Trends in Utilization and Safety of In-Hospital Coronary Artery Bypass Grafting During a Non-ST-Segment Elevation Myocardial Infarction

Gabby Elbaz-Greener, MD, MHA[a,b,c,d,#,*], Guy Rozen, MD, MHA[a,b,e,#], Fabio Kusniec, MD[a,b], Ibrahim Marai, MD[a,b], Diab Ghanim, MD[a,b], Shemy Carasso, MD[a,b], Yulia Gavrilov, PhD[f], Maneesh Sud, MD[g], Bradley Strauss, MD, PhD[g], Dennis T. Ko, MD, MSc[g,h,i,j], Harindra C. Wijeysundera, MD, PhD[g,h,i,j], David Planer, MD[c,d], and Offer Amir, MD[a,b,c,d]

Up to 10% of non-ST-segment elevation myocardial infarction (NSTEMI) patients require coronary artery bypass graft (CABG) surgery during their hospitalization. Contemporary, real-world, data regarding CABG utilization and safety in NSTEMI patients are lacking. Our objectives were to investigate the contemporary trends in utilization and outcomes of CABG in patients admitted for NSTEMI. Using the 2003 to 2015 National Inpatient Sample data, we identified hospitalizations for NSTEMI, during which a CABG was performed. Patients' sociodemographic and clinical characteristics, incidence of surgical complications, length of stay, and mortality were analyzed. Multivariate analyses were performed to identify predictors of in-hospital complications and mortality. An estimated total of 440,371 CABG surgeries, during a hospitalization for NSTEMI, were analyzed. The utilization of CABG was steady over the years. The data show increasing prevalence of individual co-morbidities as well as cases with Deyo Co-morbidity Index ≥2 (p <0.001). High, 26.4%, complication rate was driven mainly by cardiac and pulmonary complications. The mortality rate declined from 3.6% in 2003 to an average of 2.4% during 2010 to 2015. Older age, female gender, heart failure, and delayed CABG timing were independent predictors of adverse outcomes. In conclusion, utilization of in-hospital CABG as the primary revascularization strategy in patients with NSTEMI remained steady over the years. These data reveal the raising prevalence of co-morbidities during the study. High complication rate was recorded; however, the mortality declined over the years to about 2.4%. Delaying CABG was associated with small but statistically significant worsening in outcomes. **(Am J Cardiol 2020;134:32−40)**

A routine invasive strategy in non-ST-segment elevation myocardial infarction (NSTEMI) has been shown to improve clinical outcomes.[1,2] Furthermore, previous studies have proven that an early intervention is safe and associated with an improved mortality,[3] lower risk of refractory ischemia,[1] and shorter duration of hospital stay[1], compared with a delayed invasive strategy.[1,3] Approximately 5% to 10% of NSTEMI patients undergo CABG during their index hospitalization.[4] Selecting the appropriate timing for CABG in NSTEMI patients must carefully balance ischemic risk, associated with delays, and bleeding risks, related to recent antiplatelets and anticoagulant use.[5] In the absence of randomized data, the ESC/EACTS guidelines recommend that the timing for revascularization in NSTEMI patients, via percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery, should be guided by the individual patient risk stratification to immediate, early and delayed invasive or noninvasive strategies.[5] Contemporary, large-scale, real-world data regarding the utilization, timing, and safety of in-hospital CABG, in patients admitted for NSTEMI, can help us to identify the predictors of adverse outcomes and guide to improved patients' selection as well as the optimal timing for intervention. Using the National Inpatient Sample (NIS) database, our objective was to assess the trends in utilization and safety of in-hospital CABG surgery, identify the predictors of complications and mortality and the real-world relationship between the timing of in-hospital CABG and

[a]Division of Cardiovascular Medicine, Baruch Padeh Medical Center, Poriya, Israel; [b]The Azrieli Faculty of Medicine in the Galilee, Bar-Ilan University, Safed, Israel; [c]Department of Cardiology, Hadassah Medical Center, Jerusalem, Israel; [d]Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel; [e]Cardiology Division, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; [f]Biostatistical Department, TechnoSTAT Ltd, Raanana, Israel; [g]Division of Cardiology, Schulich Heart Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; [h]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; [i]Sunnybrook Research Institute, University of Toronto, Toronto, Ontario, Canada; and [j]Institute for Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada. Manuscript received June 17, 2020; revised manuscript received and accepted August 11, 2020.

Funding: None.

[#]These authors contributed equally to this study and manuscript preparation.See page 39 for disclosure information.

*Corresponding author: Tel: (972) (2)6776564; fax: (972) (2)6411028.
E-mail address: Gabby@hadassah.org.il (G. Elbaz-Greener).

0002-9149/© 2020 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjcard.2020.08.019

in-hospital outcomes, in patients who were admitted with NSTEMI.

Methods

The data were drawn from the NIS, the Healthcare Cost and Utilization Project, and Agency for Healthcare Research and Quality (AHRQ).[6] The NIS datasets include only de-identified data; therefore, this study was deemed exempt from institutional review by the Human Research Committee.

The NIS is the largest collection of all-payer data on inpatient hospitalizations in the United States. The dataset represents an approximate 20% stratified sample of all inpatient discharges from US hospitals.[7] This information includes patient-level and hospital-level factors such as patient demographic characteristics, primary and secondary diagnoses and procedures, AHRQ co-morbidities, length of stay (LOS), hospital region, hospital teaching status, hospital bed size, and cost of hospitalization. National estimates can be calculated using the patient-level and hospital-level sampling weights that are provided by NIS.

For the purpose of this study, we obtained data for the years 2003 to 2015. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) was used for reporting diagnoses and procedures in the NIS database during the study period. Of note, ICD-10-CM coding was introduced in the last quarter of 2015. For this reason, and to avoid any possible cross-coding issues during the translation, we only included the first three quarters of 2015. For each index hospitalization, the database provides a principal discharge diagnosis and a maximum of 14 or 24 additional diagnoses (depending on the year), in addition to a maximum of 15 procedures.

We identified patients 18 years of age or older with a primary diagnosis of NSTEMI based on ICD-9-CM code 410.7×, who underwent in-hospital CABG, based on ICD-9-CM procedure codes 36.1×: 36.10-36.19, 36.2, 36.91, and 36.99. We excluded the patients who had a percutaneous coronary intervention (PCI); ICD-9-CM codes 36.0× (excluding 36.03) in-hospital and before CABG during the index hospitalization. Furthermore, we excluded patients who underwent any concomitant cardiac surgery and/or additional valve surgery (ICD-9 codes 35.0-35.99), leaving NSTEMI patients, undergoing isolated CABG procedure. “Time to CABG” was defined as the time interval from hospital admission to the day of the procedure. LOS was defined as the time interval from hospital admission to hospital discharge.

The following patient demographics were collected from the database: age, gender, and race. Previous co-morbidities were identified by measures from the AHRQ. For the purposes of calculating Deyo-Charlson Co-morbidity Index (Deyo-CCI), additional co-morbidities were identified from the database using ICD-9-CM codes. Deyo-CCI is a modification of the Charlson Co-morbidity Index, containing 17 co-morbidities conditions with differential weights, with a total score ranging from 0 to 33. (Detailed information on Deyo-CCI provided in the Appendix Table 1.) Higher Deyo-CCI scores indicate to greater burden of co-morbid diseases and are associated with mortality 1 year after admission.[8] The index has been used extensively in studies from administrative databases, with proved validity in predicting short- and long-term outcomes.[9,10]

The primary outcome in this study was in-hospital mortality. The secondary outcome of interest consisted of previously reported, known in-hospital CABG-related complications[11,12] including: (1) pericardial complications (defined as tamponade, hemopericardium, pericarditis, and pericardiocentesis); (2) cardiac complications (during or resulting from procedure: defined as cardiac block, myocardial infarction, cardiac arrest, congestive heart failure, and others); (3) pulmonary complications (defined as pneumothorax/hemothorax, diaphragm paralysis, postoperative respiratory failure, and other iatrogenic respiratory complications); (4) hemorrhage/hematoma complications (defined as hemorrhage/hematoma complicating a procedure, acute posthemorrhagic anemia and hemorrhage requiring transfusion); (5) vascular complications (defined as accidental puncture or laceration during a procedure, injury to blood vessels, arteriovenous fistula, injury to retroperitoneum, vascular complication requiring surgical repair, re-open, and other vascular complications); (6) infection (defined as fever, septicemia, and postprocedural aspiration pneumonia); (7) neurological (defined as nervous system complication, unspecified, central nervous system complication, iatrogenic cerebrovascular infarction or hemorrhage cerebrovascular effect, and transient ischemic attack); (8) diaphragmatic paralysis. Detailed information on all ICD-9 CM codes, used to identify in-hospital complications, is summarized in the Appendix Table 2.

The chi-square (χ^2) test and Wilcoxon Rank Sum test were used to compare categorical variables and continuous variables, respectively. The NIS provides discharge sample weights that are calculated within each sampling stratum as the ratio of discharges in the universe to discharges in the sample.[13] Before 2012, a 20% sample of all long-term acute care hospitals in the United States, and 100% of discharges from those hospitals were retained. Beginning in 2012, however, the NIS was redesigned to construct 20% of discharge records from all (100%) hospitals in the sampling frame. These design changes, however, do not limit multiyear analysis. To account for these revisions while performing trend analysis, AHRQ developed new patient-level discharge trend weights for the years before 2012. The new trend weights (called “TRENDWT”) are intended to be used instead of the earlier NIS weights (called “DISCWT”) in years before 2012, while performing a multiyear analysis spanning year 2012. Utilizing the new weights results in improved national estimates, in addition to allowing for multiyear analysis of trends. For calculation of national estimates and correct variances, trend weight files (called ‘TRENDWT”) provided by AHRQ were used to reflect national estimates. We generated a weighted logistic regression model (using “TRENDWT”) to identify independent predictors of in-hospital complications and of in-hospital mortality. Congruent with the Healthcare Cost and Utilization Project NIS design, the hospital identification number was used as a random effect with patient-level factors clustered within hospital-level factors. We retained all predictor variables that were associated with our primary and secondary outcome with $p < 0.05$ in our final multivariable regression model. For all analyses, we used SAS software version 9.4 (SAS Institute Inc., Cary, NC.) A p value <0.05 was considered statistically significant.

Results

Out of 98,754,774 unweighted hospitalizations in the NIS database during the 1/2003 to 9/2015 period, a total of 91,673 hospitalizations were included in the analysis based on the inclusion criteria described above. After implementing the weighting method, these represented an estimated total of 440,371 hospitalizations for NSTEMI, in patients who underwent in-hospital CABG during the index hospitalization. The majority of patients (70.7%) were male and the mean age of the cohort was 65 years. Full demographic and clinical characteristics of the study population are presented in Table 1. About 62.9% of the patients were white, with high prevalence of diabetes mellitus (42.2%) and hypertension (72.1%). The prevalence of chronic obstructive pulmonary disease was 24.6%, chronic renal failure—15.3% and of history of previous myocardial infarction—9.7%.

The data reveal a relatively steady utilization of CABG in NSTEMI patients during the study period (About 34,000 surgeries a year on average). Temporal trends in baseline characteristics between the years 2003 and 2015 are shown in Appendix Table 3. A significant upward trend was observed for the majority of co-morbidities. The severity of co-morbid diseases in the study population, as indicated by Deyo-CCI, showed a steady increase over the study period (Appendix Table 3).

The "time to CABG" (3.6 days in 2003 to 3.7 in 2015, p <0.0001) and the LOS (11.4 days in 2003 to 11.18 days at 2015, p <0.001) did not change much during the study period; however, these small differences were statistically significant due to the large study population (Table 2, Figure 1).

At least 1 periprocedural complication following the CABG surgery occurred in 26.4% of the patients. Patients with 1 or more complication were older, had a higher prevalence of co-morbidities such as congestive heart failure, chronic obstructive pulmonary disease, peripheral vascular disease, and renal failure and had higher Deyo-CCI scores compared with patients without an in-hospital complication (Table 1, Figure 2).

Among the 26.4% of patients with at least 1 in-hospital complication, cardiac complications were the most common (10.1%) followed by pulmonary (9.5%) and infectious complications (4.1%). The rate of at least 1 complication increased in the overall population during the study period from 24.9% at 2003 to 28.4% at 2015 (p <0.001; Table 2, Figure 3). Although cardiac and neurological complications

Table 1
Comparison of baseline characteristics of coronary bypass grafting surgery during a non-ST-segment elevation myocardial infarction between the years 2003 and 2015

	Total	At least one complication	No complications	p value
Coronary bypass grafting surgery, n				
Total number†	91,673	24,151 (26.3%)	67,522 (73.7%)	
Weighted total number‡	440,371 (100.0%)	116,318 (26.4%)	324,053 (73.6%)	
Age (years)				<0.0001
18−44	3.6%	2.5%	4.0%	
45−59	27.7%	22.2%	29.6%	
60−74	45.5%	46.2%	45.2%	
≥75	23.3%	29.0%	21.2%	
Men	70.7%	69.1%	71.3%	<0.0001
White*	62.9%	63.1%	62.9%	<0.0001
Non-white*	16.2%	17.0%	15.9%	
Prior ischemic heart disease	93.5%	88.4%	95.3%	<0.0001
Hypertension	72.1%	67.6%	73.7%	<0.0001
Diabetes mellitus	42.2%	39.6%	43.2%	<0.0001
Chronic obstructive lung disease	24.6%	26.5%	23.9%	<0.0001
Smoker	23.6%	19.1%	25.2%	<0.0001
Obesity	19.2%	17.9%	19.7%	<0.0001
Renal failure	15.3%	18.6%	14.2%	<0.0001
Peripheral vascular disease	13.9%	16.8%	12.9%	<0.0001
Prior myocardial infraction	9.7%	8.6%	10.1%	<0.0001
Prior percutaneous coronary intervention	9.5%	8.0%	10.1%	<0.0001
Prior coronary bypass grafting	1.1%	1.0%	1.1%	0.16
Congestive heart failure	1.0%	2.7%	0.5%	<0.0001
Prior valve surgery	0.4%	0.8%	0.3%	<0.0001
Deyo-Comorbidity index, %				<0.0001
1	27.7%	23.8%	29.1%	
≥2	72.3%	76.2%	70.9%	
Mortality	2.81%	6.33%	1.56%	<0.0001

† Represents the number of observations in the NIS database.
‡ Represents total national estimates after applying sampling weights.
* 20% missing data.

Table 2
Temporal trends in complication rates, mortality, length of stay, and time to coronary bypass grafting surgery between the years 2003and 2015

	Total	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	p value
Coronary bypass grafting surgery weighted total, n	440,371	34,555	34,325	31,503	35,231	31,549	32,994	35,158	31,878	31,471	36,035	37,040	38,235	30,395	
Complications															
≥1 Complication	26.4%	24.9%	24.5%	23.9%	24.2%	25.6%	26.2%	27.3%	24.2%	25.9%	29.8%	28.4%	29.0%	28.4%	<0.001
Cardiac	10.1%	11.7%	11.2%	10.2%	10.3%	10.5%	11.1%	10.9%	10.0%	8.7%	8.9%	8.9%	9.5%	9.9%	<0.001
Pulmonary	9.5%	6.8%	6.3%	7.3%	7.5%	7.2%	7.9%	8.2%	6.5%	8.9%	14.8%	14.0%	14.0%	13.0%	<0.001
Infection	4.1%	2.3%	2.9%	2.7%	2.6%	3.2%	3.6%	4.9%	4.5%	5.0%	5.4%	5.1%	5.3%	5.1%	<0.001
Vascular	2.7%	2.7%	2.3%	2.5%	2.7%	2.9%	3.1%	2.7%	2.1%	3.1%	2.6%	2.6%	2.5%	2.7%	NS
Re-Open	2.4%	2.7%	2.2%	2.6%	2.5%	3.0%	2.7%	2.8%	2.7%	2.2%	1.9%	2.1%	2.0%	1.9%	<0.001
Hemorrhage	2.2%	1.8%	2.2%	1.9%	2.4%	3.1%	2.2%	2.6%	2.1%	2.1%	2.3%	2.0%	1.7%	1.8%	<0.001
Neurological	1.5%	2.2%	1.6%	1.7%	1.4%	1.6%	1.6%	1.9%	1.3%	1.4%	1.4%	1.0%	1.2%	1.1%	<0.001
Pericardial	0.8%	0.7%	0.8%	0.8%	0.8%	0.8%	1.0%	1.1%	0.8%	0.9%	0.75	0.9%	0.8%	0.8%	NS
Diaphragmatic Paralysis	0.1%	0.1%	0.1%	0.0%	0.0%	0.0%	0.1%	0.1%	0.0%	0.1%	0.15	0.1%	0.1%	0.1%	NS
Mortality	2.8%	3.6%	3.6%	3.3%	3.0%	3.1%	2.9%	2.8%	2.2%	2.4%	2.4%	2.3%	2.3%	2.7%	<0.001
Length of stay (days), mean ± SEM	11.44±0.05	11.4±0.17	11.92±0.17	11.61±0.15	11.46±0.15	11.81±0.15	11.54±0.16	11.46±0.16	11.04±0.16	11.36±0.16	11.47±0.10	11.24±0.09	11.26±0.09	11.18±0.10	<0.001
Time to CABG (days), mean ± SEM	3.63±0.03	3.57±0.1	3.67±0.09	3.44±0.09	3.5±0.08	3.64±0.08	3.62±0.08	3.63±0.08	3.65±0.08	3.63±0.07	3.73±0.05	3.67±0.05	3.69±O.04	3.7+0.05	<0.0001

decreased over the study period (p <0.001), they were offset by increasing trends in the rates of pulmonary and infectious complications (p <0.001). An upward trend for hemorrhagic complications was observed until 2009, decreasing thereafter. No uniform trend was observed for other in-hospital complications such as vascular or pericardial complications (Table 2).

The rate of in-hospital mortality during the study period was 2.8%. The in-hospital mortality rate decreased from 2003 to 2010 (3.6% to 2.2%) and plateaued from 2010 to 2015 (average of 2.4%; Figure 4, Table 2).

In unadjusted analysis, we found that older age, female gender, chronic obstructive pulmonary disease, renal failure, peripheral vascular disease, congestive heart failure, and increasing Deyo-CCI score were all associated with increased in-hospital complications and mortality (p <0.001). In addition, "time to CABG" in NSTEMI patients increased the odds of in-hospital complications (odds ratio 1.02, 95% confidence interval: 1.01 to 1.03) and in-hospital mortality (odds ratio 1.03, 95% confidence interval: 1.03 to 1.04; Appendix Table 4). The multivariate regression model analysis, adjusted for potential confounders is presented in Table 3. Various individual co-morbidities as well as Deyo CCI and "time to CABG" remained independent predictor of both in-hospital complications and in-hospital mortality. Interestingly, some known co-morbidities, including diabetes mellitus, essential hypertension and obesity were shown to have protective effect from the adverse outcomes, including in a multivariate analysis (p <0.001). After adjusting for potential confounders, "time to CABG" remained independent predictor of both in-hospital complications and in-hospital mortality (Table 3).

Discussion

Utilizing data from the NIS, the largest all-payer inpatient database in the United States, we identified a weighted total of 440,371 patients, who underwent CABG during their hospitalization for NSTEMI. The data show a relatively steady utilization of CABG in NSTEMI patients during the study period (2003 to 2015). That trend is consistent with previous studies that demonstrated modest increases in utilization of in-hospital CABG in NSTEMI patients during the early 1990s, remaining relatively stable thereafter.[14]

Our study reveals the raising prevalence of co-morbidities in NSTEMI patients that required an in-hospital CABG surgery over the years. Albeit the high complication rate of 26.4%, mortality rate declined over the years to about 2.4%. Older age, female gender, congestive heart failure, and delayed CABG timing were independent predictors of adverse outcomes.

We noted a 26.4% complications rate during the study period, with an increasing trend for in-hospital perioperative complications in our study population over the years. The high incidence of periprocedural complications was driven by a 10.1% cardiac and 9.2% pulmonary complications rate, in our study population, higher than previously reported. The in-hospital complications rate reported in the literature for patients who underwent CABG was usually lower than in our report.[15,16] Brown et al reported at least 1 complication in 13.6% of 114,233 Medicare beneficiaries,

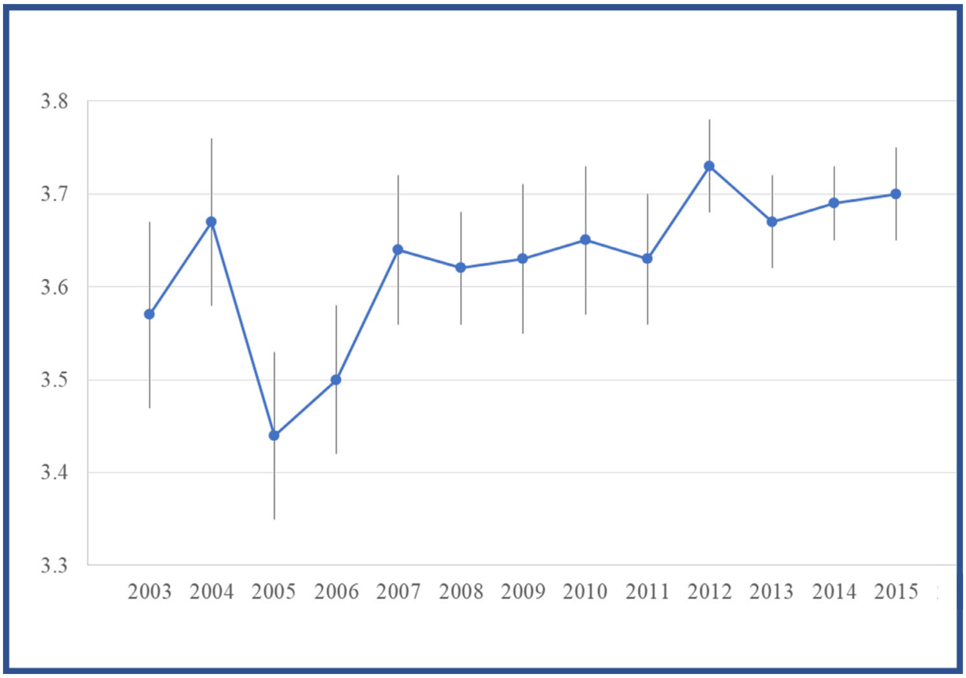

Figure 1. Time to CABG mean ± SEM between the years 2003 and 2015.

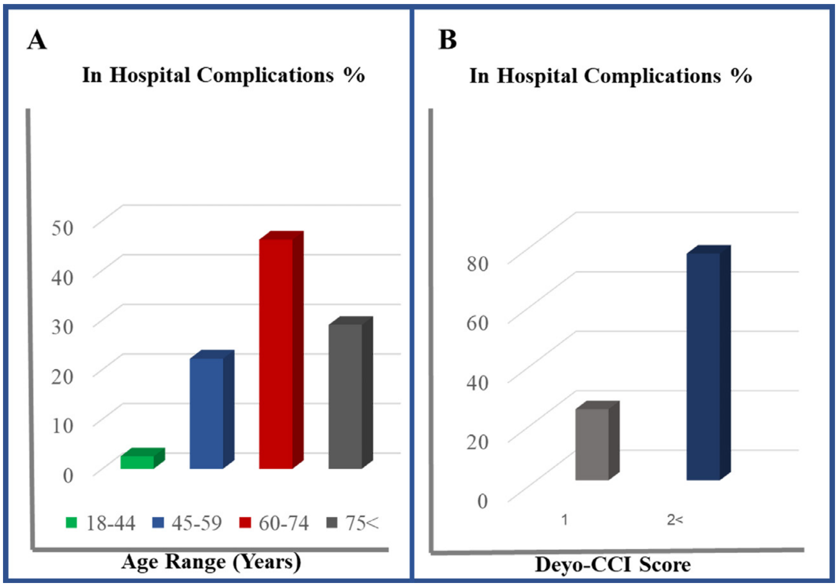

Figure 2. (A) Overall in-hospital complications by age group. (B) Overall in-hospital complication by Deyo-CCI score.

who underwent CABG in 2005 in the United States, but only 21.9% of these patients had a CABG surgery during an acute MI hospitalization.[15] Given that the outcomes of patients who underwent CABG in the setting of an acute MI are known to be less favorable,[17] higher rate of complications was expected in our study. In a more recent cross-sectional analysis of 500 patients who underwent CABG, Safaie et al reported complications rate of 21.4%, much closer to the rates shown in our study.[16] Another possible explanation for the higher complications rate in the more recent and in this study lies in the raising prevalence of patients' co-morbidities over the years. Our data show a significant increase in the prevalence of individual co-morbidities as well as cases with Deyo Co-morbidity Index ≥ 2 (65.8% in 2003, vs 77.6% in 2015) in the study population over the years that could have contributed to the high complications rate reported.

Complications are known to be an independently associated with increased periprocedural CABG mortality.[11,18–21] Interestingly, despite the higher CABG complications along with higher co-morbidities of our patients, the mortality rate was 2.8%, declining from 3.6% in 2003 to an average of 2.4% during 2010 to 2015. The observed downtrend of the mortality in our study is consistent with other

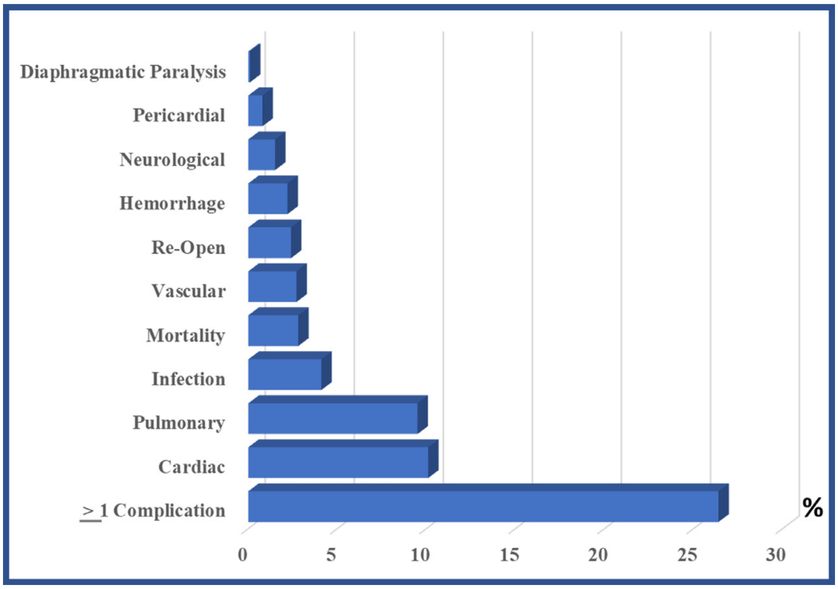

Figure 3. Types and frequencies of complication following CABG post-NSTEMI.

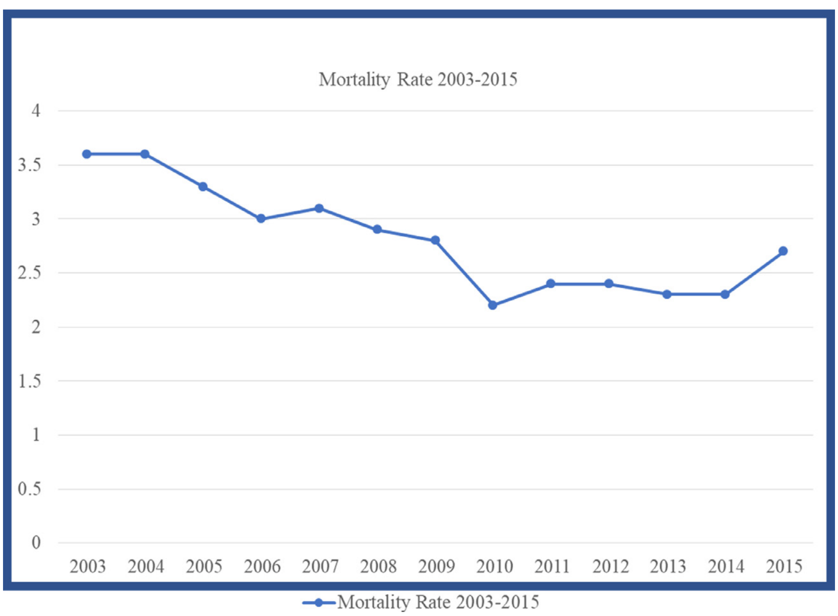

Figure 4. Mortality rate (%) during the years 2003 to 2015.

reports.[11,22] Improvements in anesthesia and surgical techniques for myocardial and brain preservation as well as better imaging and handling of the postoperative complications[23,24] have likely prevented at least some of the potential periprocedural CABG patients' mortality causes.

Furthermore, we found that delaying CABG in the index NTEMI admission was associated with small but statistically significant worsening in both periprocedural complications and mortality in this study. To our knowledge, this is the largest published cohort of NSTEMI patients that was treated in the contemporary era of aggressive pharmacological and interventional approach, in which the relationship between timing of CABG and in-hospital outcomes was analyzed. While current guidelines recommend delaying CABG in acute ST-segment elevation myocardial infarction patients for a few days or until patients are "stabilized" after their presentation,[5,25] no time reference is mentioned for NSTEMI patients due to scarcity of data.[2,5]

There are only few small studies which specifically assessed the timing of CABG surgery in NSTEMI patients with conflicting results. Some reported no differences in mortality, when comparing early versus late in-hospital CABG following NSTEMI,[26,27] whereas others have demonstrated higher mortality related to early timing of the surgery.[28,29] The data from our large, nationwide, real-world

Table 3
Multivariate analysis for predictors of In-hospital complications and in-hospital mortality, 2003 to 2015

	In-hospital complications		In-hospital mortality	
Predictors	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age, (years)		<0.001		<0.001
18-44	1.00 (reference)	N/A	1.00 (reference)	N/A
45-59	1.18 (1.13-1.23)	<0.001	0.85 (0.73-0.98)	<0.001
60-74	1.57 (1.51-1.64)	<0.001	1.63 (1.42-1.88)	<0.001
≥75	2.12 (2.03-2.22)	<0.001	3.65 (3.18-4.19)	<0.001
Deyo-Comorbidity index		<0.001		<0.001
1	1.00 (reference)	N/A	1.00 (reference)	N/A
≥2	1.24 (1.22-1.26)	<0.001	2.17 (2.06-2.28)	<0.001
Gender		<0.001		<0.001
Men	1.00 (reference)	N/A	1.00 (reference)	N/A
Female	1.03 (1.02-1.05)	<0.001	1.33 (1.28-1.38)	<0.001
Chronic obstructive lung disease		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	1.09 (1.07-1.11)	<0.001	0.96 (0.92-1.00)	<0.001
Congestive heart failure		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	5.03 (4.72-5.35)	<0.001	6.49 (6.01-7.02)	<0.001
Diabetes mellitus		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	0.72 (0.71-0.74)	<0.001	0.60 (0.58-0.63)	<0.001
Hypertension		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	0.69 (0.68-0.70)	<0.001	0.52 (0.50-0.54)	<0.001
Obesity		<.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	0.91 (0.89,0.92)	<0.001	0.75 (0.71-0.79)	<0.001
Peripheral vascular disease		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	1.23 (1.21-1.26)	<0.001	1.37 (1.31-1.44)	<0.001
Renal failure		<0.001		<0.001
No	1.00 (reference)	N/A	1.00 (reference)	N/A
Yes	1.20 (1.18-1.22)	<0.001	1.90 (1.82-1.99)	<0.001
Time to coronary artery bypass grafting (days)	1.01 (1.00-1.01)	<0.001	1.01 (1.01-1.02)	<0.001

cohort of NSTEMI patients who underwent in-hospital surgical revascularization, showed a minimal, yet statistically significant increase in complications rate and mortality with delayed CABG timing, after controlling confounders such as patients' sociodemographic and clinical characteristics.

Our study should be interpreted in the contexts of several limitations. First, the NIS database is a retrospective administrative database that contains discharge-level records and as such is susceptible to codding error and reporting may not be consistent across different institutions. Second, the NIS does not include detailed clinical information, and wherefore cannot rule out residual confounding of the association we observed. In addition, the NIS precluded using follow-up beyond the same index hospitalization. These limitations are counterbalanced by the real world, nationwide nature of the data, as well as mitigation of reporting bias introduced by selective publication of results from specialized centers.

In conclusion, the utilization of CABG as the primary revascularization strategy in patients with NSTEMI remained steady over the years. Our study reveals the raising prevalence of co-morbidities NSTEMI patients that required an in-hospital CABG surgery. High complication rate was recorded; however, the mortality declined over the years to an average of 2.4% between 2010 and 2015. Delaying CABG was associated with small but statistically significant worsening in outcomes in this study.

Author Contribution

Gabby Elbaz-Greener—study design, data interpretation, drafting the manuscript; Guy Rozen—conceptualization, drafting the manuscript; Fabio Kusniec—data analysis, data interpretation; Ibrahim Marai—data analysis, data interpretation; Diab Ghanim—critical revision of the manuscript; Shemy Carasso—critical revision of the manuscript, supervision, Yulia Gavrilov—methodology, data interpretation; Maneesh Sud—data interpretation, drafting the manuscript; Bradley Strauss—critical revision of the manuscript; Dennis T. Ko—critical revision of the manuscript; Harindra C. Wijeysundera—study design, critical revision of the manuscript; David Planer—critical revision of the manuscript; Offer Amir—critical revision of the manuscript, supervision.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The corresponding author affirms that he has listed everyone who contributed significantly to the work. The corresponding author had access to all the study data, took responsibility for the accuracy of the analysis, and had authority over manuscript preparation and the decision to submit the manuscript for publication. The corresponding author confirms that all authors read and approve the manuscript.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.08.019.

1. Katritsis DG, Siontis GC, Kastrati A, van't Hof AW, Neumann FJ, Siontis KC, Ioannidis JP. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. *Eur Heart J* 2011;32:32–40.
2. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S, Group ESCSD. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016;37:267–315.
3. Jobs A, Mehta SR, Montalescot G, Vicaut E, Van't Hof AWJ, Badings EA, Neumann FJ, Kastrati A, Sciahbasi A, Reuter PG, Lapostolle F, Milosevic A, Stankovic G, Milasinovic D, Vonthein R, Desch S, Thiele H. Optimal timing of an invasive strategy in patients with non-ST-elevation acute coronary syndrome: a meta-analysis of randomised trials. *Lancet* 2017;390:737–746.
4. Ranasinghe I, Alprandi-Costa B, Chow V, Elliott JM, Waites J, Counsell JT, Lopez-Sendon J, Avezum A, Goodman SG, Granger CB, Brieger D. Risk stratification in the setting of non-ST elevation acute coronary syndromes 1999−2007. *Am J Cardiol* 2011;108:617–624.
5. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO, Group ESCSD. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2019;40:87–165.
6. HCUP National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP), 2019. 2012-2013. Agency for Healthcare Research and Quality R, MD. Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed 27 May, 2020.
7. Steiner C, Elixhauser A, Schnaier J. The healthcare cost and utilization project: an overview. *Eff Clin Pract* 2002;5:143–151.
8. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613–619.
9. Chu YT, Ng YY, Wu SC. Comparison of different comorbidity measures for use with administrative data in predicting short- and long-term mortality. *BMC Health Serv Res* 2010;10:140–147.
10. Radovanovic D, Seifert B, Urban P, Eberli FR, Rickli H, Bertel O, Puhan MA, Erne P, Investigators AP. Validity of Charlson Comorbidity Index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS Plus registry 2002-2012. *Heart* 2014;100:288–294.
11. Moazzami K, Dolmatova E, Maher J, Gerula C, Sambol J, Klapholz M, Waller AH. In-hospital outcomes and complications of coronary artery bypass grafting in the United States between 2008 and 2012. *J Cardiothorac Vasc Anesth* 2017;31:19–25.
12. Reston JT, Tregear SJ, Turkelson CM. Meta-analysis of short-term and mid-term outcomes following off-pump coronary artery bypass grafting. *Ann Thorac Surg* 2003;76:1510–1515.
13. Hosseini SM, Moazzami K, Rozen G, Vaid J, Saleh A, Heist KE, Vangel M, Ruskin JN. Utilization and in-hospital complications of cardiac resynchronization therapy: trends in the United States from 2003 to 2013. *Eur Heart J* 2017;38:2122–2128.
14. Masoudi FA, Ponirakis A, Yeh RW, Maddox TM, Beachy J, Casale PN, Curtis JP, De Lemos J, Fonarow G, Heidenreich P, Koutras C, Kremers M, Messenger J, Moussa I, Oetgen WJ, Roe MT, Rosenfield K, Shields TP Jr., Spertus JA, Wei J, White C, Young CH, Rumsfeld JS. Cardiovascular care facts: a report from the national cardiovascular data registry: 2011. *J Am Coll Cardiol* 2013;62:1931–1947.
15. Brown PP, Kugelmass AD, Cohen DJ, Reynolds MR, Culler SD, Dee AD, Simon AW. The frequency and cost of complications associated with coronary artery bypass grafting surgery: results from the United States Medicare program. *Ann Thorac Surg* 2008;85:1980–1986.
16. Safaie N, Montazerghaem H, Jodati A, Maghamipour N. In-hospital complications of coronary artery bypass graft surgery in patients older Than 70 years. *J Cardiovasc Thorac Res* 2015;7:60–62.
17. Alkhouli M, Alqahtani F, Kalra A, Gafoor S, Alhajji M, Alreshidan M, Holmes DR, Lerman A. Trends in characteristics and outcomes of patients undergoing coronary revascularization in the United States, 2003−2016. *JAMA Netw Open* 2020;3:e1921326.
18. Hogue CW Jr., Sundt T 3rd, Barzilai B, Schecthman KB, Davila-Roman VG. Cardiac and neurologic complications identify risks for mortality for both men and women undergoing coronary artery bypass graft surgery. *Anesthesiology* 2001;95:1074–1078.
19. Hogue CW Jr., Murphy SF, Schechtman KB, Davila-Roman VG. Risk factors for early or delayed stroke after cardiac surgery. *Circulation* 1999;100:642–647.
20. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. *J Thorac Cardiovasc Surg* 1992;104:1510–1517.
21. Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R, Aggarwal A, Marschall K, Graham SH, Ley C. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. *N Engl J Med* 1996;335: 1857–1863.
22. Culler SD, Kugelmass AD, Brown PP, Reynolds MR, Simon AW. Trends in coronary revascularization procedures among Medicare beneficiaries between 2008 and 2012. *Circulation* 2015;131:362–370.
23. Grogan K, Stearns J, Hogue CW. Brain protection in cardiac surgery. *Anesthesiol Clin* 2008;26:521–538.
24. Savage EB, Cohn LH. 'No touch' dissection, antegrade-retrograde blood cardioplegia, and single aortic cross-clamp significantly reduce operative mortality of reoperative CABG. *Circulation* 1994;90:140–143.
25. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimsky P, Group ESCSD. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:119–177.
26. Davierwala PM, Verevkin A, Leontyev S, Misfeld M, Borger MA, Mohr FW. Does timing of coronary artery bypass surgery affect early and long-term outcomes in patients with non-ST-segment-elevation myocardial infarction? *Circulation* 2015;132:731–740.
27. Nichols EL, McCullough JN, Ross CS, Kramer RS, Westbrook BM, Klemperer JD, Leavitt BJ, Brown JR, Olmstead E, Hernandez F, Sardella GL, Frumiento C, Malenka D, DiScipio A, Northern New England Cardiovascular Disease Study G. Optimal timing from

myocardial infarction to coronary artery bypass grafting on hospital mortality. *Ann Thorac Surg* 2017;103:162–171.
28. Lee DC, Oz MC, Weinberg AD, Lin SX, Ting W. Optimal timing of revascularization: transmural versus nontransmural acute myocardial infarction. *Ann Thorac Surg* 2001;71:1197–1202.
29. Paparella D, Scrascia G, Paramythiotis A, Guida P, Magari V, Malvindi PG, Favale S, de Luca Tupputi Schinosa L. Preoperative cardiac troponin I to assess midterm risks of coronary bypass grafting operations in patients with recent myocardial infarction. *Ann Thorac Surg* 2010;89:696–702.