JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 1, 2018

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2017.08.016

Trends of Incidence, Clinical Presentation, and In-Hospital Mortality Among Women With Acute Myocardial Infarction With or Without Spontaneous Coronary Artery Dissection

A Population-Based Analysis

Ahmed N. Mahmoud, MD,[a] Siva Sagar Taduru, MD,[b] Amgad Mentias, MD,[c] Dhruv Mahtta, MD,[d] Amr F. Barakat, MD,[e] Marwan Saad, MD, PhD,[f] Akram Y. Elgendy, MD,[a] Mohammad K. Mojadidi, MD,[a] Mohamed Omer, MD,[b] Ahmed Abuzaid, MD,[g] Nayan Agarwal, MD,[a] Islam Y. Elgendy, MD,[a] R. David Anderson, MD,[a] Jacqueline Saw, MD[h]

ABSTRACT

OBJECTIVES The authors sought to determine the clinical characteristics and in-hospital survival of women presenting with acute myocardial infarction (AMI) and spontaneous coronary artery dissection (SCAD).

BACKGROUND The clinical presentation and in-hospital survival of women with AMI and SCAD remains unclear.

METHODS The National Inpatient Sample (2009 to 2014) was queried for all women with a primary diagnosis of AMI and concomitant SCAD. Iatrogenic coronary dissection was excluded. The main outcome was in-hospital mortality. Propensity score matching and multivariable logistic regression analyses were performed.

RESULTS Among 752,352 eligible women with AMI, 7,347 had a SCAD diagnosis. Women with SCAD were younger (61.7 vs. 67.1 years of age) with less comorbidity. SCAD was associated with higher incidence of in-hospital mortality (6.8% vs. 3.4%). In SCAD patients, a decrease in in-hospital mortality was evident with time (11.4% in 2009 vs. 5.0% in 2014) and concurred with less percutaneous coronary intervention (PCI) (82.5% vs. 69.1%). Propensity score yielded 7,332 SCAD and 14,352 patients without SCAD. The odds ratio (OR) of in-hospital mortality remained higher with SCAD after propensity matching (OR: 1.87, 95% confidence interval [CI]: 1.65 to 2.11) and on multivariable regression analyses (OR: 2.41, 95% CI: 2.07 to 2.80). PCI was associated with higher mortality in SCAD patients presenting with non-ST-segment elevation myocardial infarction (OR: 2.01; 95% CI: 1.00 to 4.47), but not with STEMI (OR: 0.62; 95% CI: 0.41 to 0.96).

CONCLUSIONS Women presenting with AMI and SCAD appear to be at higher risk of in-hospital mortality. Lower rates of PCI were associated with improved survival, with evidence of worse outcomes when PCI was performed for SCAD in the setting of non with ST-segment elevation myocardial infarction. (J Am Coll Cardiol Intv 2018;11:80–90) © 2018 by the American College of Cardiology Foundation.

From the [a]Division of Cardiovascular Medicine, University of Florida, Gainesville, Florida; [b]Department of Medicine, University of Missouri Kansas City, Kansas City, Missouri; [c]Division of Cardiovascular Medicine, University of Iowa, Iowa City, Iowa; [d]Department of Medicine, University of Florida, Gainesville, Florida; [e]UPMC Heart and Vascular Institute, University of Pittsburgh, Pittsburgh, Pennsylvania; [f]Department of Medicine, Division of Cardiovascular Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas; [g]Department of Cardiovascular Medicine/Heart and Vascular Institute, Sidney Kimmel Medical College at Thomas Jefferson University-Christiana Care Health System, Newark, Delaware; and the [h]Division of Cardiology, University of British Columbia, Vancouver General Hospital, Vancouver, British Columbia, Canada. Dr. Anderson is a consultant for Biosense Webster, a Johnson & Johnson Company. Dr. Saw has received research grants for SCAD research from the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, University of British Columbia Division of Cardiology, AstraZeneca, Abbott Vascular, St. Jude Medical, and Servier; has been a consultant for Boston Scientific, Abbott Vascular, and St. Jude Medical; has received honoraria for proctoring from Boston Scientific and St. Jude Medical; and has received speaker honoraria for SCAD from AstraZeneca, St. Jude Medical, and Sunovion. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The first two authors contributed equally to this work.

Manuscript received June 19, 2017; revised manuscript received July 30, 2017, accepted August 2, 2017.

Spontaneous coronary artery dissection (SCAD) is an infrequent disease that presents as acute coronary syndrome or sudden cardiac death, with a wide clinical spectrum of severity. Since it was first described in 1931 on an autopsy of a young woman with sudden cardiac death (1), the true prevalence of this uncommon entity has been difficult to establish. The incidence of SCAD ranges from 0.07% to 1.1% and is considered predominantly a disease of women (>90% in some cohorts) (2-6). There is a paucity of data on the outcomes of SCAD patients, especially in those presenting with acute myocardial infarction (AMI). Moreover, controversies exist on the optimum management strategies in this patient population, due to the challenges encountered during percutaneous coronary intervention (PCI) and risk of intramural hematoma propagation with angioplasty or stent deployment (7). Thus, the concrete benefit of PCI for SCAD in the setting of AMI has yet to be established.

SEE PAGE 91

The aim of this study was to conduct a population-based analysis, using the National Inpatient Sample (NIS) database, to determine the prevalence, trends, and in-hospital mortality of women with SCAD in the setting of AMI, and to evaluate the impact of PCI on in-hospital mortality.

METHODS

DATA SOURCES. The NIS database is considered the largest all-payer inpatient database in the United States, including data on more than 7 million patient discharge records each year (8). The NIS is a part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). It is constructed from billing data submitted by hospital to data organizations across the United States. NIS includes patients under Medicaid, Medicare, and private insurance, and the uninsured. The data comprise approximately 20% of stratified sample discharges from U.S. hospitals; long-term acute care and rehabilitation hospitals are not included (8). In 2012, the NIS database was redesigned for more acute representation of national estimates, where the sample records represented a random sample of discharge records from all HCUP participating hospitals rather than a random sample of hospitals from which all discharges were obtained.

The NIS data include a primary (principal) diagnosis and 24 secondary diagnoses together with 15 procedural diagnoses, all in the International Classification of Diseases-9th Edition-Clinical Modification [ICD-9-CM] coding format. The primary discharge diagnosis is usually considered the main reason for hospitalization. Other variables include sex, age, race, primary payer (e.g., Medicare, Medicaid, private, or uninsured), hospital characteristics (e.g., location, bed size, and so on), median home income (in percentile groups), day of admission (weekend or weekday), length of hospital stay, total hospital charges, and discharge status (e.g., dead or alive). A discharge weight variable is also available to calculate the national estimates of the various variables previously stated. Each record included in the NIS database is deidentified with absence of any personal identifying information.

VALIDATION OF DATA. The NIS data are crosschecked by the AHRQ annually to ensure the internal validity of the data. Data from the NIS have been compared with the American Hospital Association Annual Survey Database, the National Hospital Discharge Survey from the National Center for Health Statistics, and the Med-PAR inpatient database from Centers for Medicare & Medicaid Services in prior studies with comparable estimates (9).

PATIENT SELECTION AND INCLUSION CRITERIA. The NIS database years 2009 to 2014 were queried for women with a primary diagnosis of AMI, defined as

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CI = confidence interval

ICD-9-CM = International Classification of Diseases-9th Edition-Clinical Modification

NIS = National Inpatient Sample

NSTEMI = non-ST-segment elevation myocardial infarction

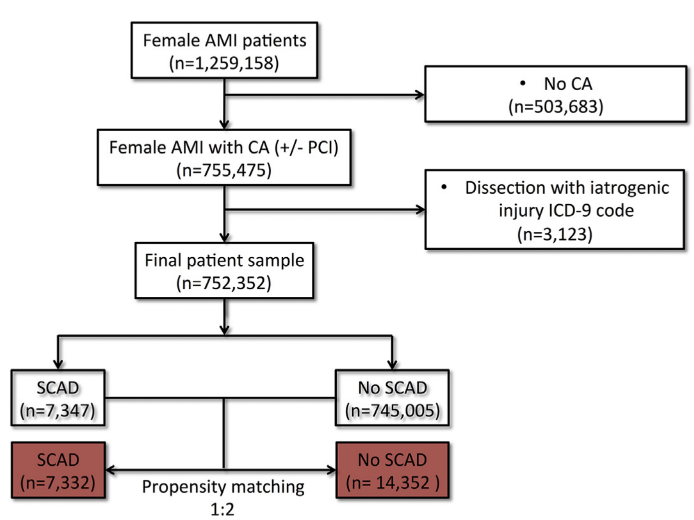
OR = odds ratio

PCI = percutaneous coronary intervention

SCAD = spontaneous coronary artery dissection

STEMI = ST-segment elevation myocardial infarction

FIGURE 1 Selection Flow Chart of Women With AMI and Concomitant SCAD



AMI = acute myocardial infarction; CA = coronary angiography; ICD-9 = the International Classification of Diseases; Ninth Edition; NIS = nationwide inpatient sample; PCI = percutaneous coronary intervention; SCAD = spontaneous coronary artery dissection.

TABLE 1 The Patients' Characteristics, Hospital Characteristics, and Outcome of Women With SCAD in the Setting of AMI

	SCAD (n = 7,347)	No SCAD (n = 745,005)	p Value	Propensity Matched SCAD (n = 7,332)	Propensity Matched No SCAD (n = 14,352)	Bias %, SMD
Clinical presentation			<0.0001			0.2
STEMI	44.9	31.4		44.8	44.5	
NSTEMI	55.1	68.6		55.2	55.5	
Day of admission						
Weekend admission	25.4	26.0	0.307	25.5	24.5	3.0
Patient demographics						
Age, yrs	61.7 ± 15.1	67.1 ± 13.2	<0.0001	61.7 ± 15.1	61.9 ± 14.1	0.1
Race			<0.0001			−1.4
White	79.1	74.5		79.2	77.1	
African American	8.7	12.7		8.6	10.8	
Hispanic	7.1	7.3		7.0	6.6	
Asian/Pacific Islander	2.0	2.0		2.0	2.6	
Native American	0.3	0.5		0.3	0.4	
Other	2.8	3.0		2.8	2.6	
Median home income			<0.0001			−0.4
0 to 25th percentile	26.8	31.7		26.7	26.7	
26th to 50th percentile	26.1	27.0		26.1	25.3	
51st to 75th percentile	24.5	23.4		24.4	26.4	
76th to 100th percentile	22.7	17.9		22.7	21.6	
Primary payment coverage			<0.0001			0.6
Medicare	59.8	43.7		43.8	46.1	
Medicaid	8.1	8.3		8.2	9.0	
Private insurance	23.7	39.0		39.0	33.7	
Self-pay	5.9	6.4		6.4	7.6	
No charge	0.6	0.7		0.7	0.7	
Other	1.9	1.9		2.0	2.8	
Smoking history	34.3	37.3	<0.0001	34.5	34.4	−0.1
Family history of CAD	12.8	10.6	<0.0001	12.8	12.4	1.6

Continued on the next page

either non-ST-segment elevation myocardial infarction (NSTEMI) (ICD-9-CM code of 410.7x) or ST-segment elevation myocardial infarction (STEMI) (ICD-CM 9 codes of 410.1x, 410.2x, 410.3x, 410.4x, 410.5x, 410.6x, 410.8x, and 410.9x). In order to ensure the diagnosis of SCAD (ICD-9-CM 414.12), 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/or PCI (ICD-9-CM codes of 00.66, 36.06, and 36.07) were included. To decrease the chances of coding errors, patients with a concomitant diagnosis code of accidental puncture or laceration during a procedure (ICD-9-CM 998.2) were excluded.

COVARIABLES AND COMORBIDITIES DEFINITIONS. To provide for a robust analysis and to minimize confounders, a large number of covariables were included in the analysis. Most of the included variables were readily supplied by the NIS database including age, sex, race (white, African American, Hispanic, Asian, and other), insurance type, median home income (0 to 25th percentile, 26th to 50th percentile, 51st to 75th percentile, and 76th to 100th percentile), day of admission, hospital bed size (large, medium, small), location (urban, urban teaching, rural), and region (Northeast, Midwest/North Central, South, and West). Other covariables and comorbidities included in the analysis (e.g., hypertension, diabetes, etc.) were either derived from the Elixhauser list of comorbidities supplied by the NIS (10) or manually coded using their specific ICD-9-CM codes. A list of ICD-9-CM codes for the covariables included in the current analysis is described in the Online Table 1.

OUTCOME DEFINITION. The main outcome of interest was in-hospital mortality (referred to as the "died" variable in the NIS database). In-hospital mortality was compared between patients with and without SCAD in both the unadjusted and propensity-matched samples.

STATISTICAL ANALYSIS. National weighted estimates were calculated using the discharge weight variable supplied by NIS. For descriptive purposes, frequencies were used to estimate categorical variables, means and standard deviations for non-skewed continuous variables, and medians with 25th to 75th

TABLE 1 Continued

	SCAD (n = 7,347)	No SCAD (n = 745,005)	p Value	Propensity Matched SCAD (n = 7,332)	Propensity Matched No SCAD (n = 14,352)	Bias %, SMD
Comorbidities						
Prior myocardial infarction	6.7	9.5	<0.0001	6,8	6,6	1.0
Prior stroke/TIA	5.3	6.5	<0.0001	5.3	5.4	−0.1
Prior PCI	8.9	13.1	<0.0001	8.9	9.7	−1.8
Prior CABG	1.5	4.7	<0.0001	1.5	1.7	−1.2
Carotid artery disease	2.4	2.0	0.013	2.0	2.5	−3.9
Dyslipidemia	64.4	57.8	<0.0001	57.9	58.3	0.6
Dementia	2.2	3.5	<0.0001	2.2	2.5	0.4
Atrial fibrillation	11.8	14.6	<0.0001	11.7	11.9	−1.6
AIDS	0	<0.2	0.030	–	–	–
Alcohol abuse	0.7	1.2	<0.0001	0.7	0.7	−0.7
Deficiency anemia	15.5	18.1	<0.0001	15.5	16.2	−2.3
Collagen vascular disease	3.1	4.0	<0.0001	3.1	3.8	−5.2
Chronic blood loss anemia	0.8	0.9	0.349	0.8	0.6	2.2
Congestive heart failure	0.4	0.5	0.362	0.4	0.4	0
Chronic pulmonary disease	20.5	23.0	<0.0001	20.5	20.6	−0.5
Coagulopathy	4.8	4.1	<0.0001	4.8	4.7	−0.07
Depression	10.3	10.5	0.620	10.4	10.7	−1.0
Diabetes, uncomplicated	21.2	32.4	<0.0001	21.2	22.5	−2.4
Diabetes, complicated	3.2	7.1	<0.0001	3.2	3.2	0.5
Drug abuse	1.3	1.7	0.022	1.3	1.4	−0.6
Hypertension	64.3	74.3	<0.0001	64.4	64.3	1.1
Hypothyroidism	15.4	17.0	<0.0001	15.5	15.3	0.7
Liver disease	1.1	1.2	0.482	1.1	1.2	−1.3
Lymphoma	0.8	0.4	<0.0001	0.8	0.7	1.3
Fluid and electrolyte disorders	20.9	21.4	0.325	20.9	19.3	2.5
Metastatic cancer	0.3	0.5	0.487	0.3	0.5	−3.2
Other neurological disorders	5.0	5.1	0.47	4.9	4.8	0.5
Obesity	17.1	18.7	0.001	17.1	17.1	0.4
Paralysis	1.5	1.3	0.003	1.5	1.2	2.0
Peripheral vascular disease	11.0	12.4	<0.0001	11	11.7	−2.4
Psychoses	2.7	2.6	0.702	2.7	2.4	1.7
Pulmonary circulation disorders	<0.2	<0.2	0.456	<0.2	<0.2	0
Renal failure	8.8	15.8	<0.0001	8.9	9.6	−1.8
Solid tumor without metastasis	1.4	0.9	<0.0001	1.4	1.1	3.1
Peptic ulcer disease	0	0	0.221	–	–	–
Valvular heart disease	<0.2	0.2	0.595	<0.2	0.2	−0.7
Weight loss	2.6	2.3	0.047	2.6	2.7	−0.9
Acute ischemic stroke	0.9	0.9	0.801	0.8	0.9	−0.4
Intracranial hemorrhage	<0.2	0.3	<0.0001	0.3	0.4	−2.8
Gastrointestinal bleeding	2.2	1.4	<0.0001	2.2	2.2	−1.5
Cardiogenic shock	9.5	5.6	<0.0001	9.5	9.3	−2.4
Acute systolic heart failure	3.5	4.6	<0.0001	3.5	3.3	1.2
Ventricular tachycardia	8.2	4.6	<0.0001	8.1	8.3	−2.4
Ventricular fibrillation	5.9	2.5	<0.0001	5.8	5.6	0.8

Continued on the next page

percentiles ranges for skewed continuous variables. Frequencies of covariables were compared between patients with and without SCAD using the Pearson chi-square test. Means were compared using independent sample Student *t* tests, whereas medians were compared using the Mood median test. A linear-by-linear association trend test (Mantel-Haenszel test for trend) was used to assess trends of categorical variables.

A propensity score match was constructed using 55 patient and hospital covariables to choose a group of controls with similar characteristics to the SCAD patient population. A nearest neighbor, 1:2 matching was adopted. The propensity score match robustness

TABLE 1 Continued

	SCAD (n = 7,347)	No SCAD (n = 745,005)	p Value	Propensity Matched SCAD (n = 7,332)	Propensity Matched No SCAD (n = 14,352)	Bias %, SMD
Hospital characteristics						
Bed size			0.880			−1.1
Small	8.5	8.3		8.3	8.0	
Medium	23.8	23.7		23.7	23.9	
Large	67.7	68.0		68.0	68.1	
Location			<0.0001			1.8
Rural	6.0	6.5		6.0	5.1	
Urban non-teaching	37.7	39.9		37.7	41.1	
Urban teaching	56.3	53.6		56.3	53.8	
Region			<0.0001			−1.4
Northeast	18.3	18.2		18.4	17.2	
Midwest/North Central	19.8	20.8		19.8	18.0	
South	39.0	43.7		39.0	44.3	
West	22.9	17.3		22.8	20.5	
Revascularization						
PCI	76.9	58.4	<0.0001	76.9	76.3	1.5
CABG	10.8	8.0	<0.0001	10.7	11.6	−4.5
Outcome						
In-hospital mortality	6.8	3.4	<0.0001	6.8	3.8	<0.0001*

Values are % or mean ± SD, except as noted. *p value by Pearson chi-square test.

AIDS = acquired immunodeficiency syndrome; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; CAD = coronary artery disease; NSTEMI = non-ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; SCAD = spontaneous coronary dissection; SMD = standardized mean difference; STEMI = ST-elevation myocardial infarction; TIA = transient ischemic attack.

was tested by evaluation of standardized mean differences (bias %) between the unmatched and matched variables with a cut level of 0.1 (11). The incidence of in-hospital mortality was compared in both groups by the Pearson chi-square test and univariable logistic regression. A subgroup analysis was performed in the matched population to evaluate the impact of different covariables on the outcome of in-hospital mortality. Covariables included in the subgroup analyses were age (above and below the median), hypertension, diabetes mellitus, acute decompensated heart failure, clinical presentation (i.e., STEMI vs. NSTEMI), and PCI.

To ensure accuracy of our estimates, we conducted a secondary analysis using multivariable backward selection logistic regression with in-hospital mortality being the dependent variable and the previously stated 58 covariates being as independent ones, using 0.05 probability of stepwise entry and 0.1 for removal. We used multiple statistical analyses models to ensure the accuracy of the effect size (12). To account for hospital cluster effect, multiple hospital variables, for example, hospital size, location, and region, were included in both the propensity score matching and multivariable regression analysis. To assess the impact of PCI on in-hospital mortality in the SCAD group, a multivariable logistic regression analysis was performed in both NSTEMI and STEMI SCAD patients with in-hospital mortality being the dependent variable and the rest of covariables together with PCI being independent variables.

All statistical analyses were performed by SPSS software version 23.0 (IBM, Armonk, New York) with a 2-sided p value of <0.05 as the cutoff for statistical significance and odds ratio (OR) with 95% confidence interval (CI) as a measure of effect size. A list of all covariables included in the propensity match construction and multivariable regression analyses is described in Online Table 2.

RESULTS

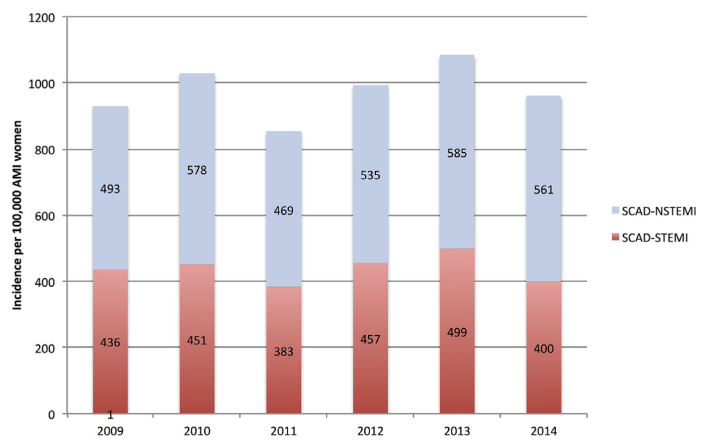
Of 1,259,158 women discharged with a primary diagnosis of AMI in the years 2009 to 2014, 752,352 women with AMI who underwent coronary angiography were included. Of these, 7,347 women had a co-diagnosis of SCAD, representing 0.98% of the women presenting with AMI (**Figure 1**). And 3,296 SCAD women had the diagnosis of STEMI, representing 44.9% of the total SCAD women with AMI. Compared with women without SCAD, women with SCAD were younger (mean age 61.7 ± 15.1 vs. 67.1 ± 13.2 years of age), with fewer risk factors for coronary artery disease. **Table 1** illustrates the incidences of various patients' and hospital characteristics of the women with SCAD and concomitant AMI.

There was a slight increase in the incidence of SCAD with time (929 vs. 961 per 100,000 women with AMI in years 2009 and 2014, respectively, $p_{trend} = 0.042$) (**Figure 2**). On the other hand, the trends of PCI use in SCAD women with AMI had decreased significantly (82.5% vs. 69.1% for 2009 and 2014 years, respectively, $p_{trend} < 0.0001$) (**Figure 3**). This was true for women with both NSTEMI and STEMI SCAD patients, with a larger trend toward lower PCI use in NSTEMI SCAD patients (Online Figure 1). The incidence of in-hospital mortality was higher with SCAD compared with patients without SCAD (6.8% vs. 3.4%, $OR_{unadjusted}$: 2.11, 95% CI: 1.92 to 2.31; $p < 0.0001$). However, the incidence of in-hospital mortality in SCAD patients appeared to be decreasing with time, 11.4% versus 5.0% for years 2009 and 2014, respectively; $p_{trend} < 0.0001$ (**Figure 3,** Online Figure 2). Of 7,347 women with SCAD in our cohort, 1,687 were <50 years of age. The different characteristics of women <50 or ≥50 years of age with SCAD are described in Online Table 3; as expected, older women had greater comorbidities compared with younger women. **Table 2** illustrates the patients' characteristics and in-hospital mortality trends of women with AMI in the setting of SCAD.

PROPENSITY-MATCHED IN-HOSPITAL MORTALITY. Propensity score matched 7,332 women with SCAD and 14,352 women without SCAD (**Figure 1**). Both groups had well-matched patient and hospital characteristics (**Table 1**). The propensity match appeared to be adequately balanced with standard mean differences <10% for all included covariables (**Table 1, Figure 4**). The incidence of in-hospital mortality was higher in SCAD patients compared with those without SCAD (6.8% vs. 3.8%, $OR_{adjusted}$: 1.87, 95% CI: 1.65 to 2.11; $p < 0.0001$). Subgroup analysis for the pre-defined covariables, illustrated that age >62 years, hypertension, and undergoing PCI were all associated with a higher incidence of in-hospital mortality in women with SCAD and AMI (**Figure 5**).

MULTIVARIABLE REGRESSION-ADJUSTED IN-HOSPITAL MORTALITY. After adjustment, the incidence of in-hospital mortality remained higher in the SCAD patients compared with patients without SCAD ($OR_{adjusted}$: 2.41, 95% CI: 2.07 to 2.80; $p < 0.0001$). **Table 3** illustrates the covariables associated with higher OR of in-hospital mortality after multivariable adjustment.

FIGURE 2 **Incidence of SCAD According to the Clinical Presentation, per 100,000 Women With AMI, Years 2009-2014**



NSTEMI = non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in **Figure 1**.

IMPACT OF PCI ON SURVIVAL IN SCAD PATIENTS. In the SCAD group, PCI was associated with increased in-hospital mortality in NSTEMI patients by both unadjusted ($OR_{unadjusted}$: 2.11, 95% CI 1.39-3.21, $p < 0.0001$) and multivariable regression adjusted analyses ($OR_{adjusted}$: 2.01, 95% CI: 1.00 to 4.47; $p = 0.02$), but not STEMI patients ($OR_{unadjusted}$: 1.37, 95% CI: 0.99 to 1.89; $p = 0.06$; and $OR_{adjusted}$: 0.62, 95% CI: 0.41 to 0.96; $p = 0.03$).

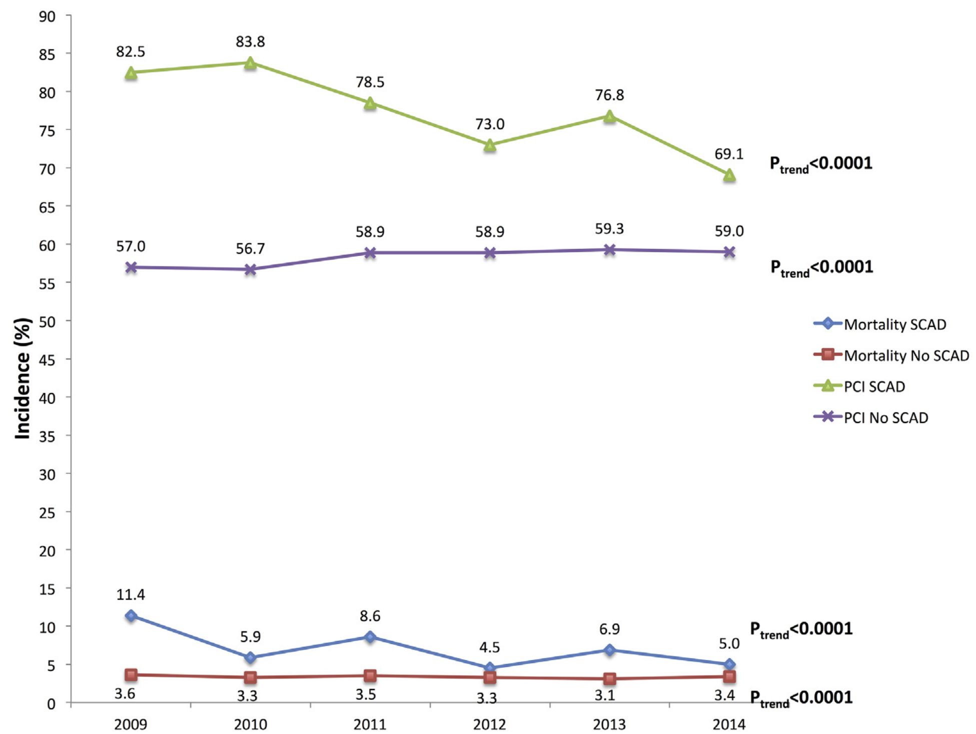
DISCUSSION

In this large population-based study, the reported prevalence of SCAD in women with AMI undergoing coronary angiography was ~1%. Women with SCAD in the setting of AMI had a higher likelihood of in-hospital mortality compared with those without SCAD. Additionally, PCI in SCAD patients appeared to be associated with an increased incidence of in-hospital mortality compared with conservative management, especially in patients presenting with NSTEMI.

To the best of our knowledge, this study is the largest study to date on women with SCAD in the setting of AMI (6,13-22). The incidence of SCAD in women with AMI in our study population was similar to prior published registries, ranging from 0.2% to 1.5%. However, this number may have underestimated the true incidence of SCAD, because SCAD might be missed by standard coronary angiography,

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 1, 2018
JANUARY 8, 2018:80–90

FIGURE 3 Trends of PCI and In-Hospital Mortality Rates in Women With and Without SCAD, Years 2009-2014



Abbreviations as in Figure 1.

TABLE 2 Trends of Patients' Characteristics and In-Hospital Mortality of Women With Spontaneous Coronary Artery Dissection in the Setting of Acute Myocardial Infarction, 2009 to 2014

	2009	2010	2011	2012	2013	2014	p Value for Trend
n	929	1029	852	992	1084	961	0.046
Clinical presentation							
STEMI	436	451	383	457	499	400	0.124
NSTEMI	493	578	469	535	585	561	0.124
Mean age (yrs)	63.9	60.3	62.5	61.6	61.7	60.6	<0.0001
Race							0.547
White	718	816	669	807	866	745	
Black	83	106	89	82	71	84	
Hispanic	63	78	52	56	98	66	
Asian	15	21	19	26	<10	26	
Native American	<10	<10	<10	<10	<10	15	
Other	46	<10	22	22	38	29	
PCI	766	863	669	725	833	664	<0.0001
Mortality	106	61	73	45	75	48	<0.0001

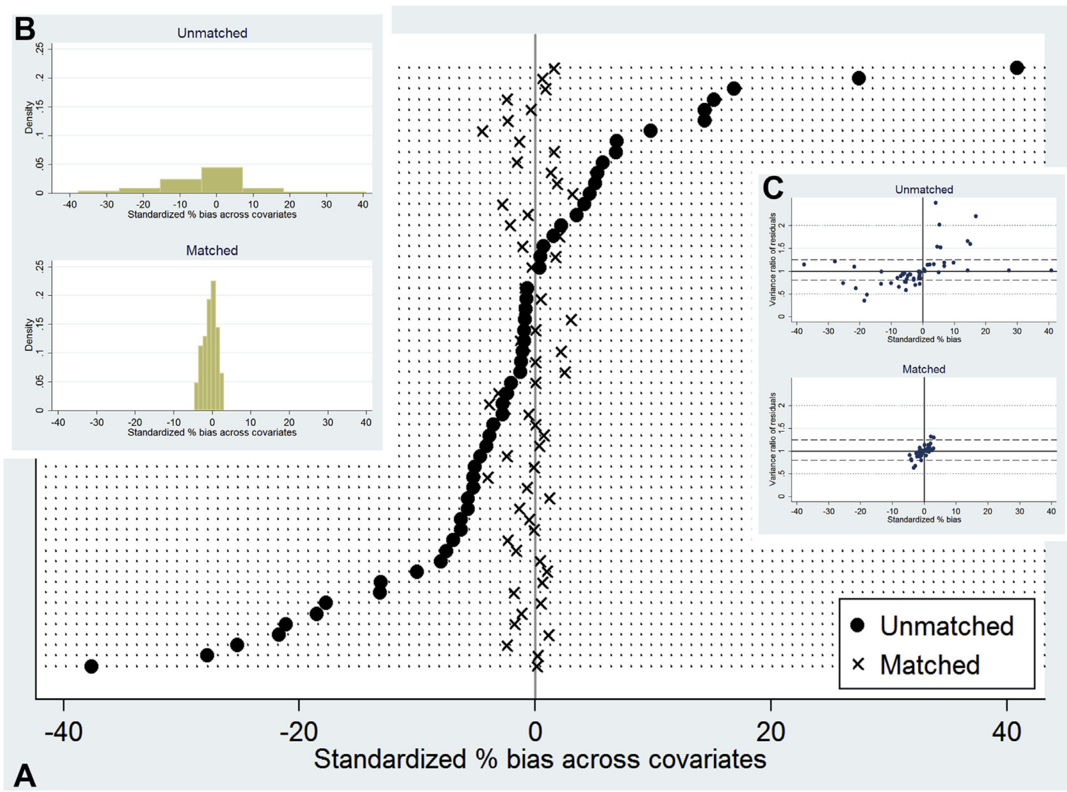
All values are per 100,000 women discharges presenting with acute myocardial infarction per year, except mean age, which is per all women discharges with spontaneous coronary artery dissection per year.

NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

especially if associated with an intramural hematoma and/or in the absence of an intimal entry point. Although the diagnostic yield of coronary angiography for SCAD is increased by the use of intravascular ultrasound or optical coherence tomography (23,24), we believe that both modalities were not widely utilized for AMI at the time these study data were collected. It is highly likely that the coronary dissection most commonly detected by angiographers in 2009 to 2014 is type I, where there is an obvious dissection plane or dye hang-up (25). This type of angiographic SCAD represents <30% of total SCAD detected on coronary angiography (22). The type 2 and 3 angiographic variants of SCAD are more likely to be missed because of lack of familiarity with these SCAD appearance, and likelihood of misdiagnosis as atherosclerotic changes (25).

Although traditionally considered a rare cause of AMI, SCAD has now been shown to be the underlying etiology in 10% to 24% of myocardial infarctions in women younger than 50 years of age (3,20,26). The average age of SCAD patients in our study was higher than previous reports; however, this finding is not surprising because SCAD had been reported before in

FIGURE 4 **Standardized Percent Bias (Standardized Mean Difference) for Each Covariable**

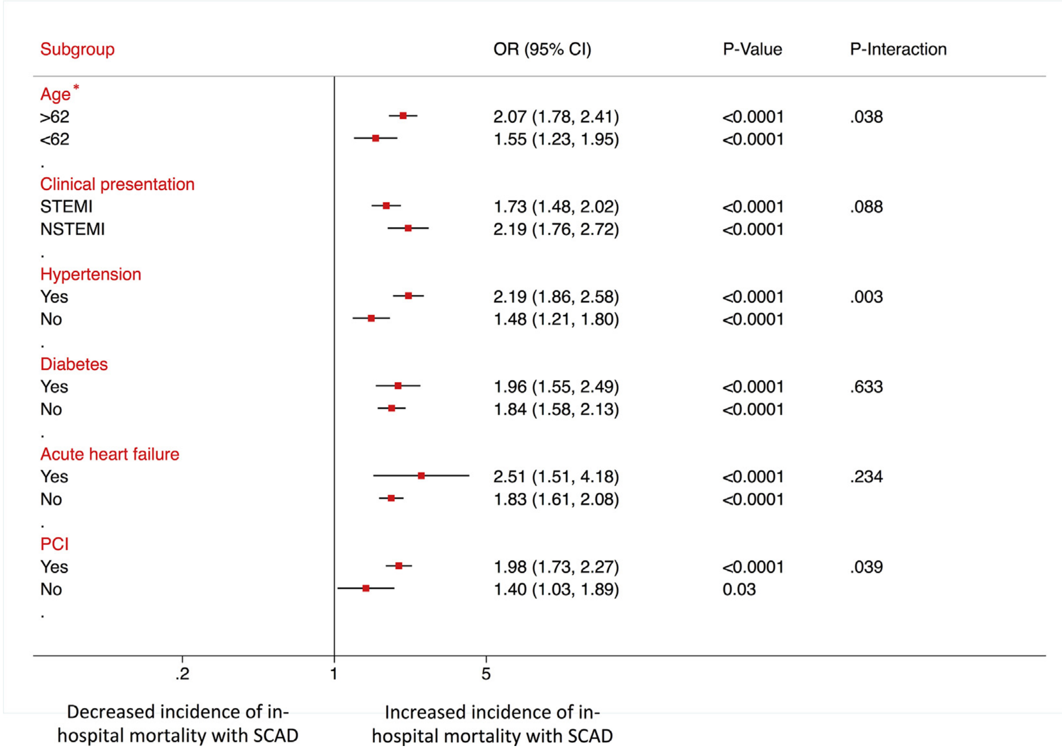


A dot plot **(A)**, a histogram **(B)**, and a scatter plot **(C)** representing the standardized percent bias (standardized mean difference) for each covariable included in the propensity score analysis, before and after matching.

elderly patients, with the oldest reported being 84 years of age (22). It is possible that the incidence of SCAD is underreported in elderly women, because the likelihood of having concomitant atherosclerotic coronary artery disease is higher, and operators may associate the dissection with the atherosclerotic process.

SCAD patients commonly present either as NSTEMI or STEMI infarction (27). The results of the current study question the benefit of PCI in SCAD patients presenting with AMI and suggest that conservative management might be associated with better short-term survival. The current findings are different from previous reports on women presenting with NSTEMI that showed a benefit of routine invasive strategy (28), and they concur with prior reports on women with SCAD illustrating that a conservative approach may be preferable (14) because the majority of SCAD lesions heal spontaneously when assessed in follow-up (22). In an observational study of 134 SCAD patients, the decision of a conservative versus revascularization approach was influenced predominantly by location of the dissection (proximal vs. distal) and level of flow impairment (Thrombosis In Myocardial Infarction [TIMI] flow grade 0 to 1 vs. 2 to 3); clinical presentation was not an influential factor. Furthermore, successful PCI was achieved in only 72% of patients who underwent PCI in that study (18). Technical failure of PCI was a major problem occurring in up to 35% of SCAD patients who underwent PCI (13). In another registry, PCI failure occurred in up to 53% of the cases, with one-half of these being in nonoccluded vessels with preserved flow (14). At the same time, SCAD lesions usually heal in the majority of patients who underwent conservative management, resulting in restoration of normal coronary flow. This also explains why long-term results with CABG may be suboptimal as venous and arterial grafts become occluded or atretic with competitive flow (13). Another major problem in SCAD patients is recurrence. Dissection recurrence usually presents in a new vessel or location different from the originally

FIGURE 5 Subgroup Analysis of In-Hospital Mortality in the Propensity-Matched Women With AMI With and Without SCAD



*Age subgroup is according to the mean age of the SCAD patients in years. CI = confidence interval; OR = odds ratio; other abbreviations as in Figures 1 and 2.

dissected vessel (14,29), with recurrence rates of 10% in the first week following presentation and up to 27% in 5 years (14). Unlike with atherosclerosis, PCI does not prevent recurrence of AMI with SCAD because it usually occurs in a different segment. In one study, SCAD recurrence was similarly high between PCI and conservatively managed patients (14). Furthermore, the majority of patients with conservatively managed SCAD have normalization of segmental wall motion abnormality and left ventricular dysfunction at follow-up (30). All of this supports the feasibility of adopting a conservative approach in SCAD patients presenting with AMI, with the option of invasive or non-invasive follow-up by computerized topography angiogram to document healing of the lesions (21).

Optimal medical therapy plays a cardinal role in the management of SCAD patients with AMI as previously described (31). Antiplatelet therapy with aspirin and adenosine di-phosphate inhibitors are frequently administered following the acute event for 1 to 12 months, followed by aspirin indefinitely. Beta-blockers are routinely administered long term to reduce arterial shear stress, especially because recent data showed lower risk of recurrent SCAD with beta-blockade (32). Selective use of statins for patients with pre-existing dyslipidemia, and selective use of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker are also indicated for patients with left ventricular dysfunction after AMI (31).

The large sample size from the NIS database provided an excellent source for further evaluation of rare diseases, such as SCAD, in a high-risk patient population presenting with AMI. The NIS database had been used to evaluate outcomes of various special patient populations on a national scale, providing accurate estimates of both the clinical presentations and outcomes (28,33).

STUDY LIMITATIONS. First, being an administrative database, the data are subject to errors in coding or misdiagnosis. For example, the definition of SCAD was based on an ICD-9-CM code; such a code could be misplaced for a patient with iatrogenic coronary

TABLE 3 Variables Associated With Higher Adjusted OR of In-Hospital Mortality in Women Presenting With AMI by Multivariable Regression Analysis

	OR (95% CI)	p Value
Age*	1.63 (1.53–1.73)	<0.0001
Hospital region (compared with Northeast)		
Midwest	1.95 (1.48–2.57)	<0.0001
South	1.98 (1.53–2.54)	<0.0001
West	1.46 (1.10–1.93)	0.008
Hospital location (compared with rural)		
Urban non-teaching hospital	1.63 (1.09–2.44)	0.017
Urban teaching hospital	1.66 (1.11–2.73)	0.014
STEMI (compared with NSTEMI)	1.66 (1.40–1.97)	<0.0001
Self pay (compared with Medicare)	1.53 (1.07–2.19)	<0.0001
Atrial fibrillation	1.23 (1.02–1.48)	0.034
Coagulopathy	1.79 (1.40–2.29)	<0.0001
Diabetes	1.64 (1.37–1.97)	<0.0001
Dementia	1.42 (1.01–2.01)	0.047
Collagen vascular disease	1.49 (1.04–2.14)	0.030
Chronic blood loss anemia	1.89 (1.03–3.47)	0.040
Congestive heart failure	6.16 (3.12–12.18)	<0.0001
Fluid and electrolytes disorders	1.32 (1.12–1.56)	0.001
Other neurological disorders	1.76 (1.34–2.30)	<0.0001
Peripheral vascular disease	1.56 (1.27–1.91)	<0.0001
Renal failure	1.91 (1.54–2.38)	<0.0001
Valvular heart disease	3.37 (1.18–9.60)	0.023
Intracranial hemorrhage	55.94 (28.87–108.38)	<0.0001
Gastrointestinal bleeding	2.16 (1.61–2.89)	<0.0001
Ventricular fibrillation	3.51 (2.84–4.32)	<0.0001
Cardiogenic shock	7.82 (6.59–9.29)	<0.0001
SCAD	2.41 (2.07–2.80)	<0.0001

*Per 10-year incremental increase in age (continuous variable).
CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

artery dissection. In an attempt to lower the chances of such error, we excluded any patient record that had a simultaneous ICD-9-CM code of "procedure injury" with the SCAD ICD-9-CM code. Second, although we evaluated all outcomes of interest after adjusting for more than 50 patient and hospital covariables, there is always the possibility of confounding biases that were not included in our analysis. Third, the NIS database lacks information regarding medical therapy, echocardiographic findings, or angiographic findings that could be used to further stratify the risk of poor outcomes in the current patient population. Fourth, the reason for choosing or deferring PCI could not be determined from the current data, with the lack of intravascular ultrasound or optical coherence tomography use data that could guide this decision. It is conceivable that patients who underwent PCI had worse geographic anatomic dissections (e.g., left main or proximal artery dissection, multivessel dissection) that were not captured in the NIS database, and may have contributed to bias for worse outcomes in this cohort. These findings support the current recommendations that conservative management should be the preferred initial strategy for management SCAD in women presenting with AMI.

CONCLUSIONS

Women presenting with AMI and concomitant SCAD have higher likelihood of in-hospital mortality compared with those without SCAD. A lower incidence of in-hospital mortality was evident in these patients with time and concurring with the decreased utilization of PCI. And thus, supporting the current recommendations that conservative management should be the preferred initial strategy for management of AMI women presenting with SCAD.

ADDRESS FOR CORRESPONDENCE: Dr. Ahmed N. Mahmoud, Department of Medicine, Division of Cardiovascular Medicine, University of Florida, 1600 SW Archer Road, Gainesville, Florida 32610. E-mail: Ahmed.Mahmoud@medicine.ufl.edu.

PERSPECTIVES

WHAT IS KNOWN? SCAD is an uncommon cause of AMI in women but more frequently encountered in those <50 years of age. PCI is commonly used to treat women with SCAD; however, there are insufficient data on the short-term outcomes of these patients.

WHAT IS NEW? In women admitted for AMI, the presence of SCAD appears to be an independent predictor of increased in-hospital mortality. The incidence of mortality might be higher with PCI compared with conservative management especially in patients presenting with NSTEMI. Thus, an initial conservative approach could be considered for management of SCAD in the setting of AMI.

WHAT IS NEXT? Further prospective studies are required to identify a subset of AMI women presenting with SCAD who could benefit from PCI. Given the rarity of this condition, registry-based randomized trials might be the most adequate method to investigate the best therapeutic approach for AMI women with SCAD.

REFERENCES

1. Pretty H. Dissecting aneurysm of coronary artery in a woman aged 42. BMJ 1931;1:667.

2. Mortensen KH, Thuesen L, Kristensen IB, Christiansen EH. Spontaneous coronary artery dissection: a Western Denmark Heart Registry study. Catheter Cardiovasc Interv 2009;74:710–7.

3. Vanzetto G, Berger-Coz E, Barone-Rochette G, et al. Prevalence, therapeutic management and medium-term prognosis of spontaneous coronary artery dissection: results from a database of 11,605 patients. Eur J Cardiothorac Surg 2009;35:250–4.

4. Nishiguchi T, Tanaka A, Ozaki Y, et al. Prevalence of spontaneous coronary artery dissection in patients with acute coronary syndrome. Eur Heart J Acute Cardiovasc Care 2016;5:263–70.

5. Hering D, Piper C, Hohmann C, Schultheiss HP, Horstkotte D. [Prospective study of the incidence, pathogenesis and therapy of spontaneous, by coronary angiography diagnosed coronary artery dissection]. Z Kardiol 1998;87:961–70.

6. Saw J, Ricci D, Starovoytov A, Fox R, Buller CE. Spontaneous coronary artery dissection: prevalence of predisposing conditions including fibromuscular dysplasia in a tertiary center cohort. J Am Coll Cardiol Intv 2013;6:44–52.

7. Walsh SJ, Jokhi PP, Saw J. Successful percutaneous management of coronary dissection and extensive intramural haematoma associated with ST elevation MI. Acute Card Care 2008;10:231–3.

8. Healthcare Cost and Utilization Project (HCUP). Overview of the National (Nationwide) Inpatient Sample (NIS). Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed May 8, 2017.

9. Epstein AJ, Polsky D, Yang F, Yang L, Groeneveld PW. Coronary revascularization trends in the United States, 2001-2008. JAMA 2011;305:1769–76.

10. Elixhauser A, Steiner C, Kruzikas D. Comorbidity software documentation. 2004. HCUP Methods Series Report# 2004-1. ONLINE February 6, 2004. US Agency for Healthcare Research and Quality. Available at: http://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp. Accessed May 8, 2017.

11. Stuart EA, Lee BK, Leacy FP. Prognostic score-based balance measures can be a useful diagnostic for propensity score methods in comparative effectiveness research. J Clin Epidemiol 2013;66:S84–90.e1.

12. Elze MC, Gregson J, Baber U, et al. Comparison of propensity score methods and covariate adjustment: evaluation in 4 cardiovascular studies. J Am Coll Cardiol 2017;69:345–57.

13. Tweet MS, Hayes SN, Pitta SR, et al. Clinical features, management, and prognosis of spontaneous coronary artery dissection. Circulation 2012;126:579–88.

14. Tweet MS, Eleid MF, Best PJ, et al. Spontaneous coronary artery dissection: revascularization versus conservative therapy. Circ Cardiovasc Interv 2014;7:777–86.

15. Alfonso F, Paulo M, Lennie V, et al. Spontaneous coronary artery dissection: long-term follow-up of a large series of patients prospectively managed with a "conservative" therapeutic strategy. J Am Coll Cardiol Intv 2012;5:1062–70.

16. McGrath-Cadell L, McKenzie P, Emmanuel S, Muller DW, Graham RM, Holloway CJ. Outcomes of patients with spontaneous coronary artery dissection. Open Heart 2016;3:e000491.

17. Rogowski S, Maeder MT, Weilenmann D, et al. Spontaneous coronary artery dissection: angiographic follow-up and long-term clinical outcome in a predominantly medically treated population. Catheter Cardiovasc Interv 2017;89:59–68.

18. Lettieri C, Zavalloni D, Rossini R, et al. Management and long-term prognosis of spontaneous coronary artery dissection. Am J Cardiol 2015;116:66–73.

19. Nakashima T, Noguchi T, Haruta S, et al. Prognostic impact of spontaneous coronary artery dissection in young female patients with acute myocardial infarction: a report from the Angina Pectoris-Myocardial Infarction Multicenter Investigators in Japan. Int J Cardiol 2016;207:341–8.

20. Rashid HN, Wong DT, Wijesekera H, et al. Incidence and characterisation of spontaneous coronary artery dissection as a cause of acute coronary syndrome-a single-centre Australian experience. Int J Cardiol 2016;202:336–8.

21. Roura G, Ariza-Solé A, Rodriguez-Caballero IF, et al. Noninvasive follow-up of patients with spontaneous coronary artery dissection with CT angiography. J Am Coll Cardiol Img 2016;9:896–7.

22. Saw J, Aymong E, Sedlak T, et al. Spontaneous coronary artery dissection: association with predisposing arteriopathies and precipitating stressors and cardiovascular outcomes. Circ Cardiovasc Interv 2014;7:645–55.

23. Saw J, Mancini GB, Humphries K, et al. Angiographic appearance of spontaneous coronary artery dissection with intramural hematoma proven on intracoronary imaging. Catheter Cardiovasc Interv 2016;87:E54–61.

24. Motreff P, Malcles G, Combaret N, et al. How and when to suspect spontaneous coronary artery dissection? Novel insights from a single-center series on prevalence and angiographic appearance. EuroIntervention 2017;12:e2236–43.

25. Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. Catheter Cardiovasc Interv 2014;84:1115–22.

26. Saw J, Aymong E, Mancini J, Sedlak T, Starovoytov A, Ricci D. Non-atherosclerotic coronary artery disease in young women. Can J Cardiol 2014;30:814–9.

27. Ho SW, Lin W, Chan KH, Seow SC. Spontaneous coronary dissection masquerading as benign fascicular ventricular tachycardia. Heart Lung Circ 2016;25:e9–11.

28. Elgendy IY, Mahmoud AN, Mansoor H, Bavry AA. Early invasive versus initial conservative strategies for women with non-ST-elevation acute coronary syndromes: Propensity matched analysis. Am J Med 2017;130:1059–67.

29. Eugène M, Siam-Tsieu V, Pillière R, Deblaise J, Dubourg O, Mansencal N. Recurrent spontaneous coronary artery dissection: Unexpected evolution and major role of emotional stress. Int J Cardiol 2015;201:316–8.

30. Franco C, Starovoytov A, Heydari M, Mancini GB, Aymong E, Saw J. Changes in left ventricular function after spontaneous coronary artery dissection. Clin Cardiol 2017;40:149–54.

31. Saw J, Mancini GB, Humphries KH. Contemporary review on spontaneous coronary artery dissection. J Am Coll Cardiol 2016;68:297–312.

32. Saw J, Humphries KH, Aymong E, et al. Spontaneous coronary artery dissection. Clinical outcomes and risk of recurrence. J Am Coll Cardiol 2017;70:1148–58.

33. Mahmoud AN, Elgendy IY, Mansoor H, et al. Early invasive strategy and in-hospital survival among diabetics with non-ST-elevation acute coronary syndromes: a contemporary national insight. J Am Heart Assoc 2017;18:e005369.

KEY WORDS acute coronary syndrome(s), mortality, propensity score matching, women

APPENDIX For supplemental figures and tables, please see the online version of this paper.