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Recurrent spontaneous coronary artery dissection in the United States

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ABSTRACT

Background: Recurrent spontaneous coronary artery dissection (SCAD) is believed to be infrequent. Predictors of recurrent SCAD are poorly characterized.
Methods: We evaluated the incidence, clinical characteristics, and predictors of recurrent SCAD using data from the Nationwide Readmissions Database from January 1, 2010, to December 30, 2016.
Results: Among 1836 SCAD patients admitted with the primary diagnosis of SCAD (61.9% female, mean age 56.1 ± 14.5, 72.9% <65 years of age), 495 patients (26.9%) had recurrent SCAD within 1 year (74.0% female, 74% <65 years of age). Multivariable analysis showed that female sex (OR 2.09; 95% CI 1.49–2.95; $p < 0.001$) was an independent predictor of recurrent SCAD within 1 year.
Conclusions: Recurrent SCAD is frequent and should be considered in younger females with a history of SCAD. Further research is needed to investigate the mechanistic links between female sex and recurrent SCAD.

1. Introduction

Spontaneous coronary artery dissection (SCAD) is a rare but important cause of acute coronary syndrome (ACS). In comparison to their counterparts with atherosclerotic ACS, patients with SCAD are at greater risk for major adverse cardiac events (MACE) and in-hospital mortality is approximately 5% [1]. The association between SCAD, arteriopathies, and inflammatory disorders remains controversial [2–6]. Few studies have reported on the incidence and predictors of recurrent SCAD [7,8]. We therefore evaluated the incidence, clinical characteristics, and predictors of recurrent SCAD using data from the Nationwide Readmissions Database from January 1, 2010, to December 30, 2016.

2. Methods

The study cohort was derived from Healthcare Cost and Utilization Project's (HCUP) National Readmission Database (NRD) between 2010 and 2016, sponsored by the Agency for Healthcare Research and Quality [9]. The NRD is one of the largest publicly available all-payer inpatient care databases from 22 states in the United States (data on approximately a sample size of 13 to 15 million discharges per year). National estimates were produced using sampling weights provided by the Agency for Healthcare Research and Quality [10].

We identified SCAD from the principle diagnosis in the NRD database using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic code (414.12) from January 2010 to September 2015 and the ICD-10-CM diagnostic code (I25.42) from October 2015 to December 2016. We then assessed for a concurrent diagnosis of acute coronary syndrome (ACS) defined as ST-elevation myocardial infarction (STEMI) (ICD-CM 9 codes of 410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.81, 410.91 and ICD-CM 10 codes of I21.3), non-ST elevation myocardial infarction (NSTEMI) (ICD-9-CM code of 410.7x and ICD-10-CM codes of I21.4),

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or unstable angina (ICD-CM 9 code 411.1 and ICD-10-CM codes of I20.x). In order to ensure the diagnosis of SCAD (ICD-9-CM 414.12), we included only patients with a procedural diagnosis of coronary angiography (ICD-9-CM codes of 88.53, 88.54, 88.55, 88.56, 37.22, or 37.23 and ICD-10-CM codes of Y84.0) and/or percutaneous coronary intervention (PCI) (ICD-9-CM codes of 00.66, 36.01, 36.02, 36.05, 36.06, or 36.07 and ICD-10-PCS 10 codes of 02703xx, 02713xx, 02723xx, and 02733xx) and excluded iatrogenic accidental puncture or laceration (ICD-9-CM codes of 998.2 and ICD-10-CM codes of I97.51). We excluded patients with age <18 years and those missing data for age, sex, or mortality. We identified recurrent SCAD as patients with a history of SCAD who were readmitted for SCAD as the principal diagnosis within 1 year. To accurately extract patients with a diagnosis of recurrent SCAD, we excluded patients with a secondary diagnosis of SCAD who were likely to include patients with persistent SCAD or those without complete resolution of the hematoma.

The primary outcome of our study was incidence of recurrent SCAD and the secondary outcome was predictors of recurrent SCAD. Patients' demographic characteristics were extracted including age and sex, primary payer, and co-morbidities such as hypertension, pulmonary hypertension, atrial fibrillation, heart failure (HF), chronic obstructive pulmonary disease (COPD), peripheral artery disease (PAD), obesity, diabetes mellitus, anemia, neurological disease, malignancy, and kidney diseases using the associated ICD-9-CM and ICD-10-CM codes. Infrequent events were not included due to data agreements [10].

Demographics, conventional risk factors, socioeconomic factors, medical management, and in-hospital outcomes were evaluated. Percentages and means ± standard deviations were computed for categorical and continuous variables, respectively. Categorical variables were compared using the Chi-squared test or Fisher's exact test, when appropriate, while continuous variables were analyzed using the 2-tailed Student's *t*-Test or the Mann–Whitney-*U* test, when appropriate. Univariable and multivariable logistic regression modeling were performed to determine predictors associated with recurrent SCAD. All analyses were conducted using R 3.4.0 and Stata version 14.2. All p-values were two-sided and statistical significance was determined at the level of $p < 0.05$.

3. Results

A total of 1836 patients were admitted for SCAD (61.9% female; mean age 56.1 ± 14.5 years), of whom 495 patients (26.9%) had recurrent SCAD within 1 year. Patients with recurrent SCAD were significantly more likely than SCAD patients without recurrence to be female (74.0% vs. 61.9%, $p < 0.001$). Recurrent SCAD patients had a higher rate of heart failure but lower rates of atrial fibrillation and ventricular arrhythmias compared with SCAD patients without recurrence ($p < 0.05$) (Table 1). There was no difference in presence of fibromuscular dysplasia between the two groups (4.7% vs. 5.9%, $p = 0.31$). The in-hospital mortality rate during hospitalization was 4.0%; patients with recurrent SCAD tended to have higher in-hospital mortality compared with SCAD patients without recurrence (5.8% vs 3.4%, $p = 0.17$). Multivariable analysis showed that female sex (OR 2.09; 95% CI 1.49–2.95; $p < 0.001$) was an independent predictor of recurrent SCAD.

Table 1
Baseline clinical characteristics of patients with SCAD and recurrent SCAD.

	SCAD (n = 1836)	Recurrent SCAD (n = 495)	P-value
Age (mean ± SD)	56.1 ± 14.5	55.4 ± 13.9	0.33
Female	61.9%	74.0%	<0.0001
Myocardial infarction	67.9%	67.3%	0.89
Heart failure	43.4%	45.7%	0.63
Peripheral vascular disease	33.8%	32.3%	0.71
Dementia	7.1%	7.2%	0.99
Chronic obstructive pulmonary disease	41.8%	44.0%	0.65
Rheumatologic diseases	8.6%	9.9%	0.67
Diabetes mellitus	44.1%	43.5%	0.91
Diabetes with complications	11.6%	10.3%	0.67
Neurological deficit	5.2%	7.2%	0.37
Chronic kidney disease	23.6%	23.3%	0.99
Hypertension	51.0%	51.6%	0.96
Atrial fibrillation	14.0%	8.1%	0.02
Fibromuscular dysplasia	5.9%	4.7%	0.31
Smoking history	24.4%	22.4%	0.61
Obesity	12.1%	9.9%	0.43
Morbid obesity	6.1%	3.6%	0.22
Hyperlipidemia	50.2%	47.5%	0.54
Cardiogenic shock	8.8%	10.3%	0.58
Ventricular arrhythmias	14.1%	7.6%	0.01
Depression	8.4%	8.5%	0.99
Anxiety	11.1%	14.4%	0.25
Admission on a weekend	16.0%	15.7%	0.98
Insurance: Medicare	30.8%	31.4%	0.95
Insurance: Medicaid	9.8%	12.1%	0.40
Insurance: private insurance	49.3%	44.0%	0.19
Insurance: self-pay	5.4%	7.2%	0.42

4. Discussion

To the best of our knowledge, this is the largest study to date reporting the incidence and outcomes of recurrent SCAD at a national level. First, we found that one-fourth of SCAD patients had recurrent SCAD. The reasons for recurrence are largely unknown. Eleid et al. [11] found that severe coronary tortuosity (defined as ≥2 consecutive curvatures ≥180°) had a borderline association with higher risk for recurrent SCAD. Although recurrent SCAD can occur with either medical management or PCI, coronary tortuosity may result in higher rates of recurrent SCAD because the pathophysiology of recurrence may relate to coronary fragility, particularly in those with the first episode of SCAD treated without intervention.

Second, female patients were more likely to have recurrent SCAD than male patients. A prior study showed that a large proportion of women reported chest pain after SCAD as well as premenstrual chest pain [12,13]. Recurrent SCAD could perhaps be related to estrogen and progesterone hormones [14–17]. One study showed only hypertension increased risk (hazard ratio: 2.46; $p = 0.011$) for recurrent SCAD [7]. However, that study was mostly female (90.5% were women). As such, SCAD studies which are female predominant (>80% of cases) may confound sex-related recurrent SCAD features. In fact, female predominant studies are common and may be due to selection bias or social media bias [18]. Besides female sex, in the present study, we were unable to identify any factors associated with an increased risk of recurrent SCAD, but the relatively small number of events may preclude definite conclusions.

In the present study, we aimed to extract patients with recurrent SCAD without including those who presented with persistent SCAD. As such, we excluded patients who carried a secondary diagnosis of SCAD and included a procedural diagnosis of coronary angiography or PCI to ensure an angiographic assessment was included in the diagnosis of the patient. As such, the number of included patients was low. To date, studies describing recurrent SCAD have found rates varying from 10 to 27% of cases, perhaps largely dependent on follow-up duration [7,19–21]. The study by Saw et al. [7], with a follow-up of 3 years, found a recurrence of SCAD in only 10% while our study found a recurrence of SCAD of 26.7% within 1 year. This difference could be due to the definition of recurrent SCAD in each analysis. For example, in the study by Saw et al. [7], recurrent SCAD was defined as de novo recurrent spontaneous dissection with new recurrent MI symptoms and enzyme elevation, which did not involve extension of dissection of the original SCAD lesion. In contrast, in the study by Tweet et al. which reported a recurrence rate of 27%[20], recurrent SCAD was defined as a clinical ACS distinct from the index event with an angiographic dissection

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plane and intramural hematoma or dissection on intravascular ultrasound or optical coherence tomography.

There are certain limitations to this study. First, although the present study reflects a national population, we identified SCAD patients based on ICD codes without reviewing the angiography. Therefore, ICD codes may underrepresent the true SCAD population. Second, we only looked for potential predictors of recurrent SCAD on a selected number of comorbidities because we were unable to identify angiographic factors such as the degree of coronary tortuosity, TIMI flow, or medications from NRD databases [11]. Third, we were unable to evaluate for recurrent SCAD that occurred >1 year, as the NRD database only includes readmission within 365 days. Therefore, this number may underestimate the number of SCAD recurrences at follow up >1 year. Fourth, we could not identify many highly relevant clinical factors, including SCAD location, vessel tortuosity, multivessel SCAD, clinical presentation (STEMI vs NSTEMI), type of initial treatment (PCI vs medical management), and type of final medical management and medications used (e.g., aspirin, beta blockers, statins). Last, we could not identify whether recurrent SCAD was in the same vessel or different vessels, as this information may shed light on the pathogenesis of recurrent SCAD.

5. Conclusions

SCAD is an uncommon disease that can present in both males and females, but female patients, particularly those with less severe comorbidities, were more likely to have recurrent SCAD. Further study is needed to explore the mechanistic link between female sex and the risk for SCAD recurrence.

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Declaration of competing interest

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