BRIEF COMMUNICATION

Acute Coronary Syndrome in Young Women due to Spontaneous Coronary Artery Dissection

Síndrome coronario agudo en mujeres jóvenes por disección coronaria espontánea

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ABSTRACT

Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome (ACS). Its prevalence is higher in young women, but its clinical characteristics and outcome remain insufficiently studied. The aim of this study was to evaluate the baseline characteristics and outcome of SCAD compared with atherosclerotic acute coronary syndrome (AACS) in young women. This prospective cohort study compared women < 60 years admitted with ACS due to SCAD with another cohort with AACS, between 2015 and 2017. A total of 49 patients were included, 7 of which (14.29%) presented SCAD. Median follow-up was 10 months (25-75 IQR: 2-18). Median age was 44 years (25-75 IQR: 38-45) in the SCAD group and 55 years (25-75 IQR: 40-58) in the AACS group (p=0.002), with greater prevalence of hypertension and dyslipidemia (69% vs. 14.3%, p=0.006 and 71% vs. 14% p=0.004, respectively). Episodes of acute stress (57.1% vs. 4.8%, p=0.001) and use of ergotamine (28.6% vs. 0%, p=0.0001) were more common in the SCAD group, and ST-segment elevation myocardial infarction was the most frequent presentation (71.4% vs. 28.6%; p = 0.02). The primary endpoint occurred in 3 patients (42.9%) of the SCAD group and was less frequent in the AACS group (9.5%, p=0.02). During follow-up, 14.9% of patients in the SCAD group and 14.8% in the AACS group presented the secondary endpoint (p=0.9). Women with SCAD had lower prevalence of cardiovascular risk factors and presented ACS with worse hemodynamic impact and more complications. The long-term outcome did not show significant differences.

Key words: Myocardial infarction - Acute coronary syndrome - Coronary artery disease

RESUMEN

La disección coronaria espontánea (DCE) es una causa infrecuente de síndrome coronario agudo (SCA). Es conocida su mayor frecuencia en mujeres jóvenes; sin embargo, sus características clínicas y evolutivas permanecen insuficientemente estudiadas. Evaluar las características clínicas y la evolución de la DCE y su comparación con el síndrome coronario agudo ateroesclerótico (SCAA) en mujeres jóvenes. Estudio de cohorte prospectivo, incluidas consecutivamente mujeres menores de 60 años que ingresaron por SCA entre 2015 y 2017, comparadas con las que presentaban (SCAA) y DCE. Se incluyeron 49 pacientes, 7 (14,29%) presentaban DCE. La media de seguimiento fue de mediana de 10 meses (Pc 25-75 2-18). La mediana de edad fue de 44 años (Pc 25-75 38-45) en grupo DCE y de 55 (Pc 25-75 49-58) en SCAA (p = 0,002), con mayor prevalencia de hipertensión arterial, dislipemia en grupo SCAA (69% vs. 14,3% p = 0,006 y 71% vs. 14% p = 0,004 respectivamente). En el grupo DCE hubo mayor estrés (57,1% vs. 4,8% p = 0,001) y uso de ergotamina (28,6% vs. 0% p = 0,0001) y se presentaron más frecuentemente como infarto agudo de miocardio con elevación del ST (71,4% vs. 28,6%; p = 0,02. El punto final primario ocurrió en 3 pacientes (42,9%) del grupo con DCE y fue menor en el SCAA (9,5%, p = 0,02. En el seguimiento, el 14,9% del grupo DCE y el 14,8% de SCAA presentaron el punto final secundario (p = 0,9). Las mujeres con DCE tuvieron menor prevalencia de factores de riesgo cardiovascular y presentaron un SCA con peor impacto hemodinámico y mayores complicaciones. La evolución a largo plazo no mostró diferencias significativas.

Palabras clave: Infarto del miocardio - Síndrome coronario agudo - Enfermedad de la arteria coronaria.

Abbreviations

AACS Atherosclerotic acute coronary syndrome	**SCAD** Spontaneous coronary artery dissection
SCA Acute coronary syndrome	

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INTRODUCTION

Spontaneous coronary artery dissection (SCAD) is a rare but serious cause of acute coronary syndrome (ACS) that is usually under-diagnosed (1), with an estimated prevalence of 0.1-1.1% among patients undergoing coronary angiography and higher prevalence in younger women. (2-4)

Symptoms of clinical presentation may range from chest pain to ST-segment elevation myocardial infarction, ventricular fibrillation and sudden death. (5, 6)

Owing to improvement in imaging techniques, the diagnosis of SCAD is increasing among patients with ACS, particularly in young women. (1)

Yet, its clinical characteristics, outcomes, and the differences with atherosclerotic ACS due to plaque rupture (AACS) are still insufficiently studied. The aim of this study was to evaluate the baseline characteristics, clinical presentation, treatments and long-term outcome of SCAD compared with AACS in young women.

METHODS

We conducted an analytical single-center, prospective cohort study. Women <60 years admitted due to an ACS between 2015 and 2017 were prospectively included. The characteristics of the patients with ACS due to SCAD were compared with those with ACS due to AACS.

The diagnosis of SCAD was defined in the coronary angiography by the presence of intimal tear with a false lumen or contrast dye stasis in the arterial wall evaluated by at least two cardiologists according to international recommendations. (3) Non-spontaneous dissections resulting in iatrogenic coronary artery trauma were excluded.

The clinical, electrocardiographic and echocardiographic characteristics were analyzed, as well as treatments and in-hospital and long-term outcome. All the patients were followed-up at an ischemic heart disease unit and underwent cardiology consultation, echocardiography and an exercise stress test or a myocardial perfusion scan, as applicable. Data were retrieved from the electronic medical records.

The primary endpoint was the composite of cardiovascular mortality, cardiogenic shock and requirement of ventricular assist devices during hospitalization. The secondary endpoint was long-term cardiovascular mortality, non-fatal myocardial infarction, new revascularization and rehospitalization due to ACS.

Statistical analysis

Discrete variables were expressed as medians and interquartile range and categorical variables as frequencies and percentages. Continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using Fisher's exact test or the chi square test, as applicable. Survival curves were built with the Kaplan-Meier method and compared using the log-rank test.

Ethical considerations

The study was approved by the institutional Teaching and Ethics Committee, and was conducted following the recommendations of the Declaration of Helsinki.

RESULTS

Among a total of 49 patients included in the study, 7 (14.29%) presented SCAD (type 1: 71.4% and type 2: 28.6%). Median follow-up was 10 months (25-75 IQR: 2-18). Median age was 44 years (25-75 IQR: 38-45) in the SCAD group and 55 years (25-75 IQR: 40-58) in the AACS group. The prevalence of hypertension and dyslipidemia was greater in this group (69% vs. 14.3%, p=0.006 and 71% vs. 14%, p=0.004, respectively) without statistically significant differences in other risk factors (Table 1).

Episodes of acute stress (57.1% vs. 4.8%, p=0.001), family history of SCAD (28.8% vs. 0%, p=0.001) and use of ergotamine (28.6% vs. 0%, p=0.0001) were more common in the SCAD group. All SCAD patients presented as acute myocardial infarction, and ST-segment elevation ACS was the most frequent presentation (71.4% vs. 28.6%; p=0.02), the left anterior descending coronary artery being more commonly affected (71.4%).

Time from symptom onset to consultation and hospital stay were similar in both groups. No significant differences in the GRACE and TIMI risk scores on hospital admission and in the risk of bleeding using the CRUSADE score were found. Medical treat-

Table 1. Baseline characteristics

	AACS (n=42)	SCAD (n=7)	p
Age, median (25-75 IQR)	56 (50-58)	46 (38-50)	0.003
HTN, n (%)	29 (69%)	1 (14.3%)	0.006
Diabetes, n (%)	7 (16.7%)	0 (0%)	0.24
Smoking, n (%)	22 (52.4%)	2 (28.6%)	0.24
Dyslipidemia, n (%)	30 (71.4%)	1 (14.3%)	0.004
Obesity, n (%)	11 (26.2%)	1 (14.3%)	0.49
FH ACAD, n (%)	14 (33.3%)	3 (42.9%)	0.62
Previous CABGS, n (%)	2 (4.8%)	0 (0%)	0.55
Previous PCI, n (%)	11 (26.2%)	1 (14.3%)	0.49
FH SCAD, n (%)	0 (0%)	2 (28.6%)	< 0.001
Puerperium, n (%)	0 (0%)	1 (14.3%)	0.14
Stress, n (%)	2 (4.8%)	4 (57.1%)	< 0.001

AASC: Atherosclerotic acute coronary syndrome. SCAD: Spontaneous coronary artery dissection. HTN: Hypertension. CABGS: Coronary artery bypass graft surgery. PCI: Percutaneous coronary intervention. FH: Family history. ACAD: Atherosclerotic coronary artery disease.

ment alone was more common in the SCAD group (p <0.001) (Table 2).

On admission, high sensitivity troponin levels were higher in ACS due to SCAD: 514 ng/l (25-75 IQR: 85-2414) vs. 32 ng/l (25-75 IQR: 11-263) in the AACS group (p=0.009). Left ventricular ejection fraction (LVEF) on admission was lower in the SCAD group (median: 51%, 25-75 IQR: 37-55 vs. 58%, 25-75 IQR: 49-63; p=0.045).

The primary endpoint occurred in 3 patients (42.9%) of the SCAD group and was significantly lower in the AACS group (9.5%, p=0.02) (Table 2), while 14.9% of the patients in the SCAD group and 14.8% in the AACS group presented the secondary endpoint (log-rank test, p=0.9). Thirty days after admission, LVEF assessed by Doppler-echocardiography showed better recovery in the SCAD group [delta +15.75% (SD: 15.33) vs. +2.6% (SD: 9); p=0.029]. Recurrence

Table 2. In-hospital outcome

Variable	AASC (n=42)	SCAD (n=7)	p
Type of ACS, n (%)			
Unstable angina	15 (35.7%)	0 (0%)	0.08
NSTEMI	15 (35.7%)	2 (28.6%)	0.53
STEMI	12 (28.6%)	5 (71.4%)	0.02
Pain-to-consultation time in hours, median (25-75 IQR)	6 (3-24)	10 (1.25-50)	0.95
GRACE risk score, median (25-75 IQR)	88 (74-108)	79 (74-97)	0.54
TIMI risk score, median (25-75 IQR)	3(2-3)	3 (1-3)	0.67
CRUSADE score, median (25-75 IQR)	30 (23-37)	33 (28-35)	0.79
Killip and Kimball class, n (%)			0.02
I	34 (81%)	4 (57.1%)	
II	5 (11.9%)	0 (0%)	
III	0 (%)	(0%)	
IV	3 (7.1%)	3 (42.9%)	
hs-cTnT on admission, median (25-75 IQR)	32 (11-263)	514 (84-2,414)	0.01
Peak hs-cTnT, median (25-75 IQR)	84 (12-997)	3,217 (1,208-4,789)	0.002
Treatment, n (%)			
Only medical	1 (2.38%)	3 (42.8%)	< 0.001
PCI	34 (80%)	3 (42.8%)	0.003
CABGS	9 (21.42%)	1 (14.2%)	0.66
Heart transplantation	0 (0%)	1 (14.2%)	
LVEF (median; Q1-Q3)	58 (49-63)	51 (37-55)	0.045
Wall motion abnormalities	27 (65.9%)	7 (100%)	0.06
SYNTAX score (median; Q1-Q3)	19 (7-33)	5 (4-7)	0.065
BARC bleeding definitions			< 0.001
1	0 (0%)	1 (14.3%)	
2	0 (0%)	0 (0%)	
3a	0 (0%)	2 (28.6%)	
3b	1 (2.4%)	0 (0%)	
4	2 (4.8%)	1 (14.3%)	
Total bleeding	3 (7.14%)	4 (57.1%)	< 0.001
Primary endpoint, n (%)			
Cardiovascular mortality	1 (2.4%)	0 (0%)	0.17
Cardiogenic shock	2 (4.8%)	2 (28.6%)	0.03
Ventricular assistance	2 (4.8%)	3 (42.9%)	0.002
Secondary endpoint, n (%)	14.8%	14.9%	log rank
Cardiovascular mortality	1 (2.4%)	0 (0%)	0.9
ACS	3 (7.1%)	1 (14.3%)	
New revascularization	4 (9.5%)	0 (0%)	
Delta LVEF after 30 days	2.6% (SD 9)	15.75% (SD 15.33)	0.029

AACS: Atherosclerotic acute coronary syndrome. SCAD: Spontaneous coronary artery dissection. ACS: Acute coronary syndrome. NSTEMI: Non-ST-segment elevation myocardial infarction. STEMI: ST-segment elevation myocardial infarction. hs-cTnT: High sensitivity cardiac troponin T. CABGS: Coronary artery bypass graft surgery. PCI: Percutaneous coronary intervention. LVEF: Left ventricular ejection fraction.

occurred in 14.28% of the patients with SCAD but did not require revascularization (Table 3).

DISCUSSION

Our study demonstrated that women with SCAD were younger and had lower prevalence of dyslipidemia and hypertension than those with AACS. In turn, ST-segment elevation ACS, higher troponin levels, lower LVEF and higher incidence of in-hospital clinical events were more common in women with SCAD.

Spontaneous coronary artery dissection is defined as a non-traumatic and non-iatrogenic separation of the coronary artery wall by intramural hemorrhage creating a false lumen, compromising anterograde blood flow and generating myocardial ischemia with or without myocardial infarction. (4, 7)

The possible predisposing factors for SCAD include fibromuscular dysplasia, peripartum state, multiparity, connective tissue disorders, systemic inflammatory conditions and hormonal therapy (8, 9-11), which may explain the lack of association with the traditional coronary risk factors related with the development of atherosclerosis.

In our study, the prevalence of SCAD in women <50 years was similar to that of previous studies, 8.7%, (5) reaching 24% in another series of young women with acute myocardial infarction. (9)

Compared with women with AACS, those with SCAD are younger (median age 46 years). In two previous studies, mean age was 43 years, and Tweet et al. reported an age of 52 years, similar to our findings. (9, 10) In addition, these women have a different cardiovascular profile, with lower prevalence of hypertension and dyslipidemia, in concordance with a comparative study published in 2017. (13)

The two largest series reported that the left anterior descending coronary artery was the vessel most commonly affected. (9, 10) However, angiographic type 1 SCAD was found in 71.4% of our patients while Saw et al. found type 2 in 67% of their patients. (9).

Presentation ECG showed ST-segment elevation in 26.1% of the patients in the study by Saw et al. and 49% in the study by Tweet et al., demonstrating that dissection produces severe involvement of the coronary artery flow. (10)

Probably, this might be associated with lower ejection fraction, higher troponin levels as expression of myocardial damage, higher incidence of cardiogenic shock and need for ventricular assistance.

Yet, and opposed to previous reports, this type of ACS presented worse hemodynamic impact and greater number of in-hospital complications. (9, 13) Interestingly, and despite the worse initial hemodynamic status and the lower number of interventional therapies (percutaneous coronary intervention or surgery), the long-term outcome was favorable as reported by other series (1, 9, 13) with greater improvement of LVEF in the long-term follow-up.

This has been reported in isolated cases in which patients may have severe left ventricular dysfunction with subsequent complete recovery. (14) However, so far no studies evaluating left ventricular function routinely on presentation and during long-term follow-up have been published.

Optimal treatment of SCAD has not been explored given that this condition is rare. There are no prospective randomized studies available to guide medical management, and it is uncertain if standard pharmacological treatment of ACS due to atherosclerotic coronary artery disease is beneficial in patients with SCAD. (10) In most patients with SCAD, conservative therapy is the strategy of choice after the diagnosis. (15) In our study, treatment was decided by a multidisciplinary team considering the patient's clinical status, symptoms and anatomy of the coronary artery involved. (1)

The recurrence of SCAD is 13-17% (9, 10) a percentage that is similar to the one reported in our study.

Despite the observational design of this study and the relatively small sample size, ii is one of the few comparative series with clinical and echocardiographic follow-up published so far.

CONCLUSIONS

Women with SCAD were younger, had lower prevalence of cardiovascular risk factors and presented ACS with worse hemodynamic impact and more complications. The long-term outcome did not show significant differences, despite medical treatment was more commonly indicated.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

Table 3. Long-term outcome

	AACS (n=42)	SCAD (n=7)	p
Secondary endpoint, n (%)	14.8%	14.9%	log rank 0.9
Cardiovascular mortality	1 (2.4%)	0 (0%)	
ACS	3 (7.1%)	1 (14.3%)	0.029
New revascularization	4 (9.5%)	0 (0%)	
Delta LVEF after 30 days	2.6% (SD 9)	15.75% (SD 15.33)	

AACS: Atherosclerotic acute coronary syndrome. SCAD: Spontaneous coronary artery dissection. ACS: Acute coronary syndrome. LVEF: Left ventricular ejection fraction.

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