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ORIGINAL ARTICLE

Predictors of in-hospital mortality in coronary artery dissection: Findings from the National Inpatient Sample 2009–2010

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Abstract

Background: *The pathophysiology of coronary artery dissection (CD) remains poorly understood and little is known about the factors predicting mortality in these patients. We aimed to study the epidemiology of CD and predictors of mortality in these patients.*

Methods: *All patients diagnosed with CD in the Nationwide Inpatient Sample 2009–2010 database using International Classification of Diseases ninth revision 414.12 were included in the study. Chronic conditions included in the analysis were diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease (CAD), obesity, alcohol use, smoking, heart failure and ventricular arrhythmias. Non-cardiovascular conditions were connective tissue disorders, fibromuscular dysplasia, Ehlers-Danlos syndrome, Marfan's syndrome, sarcoidosis, Crohn's disease, polycystic kidney disease, rheumatoid arthritis, vasculitis including giant cell arteritis, polyarteritis nodosa and Takayasu's disease, cocaine use, early or premature labor.*

Results: *The prevalence of CD in the United States was 0.02% (n = 11,255), based on the hospital admissions reviewed in the database. The mean age was 63.25 years with women (64.62 years) being older than men (62.25 years) (p < 0.001). In-hospital mortality rate was 4.2%, with women (5.5%) having higher mortality than men (3.2%) (p = 0.009). Ventricular arrhythmias (OR 5.86, p < 0.001) predicted higher mortality, while hyperlipidemia (OR 0.26, p < 0.001) and CAD (OR 0.31, p = 0.001) predicted lower mortality in multivariate analysis.*

Conclusions: *Our study demonstrated that CD was more prevalent in men but women had higher mortality than men. Age, heart failure and ventricular arrhythmias were independent predictors of increased mortality but hyperlipidemia CAD predicted lower mortality in patients with CD.* (Cardiol J 2015; 22, 2: 135–140)

Key words: coronary artery dissection, risk factors, predictors of mortality, arrhythmias

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Introduction

Coronary artery dissection (CD) is rare with a prevalence of 0.07% to 1.1%. The first case of CD was reported in 1931 [1] and about 440 cases of spontaneous coronary artery dissection (SCD) have been reported in the literature since then [2]. It is characterized by separation of the coronary arterial wall due to bleeding within the wall either from an intimal tear or a medial hematoma [3, 4]. Both processes result in compromised flow either from multiple lumens or flaps in the case of an intimal tear or luminal narrowing from the intramural hematoma, resulting in compromised antegrade blood flow. The clinical presentation is that of an acute coronary syndrome (ACS) which includes angina, non-ST elevation myocardial infarction (NSTEMI) or ST-segment elevation myocardial infarction (STEMI) and ventricular fibrillation and/or sudden cardiac death [5–7]. CD can be SCD, traumatic (as a complication of coronary angiography) [8, 9], and either atherosclerotic or non-atherosclerotic. Non-atherosclerotic SCD is associated with fibromuscular dysplasia (FMD), inflammatory and connective tissue disorders, emotional stress, exertion, post partum state and is more common in younger women [3, 4, 10]. Typically CD involves a single coronary artery, however multi vessel coronary artery dissection has also been reported [3].

CD and especially SCD remain under diagnosed and the pathophysiology is still poorly understood. The reasons include under recognition of CD as a cause of STEMI and arrhythmia related sudden cardiac death, misdiagnosis of chest pain in younger females with SCD as non-cardiac chest pain and incorrectly characterizing an intramural hematoma as spasm or atherosclerotic plaque during angiography. In addition little is known about the factors predicting mortality in CD, which till now were largely limited to case reports and small case series. The objective of our analysis was to determine the epidemiology and predictors of mortality in patients with CD.

Methods

We accessed the Nationwide Inpatient Sample (NIS) database for the period 2009 to 2010 from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality, in Rockville, MD. It is the largest all-payer hospitalization database representing up to 8 million hospital stays from 1,000 hospitals in the United States. The data represents 20% of all inpatient admissions to non-federal hospitals in the United States. All patients with primary and all listed diagnoses of CD in the NIS 2009–2010 database using International Classification of Diseases 9 (ICD-9) 414.12 were included in the study. As the ICD-9 code was restricted only to the diagnosis of CD and no other codes exist, the type of CD (spontaneous, atherosclerotic, non-atherosclerotic or iatrogenic) was uncertain. All hospitalizations of any patient aged 18 years or older were included in the analysis. Age was represented as a continuous variable while race was categorized as white, black, Asian, Hispanic, native American or others. We weighted hospital and discharge data to generate national estimates.

Outcomes

The primary outcomes of our study were predictors and prevalence of in-hospital mortality. We assessed the demographics and the prevalence of chronic conditions in patients with CD. Chronic conditions included diabetes mellitus, hypertension, hyperlipidemia, obesity, coronary artery disease (CAD), smoking and alcohol use. Non-cardiovascular conditions analyzed were connective tissue disorders, fibromuscular dysplasia, Ehlers-Danlos syndrome, Marfan's syndrome, sarcoidosis, Crohn's disease, cocaine use, polycystic kidney disease, rheumatoid arthritis, vasculitis including giant cell arteritis, polyarteritis nodosa and Takayasu's disease and early or premature labor. We also determined the prevalence of heart failure (HF) and ventricular arrhythmia (refer to supplement for ICD-9 codes used).

Statistical analysis

We analyzed the database from 2009 to 2010. Categorical variables were represented as percentages (%), while continuous variables were represented as mean ± standard deviation. Univariate regression analysis was done to determine predictors of mortality in CD. Including traditional risk factors and other factors that predicted mortality in univariate analysis, stepwise multimodel logistic regression was performed. A p value less than 0.05 was considered statistically significant. All statistical analysis was performed using STATA 10.0, Statacorp, College Station, TX. The study did not have any outside sponsorship or funding.

Table 1. Baseline demographic and clinical characteristics stratified by gender.

Variable*	Total (n = 11,255)	Males (n = 6,498)	Females (n = 4,757)	P**
Age	63.3 ± 0.3	62.3 ± 0.3	64.6 ± 0.5	< 0.001
Length of stay	4.5 ± 0.1	4.1 ± 0.1	4.9 ± 0.2	0.001
Mortality	4.2	3.2	5.5	0.008
Diabetes	30	28	33	0.02
Hypertension	70	69	71	0.21
Hyperlipidemia	64	65	63	0.39
Obesity	13	12	15	0.03
Coronary artery disease	92	94	90	0.006
Smoking	22	25	19	0.002
Alcohol	2	3	0.8	< 0.001
Heart failure	16	14	19	0.001
Ventricular arrhythmia	11	12	9	0.007
Cocaine use	0.5	0.6	0.3	0.27
Crohn's disease	0.1	0.2	0.1	0.68
Connective tissue disorder	0.4	0.2	0.7	0.12
Fibro muscular dysplasia	0.1	0.2	0.1	0.76
Marfan's syndrome	0.04	0.07	–	0.39
Sarcoidosis	0.2	0.2	0.3	0.37
Rheumatoid arthritis	1	0.8	1.2	0.54
Giant cell arteritis	0.05	–	0.11	0.24
Polycystic kidney disease	0.05	0.09	–	0.39

*Continuous variables are expressed as median (IQR). Categorical variables are expressed as %; **Pearson's χ^2 for categorical; linear regression for continuous variables.

Results

Demographics

The prevalence of CD was 0.02% (n = 11,255) of all hospital admissions reviewed during the year 2009–2010 in United States and was higher in men (57.7%) compared to women (42.3%). The mean age was 63.3 years, women were older than men (64.6 years vs. 62.3 years; p < 0.001), the mean length of stay was 4.5 days and women stayed longer than men (4.9 vs. 4.1 days; p = 0.001). Chronic conditions prevalent in our study were CAD (92%), hypertension (70%), hyperlipidemia (64%), diabetes mellitus (30%) and smoking (22%). Connective tissue disorders (0.4%), sarcoidosis (0.2%), Crohn's disease (0.1%), rheumatoid arthritis (1%), fibromuscular dysplasia (0.1%), giant cell arteritis (0.05%), polycystic kidney disease (0.05%) and Marfan's syndrome (0.04%) were the non-cardiovascular conditions included in our analysis (Table 1).

Primary and secondary outcomes

In the 11,255 hospital admissions of CD the overall in-patient mortality rate was 4.2%, HF rate was present in 16% and ventricular arrhythmias were present in 11% of this population. Women compared to men, had higher mortality (5.5% vs. 3.2%, respectively, p = 0.008), more HF (19% vs. 14%, respectively, p = 0.001) but less ventricular arrhythmia (9% vs. 12% in women, p = 0.007) (Table 1).

We also analyzed the association of various risk factors and comorbidities in predicting mortality in patients with CD. In unadjusted analysis, age (odds ratio [OR] 1.03, 95% confidence interval [CI] 1.01–1.05, p < 0.001), female sex (OR 1.74, 95% CI 1.15–2.64, p = 0.009), HF (OR 2.68, 95% CI 1.71–4.21, p < 0.001) and ventricular arrhythmias (OR 6.01, 95% CI 3.85–9.34, p < 0.001) were associated with increased mortality in patients with CD. Interestingly, hyperlipidemia (OR 0.24, 95% CI 0.15–0.37, p < 0.001) and CAD (OR 0.34, 95% CI 0.20–0.58, p < 0.001) had an inverse relationship in predicting mortality (Table 2). Gender-specific analysis showed hyperlipidemia and ventricular arrhythmia predicted mortality in both men and women. However, age (OR 1.04, 95% CI 1.01–1.067, p = 0.003) and HF (OR 3.10, 95% CI 1.72–5.59, p < 0.001) predicted mortal-

Table 2. Univariate logistic regression of risk factors predicting mortality.

Variables	Total	P	Males	P	Females	P
Age	1.03	< 0.001	1.02	0.12	1.04	0.003
Female	1.74	0.009	–	–	–	–
Length of stay	1.02	0.085	1.05	0.005	0.99	0.75
Diabetes mellitus	0.80	0.354	0.50	0.098	1.02	0.96
Hypertension	0.70	0.109	0.80	0.485	0.62	0.10
Hyperlipidemia	0.24	< 0.001	0.17	< 0.001	0.31	< 0.001
Obesity	0.97	0.932	0.38	0.188	1.38	0.38
Coronary artery disease	0.34	< 0.001	0.24	< 0.001	0.48	0.06
Smoking	0.53	0.038	0.55	0.160	0.55	0.18
Heart failure	2.68	< 0.001	1.95	0.073	3.10	< 0.001
Ventricular arrhythmia	6.00	< 0.001	8.02	< 0.001	5.29	< 0.001
Connective tissue disorder	2.69	0.354	–	–	3.21	0.29

Table 3. Stepwise multi-model logistic regression of risk factors predicting in-hospital mortality.

Model	Total	P	Males	P	Females	P
Age						
Demographic risk factors	1.03	0.003	1.02	0.171	1.04	0.009
+ Traditional risk factors	1.04	< 0.001	1.02	0.127	1.05	0.001
+ Non-CV risk factors	1.04	< 0.001	1.02	0.133	1.05	0.001
Ventricular arrhythmia						
Demographic risk factors	7.39	< 0.001	8.54	< 0.001	6.27	< 0.001
+ Traditional risk factors	6.03	< 0.001	8.17	< 0.001	4.84	< 0.001
+ Non-CV risk factors	6.00	< 0.001	8.15	< 0.001	4.73	< 0.001
Heart failure						
Demographic risk factors	2.17	0.002	1.56	0.299	2.76	0.001
+ Traditional risk factors	1.87	0.015	1.33	0.538	2.45	0.006
+ Non-CV risk factors	1.89	0.014	1.33	0.541	2.53	0.005
Hyperlipidemia						
Demographic risk factors	0.20	< 0.001	0.14	< 0.001	0.26	< 0.001
+ Traditional risk factors	0.23	< 0.001	0.16	< 0.001	0.30	0.001
+ Non-CV risk factors	0.23	< 0.001	0.16	< 0.001	0.30	0.002
Coronary artery disease						
Demographic risk factors	0.24	< 0.001	0.17	< 0.001	0.32	0.006
+ Traditional risk factors	0.32	< 0.001	0.29	0.007	0.40	0.030
+ Non-CV risk factors	0.32	< 0.001	0.29	0.007	0.40	0.030

CV — cardiovascular; + Step wise addition; Demographic factors: Age, gender and race; Traditional risk factors (or CV risk factors): Diabetes, hypertension, obesity, hyperlipidemia, coronary artery disease, smoking and alcohol use; Non-CV risk factors: C tissue disorder

ity only in females and CAD was associated with decreased mortality only in males (OR 0.24, 95% CI 0.11–0.52, p < 0.001) (Table 2).

Stepwise multimodel logistic regression showed that age (OR 1.03, 95% CI 1.01–1.05, p = 0.001), ventricular arrhythmias (OR 5.86, 95% CI 3.30–10.41, p < 0.001) and HF (OR 1.89, 95% CI 1.14–3.13, p = 0.014) were independently associated with increased mortality after adjusting for demographic factors, traditional cardiovascular and non-cardiovascular risk factors (Table 3). Hyperlipidemia (OR 0.23, 95% CI 0.14–0.39, p < 0.001) and CAD (OR 0.32, 95% CI 0.17–0.58, p < 0.001) continued to demonstrate an inverse association in predicting mortality even after adjusting for all risk factors. Gender-specific analysis showed that ventricular

arrhythmia, hyperlipidemia and CAD predicted mortality in fully adjusted models for both men and women. However, age (OR 1.04, 95% CI 1.02–1.08, p = 0.009) and HF (OR 2.53, 95% CI 1.33–4.80, p = 0.005) predicted mortality only in women and not in men (Table 3).

Discussion

Our analysis is the largest study to date on CD with a prevalence of CD (0.02%) and high mortality rate as compared to previous studies [5, 11–13] which may be attributed to the large sample size and the inclusion of all types of CD. There was an increased prevalence in men compared to women, whereas other studies demonstrated the opposite. This is probably because all types of CD were included our analysis, whereas other studies have included mostly SCD which is more prevalent in younger women with FMD. Our population also had a very low number of patients with FMD, which occurs more commonly in women with SCD [14]. Women had a higher mortality rate (5.5%) than males (3.2%), something that has been not been described before in a CD population. Not unexpectedly, we identified age, ventricular arrhythmia and HF as predictors of increased mortality in patients with CD (with advanced female age, increased prevalence of ventricular arrhythmia and HF among females in our study). However, hyperlipidemia and CAD demonstrated an inverse association with predicting mortality. This once again may be explained by the inclusion of all types of CD including atherosclerotic and iatrogenic, which may be associated with lower mortality in general and also be more likely to include patients treated with statins. Treatment with statins may be protective and may be used more frequently in patients with non-SCD since statins are known to reduce peri-procedural myocardial infarction [15], diminish the inflammatory response [13, 14, 16] and are used for primary [16, 17] and secondary prevention [18, 19] of cardiovascular death [20, 21]. Future studies may determine their role in all comers with CD.

Limitations of the study

Our analysis has several limitations since this is an observational study of a large NIS; it includes all types of CD where a review of the coronary angiograms was not possible. Previous studies have focused mostly on SCD, which may be a distinct clinical entity more common in women with FMD and postpartum status. Also, the very high percentage of patients with preexisting CAD makes it likely that high numbers of procedure related CD were included in our analysis. Since, the diagnosis of CD is easier to establish in patients with otherwise unremarkable coronary arteries (i.e. young patients) then in patients with preexisting CAD where in many cases additional imaging to coronary angiography may be needed to demonstrate a false lumen or hematoma (information that is usually not available from administrative database like NIS), it is essential to have a ICD-9 code for SCD that would help physician scientists to separate the distinct types of dissection. In addition our study excluded patients admitted to the hospital under observational status or those who were discharged home from the emergency room and those patients admitted to any federal hospital (due to absence of information recorded in the NIS database). It is possible that the actual estimate of patients with CD was greater than that recorded in the database, thereby underestimating the power of the study. Since NIS is an administrative database, diagnostic codes are subject to misclassification and there is no way to determine if secondary diagnoses represented an active problem versus past medical history. The retrospective design of the study can only demonstrate association, and hence causation between the predictors of mortality in CD cannot be determined. Information from relevant studies, such as echocardiograms, coronary angiography, computed tomography angiography, single photon emission computed tomography, and cardiac biomarker data are also not available from the NIS database.

Conflict of interest: None declared

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APPENDIX 1. International Classification of Disease, version 9 (ICD-9) codes used for coronary artery dissection identification.

Inclusion criteria	ICD-9 codes
Coronary artery dissection (any position; primary or all listed diagnosis)	414.12

APPENDIX 2. International Classification of Disease, version 9 (ICD-9) codes used for co-morbidity identification.

Co-morbidities*	ICD-9 codes
Coronary artery disease	412, 414.xx, V458.1, V458.2
Heart failure	428.xx
Hyperlipidemia	272.xx
Obesity	278.xx, 793.91, V85.21-25, V85.30-45, V85.54
Hypertension	401.x, 402.xx, 403.xx, 404.xx, 405.xx, 437.2
Diabetes mellitus	249.xx, 250.xx, 790.xx, 791.5, 791.6, V458.5, V539.1, V654.6
Ventricular arrhythmias	427, 427.1, 427.4
Alcohol use	303.xx, 305.01, 305.02, 305.03
Smoking	305.1, V15.82
Connective tissue disorder	710.xx
Marfan's syndrome	759.82
Ehlers-Danlos syndrome	756.83
Fibro muscular dysplasia	447.8
Sarcoidosis	135
Crohn's disease	555.x
Cocaine use	305.60-63, 304.20-23
Premature labor	644.xx
Rheumatoid arthritis	714.0
Giant cell arteritis	446.5
Takayasu's disease	446.7
Polyartertis nodosa	446.0
Polycystic kidney disease	753.12, 753.13, 753.14

*Primary and all listed diagnosis