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Temporal trends in the use of intra-aortic balloon pump associated with percutaneous coronary intervention in the United States, 1998–2008

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Abstract

Background—With conflicting evidence regarding the usefulness of intra-aortic balloon pump (IABP), reports of IABP use in the United States (US) have been inconsistent. Our objective was to examine trends in IABP usage in percutaneous coronary intervention (PCI) in the US, and to evaluate the association of IABP use with mortality.

Methods—Retrospective, observational study using patient data obtained from the Nationwide Inpatient Sample (NIS) database from 1998 to 2008. Patients undergoing any PCI (1,552,602 procedures) for a primary diagnosis of symptomatic coronary artery disease (CAD) and acute coronary syndrome (ACS), including non-ST elevation MI (NSTEMI) and ST elevation MI (STEMI), were evaluated.

Results—The overall use of IABP significantly decreased during the study period from 0.99% in 1998 to 0.36% in 2008 (univariate and multivariate p for trend <.0001). Patients who received IABP had substantially higher rates of shock compared to those who did not receive IABP (38.09% vs. 0.70%, p<.0001), which was associated with markedly higher in-hospital mortality rates (20.31% vs. 0.72%, p<.0001). However, IABP use significantly decreased in patients with shock (36.5% to 13.4%) and AMI (2.23% to 0.84%) (univariate and multivariate p for trend for both <.0001). A temporal reduction in all-cause PCI-associated mortality from 1.1% in 1998 to 0.86% in 2008 (univariate and multivariate p for trend <.0001) was also observed.

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Conclusions—The utilization of IABP associated with PCI significantly decreased between 1998 and 2008 in the US, even amongst patients with acute myocardial infarction and shock.

INTRODUCTION

Intra-aortic balloon pump (IABP) first became available in the 1960s for hemodynamic support in patients with cardiogenic shock resulting from acute myocardial infarction (AMI).[1] It increases coronary perfusion by inflating during diastole, and reduces afterload and decreases myocardial oxygen demand by deflating during systole. This unique mechanism enables IABP to serve as a viable hemodynamic support option in unstable patients. In the 1996 American College of Cardiology/American Heart Association (ACC/AHA) guidelines, IABP support was given a Class I recommendation for the management of shock in AMI.[2] However, due to the emergence of conflicting evidence on the usefulness of IABP, the 2013 ACC/AHA Guidelines have given IABP a Class IIb recommendation (level of evidence C) in patients with unstable angina (UA)/non-ST elevation myocardial infarction (NSTEMI) complicated with hemodynamic instability,[3] and a Class IIa (level of evidence B) for patients with cardiogenic shock after ST-elevation myocardial infarction (STEMI).[4] The 2012 European Society of Cardiology AMI Guidelines do not recommend routine IABP use in absence of shock.[5]

Much has been investigated regarding its mechanism, technique of insertion, indications, complications, and mortality benefit. However, data on current patterns of IABP use in the United States (US) are lacking. Reports from multiple centers have suggested inconsistency in its utilization in the US[6–9] and non-US centers.[10] The purpose of our study is to determine the trend of IABP utilization in the US from 1998 to 2008.

METHODS

Data Source

We analyzed data provided by The Healthcare Cost and Utilization Project (HCUP),[11] which is a family of health care databases that has been gathering a large collection of longitudinal hospital care data in the US beginning in 1988. The HCUP databases combine the data collection efforts of state data organizations, hospital associations, private data organizations, and Federal government to create a national pool of patient-level health care data, allowing researchers to investigate on a broad range of healthcare related issues.[12]

Study Patients

We examined a cohort of patients between 1998 and 2008. A total of 1,552,602 patients undergoing percutaneous coronary intervention (PCI) procedures for symptomatic coronary artery disease (CAD) and acute coronary syndrome (ACS), including NSTEMI and STEMI were identified (Figure 1). Additional patient data collected were procedure year, age, race, gender, in-hospital mortality, cost, length of stay, hypertension, AMI, CAD, congestive heart failure (CHF), transient cerebral ischemia, peripheral atherosclerosis (PVD), aortic/peripheral/visceral artery aneurysm/embolism/thrombosis, any malignancy, chronic obstructive pulmonary disease (COPD)/bronchiectasis, systemic lupus erythematosus/connective tissue disease, cardiac and circulatory congenital anomalies, shock, diabetes

mellitus (DM), coagulation and hemorrhagic disorders, heart valve disorders, peri-/endo-/myocarditis, pulmonary heart disease, chronic renal failure (CRF), hemorrhagic cerebrovascular disease (CVD), ischemic CVD, acute CVD, other CVD, disorders of lipid metabolism, anemia, prior and current tobacco use, atrial fibrillation/flutter, placement of drug-eluting stent and bare-metal stent, coronary artery bypass grafting (CABG) and percutaneous and surgical ventricular assist device placement (VAD).

Primary analysis

The primary analysis was to assess the trend of IABP use in the US over the study period, and to evaluate the association of IABP use with mortality.

Secondary analysis

The secondary analysis was to examine the trend in mortality with PCI and to determine patient characteristics associated with both IABP placement and mortality.

Statistical analyses

The study population was separated into two groups - those with IABP and those without IABP. The summary statistics on the baseline patient characteristics were generated for the entire population separated into the aforementioned groups, as well as for the subpopulations stratified by the year.

Univariate analysis was initially conducted to summarize the data. Continuous data are presented as mean +/− SD, and the nonparametric Wilcoxon rank sum tests were used to test for all continuous variables. Categorical variables are presented as category percentages and the Pearson Chi-square tests were used for test for categorical variables. All tests were two-tailed, and a P-value of less than .05 was considered significant for all tests.

The multivariate logistic regressions were fit to the data to evaluate IABP trend over the study period. Wald test with a .05 level of significance was used to test the null hypothesis of no trend. The logistic regression model was then used to assess independent predictors of IABP after adjusting for the observed baseline demographic and clinical characteristics. The logistic regression model was also used to investigate the trends for incidence of in-hospital mortality with and without IABP, as well as to assess the trends for the adjusted and unadjusted OR for the association between death and IABP over the study period.

We used a two-step propensity score method to evaluate the effect of IABP use on the mortality rate – first by estimating propensity scores using a logistic regression model with IABP as the outcome, then estimating the effect of IABP on mortality rate using the method of regression adjustment. All of our variables were accounted for. Advantage of this two-step procedure is that it allows for fitting a complicated propensity score model with interactions and higher order terms for more accurate estimation of IABP probability.[13] Fisher's Z test was used to perform the correlation test between trends in IABP use and mortality rates.

The missing data were omitted as follows: in the "No IABP group" (n=1,544,312), age (n=36, 0.002%), death (n=330, 0.02%), female sex (n=137, 0.009%), length of stay (n=21,

0.001%), mean financial cost (n=20,729, 1.3%), and race (n=419,760, 27.2%); in the "IABP" group (n=8,290), death (n=5, 0.06%), female gender (n=1, 0.01%), mean financial cost (n=211, 1.6%), and race (n=3,672, 27.3%).

All analyses were performed using SAS statistical software version 9.2 (SAS Institute Inc. Cary, NC).

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RESULTS

Trends and patterns in IABP use

The overall IABP use in the US decreased significantly during the study period from 0.99% in 1998 to 0.36% in 2008 (univariate and multivariate p for trend <.0001; Figure 2). The patients' baseline characteristics are presented in Table I. The patients who received an IABP did not differ in age or gender compared to the non-IABP group. Compared to the non-IABP group, the IABP group appeared acutely ill with substantially higher percentages of CHF (39.4% vs. 11.1%, p<.0001), AMI (84.6% vs. 34.2%, p<.0001), and shock (38.1% vs. 0.70%, p<.0001) (Table I). 10% were subsequently referred for CABG in the IABP group, compared to 0.1% in the other. The non-IABP group appeared to have a higher prevalence of chronic medical issues, such as DM, HTN, CAD, lipid disorders, and tobacco use. IABP placement was also associated with markedly higher mortality rates (20.3% vs. 0.72%, p<.0001), longer mean hospital stays (8.4 vs. 2.8 days, p<.0001), and higher mean financial hospital charges ($86,061 vs. $39,866 p<.0001) (Table I). Significant patient characteristics associated with IABP placement included shock (OR 22.6; 95% CI 21.1–24.2; p<.0001), AMI (OR 5.20; 95% CI 4.82–5.60; p<.0001), CHF (OR 2.02; 95% CI 1.89–2.16; p<.0001), and CAD (OR 1.77; 95% CI 1.61–1.95; p<.0001) (Figure 3).

Trends of IABP use in shock and AMI

There was a slight, but statically significant, increase in the percentage of patients with shock (0.88% in 1998 vs. 1.19% in 2008, univariate and multivariate p for trend <.0001) and AMI (35.5% in 1998 vs. 38.9% in 2008, univariate and multivariate p for trend <.0001) during the study period. However, the use of IABP in shock and AMI decreased. In 1998, 36.5% of patients presenting with shock were supported with IABP, which decreased to 13.4% in 2008 (univariate and multivariate p for trend <.0001; Figure 4a). The usage of IABP in patients with AMI declined from 2.23% in 1998 to 0.84% in 2008 (univariate and multivariate p for trend <.0001; Figure 4b).

All-cause mortality in PCI

The all-cause trend in PCI-associated mortality decreased over the study period from 1.1% in 1998 to 0.86% in 2008 (univariate and multivariate p for trend <.0001; Figure 5.) Patient characteristics associated with mortality included advanced age (70–80 years old; OR 3.45; 95% CI 3.06–3.88; p<.0001; >80 years old; OR 6.07; 95% CI 5.38–6.85; p<.0001), diagnosis of AMI (OR 5.13; 95% CI 4.84–5.44; p<.0001), shock (OR 13.4; 95% CI 12.6–14.3; p<.0001), hemorrhagic CVD (OR 10.8; 95% CI 9.68–11.9; p<.0001) and acute CVD (OR 25.6; 95% CI 21.9–29.8; p<.0001; Figure 6).

Death and IABP use associated with PCI

Patients with IABP had a higher mortality rate (20.3% vs. 0.72; p <.0001) (Table I). Patients who received balloon pump intervention in 1998 had a mortality rate of 22.8%, which down-trended to 17.8% in 2008 (Figure 5). When testing the overall association between IABP and mortality, patients were nearly three times more likely to die with an IABP (adjusted p<.0001; Table II). In 1998, patients were five times more likely to die with IABP intervention after adjusting for variables. However, in 2008, odds ratio for death with IABP was 2.14 (p for trend <.0001). The association between IABP and death remained statistically significant for each individual year. (Table II). Using the Fischer Z test to examine a correlation between the decline in both IABP use and mortality demonstrated a significant correlation between the two trends (adjusted p<.0001). Patients who had an IABP placed and died were more likely to be female, and have acute CVD, shock, AMI, CHF, CRF, COPD, PVD, and atrial fibrillation.

CABG and VAD in PCI

There were 1,777 patients with CABG in the no IABP group, and 892 patients in the IABP group (0.12% vs. 10.8%, Table I). Significant predictors for CABG included: AMI (OR 2.67; 95% CI 2.38–3.00; p<.0001), CAD (OR 2.94; 95% CI 2.31–3.74; p<.0001), and IABP use (OR 44.5; 95% CI 38.6–51.4 p<.0001) (See Figure 1 in supplemental files). Patients who underwent CABG were also less likely to die after adjusting for all variables (OR 0.28; 95% CI 0.21–0.38; p<.0001). The overall utilization of VAD's in PCI was fairly low, 113 out of 1,556,602 patients undergoing PCI (Table I). The use of VAD in PCI was associated with higher mortality (OR: 3.63; 95% CI 1.85–7.09; p=0.0002, Figure 6).

DISCUSSION

Through time, with advances in device technology, insertion technique from surgical to percutaneous, and increasing operator experience, IABP has been successfully employed in a wide variety of clinical settings. Although still globally used in patients with shock, accumulating data from studies have demonstrated variable results in overall use and its impact on patient mortality. To date, there have been no consistent reports on IABP use in the US. In this large and representative dataset, we observed a marked reduction in IABP usage in the US between 1998 and 2008, even among patients with shock.

After its introduction, there appeared to be an increase in IABP usage based on literature supporting a mortality benefit with initial reports of it being used in patients undergoing

coronary artery bypass grafting (CABG) pre-operatively.[14,15] Additionally, the GUSTO-1 trial demonstrated that the use of IABP was also associated with improved mortality when introduced in patients with shock treated with thrombolysis.[16] This mortality benefit was further validated by other studies, including the SHOCK and TACTICS trials.[16–19] The results of these studies, along with the potential protective effects of balloon pumping in high-risk patients,[20] a subsequent initial increase in IABP utilization at multiple centers in the United States and worldwide was noted.[6,14,21,22] However, increased utilization rates were not consistent at every center.[23] While some studies have indicated an increase in the use of IABP during our study period,[24,25] we observed the contrary, which can in part be explained by smaller sample size and limited datasets previously reported in other studies. Also, patient selection based on procedure undertaken (high-risk PCI vs. all-comer PCI) and our study period spanning greater than a decade could have potentially contributed to the differences reported.

Shock is a well-known indication for IABP consideration. However, with rates of PCI increasing steadily from as early as mid-1980s based on evidence showing improved outcomes,[26–28] there has been a decreasing trend in shock complicating AMI.[25,29–31]. Although our results demonstrated a numerically small, but significant, increase in the rates of shock and AMI, it is important to note that this was in relation to the proportion of patients who underwent PCI, and does not represent the overall incidence of shock and AMI in the US.

Examination of mortality benefit using IABP continues to be an area of investigation. Studies over the past 15 years have failed to prove a net mortality benefit when IABP is used in PCI.[32–38] Based on these studies, it is apparent there is conflicting published evidence for IABP use, with some suggesting no mortality benefit while others supporting the contrary. The growing evidence demonstrating limited mortality benefit that IABP can offer, may have contributed, at least in part, to the observed decrease in IABP utilization.

Consistent with other studies,[25,39] our study further confirms a temporal reduction in the rates in PCI-associated mortality. The mortality rates that were observed with balloon pump use are comparable to other studies,[40,41] and independent predictors for mortality - AMI, shock, hemorrhagic and acute CVD and increasing age[42,43] - are also congruous with previously published information.[29] When tested for likelihood of mortality with IABP and predictors for mortality in patients presenting for PCI, patients with shock tend to have higher mortality rates, which is backed by prior literature demonstrating high mortality rates in shock with or without IABP support.[29,31,42] A group of patients underwent CABG during the same hospitalization. A proportion of these patients who underwent CABG in the IABP group were likely referred for urgent/emergent CABG based on the higher rates of acute MI and shock observed in this group. It appears that in this select group of patients there appeared to be a mortality benefit. These findings need to be interpreted with great caution given likely significant selection bias and lack of detail about CABG procedures and indications in the NIS dataset.

There was a significant association between IABP use and mortality for each year during our study period. Although our results demonstrated a statistically significant association

between the decline in mortality and decreasing IABP use, it is critical to stress the importance that our results do not infer any causation between mortality and IABP use. Being an observational study, we are unable to establish causation between the declining IABP and mortality trends. Unexplained procedures, unaddressed confounders, differences in practice patterns, and other elements likely confounded the correlation observed. Although there was a slight increase in the overall percentage of shock and AMI, IABP application in this cohort of patients declined, with a striking decline in patients with shock. Based on these observations, perhaps IABP is being reserved for critically ill patients who require any potentially life-saving measure and, as such, is associated with a patient population in whom high mortality rates may be inevitable.

STUDY LIMITATIONS

There are several important limitations to our analysis. This is a retrospective analysis of registry data with the limitations inherent to such analyses, which precludes us from confirming causation between the trends in the utilization of IABP to mortality. The NIS database does not allow for evaluation of practice patterns, which can affect observed IABP usage. Participation in the NIS registry is voluntary and data obtained are from selected centers that participated in the registry. The NIS registry may include hospitals with a varying likelihood of following evidence-based recommendations. Therefore, the results may not be generalized to other US hospitals that were not a part of the registry. Despite multivariable adjustment, we cannot exclude the possibility that residual measured and unmeasured confounding variables might account for the observed differences. Data quality is dependent upon the accuracy and completeness of documentation and abstraction. We cannot eliminate the potential confounding introduced by over- or under-coding. Although we adjusted for multiple baseline differences, selection bias affecting physician decision-making and IABP placement decisions may influence our findings. Our results only present IABP usage associated with PCI, and do not represent overall rates of IABP usage and mortality. This study only observed in-hospital mortality. Therefore, rates and trends of out-of-hospital mortality were not accounted for and not included in this study.

CONCLUSION

IABP has traditionally been the most commonly used mechanical assist device in AMI patients complicated by shock. However, clinicians appear to be using it less in this clinical setting. Aims toward early revascularization, improvements in management of AMI from the time of symptom onset to cardiac catheterization laboratory intervention, and better primary and secondary prevention may have contributed to the downward trend in in-hospital mortality rates in PCI we observed in our study. Perhaps the evolution in the treatment of ACS and the growing evidence of limited mortality benefit with balloon pumps have played some role in the decline of IABP utilization that was observed in this study.

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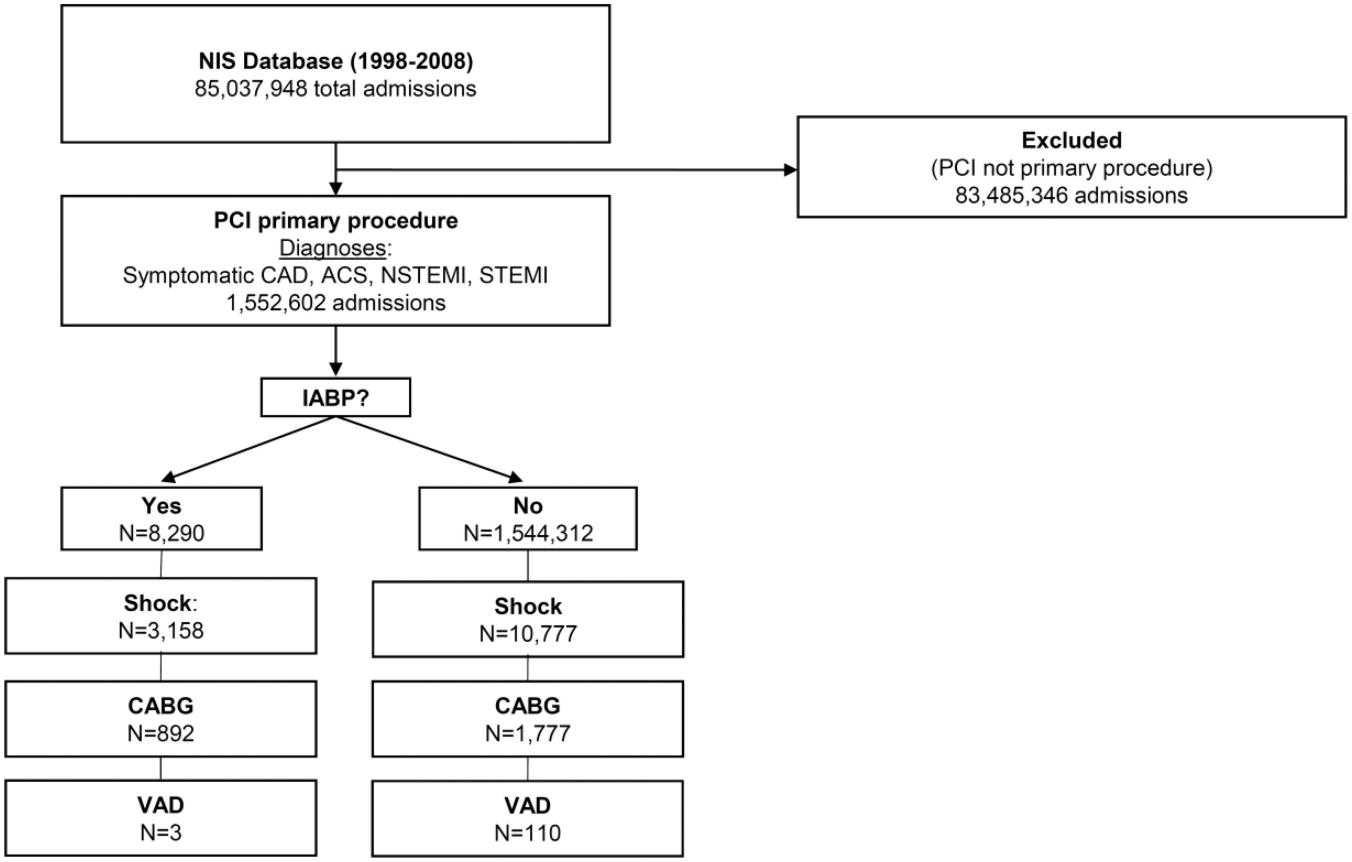


Figure 1.

Flow Diagram of study patients

NIS, Nationwide Inpatient Sample; PCI, percutaneous coronary intervention; CAD, coronary artery disease; ACS, acute coronary syndrome; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; IABP, intraaortic balloon pump; CABG, coronary artery bypass graft; VAD, ventricular assist device

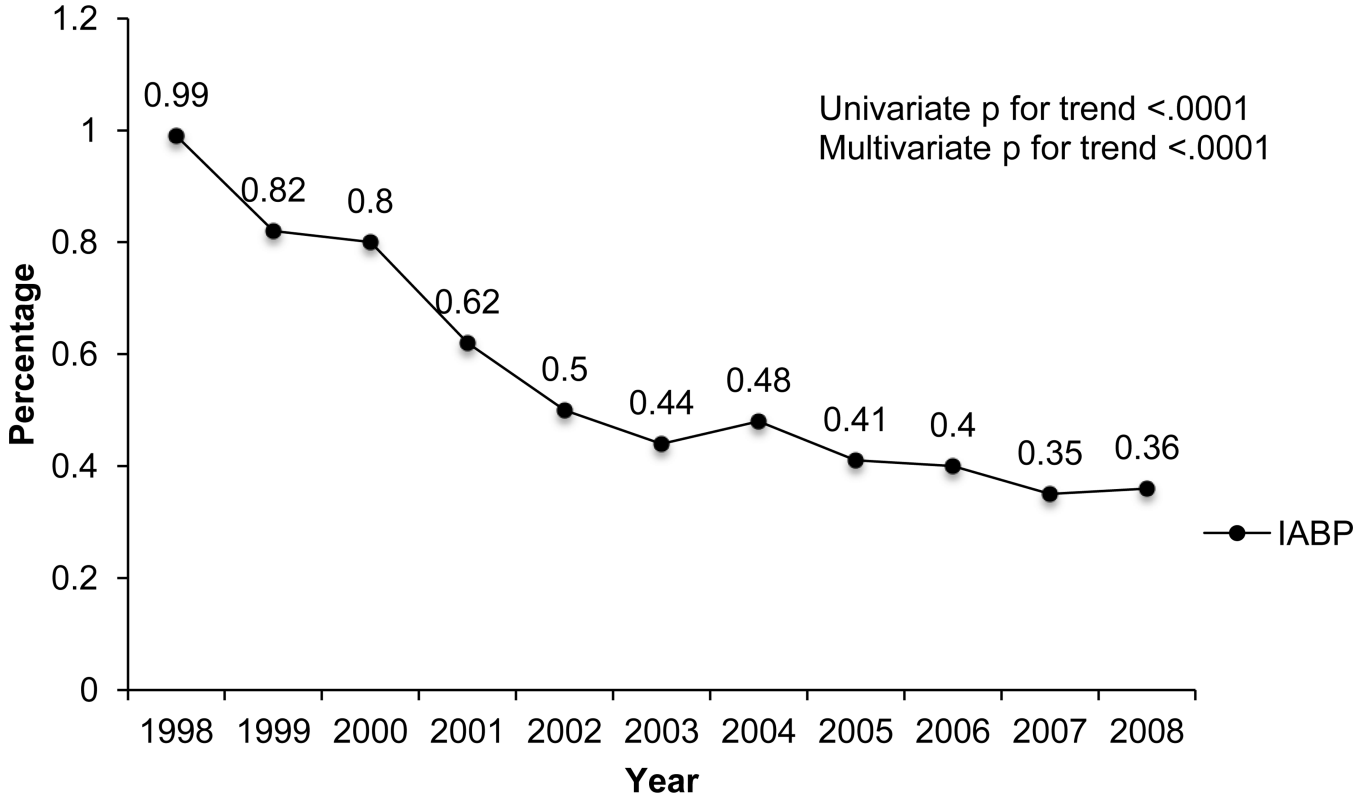


Figure 2.
Trend in overall IABP use in PCI from 1998–2008.
IABP, intraaortic balloon pump

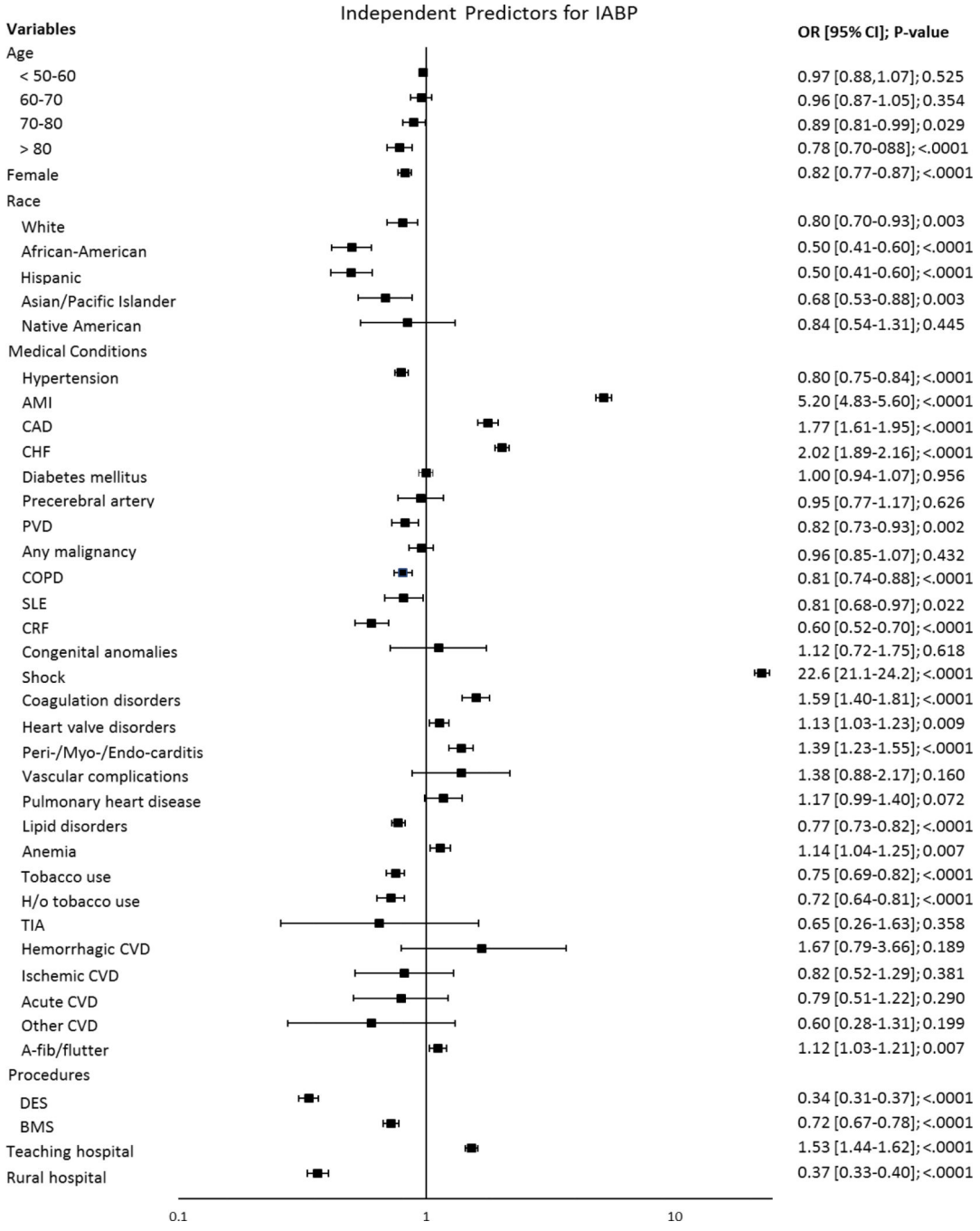
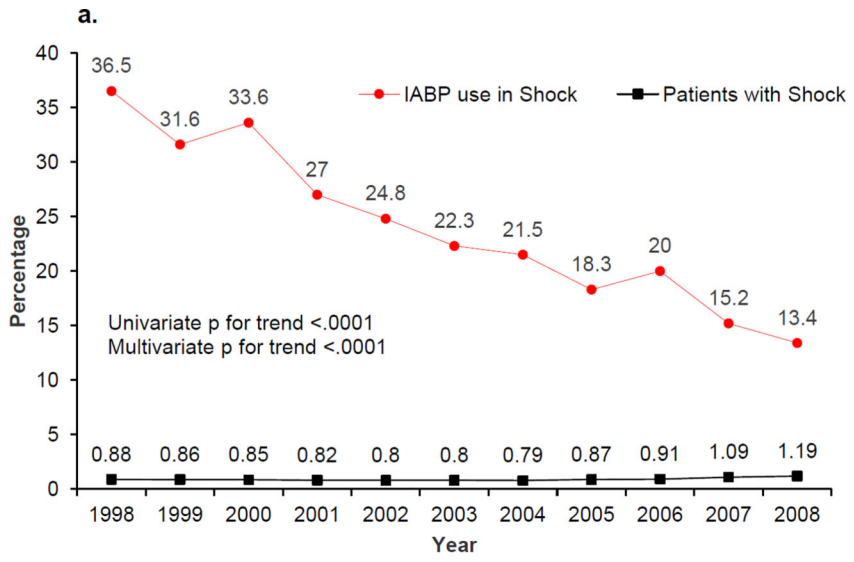


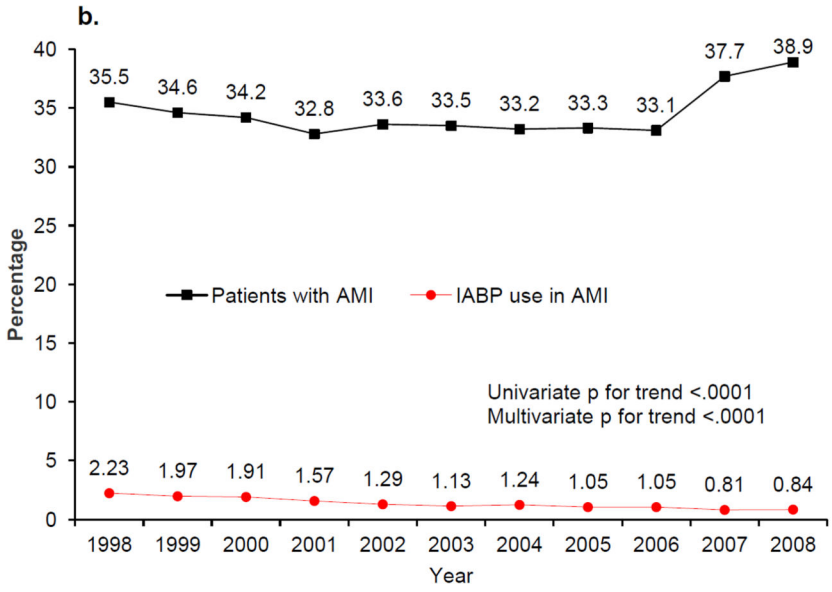
Figure 3.

Independent predictors for IABP placement in PCI.

AMI indicates acute myocardial infarction; CAD, coronary artery disease; CHF, congestive heart failure; TIA, transient ischemic attack; PVD, peripheral vascular disease; A/V/P, Aortic/peripheral/visceral; COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus; CVD, cerebrovascular disease



IABP, intraaortic balloon pump



IABP, intraaortic balloon pump; AMI, acute myocardial infarction

Figure 4.

a. Trend in overall percentage of patients with shock by year from 1998–2008. Trend in IABP use in shock by year from 1998–2008.

b. Trend in overall percentage of patients with AMI by year from 1998–2008. Trend in IABP use in AMI by year from 1998–2008.

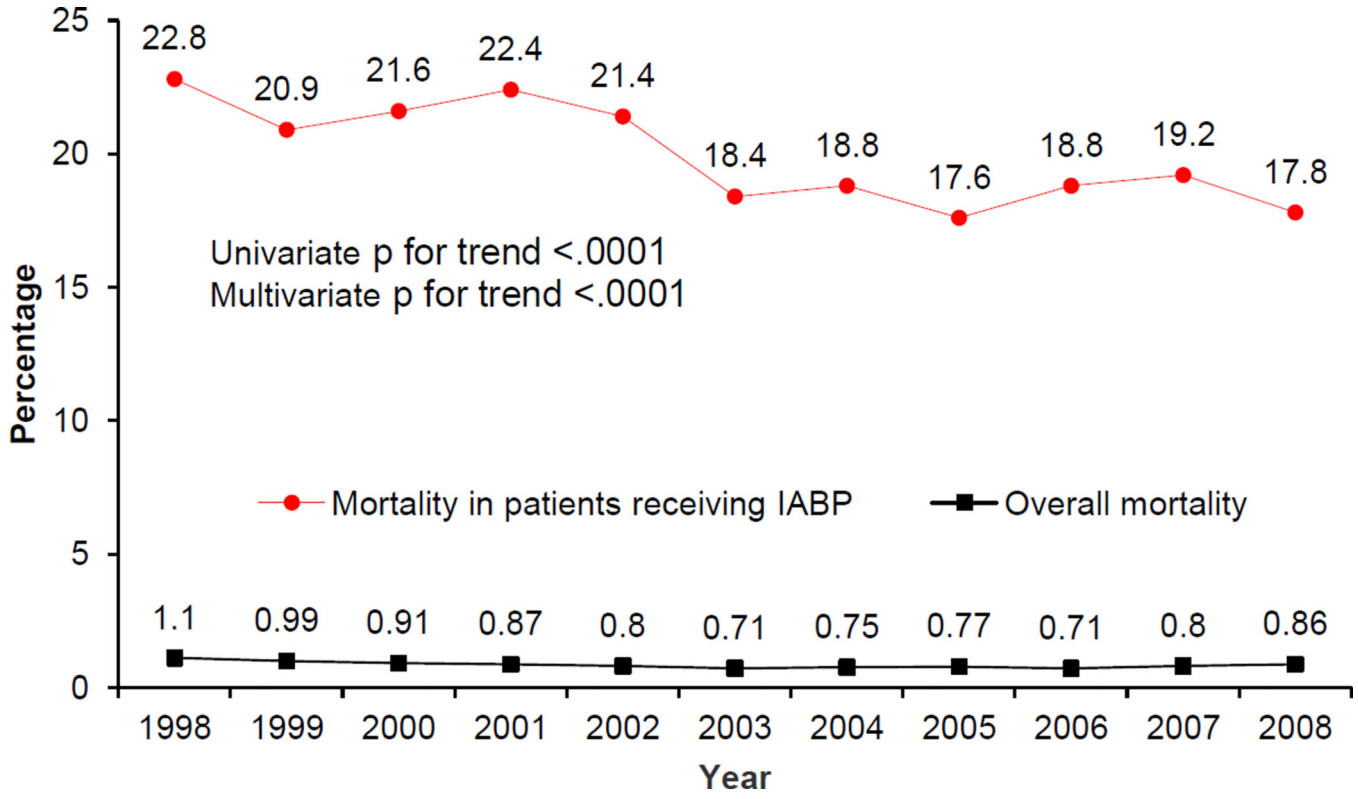


Figure 5.

Trend in all-cause, in-hospital mortality in PCI from 1998–2008.

Trend in death with IABP use in PCI from 1998–2008.

IABP, intraaortic balloon pump

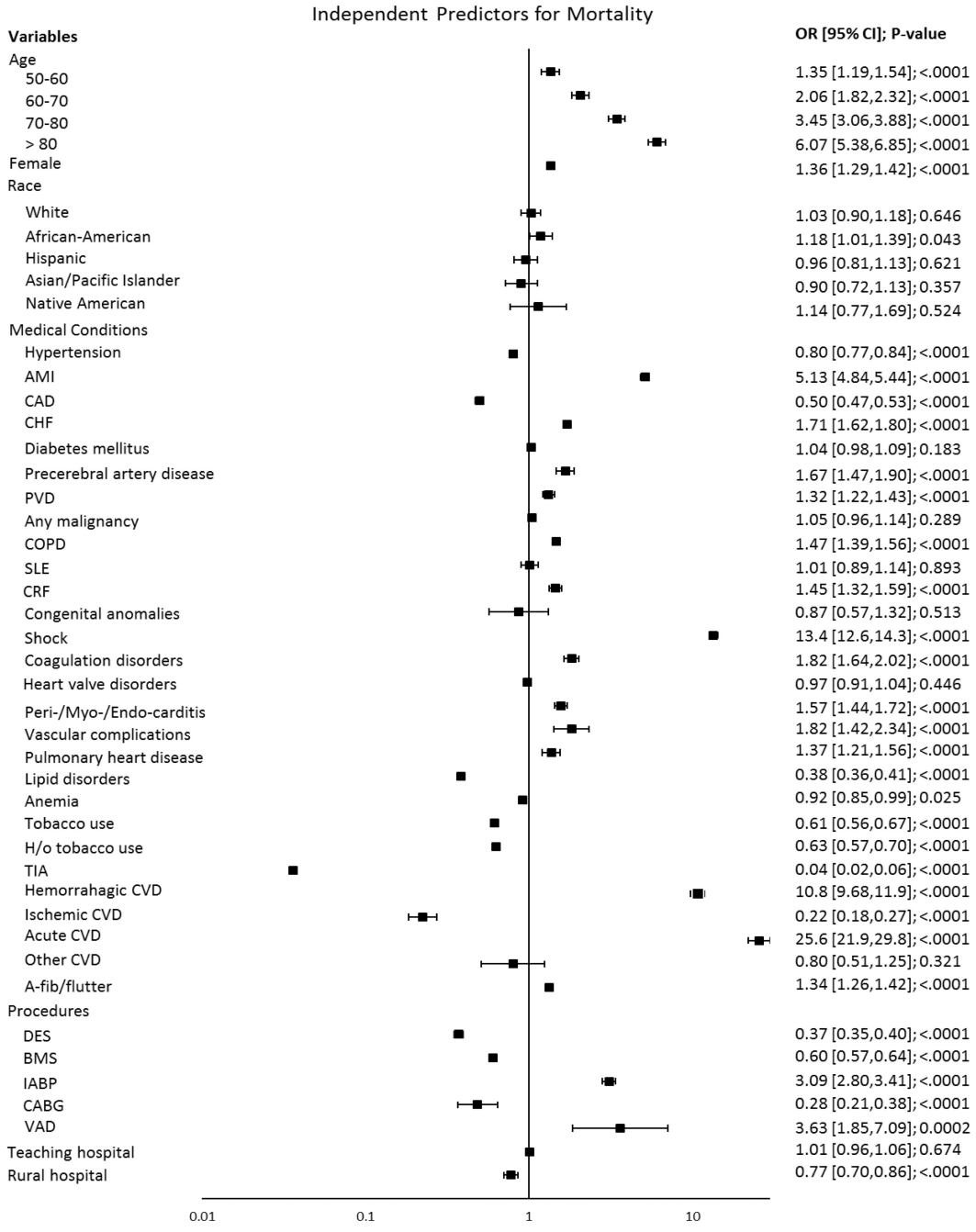


Figure 6.

Independent predictors for all-cause, in-hospital mortality in all patients undergoing PCI. AMI indicates acute myocardial infarction; CAD, coronary artery disease; CHF, congestive heart failure; TIA, transient ischemic attack; PVD, peripheral vascular disease; A/V/P, Aortic/peripheral/visceral; COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus; CVD, cerebrovascular disease; CABG, coronary artery bypass graft; VAD, ventricular assist device

Table I

Baseline patient characteristics

	No IABP [n=1,544,312]	IABP [n=8290]	*P*-value
Age, mean ± SD	64.2 ± 12.2	65. 1 ± 12.9	<.0001
Women, total (%)	528159 (34.20)	2809 (33.89)	0.5465
Race, total (%)			<.0001
White	921092 (81.91)	5054 (83.91)	
Black	75408 (6.71)	290 (4.81)	
Hispanic	68547 (6.10)	279 (4.63)	
Asian	19291 (1.72)	121 (2.01)	
Native American	4054 (0.36)	27 (0.45)	
Other	36160 (3.22)	252 (4.18)	
Died during hospitalization, total (%)	11054 (0.72)	1683 (20.31)	<.0001
Length of stay, mean ± SD	2.77 ± 3.09	8.39 ± 8.46	<.0001
Financial cost, mean ($) ± SD	39,866 ± 29,495	86,061 ± 89,133	<.0001
Hospital, total (%)			<.0001
Non-teaching	647992 (41.96)	3118 (37.61)	
Teaching	896320 (58.04)	5172 (62.39)	
Location, total (%)			<.0001
Rural	67329 (4.36)	657 (7.93)	
Urban	1476983 (95.64)	7633 (92.07)	
Medical history, total (%)			
Diabetes mellitus	446476 (28.91)	2096 (25.28)	<.0001
Hypertension	977347 (63.29)	3622 (43.69)	<.0001
AMI	528589 (34.23)	7012 (84.58)	<.0001
CAD	1485068 (96.16)	7082 (85.43)	<.0001
CHF	170801 (11.06)	3266 (39.40)	<.0001
Occlusion or stenosis of precerebral arteries	23434 (1.52)	82 (0.99)	<.0001
Other and ill-defined cerebrovascular disease	3280 (0.21)	<11* (0.11)	0.0403
TIA	2877 (0.19)	12 (0.14)	0.3814
PVD	105166 (6.81)	396 (4.78)	<.0001
A/V/P artery aneurysm/embolism/thrombosis	23369 (1.51)	160 (1.93)	0.0019
Any malignancy	95795 (6.20)	499 (6.02)	0.4890
COPD/Bronchiectasis	150720 (9.76)	1079 (13.02)	<.0001
SLE/Connective Tissue Disease	47201 (3.06)	205 (2.47)	0.0021
Cardiac and circulatory congenital anomalies	4292 (0.28)	36 (0.43)	0.0071
Shock	10777 (0.70)	3158 (38.09)	<.0001
Coagulation and hemorrhagic disorders	20893 (1.35)	541 (6.53)	<.0001
Heart valve disorders	109804 (7.11)	994 (11.99)	<.0001
Peri- endo- and myocarditis, cardiomyopathy	45014 (2.91)	585 (7.06)	<.0001
Pulmonary heart disease	21571 (1.40)	232 (2.80)	<.0001

	No IABP [n=1,544,312]	IABP [n=8290]	*P*-value
Chronic renal failure	44368 (2.87)	281 (3.39)	0.0050
Disorders of lipid metabolism	840840 (54.45)	2561 (30.89)	<.0001
Anemia	85427 (5.53)	859 (10.36)	<.0001
Tobacco use	259393 (16.80)	1144 (13.80)	<.0001
History of tobacco use	148834 (9.64)	386 (4.66)	<.0001
Ischemic CVD	25702 (1.66)	149 (1.80)	0.3451
Hemorrhagic CVD	694 (0.04)	21 (0.25)	<.0001
Acute CVD	8597 (0.56)	147 (1.77)	<.0001
Atrial fibrillation/flutter	121408 (7.86)	1436 (17.32)	<.0001
Procedure			
DES	632,917 (40.98)	1,713 (20.66)	<.0001
BMS	783,718 (50.75)	5,143 (62.04)	<.0001
CABG	1,777 (0.12)	892 (10.76)	<.0001
VAD	110 (0.01)	<11* (0.04)	0.0020

AMI indicates acute myocardial infarction; CAD, coronary artery disease; CHF, congestive heart failure; TIA, transient ischemic attack; PVD, peripheral vascular disease; A/V/P, Aortic/peripheral/visceral; COPD, chronic obstructive pulmonary disease; SLE, systemic lupus erythematosus; CVD, cerebrovascular disease; CABG, coronary artery bypass graft; VAD, ventricular assist device

* HCUP DUA prohibits the reporting of fewer than 11 observations

Table II

Association between death and IABP use by year with and without adjusting for covariates

	W/o adjusting for covariates		With adjusting for covariates	
Variable	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Overall died	35.35 (33.40,37.41)	<.0001	3.11 (2.82,3.43)	<.0001
Individual years				
1998	37.00 (31.38, 43.63)	<.0001	5.16 (3.92, 6.80)	<.0001
1999	31.71 (26.60, 37.81)	<.0001	2.94 (2.14, 4.03)	<.0001
2000	36.74 (31.25, 43.19)	<.0001	4.42 (3.32, 5.88)	<.0001
2001	39.31 (33.18, 46.58)	<.0001	5.27 (3.97, 6.99)	<.0001
2002	38.83 (32.20, 46.81)	<.0001	2.56 (1.83, 3.58)	<.0001
2003	35.73 (29.20, 43.71)	<.0001	1.98 (1.36, 2.88)	0.0004
2004	34.69 (28.54, 42.17)	<.0001	3.04 (2.14, 4.30)	<.0001
2005	30.45 (24.60, 37.70)	<.0001	2.04 (1.40, 2.96)	0.0002
2006	35.89 (29.46, 43.72)	<.0001	1.68 (1.21, 2.36)	0.0023
2007	31.99 (25.31, 40.44)	<.0001	2.18 (1.44, 3.29)	0.0002
2008	26.84 (21.34, 33.75)	<.0001	2.14 (1.47, 3.11)	<.0001

The adjusting covariates are year, age, race, gender, in-hospital mortality, cost, length of stay, hypertension, AMI, coronary atherosclerosis, congestive heart failure, occlusion or stenosis of precerebral arteries, cerebrovascular disease, transient cerebral ischemia, peripheral atherosclerosis, aortic/peripheral/visceral artery aneurysm/embolism/thrombosis, any malignancy, chronic obstructive pulmonary disease/ bronchiectasis, SLE/connective tissue disease, cardiac and circulatory congenital anomalies, shock, diabetes mellitus, coagulation and hemorrhagic disorders, heart valve disorders, peri-/endo-/myocarditis, pulmonary heart disease, chronic renal failure, hemorrhagic cerebrovascular disease (CVD), ischemic CVD, acute CVD, other cerebrovascular disease, disorders of lipid metabolism, anemia, prior and current tobacco use, atrial fibrillation/flutter, aortic valve disorder, drug-eluding stent, bare-metal stent, coronary artery bypass graft, and ventricular assist device.