

# Contemporary prevalence, trends, and outcomes of coronary chronic total occlusions in acute myocardial infarction with cardiogenic shock

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## ABSTRACT

**Background:** There are limited data on the prevalence and outcomes of chronic total occlusions (CTO) of the coronary artery in acute myocardial infarction with cardiogenic shock (AMI-CS) patients.

**Methods:** Using the National Inpatient Sample, all admissions with AMI-CS that underwent diagnostic angiography between January 1, 2008, and December 31, 2014, were included. CTO, percutaneous coronary intervention (PCI), comorbidities and concomitant cardiac arrest was identified for all admissions. Outcomes of interest included temporal trends, in-hospital mortality, and resource utilization in cohorts with and without CTO.

**Results:** In this 7-year period, 163,628 admissions with AMI-CS admissions met the inclusion criteria, with 68% being ST-elevation AMI-CS. CTO was noted in 27,343 (16.7%) admissions, with an increase in prevalence during the study period. The cohort with CTOs was more likely to be male and bearing private insurance. The CTO cohort had higher cardiovascular comorbidity, higher rates of cardiac arrest and higher use of PCI and mechanical circulatory support. The presence of a CTO was independently associated with higher in-hospital mortality (adjusted odds ratio 1.20 [95% confidence interval 1.16–1.23];  $p < 0.001$ ). The cohort with CTO had lower resource utilization (hospital stay and hospitalization costs) but was discharged more frequently to other hospitals. The presence of a CTO was associated with higher in-hospital mortality in the sub-groups of ST-elevation AMI-CS (31.5% vs. 28.7%;  $p < 0.001$ ) and non-ST-elevation AMI-CS (24.8% vs. 23.2%;  $p < 0.001$ ).

**Conclusions:** In this cohort of AMI-CS admissions that underwent diagnostic angiography, the presence of a CTO identified a higher risk cohort that had higher in-hospital mortality.

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## 1. Introduction

Acute myocardial infarction with cardiogenic shock (AMI-CS) continues to be associated with high mortality and morbidity in the contemporary era despite early percutaneous coronary intervention (PCI) [1–8]. In patients with AMI-CS, diagnostic angiography frequently reveals multivessel disease, nearly a quarter of which are chronic total occlusions (CTO) [9]. Though PCI of the culprit artery in ST-elevation myocardial infarction (STEMI) CS is recommended by both United States and European guidelines [9–12], the role of multi-vessel PCI in this population is less certain. In a recent trial, however, Thiele et al. noted no clinical benefit to complete revascularization over culprit-only revascularization in AMI-CS [9]. This has led to the European guidelines recommending against multi-vessel PCI in this setting [9,10]. Multivessel PCI might result in decrease in myocardial ischemia and salvage of greater myocardium, however this needs to be balanced against

the high contrast load. Furthermore, specifically for CTO-PCI, in addition to the high contrast load, the effort and radiation associated with revascularization, use of multiple approaches and need for multiple access sites, may not translate into an overall clinical benefit in AMI-CS [13]. Though multivessel PCI in AMI-CS has been studied previously in large national databases [14], there are limited data on the prevalence and outcomes of CTOs in AMI-CS in the contemporary era [15,16].

We sought to use a nationally-representative database to assess the presentation and outcomes of patients with CTO in AMI-CS. Given the increasingly acuity of illness and higher comorbidity burden associated with AMI-CS in the contemporary era [5], we hypothesized that there has been a steady increase in CTOs in this population.

## 2. Methods

The Healthcare Cost and Utilization Project - Nationwide/National Inpatient Sample (HCUP-NIS) is the largest all-payer database of hospitalized inpatients in the United States, containing discharge data from 20% non-federal hospitals. A retrospective cohort of admissions with a primary diagnosis of AMI (International Classification of Diseases 9 Clinical Modification [ICD-9CM] 410.x) with a secondary diagnosis of CS (ICD-9CM 785.51) that underwent diagnostic coronary angiography

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was identified between January 1, 2008, and December 31, 2014. Consistent with prior literature, presence of a coronary CTO was identified by ICD-9CM 414.2 [16]. Patient and hospital characteristics, comorbidities, and procedures were identified using previously validated methodologies (Supplementary Table 1) [1–3,5,17]. The primary outcome was the contemporary prevalence and temporal trends of CTO in admissions with AMI-CS. Secondary outcomes included the comorbidity profile, in-hospital mortality, hospitalization costs and length of stay associated with CTOs. Though the Agency for Healthcare Research and Quality has released the HCUP-NIS data till 2016, due to the change in coding practices from ICD-9CM to ICD-10CM in October 2015 we sought to restrict the data to 2014. The HCUP-NIS from 2015 and 2016 databases lack the Clinical Classification System for ICD-9CM codes used in the study. Furthermore, the ICD-10-CM codes lack extensive validation studies unlike the ICD-9CM codes and therefore need further evaluation prior to incorporation into temporal analyses [18,19].

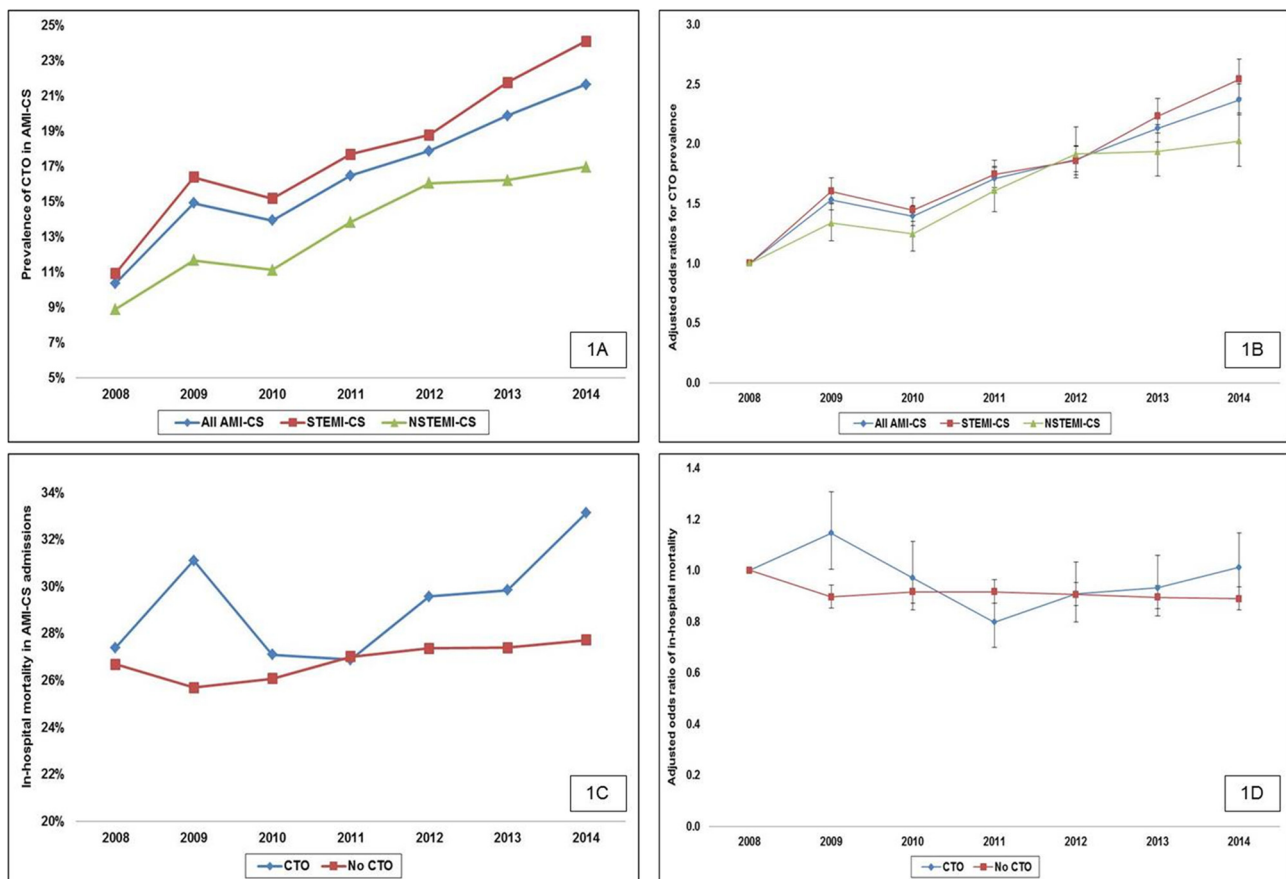
### 2.1. Statistical analysis

As recommended by HCUP-NIS, survey procedures using discharge weights provided with HCUP-NIS database were used to generate national estimates. Using the trend weights provided by the HCUP-NIS, samples from 2008 to 2011 were re-weighted to adjust for the 2012 HCUP-NIS re-design [20]. In 2012, the HCUP-NIS was re-designed to sample 20% of the national patient-level sample as compared to 2000–2011 wherein it sampled 100% of the discharges from 20% of the hospitals [20]. Using trend weights available on the HCUP-NIS

database, samples from 2000 to 2011 were retroactively re-weighted. The new sampling strategy is expected to result in more precise estimates than the previous HCUP-NIS design by reducing sampling error [21]. This methodology has been used by multiple prior studies spanning across year 2012 from the HCUP-NIS [1–5]. Odds ratio with 95% confidence interval was used to represent univariable and multivariable comparisons. Adjusted temporal trends were calculated using multivariable hierarchical logistic regression analysis incorporating age, sex, race, admission year, primary payer status, socio-economic stratum, hospital characteristics, Charlson Comorbidity Index, acute organ dysfunction, PCI, invasive hemodynamic monitoring, mechanical circulatory support and hemodialysis (referent year 2008). For the multivariate modeling, multivariable hierarchical logistic regression analysis with purposeful selection of statistically ( $p < 0.20$  by univariate analysis) and clinically relevant variables was conducted. A priori defined subgroup analysis was performed in the cohorts with STEMI and non-ST-elevation myocardial infarction (NSTEMI). Two-tailed  $p < 0.05$  was considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM Corp, Armonk NY).

### 3. Results

During this seven-year period, there were an estimated 163,628 admissions for AMI-CS that underwent diagnostic angiography, with 68% STEMIs and 32% NSTEMIs. Presence of a coronary CTO was noted in 27,343 (16.7%) admissions, with a higher prevalence in STEMI-CS (18%) vs. NSTEMI-CS (12.9%). The 7-year trends of unadjusted and



**Fig. 1.** Prevalence and in-hospital mortality with chronic total occlusions in AMI-CS. Legend: 1A: unadjusted temporal trends in the prevalence of CTO in all AMI-CS, STEMI-CS and NSTEMI-CS; 1B: adjusted temporal trends of CTO in all AMI-CS, STEMI-CS and NSTEMI-CS (referent year 2008)\*; 1C: unadjusted temporal trends in the in-hospital mortality in cohorts with and without CTO in AMI-CS; 1D: adjusted temporal trends of in-hospital mortality in cohorts with and without CTO in AMI-CS (referent year 2008)^; all  $p < 0.001$  for trend. \*Adjusted for age, sex, race, weekend admission, primary payer, socio-economic status, hospital location and teaching status, hospital region, hospital bedsize, comorbidity. ^Adjusted for age, sex, race, weekend admission, primary payer, socio-economic status, hospital location and teaching status, hospital region, hospital bedsize, comorbidity, acute organ failure, cardiac arrest, percutaneous coronary intervention, invasive hemodynamic monitoring, mechanical circulatory support, invasive mechanical ventilation, hemodialysis.

adjusted prevalence of CTO showed an increase during the study period (Fig. 1A and B). The baseline characteristics between the cohort with and without CTOs are presented in Table 1. The CTO cohort was more likely to be male, bearing private insurance (27.9% vs. 26.3%;  $p < 0.001$ ), but with comparable mean age. The cohort with CTO had greater cardiovascular comorbidities (hypertension, diabetes, hyperlipidemia, heart failure, smoking and peripheral arterial disease) than the cohort without CTOs (Table 1). The cohort with CTO had greater prevalence of cardiac arrest (23.6% vs. 21.2%) and higher use of PCI (74.8% vs. 68.2%) and mechanical circulatory support (61.5% vs. 58.4%) as compared to those without CTO ( $p < 0.001$ ). Acute kidney injury rates were similar in the cohorts with and without CTO (39.6% vs. 39.8%;  $p = 0.24$ ), however hemodialysis was used less often in the CTO cohort (3.7% vs. 4.2%;  $p < 0.001$ ).

Unadjusted in-hospital mortality was higher in the CTO cohort (29.7% vs. 26.9%; odds ratio 1.15 [95% confidence interval 1.12–1.19];  $p < 0.001$ ). The 7-year trends of unadjusted and adjusted in-hospital mortality are presented in Fig. 1C and D. The cohort with CTO had

shorter hospital length of stay ( $9.1 \pm 8.6$  vs.  $10.3 \pm 10.4$ ), lesser hospitalization costs ( $166,338 \pm 155,435$  vs.  $174,166 \pm 171,172$ ) and were transferred more frequently to other hospitals (9.9% vs. 9.4%); all  $p < 0.001$ . In a multivariable hierarchical logistic regression analysis, the presence of a CTO was independently associated with higher in-hospital mortality (odds ratio 1.20 [95% confidence interval 1.16–1.23];  $p < 0.001$ ) (Supplementary Table 2). In a priori sub-group analysis, presence of a CTO was associated with higher in-hospital mortality in the STEMI-CS (31.5% vs. 28.7%;  $p < 0.001$ ) and NSTEMI-CS (24.8% vs. 23.2%;  $p < 0.001$ ) cohorts.

#### 4. Discussion

In this nationally-representative study, CTOs were noted in nearly 17% of AMI-CS patients with a serial increase in prevalence during the study period. Admissions with STEMI had a higher prevalence of CTOs compared to NSTEMIs. The cohort with CTOs had higher severity of illness and greater use of PCI and mechanical circulatory support. The presence of a CTO was associated with higher unadjusted and adjusted in-hospital mortality, but lower resource utilization, which was consistent across sub-groups of STEMI and NSTEMI.

In this study, nearly 17% of all diagnostic angiograms in AMI-CS noted CTOs in one or more vessels, which is consistent with contemporary literature that notes CTOs in 20–29% patients with AMI-CS [15,22]. Though there are established data on the prevalence of CTOs in STEMI-CS [15,22], there are limited data in patients presenting with NSTEMI-CS. In this study we note that the cohort with STEMI had higher prevalence of CTOs compared to NSTEMI. There was a serial increase in the incidence of CTOs between 2008 and 2014. Though higher patient comorbidity and presence of significant cardiac risk factors are potential contributors, it is possible that this increase may be reflective of increased awareness and recognition. It is possible that this higher prevalence is due to improvements in coding and billing practices. The higher preponderance of male sex and risk factors of hypertension, hyperlipidemia, peripheral arterial disease and smoking in this study are comparable to the sub-study on CTOs from the Intra-aortic Balloon Pump in Cardiogenic Shock II trial [15]. These findings suggest that CTO in this patient population may be a marker of advanced comorbidities and atherosclerotic burden.

Consistent with prior literature, this study demonstrated CTOs to be associated with worse prognosis in the overall AMI cohort and in the individual STEMI and NSTEMI cohorts [15,22]. This may be hypothesized to be due to lower collateral blood flow and potentially higher myocardium at risk in CS. Furthermore, these patients are at a higher risk of ventricular arrhythmias and lower post-PCI left ventricular ejection fraction suggestive of a higher burden of cardiac morbidity during long-term follow-up [15,22]. Despite the known mortality and morbidity implications of a CTO, prior studies, including the CULPRIT-SHOCK (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock) trial have not shown a mortality benefit from CTO-PCI [9]. The lower rates of angiography and PCI in this study are consistent with prior real-world literature that reflects reluctance to perform angiography in higher risk cohorts despite robust guideline recommendations [12,23,24]. Angiography and PCI may frequently be deferred in patients with NSTEMI to evaluate for organ recovery or neurological function [25]. Further research in AMI-CS PCI, need careful delineation regarding immediate vs. staged PCI and approach to CTO-PCI in a staged manner, since the duration of this study was prior to the CULPRIT-SHOCK trial. Lastly, though the CTO cohort had shorter hospital stays and lower hospitalizations costs, they had higher rates of transfer. This is likely reflective of contemporary referral practice and highlights the need to develop centers of excellence for management of AMI-CS that present with complex coronary anatomy [6,26]. Since the HCUP-NIS does not follow patients across admissions, we are unable to ascertain this hypothesis. Further dedicated studies are needed to understand the resource utilization and inter-hospital transfers associated with complex

**Table 1**

Baseline and hospital characteristics of CTO admissions with AMI-CS.

Baseline characteristics		CTO (N = 27,343)	No CTO (N = 136,285)	p
AMI type	ST-elevation AMI	73.3	67.0	<0.001
	Non-ST elevation AMI	26.7	33.0	
Age (years)		66.3 ± 12.4	66.7 ± 12.6	<0.001
Female sex		30.4	35.7	<0.001
Race	White	67.9	67.5	0.13
	Non-White <sup>a</sup>	32.1	32.5	
Primary payer	Medicare	53.0	55.7	<0.001
	Medicaid	7.9	7.8	
	Others	39.1	36.5	
Quartile of median household income for zip code	0–25th	27.3	28.3	<0.001
	26th–50th	26.9	27.0	
	51st–75th	24.4	24.5	
Charlson Comorbidity Index	75th–100th	21.4	20.2	0.001
	0–3	28.8	27.9	
	4–6	49.3	50.5	
Comorbidities	≥7	21.9	21.6	
	Hypertension	63.9	60.0	<0.001
	Diabetes mellitus	5.3	4.8	<0.001
	Hyperlipidemia	50.0	46.7	<0.001
	Smoking	38.0	33.5	<0.001
	Alcohol	4.4	4.2	0.11
	Peripheral arterial disease	12.9	12.4	0.02
	Heart failure	53.4	52.7	0.03
	Cancer	7.5	7.6	0.62
	Chronic kidney disease	18.9	17.7	<0.001
	Liver disease	0.4	0.5	0.001
	Chronic pulmonary disease	21.3	21.0	0.21
	Stroke/transient ischemic attack	6.8	7.0	0.29
	Hemiplegia	1.3	1.3	0.71
	Connective tissue disease	7.7	7.7	0.93
Hospital teaching status and location	Rural	5.2	5.3	0.32
	Urban non-teaching	38.0	38.4	
	Urban teaching	56.8	56.3	
Hospital bed-size	Small	7.7	7.2	<0.001
	Medium	24.4	20.9	
	Large	67.9	71.9	
Hospital region	Northeast	13.1	16.2	<0.001
	Midwest	24.3	23.8	
	South	38.6	38.7	
	West	24.0	21.2	

Legend: represented as percentage or mean ± standard deviation; abbreviations: AMI: acute myocardial infarction; CS: cardiogenic shock; CTO: chronic total occlusion.

<sup>a</sup> Black, Hispanic, Asian or Pacific Islander, Native American, Others.

AMI-CS including those with CTO. Lastly, there is a crucial need to develop multi-disciplinary teams to care for complex AMI-CS patients including but not limited to optimal timing of CTO-PCI, use of appropriate mechanical circulatory support and timing of cardiac and non-cardiac organ support [5–7,27–30].

This study has several limitations, some of which are inherent to the analysis of a large administrative database. The HCUP-NIS attempts to mitigate potential errors by using internal and external quality control measures. In this database, there is no reliable way to discern if coronary revascularization was performed in the CTO or non-CTO artery during the same or a subsequent encounter. Furthermore, we are unable to discern the timing, success and complications associated with CTO PCI vs. non-CTO vessel PCI. The ICD-9CM codes for AMI and CS have been previously validated that reduces the inherent errors in the study [3,5]. However, given the moderate sensitivity of the administrative code for CS, it is possible that less severe AMI-CS admissions were missed. Importantly, though the current research methodology has been used previously to evaluate CTO admissions in the NIS dataset, a validation study on this particular ICD-9CM code is lacking [16]. It is possible that greater awareness and recognition of CTOs may have resulted in ‘upcoding’ that could have influenced the temporal trends. However, the overall frequency of CTOs in this study is consistent with prior data, making this less likely [15,22]. Lack of imaging data and extended follow-up preclude assessment of the prognostic benefit of CTO revascularization in patients with AMI-CS [9,15]. The additional burden of out-of-hospital costs and re-admissions was not captured in this single admission database.

## 5. Conclusions

In this large cohort of nationally representative AMI-CS admissions undergoing diagnostic angiography over 7-years, we noted a steady increase in the prevalence of CTOs. Presence of a CTO identified patients at higher risk for in-hospital mortality in admissions with AMI-CS. Given the paucity of data in this field, further dedicated research is needed to aid in optimizing clinical outcomes for this high-risk cohort.

## Abbreviations

AMI	acute myocardial infarction
CS	cardiogenic shock
CTO	chronic total occlusion
HCUP	Healthcare Cost and Utilization Project
ICD-9CM	International Classification of Disease-9 Clinical Modification
NIS	National/Nationwide Inpatient Sample
NSTEMI	non-ST-elevation myocardial infarction
PCI	percutaneous coronary intervention
STEMI	ST-elevation myocardial infarction

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## Declaration of competing interest

None.

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### Author contributions

Conception and design, analysis and interpretation of data: SV, GWB.  
 Drafting manuscript, critical revision, intellectual mentorship: AP, RG, GWB.  
 Final approval of the manuscript: SV, AP, RG, GWB.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2019.100414>.

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