**Temporal Trends and Predictors of Time to Coronary Angiography Following Non-ST Elevation Acute Coronary Syndromes in United States**

**Running title: Trends in Time to Coronary Angiography**

Muhammad Rashid MBBS 1,2, David L. Fischman MD3, Sara C Martinez4 MD, Quinn Capers IV MD5, Michael Savage MD3, Azfar Zaman PhD6, Nick Curzen BM,PhD7, Joie Ensor PhD1, Jessica Potts MSc1, Mohamed O. Mohamed MBChB1,2, Chun Shing Kwok MBBS1,2, Tim Kinnaird8, Rodrigo Bagur1,9, Mamas Mamas BM, BCh, DPhil1,2

1. Keele Cardiovascular Research Group, Centre for Prognosis Research, Institutes of Applied Clinical Science and Primary Care and Health Sciences, Keele University, Stoke-on-Trent, UK
2. Department of Cardiology, Royal Stoke Hospital, University Hospital North Midlands, Stoke-on-Trent, UK
3. Department of Medicine (Cardiology), Thomas Jefferson University Hospital, Philadelphia, Pennsylvania, United States
4. Division of Cardiology, Providence St. Peter Hospital, Washington, USA
5. Department of Cardiology, The Ohio State University School of Medicine, USA
6. Department of Cardiology, Freeman Hospital and Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK.
7. Coronary Research Group, University Hospital Southampton & Faculty of Medicine, University of Southampton, UK.
8. Department of Cardiology, University Hospital of Wales, Cardiff, UK
9. Division of Cardiology, Department of Medicine, London Health Sciences Centre, Western University, London, Ontario, Canada.

**Corresponding Author**

Dr Muhammad Rashid

Keele Cardiovascular Research Group,

Keele University, Stoke-on-Trent, UK

E-mail: doctorrashid7@gmail.com

Tel.: +44 (0)1612 768666

Fax: +44 (0)1782 674467

Word count: 4546

**Abstract:**

**Objectives:** This study aim to investigate the temporal trends in utilization of invasive coronary angiography (CA) at different time points and changing profiles of patients undergoing CA following NSTEACS. We also describe the association between timing of CA and in-hospital clinical outcomes.

**Methods:** We queried the National Inpatient Sample (NIS) to identify all admissions with a primary diagnosis of NSTEACS from 2004 to 2014. Patients were stratified into early (day 0,1), intermediate (day 2) and late strategy (day ≥3) according to timing of CA. Multivariable logistic regression was used to investigate the association between timing of CA and in-hospital mortality, major bleeding, stroke and Major Adverse Cerebrovascular Events (MACCE).

**Results:** A total of 4,380,827 records were identified with a diagnosis of NSTEACS, out of which 57.5% received CA. The proportion of patients undergoing early CA increased from 65.6% to 72.6% while late CA commensurately declined from 19.6% to 13.5%. Patients receiving early CA were younger (age 64 vs 70 years), more likely to be male (63.7% vs 55.3%) and of White ethnic background (68.7% vs 64.7%) compared to late CA group. Similarly, Women, weekend admissions and African Americans remain less likely to receive early CA. In-hospital mortality was lowest in the intermediate group (OR 0.30 (95% CI 0.28-0.33).

**Conclusion**: Use of early CA has increased in the management of NSTEACS; however, there remain significant disparities in utilisation of an early invasive approach in Women, African Americans, admission day and older patients in the US.

**Keywords:** Non-ST-elevation acute coronary syndrome, coronary angiography, timing, temporal trends, mortality.

**Introduction:**

Non-ST elevation acute coronary syndrome (NSTEACS) is the most frequently encountered presentation of the acute coronary syndrome (ACS) in clinical practice, accounting for almost two-thirds of total hospital admissions for ACS in the United States and Europe [1-3]. A routine invasive strategy has been shown to be associated with a reduced risk of re-infarction, repeat hospitalisation, and improved survival compared to a selective invasive or conservative approach, particularly in high-risk NSTEACS[4-6] such as those who are troponin positive. Early invasive coronary angiography (CA) helps to establish the presence and extent of coronary disease and appropriateness of revascularisation in the form of percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery.

Although an invasive approach during the index admission is now routinely practised for NSTEACS, the optimal timing of the procedure remains contentious due to conflicting results from the randomised control trials[7-9]. Specifically, meta-analyses reveal that an early invasive strategy does not reduce mortality compared with a delayed invasive strategy in all patients with NSTEACS, but there may be benefit in high-risk patients [9-12]. Moreover, the timing of CA has changed significantly in the last decade due to expansion in services and changes in guideline recommendations around the cut off for an invasive approach[13, 14]. There are limited data in contemporary practice and in national cohorts regarding temporal trends and changing characteristics of patients undergoing CA following a NSTEACS diagnosis at different time points.

The aims of current studies were to investigate the temporal trends in timing to CA and to describe changes in the profile of patients undergoing early, intermediate and late CA following admission with NSTEACS over the past decade in the United States. Our second aim was to study these trends stratified according to age, ethnicity, gender and weekday versus weekend admission. Thirdly, we investigated the independent predictors of early coronary angiography. Finally, we studied the association of in hospital mortality, MACCE, major bleeding with different time points of CA.

**Methods:**

 The data for this study were derived from National Inpatient Sample (NIS), one of the largest publically available all-payer inpatient healthcare database sponsored by the Agency for Healthcare Research and Quality (AHRQ) as a part of Healthcare Cost and Utilisation Project (HCUP)[15]. NIS collects discharge level anonymised data encompassing more than 7 million yearly hospital records. Ethical approval was not required for this study as NIS is publically available anonymised data.

 We used International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 4111 and 4107 to identify patients admitted with a primary diagnosis of NSTEACS from 2004 to 201. Data were restricted to urgent or emergency diagnoses thereby excluding elective admissions, as they do not represent a true diagnosis of NSTEACS. CA was defined as ICD-9-CM procedure codes 8853, 8854, 8855, 8856 3722 and 3723, with or without percutaneous coronary intervention (PCI) (ICD-9-CM procedure codes 0066, 3601, 3602, 3605, 3606 and 3607. Time to CA was categorised into early (day 0, 1), intermediate (day 2) and late (day ≥3). Patients who did not undergo CA comprise the conservative group.

 We also collected information on patient demographics, including age, sex, race, median household income by zip code, primary expected payer, weekend admission and comorbidities using Elixhasuer comorbidities, as defined by AHRQ. The length of stay and total cost of hospitalisation for each admission were recorded. The cost of hospitalisation was calculated using cost-to-conversion ratio to convert the reported charges into the actual cost for the payer. Additionally, hospital characteristics such as region, location, teaching status and bed size were also included. Finally, information around cardiovascular risk factors and other important relevant diagnoses such as the history of smoking, hyperlipidaemia, coronary artery disease, family history of ischemic heart disease, previous myocardial infarction or CABG, and dementia were also extracted using ICD-9-CM codes provided in supplementary table 1. The ICD-9-CM coded used for calculating Charlson comorbidity index are given in supplementary table 2.

 The in-hospital mortality is collected in NIS database as DIED variable. Whereas, other in-hospital outcomes including major bleeding, acute ischemic stroke, adverse cardiac complications, and MACCE; a composite of acute ischemic stroke, in-hospital mortality and adverse cardiac complications were obtained using ICD-9-CM codes provided in supplementary table 3.

 We compared the differences in the baseline, hospital characteristics, and crude outcomes of interest across all the four categories using descriptive statistics. Continuous variables were reported as the median and interquartile range to account for skewness of the data whereas categorical variables were presented as a number and percentage. All the analyses were undertaken using survey estimation command as recommended by AHRQ in order to account for complex survey design of NIS database. The updated AHRQ trend weights for years 2004-2011 (TRENDWT) and existing discharge weights for years 2012-2014 (DISCHWT) were used to produce national discharge-level estimates for trends analysis. Multivariable analyses were undertaken to investigate the independent predictors of early CA (0,1 day) compared late (≥3 days) and association of time to CA category with aforementioned clinical outcomes. The following covariates were adjusted for in all analyses: age, sex, elective admission, weekend admission, primary expected payer, median household income, dyslipidaemia, smoking status, previous acute myocardial infarction, previous CABG, history of IHD, previous PCI, previous CVA, family history of CAD, use of assist device or IABP, shock during hospitalisation, dementia, bed size of hospital, region of hospital, location/teaching status of hospital and 29 AHRQ comorbidities. All odds ratios (ORs) are adjusted for the aforementioned covariates and presented with the corresponding 95% confidence intervals. This methodology has previously been used for analysing data from HCUP[16-18]. STATA/MP version 14 was used to perform all statistical analysis.

**Results**

 We identified 4,380,827 records with a diagnosis of NSTEACS between 2004 and 2014, of which 1,862,123 (42.5%) were managed medically and 2,518,704 (57.5%) received CA. After excluding the records with missing information on time to CA (12%), the patients that received CA, 1,574,342 (62.5%), 302,668 (12.0%), 340,054 (13.5%) were categorised into early (day 0,1), intermediate (day 2) and late (day ≥3) CA groups respectively (Figure 1). Temporal trends in timing of CA stratified according to the three groups is depicted in Figure 2. Specifically, the proportion undergoing early CA increased from 65.6% to 72.6% with a corresponding reduction in late CA from 19.6% to 13.5%. There significant differences in the profile of the patient undergoing CA at different time points Patients receiving early CA were younger (median age 64 vs 70 years), more likely to be male (63.7% vs 55.3%) and of white ethnic background (68.7% vs 64.7%) compared to late CA group. Conversely, patient in the late CA group were more likely to be women, had higher proportions of co-existing comorbidities, and were more likely to be admitted on weekend days (Table 1). The prevalence of risk factors for coronary artery disease including smoking, dyslipidemia, previous AMI, hypertension, and peripheral vascular disease has increased in both early and intermediate groups, but with a greater proportional increase observed in the early CA group (Table 2). In contrast, patients undergoing late CA had a greater proportional increase in the non-cardiac comorbidities throughout the study period.

There were significant disparities in the secular trends of CA in patients stratified according to gender, comorbidity burden, admission day, age and ethnicity. Temporal trends in the timing of CA stratified according to gender reveal that early CA was comparatively higher in men (68.6% to 74.2%) during the study period, although there was a greater proportional increase in the use of early CA from 60.9% to 70.0% in women (Figure 3). There were significant disparities in the timing of CA use in patients with different comorbidity burden as defined by Charlson comorbidity index (Figure 4). During the 11-year study period, the use of early CA increased from 75.0% to 82.1% in patients with no comorbidity (CCI=0) compared to 47.2% to 58.3% in the CCI≥3 category. For weekend admissions (Figure 5), though the use of early CA has increased from 47.4% to 58.5% in patients admitted on a weekend, the intermediate CA group remained relatively unchanged (31.4% to 29.0%). Similar inequalities in use of early versus late CA was noted in patients from different ethnic backgrounds and age groups. Young patients aged <65 years were more likely to be managed with early CA (76.1%) compared to older patients aged >75 (63.1%) (Figure 6). Similarly, overall, higher proportions of African American received late CA compared to early CA (12.7% vs 8.9%) and this trend remained unchanged over the study period. (Figure 7). Finally, patients with private insurance were more likely to have early CA (33.5%) than late CA (16.7%), while patients on medicare were more likely to have late CA (66.4%) than early CA (49.5%). More than half of all patients treated conservatively (54.2%) were on Medicare, while only 30.8% had private insurance (Table 1).

 We also studied independent clinical and institutional predictors of early CA as shown in Table 3. The presence of haemodynamic compromise such as cardiogenic shock (OR 1.45, 95%CI 1.37-1.54) and use of intra-aortic balloon pump (OR 2.09, 95%CI 2.00-2.19) was associated with an early use of CA. Conversely, Women (OR 0.92 95%CI 0.91-0.94), weekend admission (OR 0.35 95%CI 0.34-0.36), African American (OR 0.77, 95%CI 0.74-0.81), complicated diabetes (OR 0.64, 95%CI 0.62-0.66) and chronic renal failure (OR 0.61, 95%CI 0.60-0.63) were strong negative predictors of early CA.

 Crude outcomes stratified according to the three different timings of CA are shown in Figure 8. In-hospital mortality in the early, intermediate and late were 1.8%, 1.5% and 2.3%, (p<0.0001) respectively. Lower rates for crude MACCE and bleeding was observed in the early and intermediate category compared to late CA category as depicted in Figure 8. Multivariate analysis revealed that early CA was associated with reduced in-hospital mortality (OR 0.39 95%CI 0.37-0.41), in-hospital stroke (OR 0.86 95%CI 0.80-0.92) and MACCE (OR 0.80 95%CI 0.77-0.83); however, the lowest risk was observed in intermediate category (Table 4).

**Discussion:**

 In this large, contemporary cohort of patients admitted with a diagnosis of NSTEACS in the US, there are several important observations. First, there is an increasing trend in use of early CA compared to intermediate and late CA over an 11-year period. Second, we observed significant changes in clinical characteristics and baseline risk profile of patients treated with early invasive CA compared to intermediate and late CA, so that use of early CA remains attenuated in elderly, complex and multimorbid patients despite an overall increase in adoption of early CA in NSTEACS. Third, there are significant disparities in use of early CA across different groups of patients particularly women and African Americans, who were less likely to receive early CA compared to men and caucasians. Fourth, the presence of non-cardiac comorbidities such as liver disease, peripheral vascular disease, chronic renal failure, dementia and history of alcohol disease was inversely associated with receipt of an early CA. Finally, use of CA on day 2 from admission appears to be safe and feasible in the majority of the patients admitted following NSTEACS.

 We demonstrate that women, African American and those without private insurance were less likely to undergo early CA. Women admitted with NSTEACS are older, burdened with more comorbidities and known to have higher risk of peri-procedural bleeding when compared to men[19]. However, women have higher risk of ischemic complications following NSTEACS admission such as re-infraction and repeat admission and therefore are more likely to benefit from an early invasive approach[20-22]. This is in keeping with the current AHA/ACC NSTEACS guidelines recommending an early invasive approach be adopted particularly in those with high-risk features to improve outcomes[14]. Lower utilization of invasive cardiac procedures has been reported in patients without private health insurance[23]. Consistent with literature, patients with private insurance were more likely to have early CA (33.5%) than late CA (16.7%), while patients on medicare were more likely to have late CA (66.4%) than early CA (49.5%). More than half of all patients treated conservatively (54.2%) were on Medicare, while only 30.8% had private insurance. Socioeconomic status, varying practices amongst treating physician and hospitals, lack of access to appropriate health care resources, and regional factors may be responsible for these biases in management in different patient groups when partitioned into payer categories[24-28]. Our study shows that there remain significant disparities in early aggressive treatment of these undertreated subgroup of patients and the need for development of uniform pathways to improve the outcomes in this underserved population.

 Another important finding is the significantly lower adoption of early CA in patients admitted on weekend. Previous studies reporting on “weekend effect” in acute myocardial infarction setting have mainly studied the association of clinical outcomes with a weekend admission[29]. In our large contemporary analysis, we illustrate that almost 30% of the patient admitted on weekend receive CA after 2 days compared to only 8.6% on a weekday. This trend has remained stable over the past decade.

 In our study, it appears that there exists a treatment paradox where younger and less comorbid patients selectively receive early CA in contrast to older, multimorbid patients who may have more to gain from early CA and remain less likely to receive it. The presence of non-cardiac comorbidities such as liver disease, chronic kidney disease, previous CVA, dementia, and peripheral vascular disease were strong negative predictors of early CA. Current guidelines recommend the use of early invasive strategy in patients presenting with high-risk features including ischemic electrocardiographic changes, elevated troponin levels, new CHF symptoms, left ventricular dysfunction, or haemodynamic instability[13, 14]. Presence of cardiogenic shock or use of intra-aortic balloon pump, cardiovascular risk factors such as smoking, dyslipidaemia were strongly associated with early use of CA in our study.

 Finally, we report an overall decreasing trend in in-hospital mortality, MACCE and in-hospital stroke in patients managed invasively compared to a conservative approach. Patients in the intermediate category receiving CA on day 2 appear to have lowest in-hospital mortality and MACCE, both in the unadjusted and adjusted analysis. Although it is widely believed that invasive strategy improves outcomes by reducing ischemic complications following NSTEACS, the studies have shown inconsistent results regarding the timing of CA[9, 10, 30, 31]. It is important to note that majority of these studies are conducted in the pre-P2Y12 inhibitor era with far less aggressive pharmacotherapy compared to current practices. The main benefit of early invasive approach in NSTEACS in driven by the reduction in ischemic complications such as re-infarction and future events[32-35]. It is plausible that with newer potent anti-platelet and anticoagulant use, risk of ischemic complications has reduced and an early invasive strategy can be deferred safely. Lindholm et al used data from SWEADHEART registry to study the optimal timing of invasive strategy in NSTEMI patients demonstrating a 16% relative risk reduction (HR 0.86(95%CI 0.77-0.97) in patients undergoing invasive treatment on day 2 or day 3 whereas no difference in death or MI was found on day 1[36]. National guidelines advocate a risk based approach in offering early invasive approach using validated risk scores such as Global Registry of Acute Coronary Events (GRACE) ACS score[13, 14]. It is important to mention that NIS data doesn’t capture information around haemodynamic status, ECG findings, cardiac biomarker, severity of coronary disease and GRACE ACS score, therefore a true casual inference between optimal timing of CA and in-hospital outcomes cannot be inferred from this study.

 These findings must be interpreted in the context of certain limitations. First, the time from admission to coronary angiography is calculated from admission to procedure day which may be confounded by inter-hospital transfers and unavailability of onsite coronary angiography facilities. The NIS doesn’t collect information around the haemodynamic status, ECG changes and biomarker positivity, hence risk stratification scores such as the GRACE score cannot be calculated or adjusted. This may be particularly relevant in the early invasive group, where high-risk features such as dynamic ECG changes, biomarker positivity, on-going symptoms or adverse haemodynamic profiles may be over-represented in the early invasive group, and we are unable to adjust for these features. Consequently, this may have confounded the influence of earlier angiography on mortality in these patients. Previous work has suggested that the benefit of an early invasive approach was seen predominantly in those patients with a high GRACE ACS score (GRACE >140)[37], hence we are unable to further study timing of CA as well as clinical outcomes stratified by the GRACE score. Furthermore, the NIS does not capture the severity of coronary artery disease or antiplatelet therapy that are important determinants of clinical outcomes. Finally, it is important to note that NIS is an administrative database which is subject to coding errors in both diagnosis and procedure code.

**Conclusion:**

 In this large contemporary national analysis of patients admitted with NSTEACS in the US, we observed an increasing trend in early CA associated with significant changes in baseline characteristics and risk profile of these patients compared to those receiving late CA. Although younger, healthier patients are more likely to receive early CA there remains important gender, ethnic, admission day and payment status inequalities in receipt of early CA. Women, African American, weekend admission and lack of private insurance were less likely to receive early CA. Future efforts should be focused around implementing a uniform risk guided approach in clinical practice and development of pathways to improve access to invasive CA in high-risk NSTEACS patients.

**Acknowledgement:**

The data used in this project can from HCUP Nationwide Inpatient Sample (NIS).

Healthcare Cost and Utilization Project (HCUP). 2004-2011. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp and HCUP National Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2012-2014. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/nisoverview.jsp. A full list of participating states can be found at www.hcup-us.ahrq.gov/hcupdatapartners.jsp

**Declaration of interest:**

All authors declare that there is no competing conflict of interest relevant to this study or any content presented in the manuscript.

**Funding Source:** None

**References:**

[1] McManus DD, Gore J, Yarzebski J, Spencer F, Lessard D, Goldberg RJ. Recent trends in the incidence, treatment, and outcomes of patients with STEMI and NSTEMI. Am J Med 2011;124(1):40-7.

[2] De Luca L, Olivari Z, Bolognese L, Lucci D, Gonzini L, Di Chiara A, et al. A decade of changes in clinical characteristics and management of elderly patients with non-ST elevation myocardial infarction admitted in Italian cardiac care units. Open Heart 2014;1(1):e000148,2014-000148. eCollection 2014.

[3] Puymirat E, Simon T, Cayla G, Cottin Y, Elbaz M, Coste P, et al. Acute Myocardial Infarction: Changes in Patient Characteristics, Management, and 6-Month Outcomes Over a Period of 20 Years in the FAST-MI Program (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) 1995 to 2015. Circulation 2017;136(20):1908-19.

[4] Fox KA, Anderson FA, Dabbous OH, Steg PG, Lopez-Sendon J, Van de Werf F, et al. Intervention in acute coronary syndromes: do patients undergo intervention on the basis of their risk characteristics? The Global Registry of Acute Coronary Events (GRACE). Heart 2007;93(2):177-82.

[5] Fox KA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, Shaw TR, et al. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Randomized Intervention Trial of unstable Angina. Lancet 2002;360(9335):743-51.

[6] Mehta SR, Cannon CP, Fox KA, Wallentin L, Boden WE, Spacek R, et al. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. JAMA 2005;293(23):2908-17.

[7] Katritsis DG, Siontis GC, Kastrati A, van't Hof AW, Neumann FJ, Siontis KC, et al. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. Eur Heart J 2011;32(1):32-40.

[8] Thiele H, Rach J, Klein N, Pfeiffer D, Hartmann A, Hambrecht R, et al. Optimal timing of invasive angiography in stable non-ST-elevation myocardial infarction: the Leipzig Immediate versus early and late PercutaneouS coronary Intervention triAl in NSTEMI (LIPSIA-NSTEMI Trial). Eur Heart J 2012;33(16):2035-43.

[9] Bonello L, Laine M, Puymirat E, Lemesle G, Thuny F, Paganelli F, et al. Timing of Coronary Invasive Strategy in Non-ST-Segment Elevation Acute Coronary Syndromes and Clinical Outcomes: An Updated Meta-Analysis. JACC Cardiovasc Interv 2016;9(22):2267-76.

[10] Jobs A, Mehta SR, Montalescot G, Vicaut E, Van't Hof AWJ, Badings EA, et al. Optimal timing of an invasive strategy in patients with non-ST-elevation acute coronary syndrome: a meta-analysis of randomised trials. Lancet 2017;390(10096):737-46.

[11] Neumann FJ, Kastrati A, Pogatsa-Murray G, Mehilli J, Bollwein H, Bestehorn HP, et al. Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. JAMA 2003;290(12):1593-9.

[12] Montalescot G, Cayla G, Collet JP, Elhadad S, Beygui F, Le Breton H, et al. Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. JAMA 2009;302(9):947-54.

[13] Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 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(3):267-315.

[14] Amsterdam EA, Wenger NK, Brindis RG, Casey DE,Jr, Ganiats TG, Holmes DR,Jr, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;64(24):e139-228.

[15] Anonymous Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. NIS database documentation archive. Rockville, MD; June 2016. [www.hcup-us.ahrq.gov/db/nation/nis/nisarchive](http://www.hcup-us.ahrq.gov/db/nation/nis/nisarchive) . 2018;14 March 2018.

[16] Goel K, Gupta T, Kolte D, Khera S, Fonarow GC, Bhatt DL, et al. Outcomes and Temporal Trends of Inpatient Percutaneous Coronary Intervention at Centers With and Without On-site Cardiac Surgery in the United States. JAMA Cardiol 2017;2(1):25-33.

[17] Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, et al. Trends in Coronary Angiography, Revascularization, and Outcomes of Cardiogenic Shock Complicating Non-ST-Elevation Myocardial Infarction. Am J Cardiol 2016;117(1):1-9.

[18] Kwok CS, Potts J, Gulati M, Alasnag M, Rashid M, Shoaib A, et al. Effect of Gender on Unplanned Readmissions After Percutaneous Coronary Intervention (from the Nationwide Readmissions Database). Am J Cardiol 2018;121(7):810-7.

[19] Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, et al. Acute Myocardial Infarction in Women: A Scientific Statement From the American Heart Association. Circulation 2016;133(9):916-47.

[20] Daly C, Clemens F, Lopez Sendon JL, Tavazzi L, Boersma E, Danchin N, et al. Gender differences in the management and clinical outcome of stable angina. Circulation 2006;113(4):490-8.

[21] Kunadian V, Qiu W, Lagerqvist B, Johnston N, Sinclair H, Tan Y, et al. Gender Differences in Outcomes and Predictors of All-Cause Mortality After Percutaneous Coronary Intervention (Data from United Kingdom and Sweden). Am J Cardiol 2017;119(2):210-6.

[22] Sawant AC, Josey K, Plomondon ME, Maddox TM, Bhardwaj A, Singh V, et al. Temporal Trends, Complications, and Predictors of Outcomes Among Nonagenarians Undergoing Percutaneous Coronary Intervention: Insights From the Veterans Affairs Clinical Assessment, Reporting, and Tracking Program. JACC Cardiovasc Interv 2017;10(13):1295-303.

[23] Calvin JE, Roe MT, Chen AY, Mehta RH, Brogan GX,Jr, Delong ER, et al. Insurance coverage and care of patients with non-ST-segment elevation acute coronary syndromes. Ann Intern Med 2006;145(10):739-48.

[24] Bhatt DL, Roe MT, Peterson ED, Li Y, Chen AY, Harrington RA, et al. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. JAMA 2004;292(17):2096-104.

[25] Edmund Anstey D, Li S, Thomas L, Wang TY, Wiviott SD. Race and Sex Differences in Management and Outcomes of Patients After ST-Elevation and Non-ST-Elevation Myocardial Infarct: Results From the NCDR. Clin Cardiol 2016;39(10):585-95.

[26] Malta Hansen C, Wang TY, Chen AY, Chiswell K, Bhatt DL, Enriquez JR, et al. Contemporary Patterns of Early Coronary Angiography Use in Patients With Non-ST-Segment Elevation Myocardial Infarction in the United States: Insights From the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry. JACC Cardiovasc Interv 2018;11(4):369-80.

[27] Rhudy JP,Jr, Alexandrov AW, Hyrkas KE, Jablonski-Jaudon RA, Pryor ER, Wang HE, et al. Geographic access to interventional cardiology services in one rural state. Heart Lung 2016;45(5):434-40.

[28] Capers Q, Sharalaya Z. Racial Disparities in Cardiovascular Care: A Review of Culprits and Potential Solutions. Journal of Racial and Ethnic Health Disparities 2014;1(3):171-80.

[29] Kwok CS, Al-Dokheal M, Aldaham S, Rushton C, Butler R, Kinnaird T, et al. Weekend effect in acute coronary syndrome: A meta-analysis of observational studies. Eur Heart J Acute Cardiovasc Care 2018:2048872618762634.

[30] de Winter RJ, Windhausen F, Cornel JH, Dunselman PH, Janus CL, Bendermacher PE, et al. Early invasive versus selectively invasive management for acute coronary syndromes. N Engl J Med 2005;353(11):1095-104.

[31] Milosevic A, Vasiljevic-Pokrajcic Z, Milasinovic D, Marinkovic J, Vukcevic V, Stefanovic B, et al. Immediate Versus Delayed Invasive Intervention for Non-STEMI Patients: The RIDDLE-NSTEMI Study. JACC Cardiovasc Interv 2016;9(6):541-9.

[32] Montalescot G, Wiviott SD, Braunwald E, Murphy SA, Gibson CM, McCabe CH, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial. The Lancet 2009;373(9665):723-31.

[33] Steg PG, James S, Harrington RA, Ardissino D, Becker RC, Cannon CP, et al. Ticagrelor versus clopidogrel in patients with ST-elevation acute coronary syndromes intended for reperfusion with primary percutaneous coronary intervention: A Platelet Inhibition and Patient Outcomes (PLATO) trial subgroup analysis. Circulation 2010;122(21):2131-41.

[34] Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;361(11):1045-57.

[35] Olier I, Sirker A, Hildick-Smith DJR, Kinnaird T, Ludman P, de Belder MA, et al. Association of different antiplatelet therapies with mortality after primary percutaneous coronary intervention. Heart 2018.

[36] Lindholm D, Alfredsson J, Angeras O, Bohm F, Calais F, Koul S, et al. Timing of percutaneous coronary intervention in patients with non-ST-elevation myocardial infarction: a SWEDEHEART study. Eur Heart J Qual Care Clin Outcomes 2017;3(1):53-60.

[37] Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, et al. Early versus delayed invasive intervention in acute coronary syndromes. N Engl J Med 2009;360(21):2165-75.

Table 1: Baseline characteristics of different time point of Coronary angiography

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Timing of CA | Early | Intermediate | Late | Conservative approach  |
| Number of Cases weighted (%age) | 1,574,342 (38.6%) | 302,668 (7.4%) | 340,054 (8.3%) | 1,862,123 (45.6%) |
| Age (year), Median IRQ | 64 (54-74) | 67 (57-77) | 70 (60-78) | 66 (56-75) |
| Men % | 63.7% | 58.6% | 55.3% | 49.7% |
| Ethnicity |  |  |  |  |
| White | 68.7% | 66.8% | 64.7% | 63.3% |
| Black | 8.9% | 11.2% | 12.7% | 10.0% |
| Hispanic | 6.4% | 7.7% | 8.3% | 6.4% |
| Asian/Pacific Islander | 1.7% | 1.7% | 2.0% | 1.8% |
| Native American | 0.5% | 0.5% | 0.4% | 0.4% |
| Other | 3.1% | 2.7% | 2.7% | 2.2% |
| Missing Race | 10.8% | 9.4% | 9.2% | 16.0% |
| Weekend admission | 19.4% | 53.0% | 25.1% | 26.8% |
| Primary expected payer, % |  |  |  |  |
| Medicare | 49.5% | 58.2% | 66.4% | 54.2% |
| Medicaid | 6.6% | 6.8% | 7.2% | 5.7% |
| Private Insurance | 33.5% | 25.9% | 16.7% | 30.8% |
| Self-pay | 6.6% | 5.7% | 4.5% | 5.8% |
| No charge | 0.7% | 0.7% | 0.6% | 0.5% |
| other | 3.1% | 2.7% | 2.3% | 1.9% |
| Median Household Income (percentile) |  |  |  |  |
| 0-25th | 28.2% | 30.5% | 31.9% | 30.3% |
| 26-50th | 27.5% | 27.8% | 26.7% | 27.0% |
| 51-75th | 23.9% | 23.5% | 22.8% | 22.7% |
| 76-100th | 20.4% | 18.2% | 18.6% | 20.0% |
| Comorbidities, % |  |  |  |  |
| Dyslipidaemia | 60.1% | 55.5% | 45.0% | 37.6% |
| Smoking | 40.8% | 35.8% | 29.6% | 22.4% |
| Previous AMI | 9.5% | 10.4% | 9.3% | 9.5% |
| History of IHD | 83.9% | 80.0% | 73.7% | 42.6% |
| Previous PCI | 12.1% | 12.4% | 10.0% | 7.7% |
| Previous CABG | 5.5% | 6.9% | 7.0% | 10.1% |
| Previous CVA | 3.1% | 3.7% | 3.8% | 4.0% |
| Family history of CAD | 9.2% | 6.7% | 4.0% | 3.4% |
| Valvular heart disease | 0.1% | 0.2% | 0.3% | 0.4% |
| Peripheral vascular disease | 10.7% | 13.4% | 16.0% | 11.5% |
| Multivessel PCI  | 10.8% | 8.3% | 7.6% | 0% |
| Use of assist devise or IABP | 4.4% | 2.4% | 2.8% | 0.5% |
| Shock | 2.7% | 1.6% | 2.7% | 2.2% |
| AIDS | 0.13% | 0.14% | 0.18% | 0.12% |
| Alcohol abuse | 2.9% | 3.0% | 3.4% | 2.4% |
| Deficiency anaemias | 10.8% | 15.6% | 23.2% | 20.3% |
| Chronic Blood loss anaemia | 0.6% | 0.8% | 1.8% | 1.6% |
| RA/collagen vasculardiseases | 2.1% | 2.4% | 2.5% | 2.4% |
| Congestive heart failure | 0.3% | 0.4% | 0.9% | 1.3% |
| Chronic pulmonary disease | 18.2% | 22.6% | 28.5% | 25.4% |
| Coagulopathy | 3.8% | 4.2% | 6.0% | 4.4% |
| Depression | 6.6% | 7.4% | 7.4% | 7.8% |
| Diabetes | 29.6% | 32.4% | 33.6% | 30.1% |
| Diabetes with complications | 4.8% | 7.3% | 11.6% | 7.4% |
| Drug abuse | 2.2% | 2.3% | 2.3% | 1.8% |
| Hypertension | 71.0% | 73.5% | 71.8% | 68.3% |
| Hypothyroidism | 9.1% | 10.4% | 11.2% | 12.7% |
| Liver disease | 1.1% | 1.3% | 1.8% | 1.4% |
| Lymphomas | 0.4% | 0.5% | 0.6% | 0.6% |
| Fluid and electrolyte disturbances | 13.2% | 17.9% | 27.5% | 25.1% |
| Other neurological disorders | 3.6% | 4.7% | 5.8% | 9.1% |
| Obesity | 14.9% | 15.1% | 14.3% | 9.1% |
| Paralysis | 1.0% | 1.3% | 2.0% | 2.5% |
| Psychoses | 1.7% | 2.1% | 2.6% | 2.7% |
| Pulmonary circulation disorder | 0.05% | 0.07% | 0.1% | 0.2% |
| Renal failure (chronic) | 11.8% | 18.3% | 28.6% | 24.8% |
| Peptic ulcer disease | 0.03% | 0.05% | 0.05% | 0.05% |
| Weight loss | 1.2% | 1.6% | 3.0% | 3.2% |
| Solid tumor without mets | 1.0% | 1.2% | 1.7% | 2.0% |
| Metastatic cancer | 0.4% | 0.5% | 0.7% | 1.5% |
| Dementia | 2.1% | 3.1% | 4.4% | 13.0% |
| Charlson Comorbidity Index |  |  |  |  |
| 0 | 38.9% | 29.3% | 18.8% | 23.0% |
| 1 | 33.3% | 32.8% | 30.2% | 31.5% |
| 2 | 17.4% | 22.0% | 26.8% | 24.6% |
| ≥3 | 10.4% | 15.9% | 24.2% | 20.9% |
| Hospital bed size |  |  |  |  |
| Small | 7.7% | 7.2% | 7.7% | 15.9% |
| Medium | 22.3% | 23.3% | 23.1% | 28.1% |
| Large | 70.0% | 69.5% | 69.8% | 56.0% |
| Hospital Region |  |  |  |  |
| Northeast | 20.3% | 20.1% | 23.6% | 26.3% |
| Midwest | 21.3% | 19.5% | 17.7% | 20.5% |
| South | 42.1% | 46.2% | 46.2% | 38.4% |
| West | 16.3% | 14.2% | 12.4% | 14.9% |
| Location/ Teaching status |  |  |  |  |
| Rural | 6.3% | 6.5% | 5.7% | 18.2% |
| Urban-non teaching | 38.3% | 40.9% | 40.0% | 46.9% |
| Urban- teaching | 55.4% | 52.6% | 54.3% | 34.9% |
| Length of stay, Median (IQR) | 2 (2-4) | 4 (3-6) | 6 (4-10) | 3 (2-6) |
| Total charge,$, Median (IQR) | 49757 (30830-81841) | 51034 (31227-84244) | 63602 (39026-108596) | 18078 (9841-34417) |
|  |  |  |  |  |

Table 2: Temporal trends in baseline and hospital characteristics of patients stratified according to different cut off of time to coronary angiography

|  |  |  |  |
| --- | --- | --- | --- |
| Year  | 2004 | 2005-2006 | 2007-2008 |
| Timing of CA | Early | Interm. | Late | Early | Interm. | Late | Early  | Interm. | late |
| Number of Cases weighted (%age) | 102,568 (65.6%) | 23,208 (14.8%) | 30,634 (19.6%) | 236,276 (68.4%) | 48,367 (14.0% | 60,675 (17.6%) | 245,239 (70.7%) | 46,976 (13.5%) | 54,470 (51.7%) |
| Age (year), Median IRQ | 64 (54-74) | 67 (57-77) | 71 (61-78) | 64 (54-74) | 57 (57-77) | 70 (60-79) | 64 (54-74) | 67 (57-77) | 70 (60-79) |
| Men % | 63.8% | 58.2% | 55.7% | 63.7% | 58.5% | 54.6% | 63.2% | 58.2% | 54.2% |
| Ethnicity |  |  |  |  |  |  |  |  |  |
| White | 64.6% | 62.0% | 60.2% | 63.9% | 63.9% | 62.2% | 66.2% | 64.0% | 62.7% |
| Black | 7.1% | 9.6% | 11.3% | 6.2% | 8.3% | 9.6% | 8.5% | 10.1% | 11.4% |
| Hispanic | 4.7% | 6.4% | 7.4% | 5.8% | 7.1% | 8.5% | 5.9% | 7.8% | 7.8% |
| Asian/Pacific Islander | 1.2% | 1.2% | 1.5% | 1.2% | 1.4% | 1.6% | 1.7% | 1.8% | 2.1% |
| Native American | 0.2% | 0.3% | 0.2% | 0.2% | 0.2% | 0.2% | 0.8% | 0.9% | 0.8% |
| Other | 2.3% | 2.1% | 2.2% | 3.7% | 1.7% | 1.9% | 3.3% | 2.8% | 2.9% |
| Missing Race | 19.8% | 18.3% | 17.3% | 18.9% | 17.3% | 16.0% | 13.6% | 12.6% | 12.3% |
| Weekend admission | 17.1% | 50.2% | 25.8% | 17.8% | 51.5% | 26.0% | 18.7% | 53.7% | 24.8% |
| Primary expected payer, % |  |  |  |  |  |  |  |  |  |
| Medicare | 48.0% | 55.8% | 66.8% | 48.6% | 58.0% | 66.4% | 47.7% | 56.5% | 65.4% |
| Medicaid | 5.8% | 5.8% | 6.1% | 5.7% | 6.2% | 6.5% | 5.7% | 6.3% | 6.9% |
| Private Insurance | 37.7% | 30.3% | 21.0% | 36.5% | 27.5% | 19.7% | 35.7% | 27.8% | 19.8% |
| Self-pay | 5.4% | 5.0% | 3.8% | 5.7% | 5.0% | 4.2% | 6.4% | 5.6% | 4.4% |
| No charge | 0.5% | 0.7% | 0.6% | 0.7% | 0.8% | 0.8% | 0.8% | 0.8% | 0.8% |
| other | 2.6% | 2.2% | 1.6% | 2.9% | 2.5% | 2.3% | 3.7% | 3.0% | 2.7% |
| Median Household Income (percentile) |  |  |  |  |  |  |  |  |  |
| 0-25th | 25.9% | 28.3% | 30.4% | 26.0% | 28.8% | 31.4% | 26.4% | 30.5% | 31.6% |
| 26-50th | 28.0% | 28.3% | 26.6% | 26.5% | 27.1% | 26.0% | 28.3% | 28.3% | 26.9% |
| 51-75th | 21.9% | 22.6% | 21.4% | 25.0% | 24.5% | 23.1% | 23.2% | 23.1% | 22.9% |
| 76-100th | 24.2% | 20.8% | 21.6% | 22.4% | 19.6% | 19.5% | 22.1% | 18.1% | 18.6% |
| Comorbidities, % |  |  |  |  |  |  |  |  |  |
| Dyslipidaemia | 51.6%% | 47.5%% | 35.4% | 54.1% | 49.5% | 37.2% | 57.9% | 53.0% | 40.3% |
| Smoking | 31.5% | 26.4% | 19.7% | 34.0% | 29.9% | 21.7% | 37.7% | 32.0% | 24.4% |
| Previous AMI | 8.0% | 8.5% | 7.6% | 7.7% | 9.0% | 7.7% | 8.6% | 8.7% | 7.9% |
| History of IHD | 84.4% | 80.1% | 72.0% | 84.1% | 79.1% | 71.0% | 84.0% | 79.4% | 72.4% |
| Previous PCI | 7.8% | 7.7% | 6.0% | 9.0% | 9.1% | 6.6% | 10.3% | 10.2% | 7.6% |
| Previous CABG | 5.5% | 6.2% | 6.4% | 5.3% | 6.3% | 6.0% | 5.2% | 6.4% | 6.0% |
| Previous CVA | NA | NA | NA | NA | NA | NA | 1.7% | 2.1% | 2.1% |
| Family history of CAD | 6.3% | 4.3% | 2.6% | 7.2% | 5.3% | 2.8% | 7.9% | 5.1% | 2.4% |
| Valvular heart disease | 0.1% | 0.2% | 0.4% | 0.1% | 0.1% | 0.3% | 0.1% | 0.2% | 0.3% |
| Peripheral vascular disease | 8.5% | 10.8% | 12.2% | 9.2% | 11.5% | 12.3% | 10.9% | 14.0% | 16.1% |
| Multivessel PCI  | 10.6% | 8.0% | 6.9% | 12.0% | 9.1% | 7.8% | 10.4% | 7.2% | 6.5% |
| Use of assist devise or IABP | 3.8% | 2.0% | 2.0% | 4.2% | 2.0% | 2.0% | 4.4% | 2.6% | 2.7% |
| Shock | 1.8% | 0.6% | 1.4% | 2.1% | 1.1% | 1.6% | 2.3% | 1.4% | 2.6% |
| AIDS | 0.11% | 0.17% | 0.15% | 0.1% | 0.13% | 0.16% | 0.1% | 0.17% | 0.14% |
| Alcohol abuse | 2.1% | 2.6% | 2.7% | 2.4% | 2.4% | 2.8% | 2.8% | 2.7% | 3.0% |
| Deficiency anaemias | 6.8% | 10.3% | 13.8% | 7.7% | 10.6% | 15.0% | 10.9% | 15.3% | 22.0% |
| Chronic Blood loss anaemia | 0.5% | 1.0% | 2.3% | 0.7% | 1.1% | 2.4% | 0.8% | 1.0% | 2.2% |
| RA/collagen vasculardiseases | 1.7% | 1.4% | 1.9% | 1.7% | 2.4% | 1.9% | 2.0% | 2.4% | 2.4% |
| Congestive heart failure | 0.4% | 0.3% | 1.0% | 0.3% | 0.3% | 0.8% | 0.3% | 0.6% | 0.9% |
| Chronic pulmonary disease | 15.5% | 20.0% | 26.1% | 17.2% | 21.2% | 27.7% | 18.1% | 22.1% | 28.4% |
| Coagulopathy | 2.1% | 2.9% | 4.3% | 2.6% | 2.8% | 4.1% | 3.1% | 3.5% | 5.1% |
| Depression | 4.0% | 4.4% | 4.0% | 4.7% | 5.3% | 5.0% | 5.8% | 6.4% | 6.8% |
| Diabetes | 25.7% | 28.6% | 30.6% | 26.4% | 28.8% | 29.7% | 28.2% | 31.8% | 32.7% |
| Diabetes with complications | 3.3% | 5.1% | 8.2% | 3.5% | 6.0% | 9.2% | 4.3% | 6.6% | 11.0% |
| Drug abuse | 1.3% | 1.7% | 1.4% | 1.7% | 1.9% | 1.9% | 2.0% | 2.1% | 1.9% |
| Hypertension | 61.9% | 65.5% | 62.5% | 64.6% | 66.5% | 64.5% | 68.8% | 71.1% | 70.3% |
| Hypothyroidism | 6.5% | 7.2% | 7.9% | 7.0% | 7.9% | 8.6% | 8.3% | 9.7% | 11.1% |
| Liver disease | 0.6% | 0.9% | 1.0% | 0.7% | 0.8% | 1.2% | 0.9% | 1.1% | 1.6% |
| Lymphomas | 0.3% | 0.5% | 0.6% | 0.4% | 0.4% | 0.5% | 0.4% | 0.4% | 0.6% |
| Fluid and electrolyte disturbances | 7.6% | 10.8% | 17.5% | 9.3% | 13.2% | 21.3% | 11.8% | 16.6% | 25.3% |
| Other neurological disorders | 2.5% | 2.9% | 3.7% | 2.7% | 3.7% | 4.5% | 3.3% | 4.4% | 6.0% |
| Obesity | 8.7% | 9.3% | 7.8% | 10.3% | 10.3% | 8.3% | 12.9% | 13.0% | 12.4% |
| Paralysis | 0.7% | 0.9% | 1.4% | 0.8% | 1.0% | 1.6% | 1.0% | 1.4% | 2.3% |
| Psychoses | 1.1% | 1.2% | 1.4% | 1.1% | 1.2% | 1.7% | 1.5% | 1.6% | 2.3% |
| Pulmonary circulation disorder | 0.01% | 0.02% | 0.05% | 0.03% | 0.00% | 0.04% | 0.05% | 0.09% | 0.1% |
| Renal failure (chronic) | 4.0% | 6.8% | 13.2% | 7.4% | 11.9% | 20.9% | 11.2% | 17.4% | 28.2% |
| Peptic ulcer disease | 0.06% | 0.15% | 0.1% | 0.04% | 0.07% | 0.05% | 0.02% | 0.07% | 0.07% |
| Weight loss | 0.4% | 0.5% | 1.0% | 0.6% | 0.7% | 1.6% | 0.9% | 1.1% | 2.5% |
| Solid tumor without mets | 0.9% | 1.0% | 1.4% | 0.8% | 1.1% | 1.7% | 0.9% | 1.4% | 1.6% |
| Metastatic cancer | 0.3% | 0.4% | 0.5% | 0.3% | 0.4% | 0.6% | 0.4% | 0.4% | 0.7% |
| Dementia | 1.4% | 2.0% | 2.4% | 1.5% | 2.3% | 3.2% | 1.9% | 2.5% | 3.8% |
| Charlson Comorbidity Index |  |  |  |  |  |  |  |  |  |
| 0 | 45.0% | 35.6% | 23.3% | 43.9% | 34.4% | 22.9% | 41.1% | 31.1% | 20.9% |
| 1 | 33.7% | 35.1% | 33.8% | 33.8% | 34.9% | 33.0% | 33.8% | 34.5% | 32.1% |
| 2 | 14.9% | 19.3% | 26.4% | 15.5% | 19.8% | 26.8% | 16.5% | 21.1% | 26.6% |
| ≥3 | 6.4% | 10.0% | 16.5% | 6.8% | 10.9% | 17.3% | 8.6% | 13.3% | 20.4% |
| Hospital bed size |  |  |  |  |  |  |  |  |  |
| Small | 8.6% | 5.7% | 6.0% | 5.6% | 5.8% | 5.9% | 6.3% | 6.0% | 6.0% |
| Medium | 17.1% | 20.0% | 19.6% | 21.6% | 22.8% | 23.3% | 20.7% | 21.3% | 21.9% |
| Large | 74.3% | 74.3% | 74.3% | 72.9% | 71.4% | 70.8% | 73.0% | 72.7% | 72.1% |
| Hospital Region |  |  |  |  |  |  |  |  |  |
| Northeast | 28.6% | 23.0% | 28.6% | 25.3% | 24.1% | 27.8% | 22.8% | 20.8% | 24.6% |
| Midwest | 17.5% | 17.5% | 15.3% | 17.3% | 15.9% | 12.7% | 17.7% | 17.3% | 16.1% |
| South | 41.5% | 46.6% | 44.4% | 42.9% | 47.6% | 47.9% | 44.1% | 47.3% | 47.0% |
| West | 12.4% | 12.9% | 11.7% | 14.5% | 12.4% | 12.0% | 15.4% | 14.7% | 12.3% |
| Location/ Teaching status |  |  |  |  |  |  |  |  |  |
| Rural | 6.0% | 6.4% | 5.1% | 5.0% | 6.5% | 5.1% | 6.5% | 7.6% | 7.2% |
| Urban-non teaching | 35.5% | 41.8% | 41.5% | 39.4% | 42.2% | 40.3% | 39.3% | 43.8% | 43.4% |
| Urban- teaching | 58.5% | 51.8% | 53.4% | 55.6% | 51.3% | 54.6% | 54.2% | 48.5% | 49.4% |
| Length of stay, Median (IQR) | 3 (2-5) | 4 (3-6) | 6 (5-10) | 3 (2-5) | 4 (3-6) | 7 (5-10) | 4 (2-5) | 4 (3-6) | 6 (5-10) |
| Total charge,$, Median (IQR) | 36276 (23074-56989) | 36606 (22263-58425) | 46759 (29189-77712) | 40655 (25028-64583) | 41498 (25563-66726) | 52479 (32576-86384) | 44303 (27789-73340) | 46311 (29130-76450) | 56737 (36702-98776) |
|  |  |  |  |  |  |  |  |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Year  | 2009-2010 | 2011-2012 | 2013-2014 |
| Timing of CA | Early  | Interm. | Late | Early | Interm. | Late | Early | Interm. | Late |
| Number of Cases weighted (%age) | 303,976 (71.9% ) | 56,837 (13.4%) | 62,220 (14.7%) | 328,890 (72.5%) | 60,273 (13.3%) | 64,664 (14.3%) | 357,390 (72.7%) | 67,005 (13.6%) | 67,390 (13.7%) |
| Age (year), Median IRQ | 64 (54-74) | 67 (57-77) | 69 (60-78) | 64 (55-74) | 67 (58-77) | 70 (60-79) | 65 (55-67) | 67 (58-77) | 70 (60-78) |
| Men % | 63.5% | 58.5% | 44.7% | 64.0% | 58.6% | 55.0% | 64.0% | 59.4% | 57.5% |
| Ethnicity |  |  |  |  |  |  |  |  |  |
| White | 68.4% | 66.6% | 64.0% | 71.8% | 69.3% | 67.7% | 72.0% | 70.3% | 68.2% |
| Black | 9.3% | 11.7% | 14.0% | 10.0% | 13.2% | 14.9% | 9.9% | 12.2% | 13.8% |
| Hispanic | 6.3% | 7.5% | 8.0% | 6.8% | 7.7% | 8.3% | 7.3% | 8.8% | 9.0% |
| Asian/Pacific Islander | 1.7% | 1.5% | 2.2% | 1.8% | 1.9% | 2.1% | 2.0% | 2.1% | 2.4% |
| Native American | 0.6% | 0.6% | 0.6% | 0.5% | 0.5% | 0.4% | 0.4% | 0.4% | 0.4% |
| Other | 2.7% | 2.8% | 2.9% | 3.4% | 3.3% | 3.2% | 3.0% | 2.7% | 2.9% |
| Missing Race | 11.0% | 9.3% | 8.1% | 5.8% | 4.1% | 3.3% | 5.4% | 3.6% | 3.4% |
| Weekend admission | 19.8% | 53.4% | 24.4% | 20.0% | 53.7% | 26.0% | 20.8% | 53.3% | 24.3% |
| Primary expected payer, % |  |  |  |  |  |  |  |  |  |
| Medicare | 48.4% | 56.7% | 64.9% | 50.8% | 60.1% | 67.9% | 51.3% | 60.1% | 67.6% |
| Medicaid | 6.5% | 6.7% | 7.5% | 6.8% | 7.0% | 7.2% | 7.8% | 8.0% | 8.4% |
| Private Insurance | 34.3% | 26.6% | 19.4% | 31.1% | 23.6% | 16.9% | 30.6% | 23.5% | 17.0% |
| Self-pay | 7.1% | 6.6% | 5.2% | 7.2% | 6.2% | 4.9% | 6.5% | 5.3% | 4.4% |
| No charge | 0.6% | 0.6% | 0.4% | 0.8% | 0.5% | 0.5% | 0.7% | 0.7% | 0.4% |
| other | 3.1% | 2.8% | 2.6% | 3.2% | 2.7% | 2.4% | 3.0% | 2.4% | 2.1% |
| Median Household Income (percentile) |  |  |  |  |  |  |  |  |  |
| 0-25th | 28.9% | 31.0% | 31.9% | 29.6% | 31.3% | 32.9% | 29.5% | 31.3% | 32.6% |
| 26-50th | 27.5% | 28.3% | 27.6% | 26.3% | 26.1% | 25.0% | 28.3% | 28.8% | 28.3% |
| 51-75th | 24.0% | 23.1% | 22.7% | 24.6% | 24.0% | 23.6% | 23.4% | 23.0% | 22.1% |
| 76-100th | 19.3% | 17.6% | 18.1% | 19.5% | 18.6% | 18.5% | 18.8% | 16.8% | 17.0% |
| Comorbidities, % |  |  |  |  |  |  |  |  |  |
| Dyslipidaemia | 60.8% | 56.1% | 45.9% | 63.4% | 59.5% | 51.2% | 64.0% | 60.1% | 53.1% |
| Smoking | 41.0% | 35.6% | 30.4% | 43.7% | 39.3% | 34.9% | 47.1% | 42.8% | 39.6% |
| Previous AMI | 9.4% | 9.9% | 9.6% | 10.4% | 11.7% | 10.8% | 11.0% | 12.4% | 11.1% |
| History of IHD | 84.7% | 80.6% | 74.9% | 84.1% | 81.1% | 76.0% | 82.7% | 79.3% | 74.9% |
| Previous PCI | 12.0% | 12.0% | 10.2% | 13.9% | 15.4% | 12.7% | 15.0% | 15.8% | 14.0% |
| Previous CABG | 5.1% | 6.6% | 7.2% | 5.7% | 7.3% | 7.7% | 5.9% | 7.5% | 8.1% |
| Previous CVA | 3.7% | 4.6% | 5.2% | 4.5% | 5.6% | 6.3% | 5.0% | 6.3% | 6.7% |
| Family history of CAD | 10.1% | 6.7% | 4.4% | 10.2% | 7.8% | 5.0% | 10.9% | 8.4% | 5.9% |
| Valvular heart disease | 0.1% | 0.2% | 0.3% | 0.1% | 0.2% | 0.3% | 0.07% | 0.1% | 0.2% |
| Peripheral vascular disease | 10.8% | 13.5% | 16.5% | 11.4% | 14.7% | 18.1% | 11.5% | 14.0% | 18.5% |
| Multivessel PCI  | 9.7% | 7.2% | 6.5% | 10.8% | 8.6% | 8.3% | 11.3% | 9.0% | 8.9% |
| Use of assist devise or IABP | 4.6% | 2.5% | 2.8% | 4.6% | 2.4% | 3.5% | 4.2% | 2.5% | 3.2% |
| Shock | 2.8% | 1.7% | 2.7% | 3.1% | 1.8% | 3.3% | 3.1% | 2.0% | 3.7% |
| AIDS | 0.15% | 0.11% | 0.22% | 0.14% | 0.13% | 0.16% | 0.13% | 0.16% | 0.21% |
| Alcohol abuse | 2.9% | 3.1% | 3.4% | 3.1% | 3.3% | 3.8% | 3.3% | 3.4% | 3.9% |
| Deficiency anaemias | 11.4% | 16.5% | 25.2% | 12.3% | 18.7% | 28.7% | 11.9% | 17.8% | 28.5% |
| Chronic Blood loss anaemia | 0.6% | 0.8% | 1.8% | 0.5% | 0.8% | 1.5% | 0.5% | 0.5% | 1.2% |
| RA/collagen vasculardiseases | 2.1% | 2.3% | 2.4% | 2.3% | 2.7% | 3.0% | 2.5% | 2.6% | 2.9% |
| Congestive heart failure | 0.4% | 0.5% | 1.3% | 0.3% | 0.4% | 1.0% | 0.2% | 0.4% | 0.9% |
| Chronic pulmonary disease | 17.9% | 22.2% | 27.4% | 18.9% | 23.5% | 29.8% | 19.4% | 24.3% | 30.2% |
| Coagulopathy | 3.9% | 4.1% | 6.2% | 4.4% | 5.1% | 7.5% | 4.7% | 5.3% | 7.5% |
| Depression | 6.7% | 7.4% | 7.6% | 7.6% | 8.5% | 9.6% | 8.3% | 9.4% | 9.6% |
| Diabetes | 29.4% | 32.2% | 33.3% | 31.5% | 34.8% | 36.0% | 32.1% | 34.7% | 37.3% |
| Diabetes with complications | 4.5% | 6.9% | 11.3% | 5.4% | 8.6% | 13.3% | 6.0% | 8.7% | 14.4% |
| Drug abuse | 2.1% | 2.1% | 2.3% | 2.4% | 2.5% | 2.7% | 2.7% | 2.8% | 2.8% |
| Hypertension | 71.3% | 73.4% | 72.5% | 74.3% | 77.6% | 77.0% | 76.1% | 79.4% | 78.0% |
| Hypothyroidism | 9.0% | 10.8% | 11.0% | 10.1% | 12.3% | 13.0% | 10.8% | 11.8% | 13.5% |
| Liver disease | 1.0% | 1.2% | 1.8% | 1.2% | 1.5% | 2.1% | 1.4% | 1.9% | 2.6% |
| Lymphomas | 0.3% | 0.6% | 0.7% | 0.4% | 0.5% | 0.6% | 0.4% | 0.6% | 0.7% |
| Fluid and electrolyte disturbances | 13.4% | 17.3% | 28.5% | 15.2% | 20.8% | 32.0% | 16.4% | 22.4% | 34.2% |
| Other neurological disorders | 3.5% | 4.7% | 6.2% | 3.9% | 5.4% | 6.8% | 4.3% | 5.7% | 6.8% |
| Obesity | 14.8% | 14.7% | 14.2% | 17.2% | 18.1% | 18.0% | 19.1% | 19.9% | 21.0% |
| Paralysis | 1.0% | 1.3% | 2.2% | 1.1% | 1.3% | 2.2% | 1.0% | 1.5% | 2.3% |
| Psychoses | 1.8% | 2.3% | 2.6% | 2.0% | 2.5% | 3.3% | 2.2% | 2.8% | 3.4% |
| Pulmonary circulation disorder | 0.07% | 0.1% | 0.2% | 0.05% | 0.1% | 0.1% | 0.04% | 0.08% | 0.1% |
| Renal failure (chronic) | 12.5% | 19.5% | 31.0% | 14.0% | 22.9% | 34.0% | 14.7% | 22.5% | 35.3% |
| Peptic ulcer disease | 0.02% | 0.02% | 0.04% | 0.03% | 0.05% | 0.05% | 0.02% | 0.02% | 0.04% |
| Weight loss | 1.4% | 1.5% | 3.0% | 1.5% | 2.3% | 4.3% | 1.6% | 2.2% | 4.3% |
| Solid tumor without mets | 1.0% | 1.2% | 1.6% | 1.0% | 1.1% | 1.8% | 1.0% | 1.3% | 1.8% |
| Metastatic cancer | 0.4% | 0.5% | 0.7% | 0.4% | 0.5% | 0.8% | 0.4% | 0.5% | 0.7% |
| Dementia | 2.3% | 3.2% | 4.6% | 2.5% | 3.6% | 5.6% | 2.4% | 3.6% | 5.2% |
| Charlson Comorbidity Index |  |  |  |  |  |  |  |  |  |
| 0 | 38.8% | 29.9% | 18.7% | 36.2% | 25.8% | 15.8% | 34.8% | 25.1% | 14.4% |
| 1 | 33.3% | 32.8% | 30.3% | 33.0% | 31.1% | 27.7% | 32.5% | 30.8% | 26.6% |
| 2 | 17.6% | 21.9% | 26.1% | 18.3% | 23.6% | 26.9% | 19.1% | 23.5% | 27.8% |
| ≥3 | 10.2% | 15.4% | 24.9% | 12.4% | 19.5% | 29.6% | 13.6% | 20.5% | 21.1% |
| Hospital bed size |  |  |  |  |  |  |  |  |  |
| Small | 7.3% | 6.6% | 6.6% | 7.6% | 7.5% | 7.5% | 10.3% | 9.8% | 9.6% |
| Medium | 19.4% | 20.7% | 21.4% | 23.8% | 24.8% | 23.3% | 26.4% | 27.1% | 26.7% |
| Large | 73.3% | 72.6% | 72.0% | 68.6% | 67.7% | 69.2% | 63.2% | 63.1% | 63.7% |
| Hospital Region |  |  |  |  |  |  |  |  |  |
| Northeast | 19.1% | 19.2% | 21.9% | 17.6% | 18.2% | 20.9% | 17.0% | 18.3% | 21.1% |
| Midwest | 21.9% | 18.5% | 17.6% | 23.4% | 20.9% | 19.8% | 24.9% | 23.7% | 22.6% |
| South | 41.8% | 47.5% | 47.1% | 41.6% | 45.6% | 46.7% | 40.7% | 43.6% | 43.7% |
| West | 17.2% | 14.7% | 13.4% | 17.4% | 15.3% | 12.6% | 17.4% | 14.4% | 12.6% |
| Location/ Teaching status |  |  |  |  |  |  |  |  |  |
| Rural | 7.3% | 6.7% | 5.9% | 6.2% | 5.6% | 5.3% | 6.4% | 6.3% | 5.2% |
| Urban-non teaching | 41.4% | 44.4% | 42.4% | 40.4% | 42.3% | 41.3% | 33.0% | 33.3% | 33.2% |
| Urban- teaching | 51.3% | 48.9% | 51.7% | 53.4% | 52.0% | 53.4% | 60.6% | 60.4% | 61.6% |
| Length of stay, Median (IQR) | 3 (2-5) | 4 (3-6) | 6 (5-10) | 2 (2-4) | 3 (3-6) | 6 (4-10) | 2 (2-4) | 3 (3-6) | 6 (4-10) |
| Total charge,$, Median (IQR) | 49564 (31416-81416) | 52157 (31902-86213) | 66233 (40732-112689) | 54826 (35027-89429) | 56866 (36117-92808) | 74067 (45924-125048) | 61279 (38541-99171) | 63391 (39589-102309) | 78990 (49389-132442 |

Table 3: Independent predictors of early coronary angiography

|  |  |  |
| --- | --- | --- |
| Variable  | Odd Ratio | 95% confidence interval  |
| Age | 0.98 | 0.98 | 0.98 |
| Weekend admission | 0.35 | 0.34 | 0.36 |
| Female | 0.92 | 0.91 | 0.94 |
| African American (Ref White) | 0.77 | 0.74 | 0.81 |
| Alcohol abuse | 0.81 | 0.77 | 0.85 |
| Chronic deficiency anaemia | 0.74 | 0.72 | 0.76 |
| Chronic blood loss | 0.61 | 0.56 | 0.66 |
| Congestive heart failure | 0.81 | 0.72 | 0.92 |
| Depression | 0.92 | 0.89 | 0.95 |
| Diabetes mellitus  | 0.86 | 0.84 | 0.87 |
| Diabetes mellitus with complications | 0.64 | 0.62 | 0.66 |
| Liver disease | 0.76 | 0.71 | 0.81 |
| Lymphoma | 0.79 | 0.71 | 0.88 |
| Metastatic cancer | 0.82 | 0.73 | 0.91 |
| Obesity  | 0.94 | 0.91 | 0.96 |
| Paralysis | 0.78 | 0.73 | 0.84 |
| Peripheral vascular disease | 0.90 | 0.88 | 0.92 |
| Renal failure | 0.61 | 0.60 | 0.63 |
| Cancer | 0.78 | 0.73 | 0.83 |
| Weight loss | 0.82 | 0.77 | 0.88 |
| Smoking | 1.15 | 1.12 | 1.17 |
| Dyslipidemia | 1.21 | 1.19 | 1.24 |
| Ischemic heart disease | 1.32 | 1.29 | 1.36 |
| Family history of coronary artery disease | 1.28 | 1.23 | 1.34 |
| Previous myocardial infarction  | 0.92 | 0.90 | 0.95 |
| Previous Cerebrovascular accident | 0.92 | 0.88 | 0.96 |
| Previous coronary artery bypass graft | 0.84 | 0.81 | 0.87 |
| Cardiogenic Shock | 1.45 | 1.37 | 1.54 |
| Intra-aortic balloon pump | 2.09 | 2.00 | 2.19 |
| Dementia | 0.84 | 0.80 | 0.87 |

Table 4: Association between timing of coronary angiography and clinical outcomes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Clinical outcome | Reference No Cath | Day=0,1 | Day=2 | Day≥3 |
| MACCE | 1.00 | 0.80 (0.77-0.83), p<0.001 | 0.66 (0.63-0.70), p<0.001 | 0.65 (0.62-0.78), p<0.001 |
| In hospital mortality | 1.00 | 0.39 (0.37-0.41), p<0.001 | 0.30 (0.28-0.33), p<0.001 | 0.33 (0.31-0.35), p<0.001 |
| In-hospital stroke | 1.00 | 0.86 (0.80-0.92), p<0.001 | 0.97 (0.93-1.02), p=0.8 | 1.19 (1.10-1.28), p<0.001 |
| Cardiac Complications | 1.00 | 4.71 (4.09-5.41),p<0.001  | 4.00 (3.47-4.61),p<0.001 | 3.49 (3.03-4.02), p<0.001 |
| Bleeding complications | 1.00 | 1.16 (1.11-1.22), p<0.001 | 1.15 (1.10-1.21), p<0.001 | 1.43 (1.37-1.49), p<0.001 |

Figure legends:

Figure 1: Flow diagram of included/excluded records

Figure 2: Temporal trends in time to coronary angiography stratified according early, intermediate and late

Figure 3: Trends in Timing of Coronary angiography stratified according to Gender

Figure 4: Temporal trends in time to coronary angiography and comorbidity burden as defined by Charlson comorbidity index

Figure 5: Trends in timing of coronary angiography stratified according to weekday versus weekend admission

Figure 6: Relationship between age and time to coronary angiography

Figure 7: Trends in timing of coronary angiography stratified according to Ethnicity

Figure 8: Crude outcomes stratified according to timing of Coronary angiography