National Trends and Outcomes of Percutaneous Coronary Intervention in Patients ≥ 70 Years of Age With Acute Coronary Syndrome (from the National Inpatient Sample Database)

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Several randomized trials have demonstrated the benefits of an invasive strategy for older patients with acute coronary syndromes (ACS); however, there are limited real-world data of the temporal trends in the use of percutaneous coronary intervention (PCI) in this population. This was a retrospective observational analysis. We queried the National Inpatient Sample database from 1998 to 2013 for patients aged ≥ 70 years who had non−ST-elevation acute coronary syndrome (NSTE-ACS) or ST-elevation myocardial infarction (STEMI). We reported the temporal trends of PCI and in-hospital mortality. A total of 6,720,281 hospitalizations with ACS were identified in advanced age patients, 18.3% of whom also underwent PCI. There was an upward trend in the rate of PCI in older adults ≥ 70 years with any ACS from 9.4% in 1998 to 28.3% in 2013 ($p < 0.001$), as well as in cases of PCI for NSTE-ACS (7.3% in 1998 vs 24.9% in 2013, $p < 0.001$) and PCI for STEMI (11% in 1998 vs 35.7% in 2013, $p = 0.002$). This upward trend was consistent in all age categories (70 to 79), (80 to 89) and ≥ 90 years. Despite an increase in the prevalence of comorbidities for ACS hospitalizations aged ≥ 70 years who received PCI, the in-hospital mortality rate showed a downward trend ($p < 0.001$). Multivariate analysis adjusting for various comorbidities showed that PCI was associated with lower in-hospital mortality and length of hospital stay among elderly with NSTE-ACS and STEMI. In conclusion, in this 16-year analysis there was an increase in the rate of PCI procedures among older adults with ACS. PCI was independently associated with lower mortality in elderly patients with ACS. **Published by Elsevier Inc. (Am J Cardiol 2019;123:25−32)**

The advancement of medical therapy and percutaneous coronary interventions (PCI) have reduced mortality rates in patients with acute coronary syndrome (ACS).[1,2] However, age remains a significant confounding factor that leads to reduced adherence to guideline-directed therapies and invasive strategies for stable Coronary Artery Disease (CAD) and ACS,[3] a pattern that is largely based on physicians' discretion.[4−6] Despite that, the risk of complications and mortality remain higher in older compared with younger population. A previous study demonstrated that the use of appropriate guideline-directed therapies in elderly patients has increased in the last 2 decades with no increase in the risk of in-hospital mortality despite an increase in the age and comorbidities of the included cohorts.[3] Another US population-based study (1991-2006) including patients > 75 years of age, suggested some improvement in the post-PCI outcomes over the study period despite a significant increase in their comorbidities.[7] Importantly, recent randomized trials have demonstrated the merit of an early invasive strategy in patients with non-ST-elevation ACS (NSTE-ACS) in this population.[8,9] Previous non−US-based cohorts have demonstrated beneficial outcomes with PCI in elderly with ACS;[3,10] however, no contemporary US cohorts have addressed the practice and outcomes of PCI for elderly with ACS. Thus, we aimed to examine the temporal use and outcomes of PCI in elderly with ACS using the largest inpatient database in the United States.

Methods

We analyzed data from the Nationwide Inpatient Sample (NIS) database, the largest publicly available all-payer inpatient care database in the United States.[11] This database contains over a 100 clinical and nonclinical data elements

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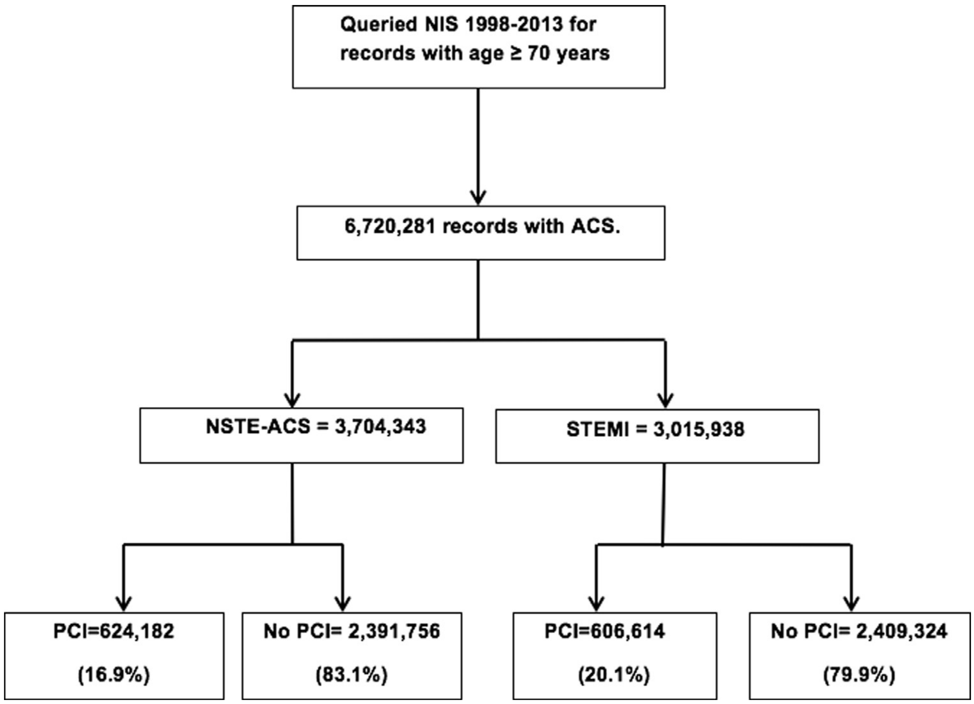

Figure 1. Study flow sheet. ACS = acute coronary syndrome; NSTE-ACS = Non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

from ~7 million unweighted hospital stays, representing roughly 20% of hospital admissions in the United States. Data from this database have been analyzed and used in different studies reporting trends and inpatient outcomes of disease.[12−14] This study was exempt from institutional review board evaluation, as the data used are de-identified and publicly available. We queried the NIS database from 1998 to 2013 to identify patients ≥70 years who have International Classification of Diseases, Ninth Edition diagnostic codes of non−ST-elevation myocardial infarction (NSTEMI), unstable angina or ST-elevation myocardial infarction (STEMI). For NSTEMI and unstable angina, we only used primary diagnostic codes to avoid patients with type 2 MI (Supplemental Table 1).[11,15] NSTE-ACS included cases with unstable angina or NSTEMI.

The aim of the study was to evaluate the temporal trends of PCI procedures performed in those ≥70 years with ACS, and was further stratified into NSTE-ACS or STEMI. We also analyzed in-hospital mortality and length of hospital stay. We excluded cases with missing data on our main outcomes of interest; in-hospital mortality, and length of hospital stay. In the cohort with NSTE-ACS and STEMI, multivariate analysis was conducted for in-hospital mortality and length of hospital stay, controlling for various baseline characteristics and comorbidities. The multivariate model included age, gender, race, congestive heart failure, hypertension, diabetes mellitus, renal failure, obesity, valvular heart disease, and anemia. Clinical characteristics and inpatient outcomes were reported using International Classification of Diseases, Ninth Edition codes, Clinical Classifications Software codes and Elixhauser comorbidities as reported by Healthcare Cost and Utilization Project (Supplemental Table 1). We described baseline characteristics and clinical outcomes according to 3 age groups (70 to 79, 80 to 89, and ≥90).

Statistical analyses were performed using SPSS Statistics 22. We analyzed data from the national estimates using the new trend weights provided by the NIS.[11,15] Categorical variables were reported as counts and percentage while continuous variables were reported as mean ± standard deviation or median and interquartile range depending on if they were normally distributed or not. Baseline characteristics were compared using chi-square test and the effect size was presented using phi coefficient. Outcome variables were compared using different techniques; logistic regression was used in case of in-hospital mortality and gamma regression with a logarithmic link was used in case of right skewed outcomes (length of stay). The effect size of in-hospital mortality and length of stay was quantified using hazard ratio (HR) and the incident rate ratios (IRR) respectively. To estimate the over-time changes during the period from 1998 to 2013, we used time series plots and interrupted time series regression models. We corrected the models for the serially auto-correlated nature of the observations. Time series analyses were performed in R 3.1.3[16] using the nlme package.[17]

Results

Over a 16-year period (1998 to 2013), we identified 6,724,005 hospitalizations aged ≥70 years who had a diagnosis of ACS. After excluding cases with missing data on mortality (3,201) and length of hospital stay (523), results yielded 6,720,281 hospitalizations. Among those 3,704,343 (55.1%) had NSTE-ACS and 3,015,938 (44.9%) had STEMI. PCI was performed in 1,230,796 (18.3%) of records with ACS: 624,182 (16.9%) of records with NSTE-

Table 1
Comparison of baseline characteristics among elderly ≥70 years with acute coronary syndrome who had percutaneous coronary intervention during the period from 1998 to 2013

	1998 to 2003 (N = 399,720)		2004 to 2007 (N = 324,976)		2008 to 2013 (N = 506,101)			
Baseline characteristics	n	%	n	%	n	%	*φ*	*p Value*
Female	188,268	(47.1%)	151,777	(46.7%)	223,752	(44.2%)	.03	(<.001)
Hypertension	230,239	(57.6%)	213,443	(65.7%)	379,439	(75.0%)	.14	(<.001)
Diabetes mellitus	92,335	(23.1%)	79,278	(24.4%)	144,703	(28.6%)	.05	(<.001)
Diabetes with complication	12,391	(3.1%)	10,653	(3.3%)	23,780	(4.7%)	.04	(<.001)
Congestive heart failure	42,370	(10.6%)	2,342	(0.7%)	3,511	(0.7%)	.25	(<.001)
Obesity*	1,599	(0.4%)	2,672	(0.8%)	8,409	(1.7%)	.05	(<.001)
Smoking	24,509	(6.0%)	24,955	(7.7%)	47,052	(9.3%)	.05	(<.001)
Chronic kidney disease	20,385	(5.1%)	34,633	(10.7%)	98,935	(19.6%)	.16	(<.001)
Chronic lung disease	70,351	(17.6%)	60,701	(18.7%)	97,564	(19.3%)	.01	(<.001)
Peripheral vascular disease	12,791	(3.2%)	36,947	(11.4%)	70,261	(13.9%)	.16	(<.001)
Anemia**	44,368	(11.1%)	43,248	(13.3%)	78,473	(15.5%)	.06	(<.001)
Valvular heart disease	362	(0.1%)	667	(0.2%)	975	(0.2%)	.00	(<.001)

ϕ Phi is used instead of chi-square value to show the strength of association.
* Obesity was defined as body mass index >30.
** Anemia was defined as hemoglobin of less than 13.5 g/dL in men and less than 12.0 g/dL in women.

ACS and 606,614 (20.1%) of those with STEMI. Study flow sheet is outlined in Figure 1. From 1998 to 2013, there was an increase in comorbidities' burden among elderly with ACS receiving PCI (Table 1). Baseline characteristics for records with NSTE-ACS and STEMI are outlined in Tables 2 and 3. PCI for elderly with ACS was more commonly performed in urban teaching hospitals (48%) compared with urban nonteaching (35%), rural (5%), and other unclassified hospitals (12%) ($p < 0.001$; Supplemental Figure 1).

The rate of PCI in hospitalizations with ACS aged ≥70 years was 9.4% in 1998 compared with 28.3% in 2013 with an annual increase of 1.6% (95% confidence interval [CI]: 1.4 to 2.0; $p < 0.001$) (Figure 2). A similar upward trend was observed among all age categories (70 to 79 years), (80 to 89 years), and ≥90 years ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively) (Supplemental Figure 2). Among patients with ACS aged ≥90 years, 0.2% were ≥100 years of age. In-hospital mortality among hospitalizations with ACS ≥70 years who underwent PCI was 62.4 per 1,000 PCI in 1998 compared with 46.9 per 1,000 PCI in 2013 with a significant downward trend ($p < 0.001$) (Figure 3; Table 4).

Among those aged ≥70 years with NSTEMI, 7.3% underwent PCI in 1998 compared with 24.9% in 2013 (Figure 4, panel A). During the period from 1998 to 2006,

Table 2
Baseline characteristics among elderly patients with non−ST-elevation acute coronary syndrome during the period from 1998 to 2013

	No PCI (N = 3,080,161,83%)		PCI (N = 624,182, 17%)		Comparison	
Baseline characteristics	n	%	n	%	ϕ	(p Value)
Female	1,641,844	(53.3%)	284,101	(45.5%)	−.06	(<.001)
Ethnicity						
White	2,040,527	(66.2%)	413,492	(66.2%)	.00	(.976)
Black	190,782	(6.2%)	28,516	(4.6%)	−.03	(<.001)
Hispanic	153,315	(5.0%)	28,882	(4.6%)	−.01	(<.001)
Asian Pacific Islander	48,882	(1.6%)	8,380	(1.3%)	−.01	(<.001)
Others	61,694	(2.0%)	17,327	(2.8%)	.02	(<.001)
Hypertension	1,463,012	(47.5%)	383,564	(61.5%)	.05	(<.001)
Diabetes mellitus	622,292	(20.2%)	153,966	(24.7%)	.01	(<.001)
Congestive heart failure	33,100	(1.1%)	8,449	(1.4%)	.003	(<.001)
Obesity*	116,131	(3.8%)	39,187	(6.3%)	.04	(<.001)
Smoking	134,398	(4.4%)	43,767	(7.0%)	.05	(<.001)
Chronic kidney disease	500,939	(16.3%)	92,672	(14.8%)	−.05	(<.001)
Chronic lung disease	554,025	(18.0%)	108,022	(17.3%)	−.04	(<.001)
Peripheral vascular disease	296,392	(9.6%)	75,487	(12.1%)	.03	(<.001)
Anemia**	594,550	(19.3%)	90,328	(14.5%)	−.05	(<.001)
Valvular heart disease	10,569	(0.3%)	240	(0.1%)	−.03	(<.001)

ϕ Phi is used instead of chi-square value to show the strength of association.
* Obesity was defined as body mass index >30.
** Anemia was defined as hemoglobin of less than 13.5 g/dL in men and less than 12.0 g/dL in women.
PCI = percutaneous coronary intervention.

Table 3
Comparison of baseline characteristics among elderly patients with ST-elevation acute myocardial infarction during the period from 1998 to 2013

	No PCI (N = 2,409,324;80%)		PCI (N = 606,614; 20%)		Comparison	
Baseline characteristics	n	%	n	%	ф	(p Value)
Female	1,311,638	(54.4%)	279,597	(46.1%)	−.067	(< .001)
Ethnicity						
White	1,573,642	(65.3%)	398,082	(65.6%)	.003	(< .001)
Black	117,780	(4.9%)	21,134	(3.5%)	−.027	(< .001)
Hispanic	92,355	(3.8%)	25,147	(4.1%)	.006	(< .001)
Asian Pacific Islander	36,180	(1.5%)	8,539	(1.4%)	−.003	(< .001)
Others	41,202	(1.7%)	15,912	(2.6%)	.027	(< .001)
Hypertension	820,408	(34.1%)	293,153	(48.3%)	.070	(< .001)
Diabetes mellitus	348,936	(14.5%)	102,795	(16.9%)	−.014	(< .001)
Congestive heart failure	229,412	(9.5%)	13,130	(2.2%)	−.165	(< .001)
Obesity*	14,637	(0.6%)	4,548	(0.7%)	.007	(< .001)
Smoking	88,331	(3.7%)	52,748	(8.7%)	.095	(< .001)
Chronic kidney disease	244,999	(10.2%)	47,773	(7.9%)	−.075	(< .001)
Chronic lung disease	335,416	(13.9%)	75,929	(12.5%)	−.066	(< .001)
Peripheral vascular disease	151,169	(6.3%)	44,722	(7.4%)	.018	(< .001)
Anemia**	409,680	(17.0%)	73,673	(12.1%)	−.053	(< .001)
Valvular heart disease	66,164	(2.7%)	1,664	(0.3%)	−.096	(< .001)

ф Phi is used instead of chi-square value to show the strength of association.
* Obesity was defined as body mass index > 30.
** Anemia was defined as hemoglobin of less than 13.5 g/dL in men and less than 12.0 g/dL in women.
PCI = percutaneous coronary intervention.

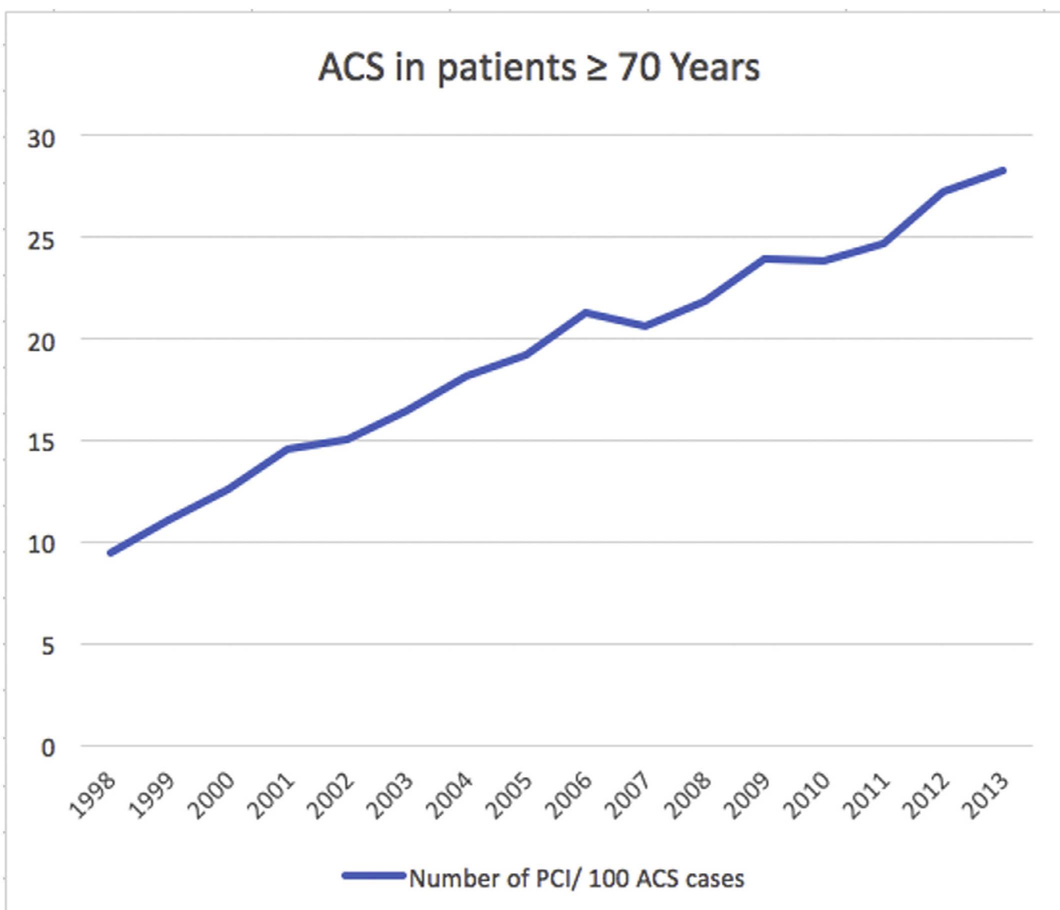

Figure 2. Temporal trends in the rate of PCI procedures for elderly with ACS ≥ 70 years; ACS = acute coronary syndrome; PCI = percutaneous coronary intervention.

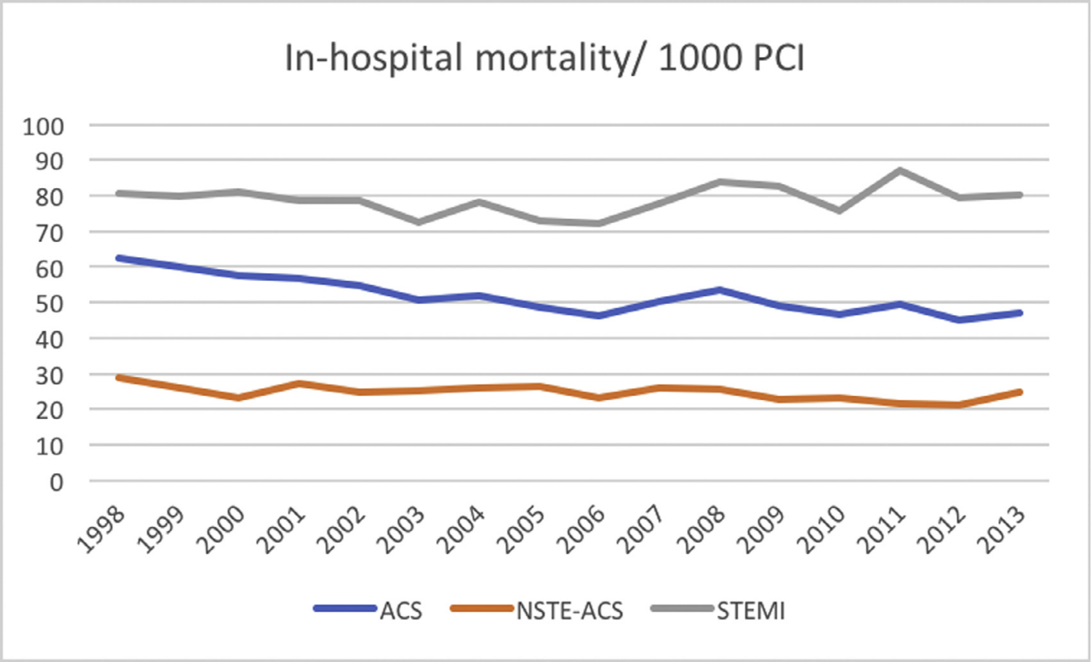

Figure 3. Temporal trends in in-hospital mortality for elderly with ACS, NSTE-ACS, and STEMI of age ≥70 years who underwent PCI. ACS = acute coronary syndrome; NSTE-ACS = Non−ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

there was an annual increase of 1.6% (95% CI: 1.4 to 1.7; $p < 0.001$) in the incidence rate of PCI. While, during the period from 2006 to 2013, there was a slower annual increase of 1.0% (95% CI: 1.01 to 1.2; $p < 0.001$) in the trend of PCI. Similar trends were observed in all age categories (70 to 79 years), (80 to 89 years), and ≥90 years (Supplemental Table 2). In-hospital mortality among those with NSTE-ACS ≥70 years who underwent PCI was 28.7 per 1,000 PCI in 1998, compared with 24.7 per 1,000 PCI in 2013 with a significant downwards trend ($p = 0.007$; Figure 3). Multivariate analysis showed that those with NSTE-ACS aged ≥70 who underwent PCI were associated with lower in-hospital mortality (2.4% vs 7.1%; HR = 0.474; 95% CI: 0.455 to 0.494; $p < 0.001$) and shorter median length of hospital stay (3 vs 4 days; IRR = 0.829; 95% CI: 0.827 to 0.831; $p < 0.001$) compared with those who did not undergo PCI.

Among hospitalizations with STEMI aged ≥70 years, 11% underwent PCI in 1998 compared with 35.7% in 2013 with an upward trend of 1.3% (95% CI: 1.1 to 1.5; $p = 0.002$) that increased after 2006 (trend change = 0.6%; 95% CI: 0.3 to 0.9; $p = 0.002$; Figure 4, panel B). Similar trends were also reproducible in different age categories (Supplemental Table 3). In-hospital mortality among those with STEMI ≥70 years who underwent PCI was 80.6 per 1,000 PCI in 1998, compared with 80.1 per 1,000 PCI in 2013 with nonsignificant change of trend ($p = 0.499$; Figure 3). Multivariate analysis showed that PCI in records with STEMI aged ≥70 was associated with lower mortality (7.9% vs 23.5%; HR = 0.439; 95% CI: 0.428 to 0.450; $p < 0.001$) and shorter hospital stay (4 vs 5 days; IRR = 0.744; 95% CI: 0.742 to 0.746; $p < 0.001$).

Discussion

In this observational nationwide analysis including 6,720,281 hospitalizations, we describe the national trends and outcomes of PCI in the elderly with ACS. From 1998 to 2013, our analysis showed an upward trend in the rate of PCI among elderly ≥70 years with any ACS, as well as in cases of NSTE-ACS and STEMI. This upward trend was consistent in all age categories (70 to 79), (80 to 89), and ≥90 years. Also, there was an increase in the comorbidities burden along the study years in elderly with ACS who

Table 4
Rate of percutaneous coronary intervention and in-hospital mortality in acute coronary syndrome patients aged ≥70 years

Year	PCI cases (70 to 79 years)	In-hospital mortality (70 to 79 years)*	PCI cases (80 to 89 years)	In-hospital mortality (80 to 89 years)*	PCI cases (≥90 years)	In-hospital mortality (≥90 years)*
1998 to 2001	169,801	47.7	71,204	81.8	4,168	116.4
2002 to 2005	202,266	42.2	105,868	65.4	8,259	98.0
2006 to 2009	200,875	39.9	118,753	61.8	11,669	96.4
2010 to 2013	204,195	35.9	118,302	60.5	14,802	90.4

PCI = percutaneous coronary intervention.
* rate per 1,000 PCI case.

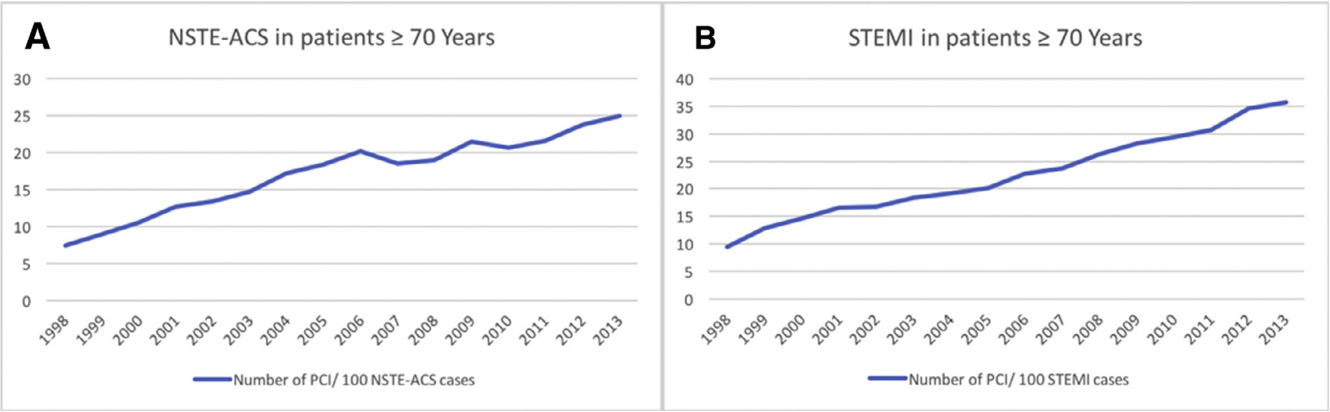

Figure 4. Panel A: temporal trends in the rate of PCI procedures for elderly ≥70 years with NSTE-ACS. Panel B: temporal trends in rate of PCI procedures for elderly ≥70 years with STEMI. NSTE-ACS = Non−ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

received PCI. In-hospital mortality rate decreased among the overall hospitalizations for ACS aged ≥70 years who received PCI as well in cases of NSTE-ACS ≥70 years who received PCI. In hospitalizations for STEMI ≥70 years who received PCI no change in the rate of in-hospital mortality was observed. Adjusted analysis showed that cases with NSTE-ACS or STEMI of age ≥70 who received PCI were associated with lower in-hospital mortality and shorter length of stay.

Many concerns exist regarding the utility of PCI in elderly patients with CAD. As part of the aging process, coronary arteries in elderly tend to have more calcifications, dilatation, and tortuosity.[18,19] Elderly have higher associated comorbidities, and are more prone to peri-procedural complications including renal failure and bleeding.[18,20] As a result, older patients with CAD are associated with higher morbidity, mortality, and functional decline compared with their younger counterparts.[6,18] Adherence to guidelines-recommended treatment is associated with reduced morbidity and mortality for patients with CAD.[3] Many studies suggest that older patients with CAD are suboptimally treated with guidelines-recommended therapies, including PCI.[21]

Our analysis showed an increase in the rate of PCI in NSTE-ACS for those aged ≥70 years, with a concomitant decrease in in-hospital mortality rate. The observed increase in PCI rate is consistent with previous studies.[1,3] A multicenter study in Switzerland conducted by Schoenenberger et al on 13,662 patients aged ≥70 years with ACS showed an upward trend in the use of PCI between 2001 and 2012.[3] In the present study, adjusted analysis showed a reduction in in-hospital mortality and length of stay among those with NSTE-ACS aged ≥70 who underwent PCI. A recent randomized trial showed that in patients aged ≥80 with NSTE-ACS, early invasive approach was superior to conservative treatment in the composite outcome of myocardial infarction, need for urgent revascularization, stroke, and death. Other studies have demonstrated similar results for superiority of early invasive approach for broad population of NSTE-ACS patients including the elderly,[4,9,10] which is supported by major societies' guidelines for NSTE-ACS.[22]

A similar upward trend in PCI rate was also demonstrated in hospitalizations with STEMI aged ≥70 years. However, there was no change in the trend of in-hospital mortality during the study period. Globally, multiple studies have reported an upward trend in primary PCI in elderly patients with STEMI.[23−25] A multicenter study in the United Kingdom conducted from 2005 to 2011 reported an increase in primary PCI in octogenarians presenting with STEMI, with no change in in-hospital mortality rates.[25] Also, data from Swedish Coronary Angiography and Angioplasty Registry showed an upward trend in primary PCI in patients ≥ 80 years from 2001 to 2010.[23] Our adjusted analysis also showed a lower in-hospital mortality and length of stay in hospitalizations of age ≥70 years with STEMI who underwent PCI compared with those who did not.

This current analysis is the first contemporary analysis for trends and outcomes of PCI in the elderly with ACS in the United States. During the 16-year study period, guidelines have evolved, and recommendations have been stronger toward no age discrimination when deciding on invasive management.[26,27] Our analysis showed an increase in the rate of PCI procedures in the elderly with ACS during the study years. The increase in PCI numbers for ACS might be related to evolution of new interventional therapeutics as well as increased comfort and experience with PCI in the elderly. However, the magnitude of such increase in the PCI numbers did not meet the recommendations of the current guidelines for appropriate practice. Our analysis showed that the higher proportion of elderly with ACS is conservatively treated. Specifically, the rates of PCI in elderly with STEMI (20.1%) were discordant with the consecutive clinical evidence and practice guidelines. This study supports previous reports that adherence to guidelines therapy is suboptimal in the elderly population.[4,10] Our study also showed that PCI was independently associated with lower mortality in elderly with NSTE-ACS and STEMI.

The NIS is a time-discrete administrative database, where patients' data are related to a certain hospitalization period. As with any administrative dataset, there can be potential coding errors and incomplete or missing documentation. In attempts to mitigate potential errors, multiple internal and external quality control measures are conducted to validate the NIS. Many useful data for our study could not be retrieved, that include clinical variables, medications information, laboratory data, and long-term outcomes. Also, other factors which might affect the decision to perform PCI such as bleeding diathesis and other cardiac imaging results are not included in the NIS database. Despite the robust analysis and adjusting for variable risk factors, presence of unmeasured confounders is possible given the observational nature of this analysis. Data on transferred patients were not available, which may have underestimated the prevalence of PCI. Despite these limitations, this study fills the current gap in literature regarding the true volume and outcomes of PCI in the elderly in the United States.

Declaration of Interest

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.amjcard.2018.09.030.

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