortality compared to men. In this study, we aim to retrospectively assess the clinical characteristics and angiographic profile of ACS in women compared to men in two tertiary care centers in Dakar. **Methods:** In this study, we retrospectively analyzed and compared data between men and women among 133 patients who underwent coronary angiogram for ACS in 2 tertiary centers from February 2019 to January 2020. **Results:** A total of 133 patients were included in our study of whom 97 (72.9%) were men. The mean age was 58 ± 13.6 years. Women were older than men (61.4 ± 14.3 years vs 56.6 ± 13.5 years ($p = 0.07$). Hypertension, sedentary lifestyle and obesity were significantly more frequent in women (69.4%, 52.7% and 19.4%) when compared to men (38.8%, 25.7% and 6.19%) respectively, ($p = 0.001$; 0.002 and 0.03). Smoking was less frequent in women (2.8%) than in men (44.3%), ($p < 0.001$). The mean time from diagnosis to coronary angiography was not statistically different regardless of the presentation mode. On coronary angiogram, single vessel disease was most common (36.1% of men vs 33.3% of women) followed by triple vessel disease (24.7% vs 19.4% respectively). The left anterior descending artery was the most commonly affected vessel (84.4% of men vs. 61.1% of women) in both sexes followed by the left circumflex artery. The left main stem was diseased similarly in both sexes (around 8%). The majority of patients had low SYNTAX score but more often women than men (97.2% vs 92.78%, $p = 0.04$). Among all the patients, 65 (48.9%) underwent PCI with no statistical difference between men and women. **Conclusion:** In our study,

women with ACS were older, had more cardiovascular risk factors but less angiographic extent of disease than men.

Keywords

Sex Differences, Acute Coronary Syndrome, Senegal

1. Background

Considered as rare for a longtime, coronary artery disease (CAD) is increased, along with adoption of western lifestyle in Sub-Saharan Africa [1]. CORONAFRIC, the first prospective and multicenter study conducted in 13 West-African countries revealed a CAD relative incidence rate of 3.17% [2]. CORONAFRIC 2 published in 2017, revealed an incidence rate of 24% of CAD [2]. In Senegal, CAD is the second leading cause of death in the general population after neonatal disorders and the first one after 50-year-old [3]. The acute coronary syndrome (ACS) incidence rose from 5% to 12% in Dakar during the last 20 years [4]. This increase in prevalence did not spare neither women nor men and according to current data, the former paid the heaviest price in terms of mortality compared to men [5]. CAD is responsible for 4 to 6 times more death than breast cancer [2].

In the present study, we aim to retrospectively assess the clinical characteristics and angiographic profile of ACS in women compared to men in a tertiary care center in Dakar.

2. Methods

2.1. Study Design

This was a retrospective descriptive and analytic study in 2 tertiary cardiology centers in Dakar from February 2019 to January 2020.

2.2. Patient Selection

All consecutive patients diagnosed with acute coronary syndrome (ACS) who underwent coronary angiography in the department of cardiology of Principal Hospital of Dakar and Aristide Le Dantec Hospital over a period of 1 year (February 1st, 2019-January 31st, 2020) were enrolled in the study.

Patients admitted for ACS who did not undergo coronary angiography were excluded from the analysis.

2.3. Data Collection

Data for each patient were recorded on predefined data collection forms.

We used patients' medical records and electronic files of the interventional unit. First, we noted in the files all the patients received for acute coronary syndrome. Then we selected from these patients those who had undergone coronary angiography. The following data were then collected from eligible patients:

- Sociodemographic characteristics: age, sex, occupation, date of hospitalization;
- History and risk factors for cardiovascular disease: hypertension, type 2 diabetes mellitus, active smoking, sedentary lifestyle, dyslipidemia, obesity, family history of premature coronary artery disease, history of stroke, peripheral artery disease (PAD), myocardial infarction (MI) and percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).
- Clinical findings: symptoms (chest pain, dyspnea, vomiting), physical examination data (hemodynamic parameters, KILLIP stage).
- Laboratory findings: fasting blood glucose, troponin, lipid profile;
- Electrocardiogram (ECG): repolarization abnormalities, rhythm and conduction disorders;
- Echocardiogram: wall motion abnormalities, left ventricular ejection fraction (LVEF), and valvular heart disease and systolic pulmonary artery pression.

2.4. Coronary Angiography

Coronary angiography was performed with GE Allura through the femoral or radial approach with at least 2 orthogonal views for each vessel. The delay between diagnosis and coronary angiography was reported. Visual assessment by two experienced operators was used to quantify and locate coronary lesions before categorizing them, according to the number of major coronary arteries involved, as single (SVD), double (SVD) or triple vessel disease (TVD). The lesions were classified according to the ACC/AHA classification into three categories A, B, C and graded as follows:

- Obstructive: ≥50% of luminal diameter reduction.
- Non-obstructive disease: <50% of the luminal diameter reduction and/or irregularities of the lumen.
- Normal epicardial coronary arteries: no stenosis and no lumen irregularities.

The quality of the antegrade flow of the downstream bed was also assessed by the TIMI flow. The severity of the coronary lesions was appreciated using the SYNTAX score.

Regarding PCI, primary PCI designated angioplasty performed within 12 hours of symptom onset on the culprit artery, and without prior use of thrombolytic therapy and rescue PCI for STEMI (or STEMI equivalent) after failed full-dose lytics. The type (drug eluting stent (DES) or bare metal stent (BMS) and number of stents were noted.

The PCI was successful when at least a 20% reduction in the initial lesion with residual stenosis < 50% of the artery lumen diameter and a TIMI 3 flow was achieved. Failure of PCI as failure of the angioplasty guidewire to cross a lesion or as "no-reflow" defined as no coronary flow after stenting or "low flow" as a slowing of coronary flow after stenting.

2.5. Ethical Clearance

The study was conducted according to the principles outlined in the Declaration

of Helsinki. This study was approved by the National Medical Ethics Committee of Senegal. Written consent was obtained from all participants, and permission to access data was granted in the ethics committee approval.

2.6. Statistical Analysis

The parameters studied were recorded on electronic case report form and then analyzed using Epi info software version 3.5.4.

Quantitative variables were expressed as mean ± standard deviation, and qualitative variables as percentage.

Means and percentages were compared using Student's t test, Chi-square test, and Fischer's exact test, respectively, depending on their applicability. Any difference of less than 0.05 was considered statistically significant.

3. Results

A total of 133 patients were included in our study. Of these, 97 (72.9%) were men and 36 (27.1%) were women.

The mean age of male and female patients was 56.6 ± 13.52 years and 61.4 ± 14.29 years respectively. Most of the patients (62.5%) were in the age group of 60 - 69 years with 34.7% men versus 27.8% women. Women were, on average, older than men (61.4 ± 14.29 years vs 56.6 ± 13.52 years (p = 0.07). Table 1 describes the baseline characteristics of the patients.

The most common risk factor was hypertension, followed by type 2 diabetes, smoking, sedentary lifestyle, and obesity. Hypertension, sedentary lifestyle and obesity were significantly more frequent in women (69.4%, 52.7% and 19.4%) compared to men (38.8%, 25.7% and 6.19%) respectively, (p = 0.001; 0.002 and 0.03). In contrast, smoking was significantly lower in women (2.8% vs. 44.3%, p = 0.000). Type 2 diabetes was also more frequent in women (38.89% vs 26.80%) but that difference was not statistically significant, (p = 0.08).

Most of the patients had at least one cardiovascular risk factor. However, there was no risk factor in 8% of women and 16% of men.

Regardless of the type of ACS, chest pain was the most common symptom. Approximately half of the patients reported typical chest pain (48.45% in men vs 55.56% in women) with no significant difference between the two sexes. Atypical chest pain was found in 11 (30.56%) women and 31 (31.96%) men, (p = 0.64). Women experienced more digestive symptoms, characterized by nausea and vomiting, (27.78% vs. 10.31% p = 0.04).

Repolarization disorders were located mainly in the anterior territory on the 12-lead electrocardiogram and STEMI was the most common presentation (57.7% of men vs 52.8% of women).

Echocardiogram was conducted in 111 patients (83.4%). Most of the patients had a preserved left ventricular ejection fraction (LVEF). The mean LVEF was 56.3% ± 19.4. Women had, on average, a better LVEF compared to men (63.1 ± 22.6 versus 53.7 ± 17.5), p = 0.02.

Table 1. Baseline characteristics of patients.

Characteristics	Women (n = 36), n (%)	Men (n = 97), n (%)	P value
Age (years), median (SD)	*61.4 (14.29)*	*56.6 (13.52)*	*0.07*
Hypertension	*25 (69.44%)*	*40 (41.24%)*	*0.001*
Diabetes	*14 (38.89%)*	*26 (26.80%)*	*0.08*
Smoking	*1 (2.78%)*	*43 (44.33%)*	*<0.001*
Sedentary lifestyle	*19 (52.78%)*	*25 (25.77%)*	*0.002*
Obesity	*7 (19.44%)*	*6 (6.19%)*	*0.03*
Dyslipidemia	*2 (5.56%)*	*11 (11.34%)*	*0.27*
Chest pain			
Typical	*20 (55.56%)*	*47 (48.45%)*	*0.54*
Atypical	*11 (30.56%)*	*31 (31.96%)*	*0.64*
Digestive signs	*10 (27.78%)*	*10 (10.31%)*	*0.04*
Repolarization abnormalities location			
Anterior	*22 (61.1%)*	*62 (63.9%)*	*0.76*
Inferior	*13 (36.1%)*	*34 (35.1%)*	*0.56*
Lateral	*11 (30.6%)*	*18 (18.6%)*	*0.14*
Diagnosis at admission			
STEMI	*19 (52.8%)*	*56 (57.7%)*	*0.61*
Non-STEMI	*17 (47.2%)*	*41 (42.2%)*	*0.41*
Classification Killip			
I	*27 (75%)*	*80 (82.4%)*	
II	*4 (11.1%)*	*12 (12.3%)*	
III	*0 (0%)*	*1 (1.1%)*	
IV	*1 (2.7%)*	*1 (1.1%)*	
LVEF (%), mean (SD)	*63.1 (22.6)*	*53.7 (17.5)*	
>50	*24 (77.4%)*	*48 (60%)*	*0.02*
30 - 50	*5 (16.1%)*	*26 (32.5%)*	
<30	*2 (6.5%)*	*6 (7.5%)*	

Non-STEMI: Non-ST segment-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; LVEF: Left ventricular ejection fraction.

Among patients with documented STEMI diagnosis, 24.8% received thrombolysis (13.7% of men vs 11.1% of women). The average delay of thrombolysis was 4.56 hours in men (range from 2 to 13 hours) vs 7.9 hours in women (range from 1 to 9 hours), p = 0.15 (Table 3).

The radial access was most commonly used (87.6% of men vs. 83.3% of women) followed by the femoral approach 12.4% and 13.9% respectively with no difference between both sexes.

The mean time from diagnosis to coronary angiography in STEMI patients was slightly shorter in women (28.8 ± 93.3 h in women (range from 1 and 154 h) when compared to men (31.2 ± 127.2 h (range from 1 and 288 h). The difference was not statistically significant (p = 0.85). In non-STEMI patients, the delay was quite similar (4.41 ± 4.1 days with extremes of 0.5 and 16.4 days in men and 4.33 ± 3.2 days with extremes of 0.30 and 9 days in women), p = 0.95.

Normal epicardial coronary arteries were found in 12.4% of men and 25% of women. A small number (4 men and 3 women) had nonobstructive coronary artery disease (CAD). Among those with obstructive CAD, SVD was the most common (36.1% of men vs 33.3% of women) followed by the TVD (24.7% vs 19.4% respectively). The LAD was the most common culprit vessel (84.4% of men vs. 61.1% of women) in both sexes followed by the LCX involvement (72.2% of men vs. 44.4% of women) than the RCA (64.9% of men vs. 47.2% of women). The left main stem was involved in 8.2% of men and 8.3% of women. Type A and B1 were the most frequent lesions with 85.19% in male (n = 69) vs 62.5% in female (n = 15) respectively then 67.9% in male (n = 55) vs 45.83% in female (n = 11). The majority of the patients had low SYNTAX score (between 0 and 22) and more frequent in women than men (97.2% vs. 92.78%, p = 0.04). There was no case of coronary artery dissection.

The angiographic characteristics are described in Table 2.

Among the 133 patients, 65 (48.9%) underwent PCI with 49.5% of men and 47.2% of women. A stent was implanted in 37 (77.1%) men and 13 (81.3%) women. DES was the most common stent used (89.6% men vs 82.4% in women) (Table 3).

Table 2. Angiographic characteristics of the patients.

Parameters	Women (n = 36), n (%)	Men (n = 97), n (%)	P value
CAG performed	*36* (*100%*)	*97* (*100%*)	
Delay from diagnosis to CAG mean (*SD*)			
STEMI (*hours*)	*28.8* (*93.3*)	*31.2* (*127.2*)	*0.85*
Non-STEMI (*days*)	*4.33* (*3.2*)	*4.41* (*4.1*)	*0.95*
Radial approach	*31* (*86.1%*)	*85* (*87.6%*)	*0.25*
Femoral approach	*5* (*13.9%*)	*12* (*12.4%*)	*0.25*
Normal coronary arteries	*9* (*25%*)	*12* (*12.4%*)	*0.30*
Spontaneous dissection	*0*	*0*	
Non-obstructive CA	*3* (*8.3%*)	*4* (*4.1%*)	
CA obstruction degree			
50% - 70% stenosis	*18* (*50%*)	*81* (*83.5%*)	*<0.001*
70% - 90% stenosis	*13* (*36.1%*)	*58* (*59.8%*)	*0.01*
90% - 99% stenosis	*7* (*19.4%*)	*26* (*26.8%*)	0.38
100% occlusion	*12* (*33.3%*)	*76* (*78.4%*)	*<0.001*
CTO	*3* (*8.3%*)	*1* (*1%*)	0.06
Number of vessels			
SVD	*12* (*33.3%*)	*35* (*36.1%*)	0.30
DVD	*5* (*13.9%*)	*22* (*22.7%*)	
TVD	*7* (*19.4%*)	*24* (*24.7%*)	
LM involvement	3 (8.3%)	*8* (*8.2%*)	
LAD	22 (61.1%)	*82* (*84.4%*)	0.04
LCX	16 (44.4%)	*70* (*72.2%*)	<0.001
RCA	17 (47.2%)	*63* (*64.9%*)	0.03

Continued

ACC/AHA lesion type			
A	15 (62.5%)	*69* (*85.2*%)	0.22
B1	11 (45.8%)	*55* (*67.9*%)	0.17
B2	7 (29.2%)	*34* (*41.98*%)	0.32
C	16 (66.7%)	*26* (*32.1*%)	0.13
SYNTAX score			
0 - 22	35 (97.2%)	*90* (*92.7*%)	0.04
23 - 33	0	*7* (*7.3*%)	0.16
>33	1 (2.8%)	*0*	0.84

CAG: Coronary angiogram; CA: coronary artery; SVD: Single-vessel disease; DVD: double-vessel disease; TVD: Triple-vessel disease; LM: Left main coronary artery; LAD: Left anterior descending coronary artery; LCX: Left circumflex coronary artery; RCA: Right coronary artery; CTO: Chronic total occlusion.

Table 3. Reperfusion treatment.

Modalities	Women (n = 36), n (%)	Men (n = 97), n (%)	P value
Thrombolysis	*4* (*11.1*%)	*13* (*13.7*%)	
Delay of thrombolysis, (*h*)	7.9	4.56	*0.15*
PCI	17 (47.2%)	48 (49.5%)	*0.82*
Thrombectomy	0	2 (4.2%)	
Stent implantation	13 (81.3%)	37 (77.1%)	*0.79*
DES	14 (82.4%)	43 (89.6%)	*0.28*
BMS	3 (17.6%)	3 (6.3%)	*0.28*

PCI: Percutaneous coronary artery intervention; DES: Drug eluting stent; BMS: Bare metal stent.

4. Discussion

In our series we found a percentage of 72.9% of men versus 27.1% of women, *i.e.* a clear male predominance (sex ratio = 2.6) which is in agreement with the study of Hao *et al.* (74% of men vs 25% of women) as well as the French Registry of Acute ST-elevation or non-ST-elevation myocardial infarction (ratio 1:2.8) and the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) registry on ACS patients (ratio 1:2.7) [6] [7]. Women usually experience atypical chest pain or digestive symptoms leading hence to late or misleading diagnosis which explain at least partially the bad outcomes associated with ACS in women. This could explain their low representativeness [8].

The women of our cohort were older and had more risk factors including hypertension, diabetes, obesity and sedentary lifestyle than men. These observations were largely reported in the literature [8] [9] [10].

Older women have more acute coronary syndrome because of the vascular transition that occurs during menopause, making them vulnerable and prone to cardiovascular disease. In fact, before menopause, ovarian hormones have a vascular-protective role, which allows women during their genital period to develop less cardiovascular disease than men of the same age.

In the INTERHEART study, hypertension was one of the most frequent cardiovascular risk factors in female patients with ischemic heart disease. It was associated with 29% of myocardial infarction in women and 15% in men [11].

The more frequent sedentary lifestyle and obesity may be due to cultural considerations. In fact, obesity is considered as a sign of wealth, beauty and even good health in sub-Saharan Africa. Furthermore, the belief that weight loss is associated with certain pathologies is widespread and certain ethnic groups promote voluntary female obesity [12]. In addition, physical activity, is thought to be for men only.

In contrast, smoking was less frequent among women in our cohort and might be due to social and religious considerations too. Smoking is seen as against good standard of life in our community.

As already demonstrated, typical chest pain remains the most common presentation during ACS regardless of the age in men and women [13]. However, women are more prone to experience atypical chest pain and digestive signs explaining the higher rate of misdiagnosing ACS. The similar rates of atypical chest pain between women and men in our study may be explained by the female's small sample in our cohort and the retrospective pattern of our study leading to a potential information bias.

Both men and women presented most often with STEMI with a lower frequency in women but without statistical difference. Whereas in the GUSTO IIb trial, men were more likely to develop STEMI than women do [14] confirmed more recently by the large Get with The Guidelines-Coronary Artery Disease registry [15].

In our study delay from diagnosis to coronary angiogram did not differ between men and women, regardless of the ACS type. Non-obstructive coronary artery disease was more common in female patients and might, in ACS context, be related to myocardial infarction with non-obstructive coronary artery (MINOCA). As reported in the literature, MINOCA is more frequent in women [16]. Fortunately, cardiologists are more and more aware of this condition, far from benign [17] [18], due to the growing literature in that field [19] [20].

The extent of coronary artery disease is globally low in both genders as showed by the more frequent SVD, the low SYNTAX score and the higher rates of types A and B lesions. Nevertheless, women had less extensive and severe CAD than men, as reported in the literature.

Generally, women are less likely to undergo coronary angiography than men and therefore have less access to percutaneous coronary intervention (PCI). This difference may contribute to explaining excess female mortality. However, in our cohort PCI was performed roughly at the same proportions in both gender (in 47.2% of women vs 49.5% of men). Several studies such as Spirit Women study [9] have shown the same effectiveness of revascularization in both sexes in acute coronary syndrome. According to that study, the success rates of angioplasty have indeed improved, with even better results in women in terms of restenosis or thrombosis for the new generation stents. Similarly, the radical approach has

led to a reduction of vascular complications. The results of modern treatments are therefore as good in women as in men.

Limitations

The main limitations of our study are the small sample of the cohort and the retrospective nature which is prone to information bias.

5. Conclusion

In this retrospective study, women with ACS are older, have more traditional risk factor of cardiovascular disease and less extensive coronary artery disease than men.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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