Impact of family history of coronary artery disease on in-hospital clinical outcomes in ST-segment myocardial infarction

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Background: Patients with a family history of coronary artery disease (FHxCAD) are at increased risk for development of myocardial infarction (MI). However, the data on the influence of FHxCAD on in-hospital clinical outcomes post ST-segment myocardial infarction (STEMI) is limited. Hence, we evaluated the impact of FHxCAD on in-hospital clinical outcomes post STEMI in an unselected nationwide cohort.

Methods: Nationwide Inpatient Sample (NIS) database [2003–2011] was used to compare differences in all-cause in-hospital mortality and adverse clinical events (cardiogenic shock, acute cerebrovascular events and use of intra-aortic balloon pump) between patients with and without FHxCAD.

Results: A total of 2,123,492 STEMI admissions were identified, of which 7.4% (n=158,079) patients were with FHxCAD and 92.6% (n=1,965,413) were without FHxCAD. The FHxCAD group had lower in-hospital mortality [1.4% *vs.* 8.1%; adjusted odds ratio (OR): 0.42, 95% confidence interval (CI): 0.41–0.44; P<0.001] when compared with no-FHxCAD group. They underwent a significantly higher number of coronary interventions, and were less likely to develop cardiogenic shock, acute cerebrovascular events and to require intra-aortic balloon pump during hospitalization.

Conclusions: This large sample size study demonstrates that STEMI patients with FHxCAD had lower in-hospital mortality and adverse clinical events in comparison to patients with no-FHxCAD. Further research is warranted to determine whether the superior outcomes in FHxCAD patients with STEMI are related to differences in strategies related to diet, exercise, use of medications or coronary interventions.

Keywords: Coronary artery disease; myocardial infarction (MI); family history; mortality; ST-segment myocardial infarction (STEMI)

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Introduction

Family history of coronary artery disease (FHxCAD) is an established risk factor for the development of acute myocardial infarction (AMI) (1). However, data relating to impact of FHxCAD on post-ST-segment myocardial infarction (STEMI) clinical outcomes is limited (2-5). In this study, we evaluated the impact of FHxCAD on in-hospital outcomes in 2,123,492 STEMI patients using Nationwide Inpatient Sample (NIS) database from 2003–2011.

Methods

NIS is the largest publicly available all-payer inpatient database available in the United States and it is sponsored by the Agency for Healthcare Research and Quality (6). We used International Classification of Diseases, ninth edition; Clinical Modification (ICD-9-CM) codes (410.01, 410.11, 410.21, 410.31, 410.41, 410.51, 410.61, 410.81, 410.91) to identify all patients ≥18 years of age admitted with a primary diagnosis of STEMI. FHxCAD was then identified using ICD-9-CM code, V.173, and all others were considered as patients with no-FHxCAD. Our primary outcome measure was all-cause in-hospital mortality, defined as "died" during the index hospitalization in the NIS database. Secondary outcomes were identified using ICD-9 and clinical classification software (CCS) codes, and included the following: acute cerebrovascular event (CCS-109), cardiogenic shock (ICD-9 CM-785.51), and intra-aortic balloon pump use (ICD-9 CM-37.61) during the hospitalization.

Baseline patient characteristics used included demographics (age, gender, race, primary expected payer, weekday *vs.* weekend admission, median household income for patient's zip code), all Elixhauser co-morbidities as defined by the Agency for Healthcare Research and Quality (7) (acquired immune deficiency syndrome, alcohol abuse, deficiency anemia, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, chronic renal failure, coagulopathy, depression, diabetes (uncomplicated), diabetes (with chronic complications), drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurologic disorders, obesity, paralysis, peripheral vascular disease, psychosis, pulmonary circulation disorders, solid tumor without metastasis, valvular heart disease, and weight loss), and data on hospital characteristics such as hospital region (Northeast, Midwest, South, and West), bed size (small, medium, and large), location (rural, urban), and teaching status. In addition, other clinically relevant co-morbidities were identified using the following codes: smoking (ICD-9 CM-V15.82, 305.1), dyslipidemia (CCS-53), previous myocardial infarction (MI) (ICD-9 CM-412), previous percutaneous coronary intervention (ICD-9 CM-V45.82), previous coronary artery bypass graft (ICD-9 CM-V45.81), carotid artery disease (ICD-9 CM-433.10), and atrial fibrillation (ICD-9 CM-427.31). The type of invasive coronary intervention such as diagnostic coronary angiography (ICD-9 CM: 37.22–37.23 and 88.52–88.57), percutaneous coronary intervention (ICD-9 CM: 00.66, 36.01, 36.02, 36.05, 36.06 and 36.07) and coronary artery bypass grafting (ICD-9 CM: 36.10–36.19) was also identified. Weighted data was used for all analyses.

Baseline patient and hospital characteristics were compared using Pearson's Chi-square test for categorical variables and the Student *t*-test for continuous variables. Multivariable unconditional logistic regression was used to examine the association of FHxCAD with primary and secondary outcomes. The regression models were adjusted for patient demographics, hospital characteristics and all comorbidities listed in *Table 1*. Statistical analysis was performed using SPSS 23.0 (IBM Corp., Armonk, NY, USA). A two-sided P value of <0.05 was used to identify statistical significance.

Results

A total of 2,123,492 STEMI hospitalizations, with 7.4% (n=158,079) patients with FHxCAD and 92.6%

Table 1 Baseline demographics, hospital and admission characteristics, and comorbidities of STEMI patients

Variable	Overall	No FHxCAD	FHxCAD	P value
Number of cases (weighted)	2,123,492	1,965,413	158,079	<0.001
Age, mean ± SD (years)	65.1±14.7	65.8±14.6	56.2±11.9	<0.001
Women (%)	35.6	36.3	26.6	<0.001
Race (%)				<0.001
White	79.2	78.8	84.5	
African American	7.6	7.8	5.3	

Table 1 (*continued*)

Table 1 (*continued*)

Variable	Overall	No FHxCAD	FHxCAD	P value
Hispanic	7.2	7.4	5.2	
Asian or Pacific Islander	2.2	2.2	1.4	
Native American	0.5	0.5	0.5	
Other	3.3	3.1	3.3	
Primary expected payer (%)				<0.001
Medicare	48.7	50.8	23.5	
Medicaid	5.6	5.6	5.6	
Private insurance	34.8	33.2	54.9	
Self-pay	7.1	6.8	10.5	
No charge	0.6	0.6	1.1	
Other	3.2	3.1	4.4	
Median household income (%)				<0.001
0 to 25th percentile	27.2	27.5	23.9	
26th to 50th percentile	27.6	27.7	25.9	
51st to 75th percentile	24.4	24.2	26.2	
76th to 100th percentile	20.8	20.6	24.0	
Weekend admission	26.8	26.7	28.1	<0.001
Elective admission	7.9	7.9	8.1	0.001
Hospital characteristics (%)				
Region				<0.001
Northeast	16.9	17.0	16.5	
Midwest	24.6	24.6	24.0	
South	39.7	39.5	41.3	
West	18.9	18.2	18.9	
Bed size				<0.001
Small	9.8	10.0	7.4	
Medium	22.9	23.0	22.0	
Large	67.3	67.1	70.7	
Urban location	87.8	87.4	92.4	<0.001
Teaching hospital	45.4	45.3	47.5	<0.001
Comorbidities*				
Smoking	34.8	32.8	60.0	<0.001
Diabetes mellitus (uncomplicated)	23.2	23.6	19.0	<0.001
Diabetes mellitus (complicated)	3.3	3.4	1.7	<0.001
Hypertension	56.6	56.7	55.4	<0.001

Table 1 (*continued*)

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Variable	Overall	No FHxCAD	FHxCAD	P value
Dyslipidemia	47.4	46.1	63.6	<0.001
Alcohol abuse	2.7	2.7	3.1	<0.001
Obesity	8.8	8.4	13.9	<0.001
Prior MI	7.1	7.1	7.0	0.074
Prior percutaneous coronary intervention	8.1	8.0	8.9	<0.001
Prior coronary artery bypass grafting	4.2	4.3	1.9	<0.001
Atrial fibrillation	12.9	13.5	6.1	<0.001
Congestive heart failure	0.6	0.6	0.1	<0.001
Carotid artery disease	0.9	0.9	0.6	<0.001
Peripheral vascular disease	7.3	7.5	4.9	<0.001
Renal failure	8.3	8.8	2.6	<0.001
Chronic pulmonary disease	16.4	16.8	11.5	<0.001
Pulmonary circulation disorders	<0.1	<0.1	<0.1	<0.001
Valvular disease	0.2	0.2	0.0	<0.001
Acquired immune deficiency syndrome	0.1	0.1	0.1	0.006
Deficiency anemia	9.8	10.2	5.6	<0.001
Rheumatoid arthritis/collagen vascular diseases	1.8	1.8	1.3	<0.001
Chronic blood loss anemia	0.9	1.0	0.4	<0.001
Coagulopathy	3.4	3.5	2.1	<0.001
Depression	4.6	4.6	4.6	0.422
Drug abuse	1.8	1.7	2.2	<0.001
Hypothyroidism	6.9	7.1	5.0	<0.001
Liver disease	0.8	0.8	0.6	<0.001
Lymphoma	0.4	0.4	0.2	0.003
Fluid and electrolyte disorder	15.2	15.7	8.7	<0.001
Metastatic cancer	0.8	0.8	0.2	<0.001
Other neurologic disorders	4.7	4.9	2.0	<0.001
Paralysis	1.3	1.3	0.3	<0.001
Psychoses	1.5	1.5	1.2	<0.001
Solid tumor without metastasis	1.2	1.3	0.4	<0.001
Peptic ulcer disease	0.0	0.0	0.0	0.055
Weight loss	1.4	1.5	0.3	<0.001

*, co-morbidities were extracted using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Clinical Classifications Software (CCS) Codes. FHxCAD, family history of coronary artery disease; no-FHxCAD, no family history of coronary artery disease; STEMI, ST-segment elevation myocardial infarction; MI, myocardial infarction.

Table 2 In-hospital clinical outcomes between STEMI patients with and without FHxCAD

In-hospital outcomes	Overall	No FHxCAD	FHxCAD
In-hospital mortality			
Percentage (%)	9.2	9.8	1.7
Unadjusted OR (95% CI)		Reference	0.16 (0.15–0.17)
Adjusted OR (95% CI)		Reference	0.45 (0.43–0.47)
Acute cerebrovascular event			
Percentage	1.6	1.7	0.4
Unadjusted OR (95% CI)		Reference	0.25 (0.23–0.27)
Adjusted OR (95% CI)		Reference	0.54 (0.50–0.59)
Cardiogenic shock			
Percentage (%)	8.1	8.5	3.7
Unadjusted OR (95% CI)		Reference	0.41 (0.40–0.42)
Adjusted OR (95% CI)		Reference	0.61 (0.60–0.63)
Intra-aortic balloon pump use			
Percentage (%)	8.5	8.6	6.7
Unadjusted OR (95% CI)		Reference	0.76 (0.75–0.78)
Adjusted OR (95% CI)		Reference	0.81 (0.79–0.83)

STEMI, ST-segment elevation myocardial infarction; FHxCAD, family history of coronary artery disease; no-FHxCAD, no family history of coronary artery disease; OR, odds ratio; CI, confidence interval.

(n=1,965,413) with no-FHxCAD were identified during the study period (*Table 1*). FHxCAD patients were younger (mean age: 56.2 *vs.* 65.8 years; P<0.001), more likely men (74.4%), private insurers (54.9%) and of white race (79.2%). They belonged to higher socioeconomic status, and presented to hospitals with the following characteristics: large bed-size (70.7% *vs.* 67.1%), urban location (92.4% *vs.* 87.4%), and teaching status (47.5% *vs.* 45.3%) when compared with no-FHxCAD patients. The prevalence of hypertension, diabetes (both uncomplicated and complicated), congestive heart failure, chronic pulmonary disease, peripheral vascular disease, carotid artery disease, renal failure and history of coronary artery bypass grafting was significantly lower in FHxCAD patients when compared with no-FHxCAD patients (all P<0.001). Furthermore, hyperlipidemia, obesity, alcoholism, smoking, and history of percutaneous coronary intervention were more prevalent in the FHxCAD group than the no-FHxCAD group (all P<0.001) (*Table 1*). FHxCAD group underwent significantly higher invasive coronary interventions such as diagnostic coronary angiography (87.4% *vs.* 68.4%), percutaneous coronary intervention (75.4% *vs.* 55.3%) and coronary artery bypass grafting (9.5% *vs.* 8.3%) on comparison with no-FHxCAD (all P<0.001).

The mortality rate was significantly lower in FHxCAD group (1.4%) *vs.* no FHxCAD group (8.1%) [unadjusted odds ratio (OR): 0.16; 95% confidence interval (CI): 0.15–0.17; P<0.001]. After multivariate adjustment, the difference continued to remain significant (adjusted OR: 0.43, 95% CI: 0.45–0.47; P<0.001) (*Table 2*). Additionally, FHxCAD patients had significantly lower acute cerebrovascular disease and cardiogenic shock events post STEMI presentation. Moreover, they required lower use of intra-aortic balloon pump during the hospital stay (*Table 2*). *Table 3* describes the in-hospital outcomes stratified by age groups for those with FHxCAD and *Table 4* shows the predictors of in-hospital adverse outcomes.

Discussion

In this large sample study with 2,123,492 STEMI patients, even after multivariate adjustment for hospital and admission characteristics, patient demographics and comorbidities, patients with positive FHxCAD

Table 3 Adjusted OR for adverse in-hospital outcomes stratified by age groups for those with FHxCAD

Age group (years)	Clinical outcome	
	In-hospital mortality	Cardiogenic shock
18–40	0.37 (0.19–0.71)	0.42 (0.29–0.63)
41–50	0.47 (0.35–0.63)	0.61 (0.52–0.71)
51–60	0.39 (0.31–0.48)	0.61 (0.54–0.69)
61–70	0.50 (0.41–0.60)	0.61 (0.53–0.70)
71–80	0.47 (0.38–0.58)	0.61 (0.51–0.73)
81–90	0.66 (0.52–0.82)	0.68 (0.51–0.89)
91–100	0.35 (0.16–0.77)	0.56 (0.17–1.81)

The data represent adjusted OR (95% CI). FHxCAD, family history of coronary artery disease; OR, odds ratio; CI, confidence interval.

Table 4 Predictors of adverse in-hospital clinical outcomes

Clinical variable	Clinical outcome	
	In-hospital mortality	Cardiogenic shock
Atrial fibrillation	1.18 (1.15–1.22)	1.47 (1.42–1.52)
Renal failure	1.66 (1.60–1.72)	1.23 (1.18–1.28)
Fluid-electrolyte abnormalities	2.42 (2.35–2.49)	2.67 (2.59–2.75)
Diabetes	1.16 (1.12–1.19)	1.09 (1.05–1.12)
Chronic lung disease	1.11 (1.07–1.15)	1.15 (1.11–1.19)
Congestive heart failure	1.27 (1.12–1.44)	2.90 (2.60–3.25)

The data represent adjusted OR (95% CI). OR, odds ratio; CI, confidence interval.

had significantly lower in-hospital mortality and acute cerebrovascular and cardiogenic shock events post STEMI. To the best of our knowledge, our study is by far the largest nationwide study till date to report the prognostic influence of FHxCAD on post STEMI clinical outcomes.

Prior smaller size investigations have reported similar results with respect to post MI in-hospital and long-term mortality (2-5). Data from a Canadian registry reported FHxCAD to be associated with significant reduction in long term all-cause mortality post MI (hazard ratio: 0.77, 95% CI: 0.73–0.80) (5). Similar results were demonstrated in an Israeli study with protective effect of FHxCAD at 30-day (OR: 0.50, 95% CI: 0.22–0.99) and 1-year mortality (OR: 0.58, 95% CI: 0.42–0.80) post MI (4). In contrast, Kim *et al.* in a large Korean nationwide prospective study compared post MI clinical outcomes in 11,612 acute MI patients and found out that FHxCAD was associated with increased risk of cardiac death and major adverse cardiovascular events (3). While data in US population is limited, a study based on US national registry of MI reported positive effects on short-term survival were also seen in MI patients (OR: 0.71, 95% CI: 0.69–0.73), similar to our study results (2). We observed a stronger relationship between FHxCAD and STEMI clinical outcomes from those reported earlier, which we believe can plausibly be due to differences in sample size, racial distribution, types of MI (NSTEMI and STEMI both *vs.* STEMI only in ours) and use of different types of covariates in regression model. We adjusted extensively from factors ranging from patient demographics to hospital characteristics to clinical comorbidities. Our study is the largest US study till date in which the positive survival impact of FHxCAD on in-hospital mortality persisted even after extensive adjustment for different factors.

The observations from our study can be explained by several potential reasons. Possibly, FHxCAD can positively influence the patients' utilization and compliance of cardiovascular medications. A recent multicenter prospective study based on the APPROACH registry reported FHxCAD patients were more likely to be on cardiovascular medications such as aspirin, beta-blockers, statins, angiotensin converting enzyme inhibitors and angiotensin receptor blockers (5). Also, FHxCAD patients are more likely to be physically active, and consume healthy daily diet consisting of fruits and vegetables (8). In addition, patients with positive family history are more aware of future cardiovascular risk and also present earlier for the management of important modifiable risk factors such as hypertension (9). Furthermore, similar to our findings, higher utilization of life saving coronary interventions such as percutaneous coronary intervention and coronary artery bypass grafting has been reported by other studies in patients with FHxCAD (4,5). Also in our study, FHxCAD patients were likely to present to urban, bigger bed-size hospitals and academic institutions, which might have possibly led to the differences in approach and utilization of medical therapies. Moreover, a higher proportion of no-FHxCAD patients in our study had lower median household income, and were also more likely to be medicare insurers. Both economic and insurance has been previously associated with increased in-hospital mortality post MI due to differences in utilization of standard practice, health-care delivery systems and performance of emergency services (10,11). In addition, lower socioeconomic status has been associated with

independent predictors of mortality such as poorer functional capacity and impaired heart rate recovery (12).

This study has several limitations, majorly due to the use of an administrative database and the retrospective nature of the study. NIS database has limited clinical information and is prone to coding errors or under coding. The prevalence of FHxCAD in our study was lower (7.4%) in comparison to those reported by earlier studies (15–30%) (2,4,5). Additionally, although we adjusted for multiple variables in regression model, the possibility of lack of adjustment for undiscovered confounding variables and treatment details cannot be ignored. The data from NIS database is collected at the level of hospitalization and is not individualized. This makes assessment of reasons behind individual patient specific issues, such as differences in insurance status, economic status and utilization of invasive coronary interventions, not possible. Lastly, post discharge follows up data and exact cause of death is not available.

Conclusions

In summary, FHxCAD was associated with lower risk adjusted in-hospital mortality and adverse clinical outcomes, in our large national unselected cohort of STEMI patients. Further research is warranted to determine whether the superior outcomes in FHxCAD patients with STEMI are related to differences in modifiable factors such as dietary habits, daily lifestyle activities, medications or coronary interventions.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Informed consent is not applicable to this study as it is a retrospective study from a publicly open database.

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