Admissions Rate and Timing of Revascularization in the United States in Patients With Non-ST-Elevation Myocardial Infarction

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Clinical trials have shown improved outcomes with an early invasive approach for non-ST-elevation myocardial infarction (NSTEMI). However, real-world data on clinical characteristics and outcomes based on time to revascularization are lacking. We aimed to analyze NSTEMI rates, revascularization timing, and mortality using the 2016 Nationwide Readmissions Database. We identify patients who underwent diagnostic angiography and subsequently received either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Finally, revascularization timing and mortality rates (in-hospital and 30-day) were extracted. Our analysis included 748,463 weighted NSTEMI hospitalizations in 2016. Of these hospitalizations, 50.3% (376,695) involved diagnostic angiography, with 34.1% (255,199) revascularized. Of revascularized patients, 77.6% (197,945) underwent PCI and 22.4% (57,254) underwent CABG. Patients with more comorbidities tended to have more delayed revascularization. PCI was most commonly performed on the day of admission (32.9%; 65,155). This differs from CABG, which was most commonly performed on day 3 after admission (13.7%; 7,823). The in-hospital mortality rate increased after day 1 for PCI patients and after day 4 for CABG patients, whereas 30-day in-hospital mortality for both populations increased as revascularization was delayed. Our study shows that patients undergoing early revascularization differ from those undergoing later revascularization. Mortality is generally high with delayed revascularization, as these are sicker patients. Randomized clinical trials are needed to evaluate whether very early revascularization (<90 minutes) is associated with improved long-term outcomes in high-risk patients. **(Am J Cardiol 2020;134:24−31)**

The presentation of non-ST-elevation myocardial infarction (NSTEMI) commonly involves vessel thrombosis but not always total vessel occlusion, thus accounting for the heterogeneity of presentation.[1] The incidence of NSTEMI is estimated to be twice that of ST-elevation myocardial infarction (STEMI).[2,3] Nonetheless, the current standard of care for NSTEMI patients is largely uniform, with the most consistent approach being hospitalization and coronary angiography within the next several days, with the timing guided by validated risk scores.[4,5] Clinical trials in NSTEMI have shown improved outcomes with an early invasive approach.[6,7] However, meta-analyses have shown conflicting outcomes with early revascularization.[8−10] These trials have not established criteria or time after NSTEMI presentation for early revascularization such as with STEMI (<90 minutes). Also, real-world data on mortality rates based on time to revascularization are limited. This study aimed to evaluate the overall real-world incidence of NSTEMI, time to revascularization, in-hospital and 30-day in-hospital mortality on the basis of time to revascularization using the 2016 Nationwide Readmissions Database (NRD).

Methods

The study cohort was obtained from the NRD, which is part of a family of databases and software tools developed for the 2016 Healthcare Cost and Utilization Projects, sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NRD is one of the largest publicly available all-payer inpatient-care databases in the United States, representing 49.3% of total US hospitalizations. The NRD includes de-identified patient-level public discharge data from 22 states on approximately 18 million unweighted discharges per year. The NRD may be used to evaluate the roughly 36 million annual discharges in the United States, with data elements including hospital characteristics, patient demographics, chronic co-morbidities, procedures, primary and secondary discharge diagnoses, payment source, and total costs overall.[11] The details regarding the NRD data are available online (https://www.hcup-us.ahrq.gov/).

The 2016 NRD uses the International Classification of Diseases, Tenth Revision (ICD-10) coding system. Using this database, we identified all hospitalizations with the ICD-10 code representing NSTEMI as the primary discharge diagnosis. Given the nature of NRD reporting,

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all NSTEMI types, except for periprocedural NSTEMIs, were included on the basis of ICD-10 codes. Patients admitted in December were excluded, as it was not possible to assess these patients' 30-day readmissions. In addition, we excluded any invalid or inconsistent data as outlined by AHRQ in 2016.

NSTEMI patients who underwent diagnostic coronary angiography and those who received PCI or CABG were identified using the associated ICD-10 procedure code. Then we calculated the time to revascularization on the basis of the difference between the date of admission and the date of procedure, identifying this as same day (day 0), day 1, day 2, and up through the maximum observed of day 10. Finally, we calculated in-hospital and 30-day in-hospital mortality on the basis of the day of revascularization. Given that these groups are inherently different in multiple aspects, we reported crude percentages without comparisons for all mortality results. The 30-day in-hospital mortality rate was calculated using the ratio of patients who died in the hospital during 30-day readmission after the index procedure compared with the total number of 30-day readmissions.

In order to obtain a national estimate, we applied a weighted adjustment with variance to the total number of patients observed in the NRD. This statistical technique allows for correction for the discrepancies between the observed sample in the NRD and the national estimate.[12] We report weighted estimates in the manuscript to represent nationwide trends.

We converted ICD-10 codes using clinical classification software tools provided by AHRQ. Patient demographic characteristics and hospital characteristics such as bed size and teaching status were also retrieved from the NRD. SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was used for statistical analyses.

Results

In 2016, there were 748,463 weighted hospitalizations for NSTEMI in the United States, of which 50.3% (376,695) involved diagnostic angiography. Of these patients, 67.7% (255,199) were revascularized, with PCI accounting for 77.6% (197,945) of revascularizations and CABG 22.4% (57,254) (Figure 1).

Baseline characteristics for the weighted NSTEMI patient cohort are described in Table 1. Patients who did not receive an angiogram were older and sicker with an overall higher prevalence of co-morbidities, including heart failure, hypertension with complications, chronic kidney disease, chronic obstructive pulmonary disease, cerebrovascular disease, and neoplastic disorders. Patients not undergoing angiography were also more likely to have Medicare insurance and had a higher 30-day readmission rate. They were less likely to have hypertension or hyperlipidemia than patients who received coronary angiography.

Among patients undergoing coronary angiography, the procedure occurred on the same day as admission (day 0) in 27.8% (104,754) of patients, on day 1 in 30.3% (114,324), on day 2 in 13.8% (51,889), on day 3 in 7.8% (29,335), and on day 4 or later in 20.1% (Figure 2). Of all patients undergoing PCI, revascularization was performed in 32.9% (65,155) on day 0, 31.6% (62,467) on day 1, 13.0% (25,677) on day

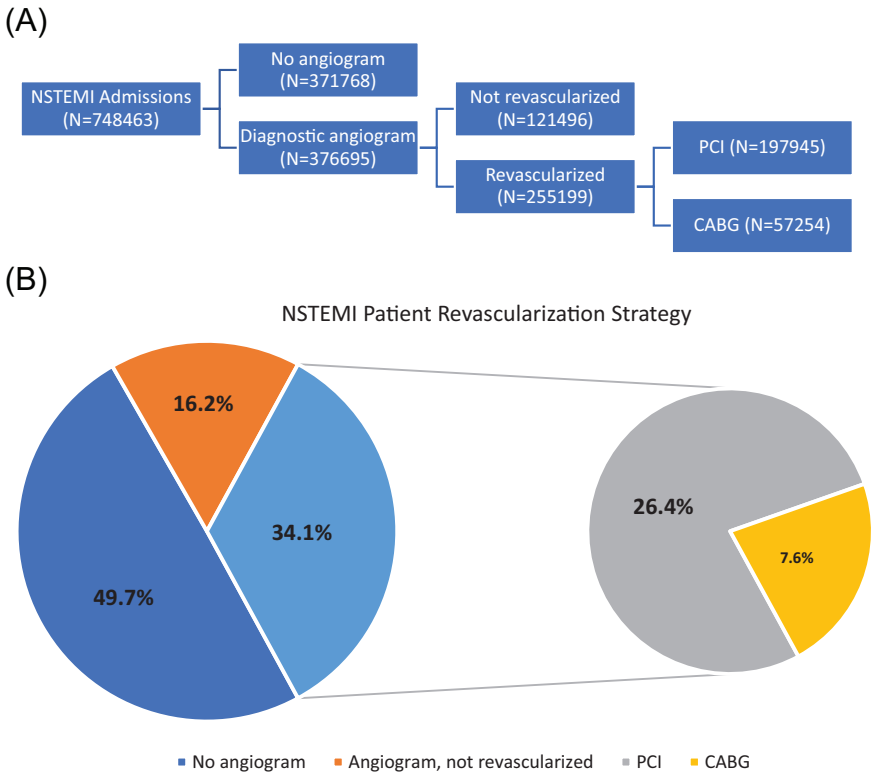


Figure 1. (A) In-hospital management of NSTEMI patients. (B) NSTEMI patient revascularization strategy.

2, and then gradually decreasing through day 10. In contrast, only 7.0% (3,985) of patients who underwent CABG were revascularized on day 0. The rate of CABG revascularization gradually increased with each hospital day, reaching a maximum on day 3, with 13.7% (7,823) of CABG procedures, before gradually decreasing through day 10. Findings of timing of revascularization from NSTEMI admission are depicted in Figure 3. Baseline characteristics for PCI patients based on day of revascularization are described in Table 2, and baseline characteristics for CABG patients based on day of revascularization are described in Table 3. Overall, the prevalence of comorbidities increased in the PCI group as revascularization was delayed. However, the prevalence of comorbidities did not differ in the CABG group on the basis of time to revascularization. Acuteness, as might be assessed by the Global Registry of Acute Coronary Events (GRACE) score, was not available.[13]

The 30-day readmission rate was highest for patients who were admitted for an NSTEMI and did not receive a coronary angiography (17.3%). In contrast, the readmission rate was lower for those who received a coronary angiography without intervention (15.6%) and even lower for those who received revascularization (PCI 11.6% and CABG 12.7%) (Table 1). The 30-day readmission rate for PCI was the lowest when it was performed on day 0 (9.0%) and increased for every day that it was delayed (Table 2). The 30-day readmission rate for CABG was higher on day 0 (10.8%) and if the CABG was delayed. CABG 30-day readmission rates were the lowest when it was performed on day 2 (9.6%) and increased for every day following day 2 (Table 3).

For PCI patients, the crude in-hospital mortality rate initially decreased from 2.1% on day 0 to a minimum of 1.5% on day 1 before steadily increasing to a maximum of 6.6% on day 10 (Figure 4). For CABG patients, in-hospital mortality was 3.2% on day 0 and decreased to a minimum 2.2% on day 4, before steadily increasing to a maximum of 5.0% on day 10 (Figure 4).

For PCI, adjusted 30-day in-hospital mortality for revascularization on day 0 was 3.5%, and that rate continued to increase on the basis of time to revascularization before peaking at 9.7% on day 6, then decreased through day 10 (Figure 4). In contrast, for CABG (Figure 4), crude 30-day in-hospital mortality for day 0 was 3.2%, but that rate decreased on day 1 (2.6%) and day 2 (2.6%), with an upward trend after day 3.

Discussion

We found that half of the NSTEMI hospitalizations in 2016 involved diagnostic angiography, with 34% revascularized. In the PCI group, most patients underwent revascularization on the day of admission or the next day, while revascularization in the CABG group was delayed, peaking at day 3. In-hospital mortality rates were highest for same-day PCI and trended downward on subsequent days but again increased if PCI was delayed beyond day 3. However, 30-day in-hospital mortality during readmission after PCI continued to increase as the revascularization was delayed. In the CABG group, the highest in-hospital mortality was

Table 1
Baseline characteristics of NSTEMI patients (n = 748,463)

Variable	No Angiogram (N=371,768)	Angiogram (N=376,695)		
		No Revascularization (N=121,496)	PCI (N=197,945)	CABG (N=57,254)
Mean age (years)	73.8 ± 13.7	67.0 ± 13.1	66.1 ± 12.5	66.0 ± 10.7
Men	52.0%	53.5%	65.3%	72.2%
Comorbidities				
Cardiac arrythmia	41.4%	32.4%	24.3%	43.1%
Conduction disorder	16.5%	14.6%	12.1%	11.6%
Heart failure	52.5%	43.5%	29.7%	39.3%
Hypertension	39.9%	52.3%	58.3%	60.9%
Hypertension with complications	42.4%	33.2%	27.1%	31.0%
Hyperlipidemia	51.6%	63.4%	72.7%	77.0%
Diabetes Mellitus	42.2%	42.0%	42.5%	50.9%
Chronic Kidney Disease	59.1%	38.4%	30.2%	39.3%
Chronic Obstructive Pulmonary Disease	26.3%	23.0%	16.9%	20.7%
Asthma	6.1%	7.6%	5.9%	5.8%
Cerebrovascular disease	12.5%	7.6%	5.6%	12.2%
Peripheral vascular disease	16.9%	18.2%	16.1%	18.8%
Coagulopathy	12.7%	6.9%	4.7%	23.2%
Anemia	40.4%	24.9%	19.0%	63.3%
Neoplastic disorder	11.4%	5.9%	4.1%	4.3%
Other characteristics				
Medicare/Medicaid	84.9%	73.0%	66.3%	66.0%
Hospital Bed size - Medium	29.4%	28.4%	28.5%	24.9%
Hospital Bed size - Large	55.3%	61.5%	62.2%	67.9%
Teaching Hospital	78.2%	76.2%	76.4%	81.0%
Weekend admission	26.4%	26.3%	25.8%	23.8%
30-Day Readmission Rate	17.3%	15.6%	11.6%	12.7%

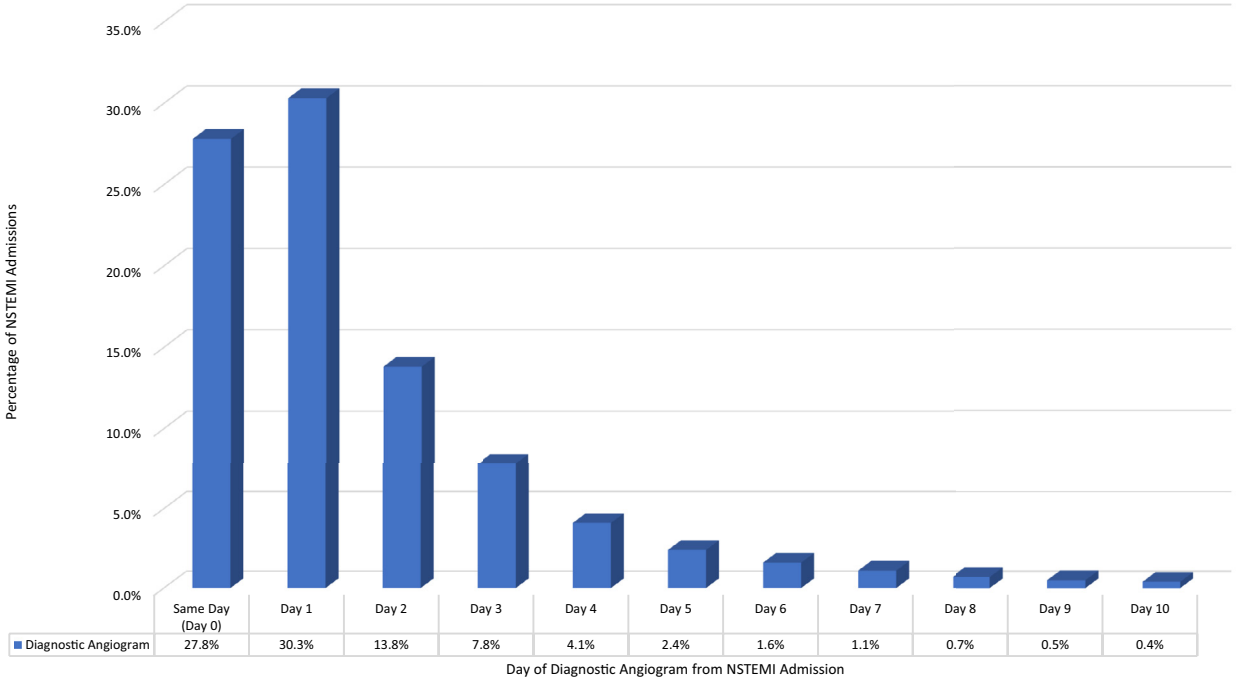


Figure 2. Timing of diagnostic angiogram based on NSTEMI admission date.

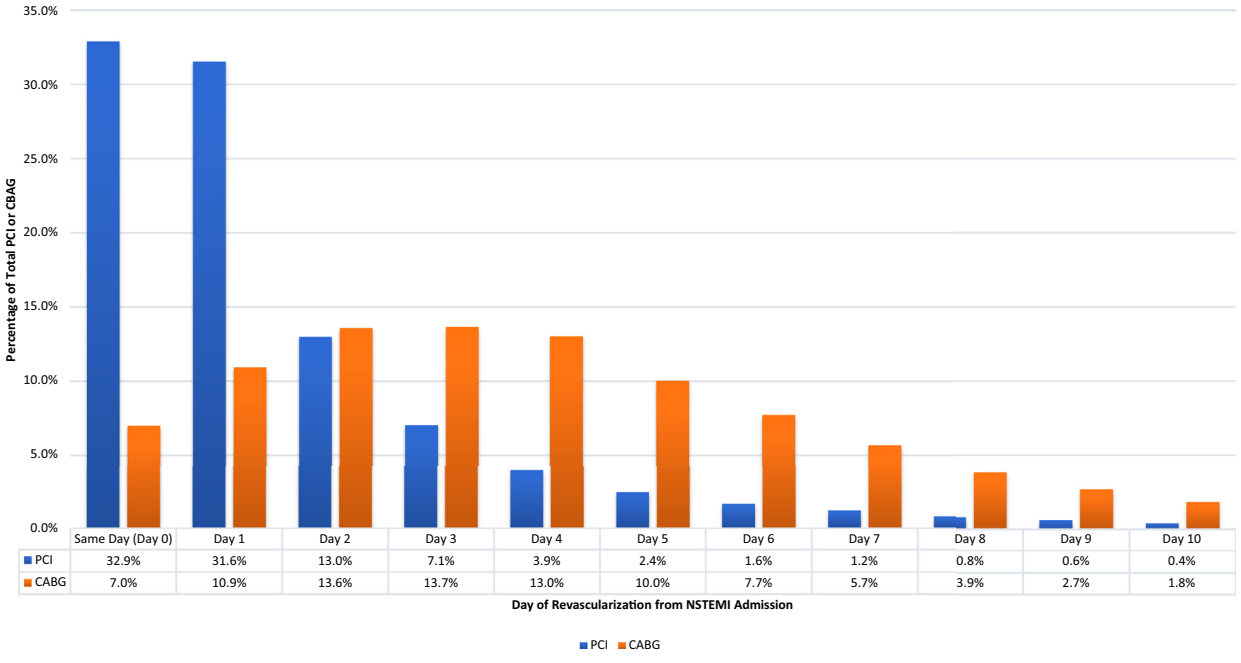


Figure 3. Timing of revascularization based on NSTEMI admission date.

in the group that underwent emergent, day-of-admission surgery.

The incidence of NSTEMI continues to increase in the United States.[3] Although the treatment of STEMI with prompt reperfusion is an established strategy, treatment of NSTEMI is guided by the patient's clinical condition and risk factors but with uncertainty as to the best timing for an invasive strategy. The most consistent approach remains to hospitalize the patients, initiate medical therapy, and then perform an invasive strategy within several days, on the basis of clinical presentation.[4,5] Clinical trials have shown benefit with an early invasive approach,[6,7,14] and guidelines[15] have recommended an early revascularization strategy within 24 hours of admission for high-risk subgroups. Consistent with the guidelines, the majority of patients in this real-world analysis were revascularized within 1 day of hospitalization

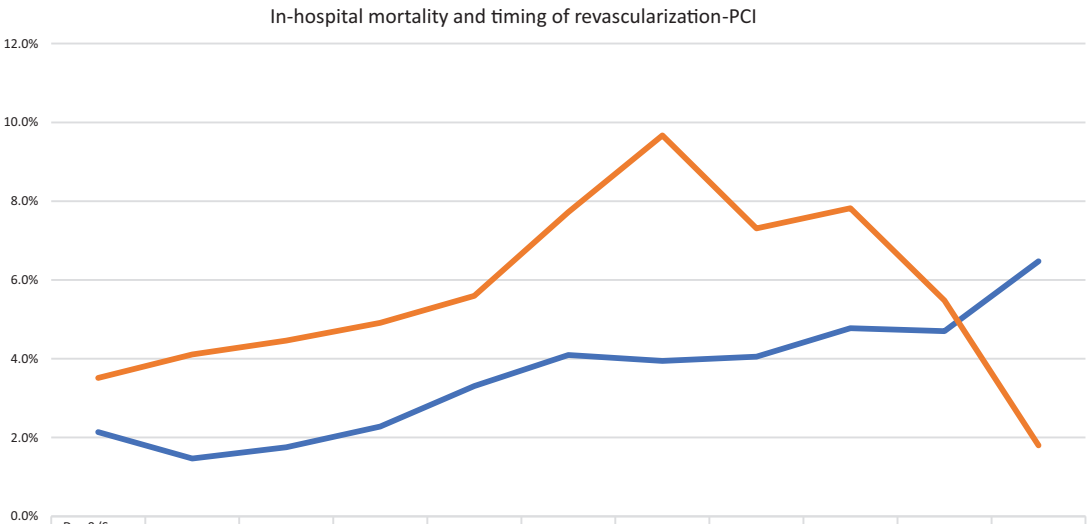
Table 2
Baseline characteristics of PCI patients based on day of revascularization (n = 197,945)

Variable	Days from Admission					
	0 (N=65,155)	1 (N=62,467)	2 (N=25,677)	3 (N=13,950)	4 (N=7,675)	5-10 (N=13,999)
Mean age (years)	64.2 ± 12.5	65.2 ± 12.4	67.4 ± 12.4	68.6 ± 12.4	70.0 ± 12	71.0 ± 11.4
Men	68.5%	66.6%	63.1%	60.2%	58.2%	58.0%
Comorbidities						
Cardiac arrythmia	19.8%	20.0%	26.1%	30.3%	35.1%	40.8%
Conduction disorder	10.5%	11.1%	13.1%	14.4%	14.9%	16.1%
Heart failure	19.6%	22.6%	33.8%	42.0%	51.0%	64.2%
Hypertension	62.4%	61.7%	57.1%	53.9%	49.2%	41.6%
Hypertension with complications	18.2%	22.4%	31.9%	37.5%	44.1%	53.1%
Hyperlipidemia	72.0%	73.8%	74.3%	73.0%	71.7%	68.9%
Diabetes Mellitus	36.4%	39.8%	46.1%	50.4%	55.0%	57.7%
Chronic Kidney Disease	19.9%	24.3%	34.5%	41.6%	50.1%	62.3%
Chronic Obstructive Pulmonary Disease	12.7%	14.5%	18.8%	22.4%	25.6%	29.5%
Asthma	5.1%	5.8%	6.2%	6.8%	7.4%	7.1%
Cerebrovascular disease	3.7%	4.4%	6.2%	7.9%	8.9%	11.8%
Peripheral vascular disease	11.9%	13.7%	17.7%	20.6%	25.6%	28.3%
Coagulopathy	3.4%	3.4%	4.9%	6.1%	7.8%	10.1%
Anemia	12.1%	13.7%	20.6%	26.4%	34.4%	45.3%
Neoplastic disorder	3.0%	3.4%	4.6%	4.7%	6.8%	8.2%
Other characteristics						
Medicare/Medicaid	59.2%	62.5%	70.9%	75.0%	80.1%	83.6%
Hospital Bed size - Medium	30.2%	28.6%	28.1%	28.2%	28.1%	24.1%
Hospital Bed size - Large	59.5%	61.8%	63.2%	63.6%	64.6%	69.3%
Teaching Hospital	77.1%	76.0%	75.8%	76.2%	76.8%	78.9%
Weekend admission	18.2%	24.5%	48.0%	29.1%	27.4%	21.8%
30-Day Readmission Rate	9.0%	9.4%	12.5%	14.6%	17.1%	22.0%

Table 3
Baseline characteristics of CABG patients based on day of revascularization (n = 57,254)

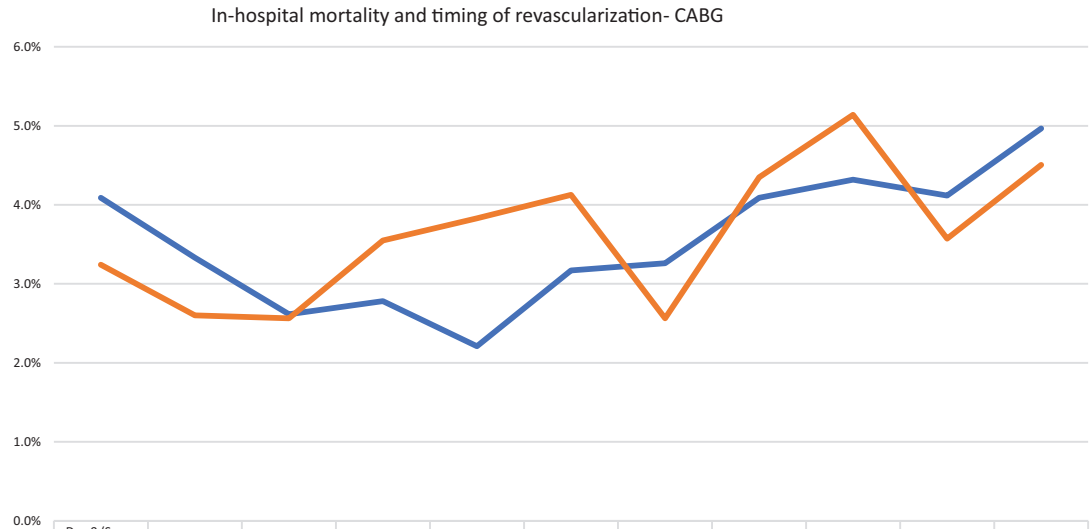
Variable	Days from Admission					
	0 (N=3,985)	1 (N=6,257)	2 (N=7,778)	3 (N=7,823)	4 (N=7,463)	5-10 (N=18,218)
Mean age (years)	65.3 ± 11	65.6 ± 10.5	65.6 ± 10.7	65.4 ± 10.7	65.8 ± 10.8	66.2 ± 10.6
Men	74.2%	73.6%	74.5%	75.3%	72.5%	69.7%
Comorbidities						
Cardiac arrythmia	41.3%	40.9%	39.7%	39.6%	40.4%	45.7%
Conduction disorder	9.0%	9.8%	10.9%	11.2%	11.5%	12.9%
Heart failure	31.9%	26.8%	28.6%	32.7%	34.7%	48.0%
Hypertension	61.8%	65.5%	67.2%	64.9%	65.4%	56.4%
Hypertension with complications	23.1%	21.1%	22.9%	26.4%	27.5%	38.6%
Hyperlipidemia	71.4%	75.4%	78.3%	78.8%	79.9%	77.2%
Diabetes Mellitus	43.1%	41.7%	47.4%	50.2%	50.9%	55.3%
Chronic Kidney Disease	32.0%	28.7%	29.6%	33.4%	34.4%	47.3%
Chronic Obstructive Pulmonary Disease	18.5%	17.0%	17.9%	18.9%	19.0%	23.9%
Asthma	6.0%	5.3%	5.6%	5.5%	5.5%	6.0%
Cerebrovascular disease	9.0%	8.1%	9.7%	11.0%	11.4%	14.7%
Peripheral vascular disease	18.2%	14.5%	15.5%	16.3%	17.1%	22.1%
Coagulopathy	24.8%	23.2%	22.2%	22.8%	21.2%	23.0%
Anemia	60.2%	57.8%	57.6%	61.3%	60.4%	66.9%
Neoplastic disorder	2.7%	2.7%	3.2%	3.0%	3.8%	5.3%
Other characteristics						
Medicare/Medicaid	63.4%	60.3%	61.1%	63.9%	64.1%	70.2%
Hospital Bed size - Medium	24.3%	25.8%	26.6%	26.0%	25.3%	23.7%
Hospital Bed size - Large	66.4%	66.3%	66.3%	66.9%	68.3%	70.3%
Teaching Hospital	82.8%	79.2%	80.7%	79.8%	79.5%	82.8%
Weekend admission	9.9%	16.6%	26.6%	28.9%	29.9%	23.3%
30-Day Readmission Rate	10.8%	10.7%	9.6%	11.7%	11.9%	14.6%

(A)



	Day 0 (Same Day)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
In-hospital mortality	2.1%	1.5%	1.8%	2.3%	3.3%	4.1%	3.9%	4.1%	4.8%	4.7%	6.5%
30-day in-hospital mortality	3.5%	4.1%	4.5%	4.9%	5.6%	7.7%	9.7%	7.3%	7.8%	5.5%	1.8%

(B)



	Day 0 (Same Day)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
In-hospital mortality	4.1%	3.3%	2.6%	2.8%	2.2%	3.2%	3.3%	4.1%	4.3%	4.1%	5.0%
30-day in-hospital mortality	3.2%	2.6%	2.6%	3.5%	3.8%	4.1%	2.6%	4.3%	5.1%	3.6%	4.5%

Figure 4. (A) In-hospital and 30-day in-hospital mortality rate based on timing of PCI revascularization from admission date. (B) In-hospital and 30-day in-hospital mortality rate based on timing of CABG revascularization from admissions date.

(54.0%), with mortality initially decreasing on days 1 and 2 before steadily increasing with longer delay. Similar findings were reported in a recent large, real-world PCI registry by Iantorno et al.[16]

The VERDICT trial[17] showed that very early revascularization (median 4 hours after randomization) improved outcomes in comparison with standard strategy (<24 hours) in the subgroup of patients with high risk scores. In addition, more recent data from the EARLY trial (ClinicalTrials.gov NCT02750579)[18] demonstrated that at 30 days, cardiovascular death or recurrent ischemia was drastically lower with an early invasive strategy (<2 hours) than with a delayed invasive strategy (12 to 72 hours). However, this was driven mostly by recurrent ischemia, and there was no difference in cardiovascular death or MI specifically between the 2 groups. To date, there are no randomized trials specifically in high-risk NSTEMI patients evaluating whether a very early strategy of <90 minutes from presentation to revascularization, as employed with STEMI, would be beneficial in the NSTEMI population.

Although the pathophysiological processes of STEMI and NSTEMI are different, with the artery more likely to be partially patent in NSTEMI, ensuring minimal myocardial blood flow, this flow might not be sufficient to prevent necrosis. Furthermore, arteries supplying the lateral or posterior wall of the left ventricle may be totally occluded but without ST-elevation on the electrocardiogram.

We found higher rates of baseline comorbidities in the group in which revascularization was delayed. Prior studies have shown racial, age, and gender bias by clinicians in performing revascularization in patients with acute myocardial infarction.[3,19] The study by Iantorno et al[16] and an analysis from the ACTION registry[20] also showed higher baseline comorbidities in the delayed PCI group. These patients would probably have higher risk scores and would have benefitted from early revascularization. It was also noted in our analysis that if revascularization was delayed beyond a certain point (day 1 for PCI patients and day 4 for CABG patients), crude in-hospital mortality rates increased. The significant selection bias concerning time to intervention precludes using observational data to determine the time for initiating an invasive strategy. Thus, there is a need for a randomized trial.

Our study has limitations. We used the NRD, which is an administrative database derived from ICD-10 billing codes and relies on the physician to properly code for all admissions. Furthermore, NRD cannot be used to calculate patients' risks scores or if noninvasive ischemic evaluation was performed before angiography. Thus, we are unable to fully risk-stratify the patients on the basis of presentation. In addition, ICD-10 billing does not distinguish between Type I and Type II NSTEMI, so there is some variability in the patients' presentations. Second, the NRD dataset includes non-PCI/CABG-capable hospitals; however, we were unable to fully capture the timing of these patients being transferred to a PCI/CABG-capable facility. However, the delay of primary revascularization due to being transferred to another hospital reflects real-world experience. Third, a propensity-matched analysis cannot be performed in this cohort because there are likely to be multiple unmeasured confounding variables that cannot be accounted for. Similarly, a multivariable analysis cannot be performed using time to revascularization as an independent variable, as the groups were different in multiple aspects. The study hypothesis was to report descriptive data of clinical characteristics and outcomes based on time to revascularization. Only a randomized clinical trial with appropriate distribution of patients in the study and control arms can derive a causal attribution. Fourth, the NRD is limited to a follow-up window of 30 days, so we are unable to report on long-term follow-up. And finally, 30-day in-hospital mortality outcomes in our analysis include patients who died during a readmission. This outcome does not include all deaths within the 30-day period. Nevertheless, these real-world clinical data provide up-to-date trends of crude in-hospital and 30-day in-hospital mortality on the basis of time to revascularization in this large, national population and are hypothesis-generating, indicating a need for a randomized clinical trial.

In conclusion, NSTEMI occurs more often than STEMI. Variables describing patient populations and, almost certainly, acuteness of presentation will vary by day after presentation when revascularization is performed. Thus, mortality varied, with in-hospital mortality increasing after day 1 for PCI patients and after day 4 for CABG patients, whereas 30-day in-hospital mortality increased as revascularization was delayed. Indeed, patients with more comorbidities tended to be revascularized later, despite evidence from clinical trials supporting early revascularization in high-risk populations. In this analysis, confounding variables, some of them unmeasurable, prevent causal attribution of the influence of delay on mortality. Randomized clinical trials are urgently needed to evaluate whether high-risk NSTEMI patients treated similarly to STEMI patients, with prompt reperfusion, would have better outcomes.

Authors' Contribution

Brian C. Case, MD: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing original draft and review & editing. **Charan T. Yerasi, MD:**Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing original draft and review & editing. **Yanying Wang, PhD:** Data curation; Formal analysis; Methodology. **Brian J. Forrestal, MBBS:**Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing original draft and review & editing. **Joshua Hahm, MS:**Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing review & editing. **Sarahfaye Doman, MPH:** Data curation; Formal analysis; Methodology; Supervision; Project administration. **William S. Weintraub, MD:**Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing – review & editing. **Ron Waksman, MD:**Conceptualization; Methodology; Project administration; Supervision; Validation; Visualization; Writing – review & editing.

Disclosure

Conflicts of interest: Ron Waksman—Advisory Board: Amgen, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Consultant: Amgen, Biotronik, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Grant Support: AstraZeneca, Biotronik, Boston Scientific, Chiesi; Speakers Bureau: AstraZeneca, Chiesi; Investor: MedAlliance. William S. Weintraub—Consultant and grants: Amarin; Advisory board: AstraZeneca; Consultant: scPharmaceuticals.

*All other authors:*None to report.

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