Journal of the American Heart Association

ORIGINAL RESEARCH

Outcomes of Elderly Patients Undergoing Left Atrial Appendage Closure

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BACKGROUND: Elderly patients have a higher burden of comorbidities that influence clinical outcomes. We aimed to compare in-hospital outcomes in patients ≥80 years old to younger patients, and to determine the factors associated with increased risk of major adverse events (MAE) after left atrial appendage closure.

METHODS AND RESULTS: The National Inpatient Sample was used to identify discharges after left atrial appendage closure between October 2015 and December 2018. The primary outcome was in-hospital MAE defined as the composite of post-procedural bleeding, vascular and cardiac complications, acute kidney injury, stroke, and death. A total of 6779 hospitalizations were identified, of which, 2371 (35%) were ≥80 years old and 4408 (65%) were <80 years old. Patients ≥80 years old experienced a higher rate of MAE compared with those aged <80 years old (6.0% versus 4.6%, *P*=0.01), and this difference was driven by a numerically higher rate of cardiac complications (2.4% versus 1.8%, *P*=0.09) and death (0.3% versus 0.1%, *P*=0.05) among individuals ≥80 years old. In patients ≥80 years old, higher odds of in-hospital MAE were observed in women (1.61-fold), and those with preprocedural congestive heart failure (≈2-fold), diabetes (≈1.5-fold), renal disease (≈2.6-fold), anemia (≈2.7-fold), and dementia (≈5-fold). In patients <80 years old, a higher risk of in-hospital MAE was encountered among women (≈1.4-fold) and those with diabetes (≈1.3-fold), renal disease (≈2.6-fold), anemia (≈2-fold), and dyslipidemia (≈1.2-fold).

CONCLUSIONS: Patients ≥80 years old had higher rates of in-hospital MAE compared with patients aged <80 years old. Female sex and the presence of heart failure, diabetes, renal disease, and anemia were factors associated with in-hospital MAE among both groups.

Key Words: anticoagulation ■ atrial fibrillation ■ comorbidities ■ elderly ■ left atrial appendage closure ■ octogenarians ■ stroke

The prevalence of atrial fibrillation increases with age,[1] as does the risk of cerebrovascular accidents.[2–5] Moreover, its has been shown that individuals aged 80 years or older have >20% of atrial fibrillation–related strokes[5] and these are often more severe in terms of disability and mortality.[5–7] While oral anticoagulation therapy is the mainstay for thromboembolic cerebrovascular accidents prevention,[6,8] elderly patients are at increased risk of bleeding events[3,9]; hence, these drugs are often underused, mainly because of advanced age or the perceived high-risk of bleeding complications, falls, or even polypharmacy.[3,6,7,10]

Studies have demonstrated the safety and efficacy of left atrial appendage closure (LAAC) to reduce the risk of stroke in patients with atrial fibrillation,[11–13] and current guidelines recommend LAAC for individuals in whom long-term oral anticoagulation is considered either suboptimal or contraindicated.[6,8] Patients referred for LAAC often present with overlapping risks

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This manuscript was sent to Marwan Refaat, MD, Guest Editor, for review by expert referees, editorial decision, and final disposition.

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.021973

For Sources of Funding and Disclosures, see page 13.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This study represents a comprehensive appraisal on age-related differences and in-hospital outcomes following left atrial appendage closure.
- Patients ≥80 years old had higher rates of in-hospital complications compared with patients <80 years old.
- Burden of comorbidities was associated with in-hospital adverse events following left atrial appendage closure in patients ≥80 years old and those aged <80 years old.

What Are the Clinical Implications?

- These findings have significant implications for the understanding of how age-related outcomes may differ in patients undergoing left atrial appendage closure.

Nonstandard Abbreviations and Acronyms

CHA_2DS_2-VASc	Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, prior stroke or transient ischemic attack, age 65 to 74 years, vascular disease (including previous myocardial infarction), and female sex
LAAC	left atrial appendage closure

of systemic thromboembolism and bleeding events. In addition, elderly patients are generally frailer and have higher comorbidity burden, both of which often co-exist and influence clinical outcomes.[14,15] Therefore, we aimed to compare in-hospital outcomes in patients ≥80 years old to younger patients, and to determine the factors associated with increased risk of adverse events after LAAC.

METHODS

Data Source

We conducted a cohort-based observational study using the National Inpatient Sample (NIS) database, a nationally representative and all-payer publicly available database of hospitalized patients in the United States. The NIS database was developed by the Agency for Healthcare Research and Quality as a part of the Healthcare Cost and Utilization Project, which includes hospital information for >7 million hospital discharges annually and ≈20% stratified weighted sample of all discharges from United States community hospitals.[16] The authors declare that all supporting data are available within the article and its online supplementary files. Institutional review board and ethics committee approval was obtained from The Western University Health Science Research Ethics Board, and patient consent was not required because of the nature of this study.

Study Population

Between October 2015 and December 2018, hospitalizations for LACC, as a primary procedure, were identified using the *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) procedure code 02L73DK (occlusion of left atrial appendage with intraluminal device, percutaneous approach). For this study, individuals were divided into 2 groups, those ≥80 years old and those <80 years old, and *ICD-10-CM* codes were used to identify patient's baseline characteristics through the Charlson comorbidity index[17] (CCI, Table S1), and the Elixhauser comorbidity score[18] (ECS, Table S2). The CHA_2DS_2-VASc score was used to estimate the thromboembolic risk.

Outcome Measures

The primary outcome of interest was the occurrence of in-hospital major adverse events (MAE). In-hospital MAE were identified using *ICD-10-CM* codes and detailed in Table S3, and this included a composite of postprocedural bleeding, cardiac and vascular complications, acute kidney injury, stroke, or transient ischemic attack and death.

Statistical Analysis

Categorical variables are expressed as counts and percentages and continuous variables are presented as mean±SD or median (interquartile range [IQR]) according to variable distribution. Because of Healthcare Cost and Utilization Project data use agreement, variables in tables with <10 discharge records are displayed as "<10". Differences between patients ≥80 and <80 years old were evaluated using 2-sided Student *t* test or Wilcoxon rank-sum test for continuous variables and the χ^2 test for categorical variables, accordingly, adjusting for a survey sampling design. *P* values for each variable were computed adjusting for sampling discharge-level weights, cluster, and strata provided by NIS and as recommended by Agency for Healthcare Research and Quality during survey-specific analysis.

The Cochran-Armitage trend test was used for detecting linear trends for complications over the time. Length of stay was calculated by subtracting the admission date from the discharge date. Hospital

volumes were determined based on the annual number of LAAC performed by each hospital in a given year.

Factors associated with the primary outcome for patients ≥80 and <80 years old were assessed separately. We first conducted the univariate analysis for each outcome with a single variable; then, the variables associated with outcome variable from univariate analysis with a *P* value of <0.10 were included in multivariable models along with comorbidities. In addition, clinically relevant variables, chosen a priori, such as age, sex, and race were also included in multivariable models.

To account for the 2-level hierarchical structure of the NIS database (patients are nested within hospitals), multilevel modeling was applied, allowing the intercepts to vary across hospitals for in-hospital MAE with adjustment of the sampling weight. To assess the effect of age ≥80 years old in the whole cohort, the multilevel logistic regression model was fitted first adjusting for, in addition to sex, race and relevant comorbidities, then separately for patients ≥80 and <80 years old.

Area under the receiver operating characteristic curve analysis was conducted for each model to assess its discrimination ability for in-hospital MAE. The goodness-of-fit of the model was assessed using Akaike information criterion and comparatively, a lower Akaike information criterion indicates that a model fits the data better. The model's calibration was evaluated by the Brier score that was calculated from mean squared error of prediction for each model. Differences were considered statistically significant at *P* values of <0.05. Statistical analyses were performed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

A total of 6779 hospitalizations were identified in the NIS dataset as having undergone LAAC as a primary procedure between October 1, 2015 and December 31, 2018. Of these, 2371 (35%) were ≥80 years old (mean age 84.1±3.0 years old) and 4408 (65%) were <80 years old (mean age 71.6±6.3 years old). Interestingly, while the CCI was lower in patients ≥80 years old compared with <80 years old (1.9±1.7 versus 2.1±1.7, *P*<0.001),

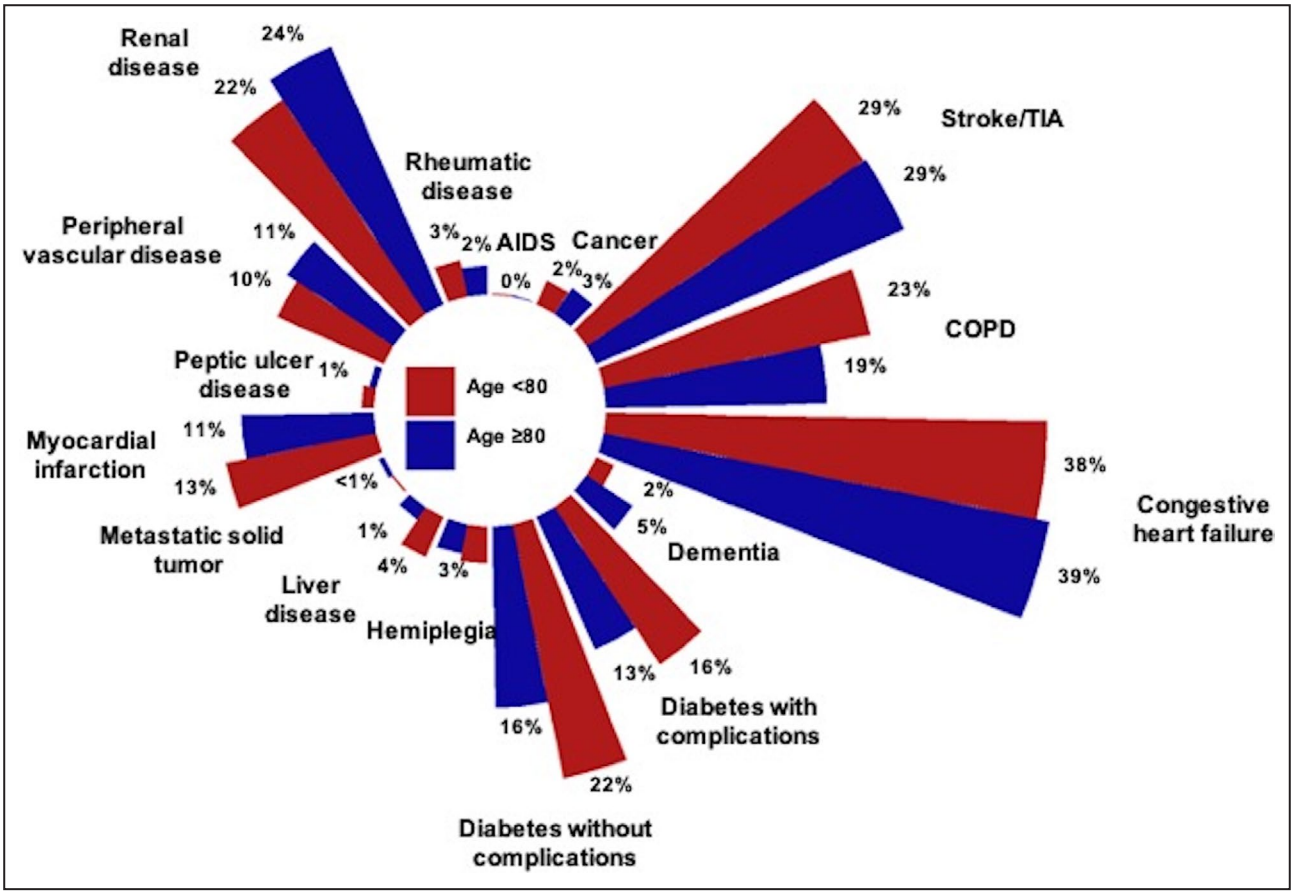


Figure 1. Proportion of components in Charlson Comorbidity Index.
Because of the very low proportions, mild liver disease and moderate–severe liver disease were pooled, leading to 16 variables instead of 17. COPD indicates chronic obstructive pulmonary disease; and TIA, transient ischemic attack.

the ECS was higher in those ≥80 years old compared with <80 years old (9.9±5.7 versus 9.6±5.9, *P*=0.03). The group-based distribution of CCI and ECS are presented in Figures 1 and 2, respectively. Patients ≥80 years old showed a higher CHA_2DS_2-VASc score (4.7±1.4 versus 4.0±1.5, *P*<0.001) and 100% of them presented with a high thromboembolic risk (CHA_2DS_2-VASc score ≥2, Figure 3) while 97% in the <80 years old cohort did (Table 1). Remaining baseline characteristics are presented in Table 1.

In-Hospital Complications

The composite of in-hospital MAE occurred in 5.1% of patients, with statistical difference between patients ≥80 and <80 years old (6.0% versus 4.6%, *P*=0.01); and this difference was mainly driven by the numerically higher rate of cardiac complications (2.4% versus 1.8%, *P*=0.09) and death (0.3% versus 0.1%, *P*=0.05) among individuals ≥80 years old as compared with <80 years old (Table 1).

A quarterly analysis indicates that the number of LAAC procedures increased over time. Based on the Cochran-Armitage trend test, while the incidence of in-hospital MAE significantly decreased from 16.7% in October to December 2015 to 7.6% in October to December 2018 in patients ≥80 years old (P_{trend}=0.02), it remained steady (6.0%–6.5%, P_{trend}=1.00) among those <80 years old (Figure 4).

To further evaluate the factors associated with in-hospital MAE, the patient's baseline, and periprocedural characteristics according to age ≥80 and <80 years old are detailed in Table 2. Patients in the ≥80-year-old group who experienced in-hospital MAE had more previous history of diabetes (39% versus 27%, *P*=0.003), congestive heart failure (51% versus 37%, *P*=0.003), renal disease (42% versus 23%, *P*<0.001), dementia (9.2% versus 4.5%, *P*=0.01), depression

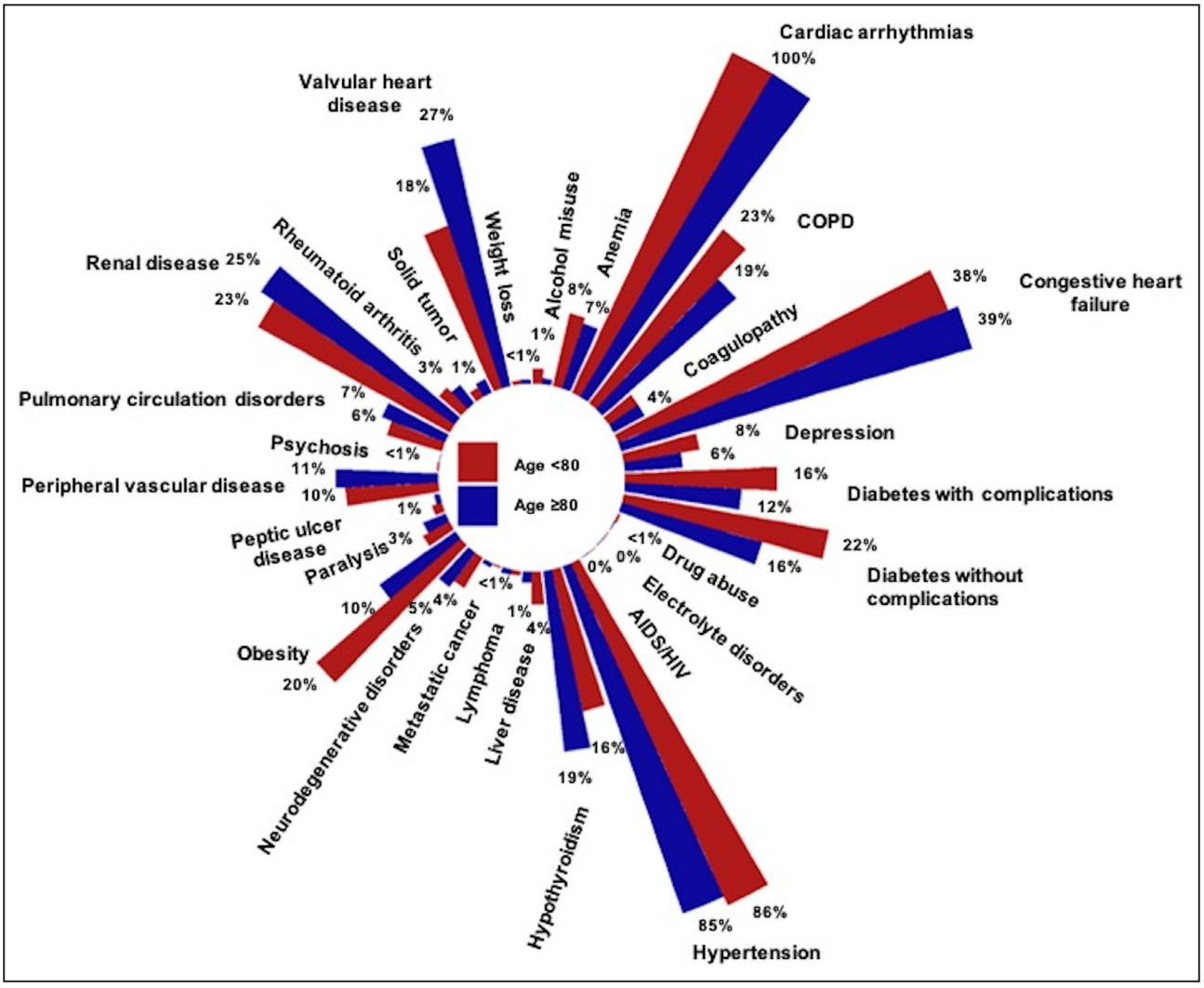


Figure 2. Proportion of components in Elixhauser Comorbidity Score.
Because of the very low proportions, deficiency anemia and blood loss anemia were pooled, leading to 29 variables instead of 30.

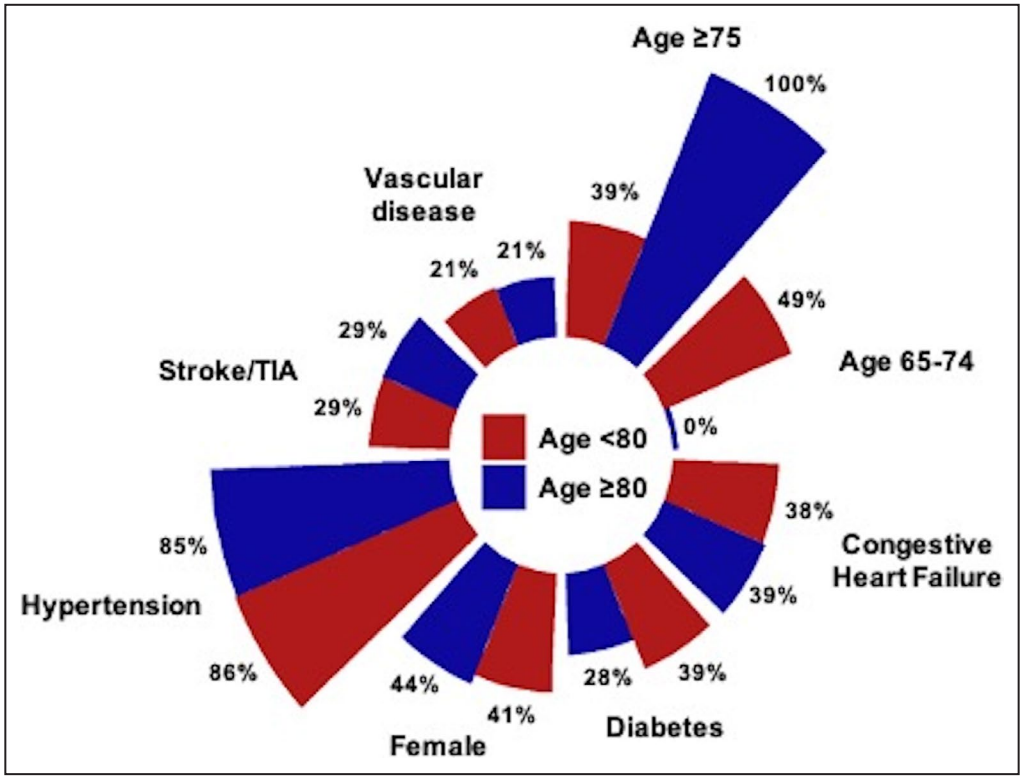


Figure 3. Proportion of components in CHA_2DS_2-VASc score.
CHA_2DS_2-VASc indicates Congestive heart failure, Hypertension, Age ≥75 years, Diabetes, prior Stroke or transient ischemic attack, Vascular disease (including previous myocardial infarction), Age 65 to 74 years, Sex category; and TIA, transient ischemic attack.

(13% versus 5.7%, *P*<0.001), and anemia (35% versus 16%, *P*<0.001). Patients in the <80-year-old group who experienced in-hospital MAE had more previous history of dyslipidemia (67% versus 60%, *P*=0.03), diabetes (47% versus 38%, *P*=0.01), congestive heart failure (49% versus 38%, *P*=0.001), renal disease (42% versus 21%, *P*<0.001), and anemia (33% versus 16%, *P*<0.001). In both cohorts, the proportion of patients with in-hospital MAE increased with the increase in comorbidity burden as assessed by the CCI (2.7±1.8 versus 1.8±1.9, in patients ≥80 years old and 2.7±2.0 versus 2.1±1.7 in those <80 years old, *P*<0.001 for both), and ECS (11.6±6.2 versus 9.9±5.6, *P*=0.001, in patients ≥80 years old, and 11.93±6.6 versus 9.5±5.9, *P*<0.001, in those <80 years old), Table 2.

Length of Hospital Stay and Cost

The overall median length of stay was similar for patients ≥80 and <80 years (*P*=0.38), Table 1. The length of stay was significantly longer among those ≥80 years old and <80 years old who experienced in-hospital MAE compared with counterparts who did not experience in-hospital MAE (Wilcoxon rank-sum test, *P*<0.001, for both). Patients ≥80 years old and <80 years old who experienced in-hospital MAE had a significantly higher index cost compared with those who did not have complications ($28 727; IQR, $21 145–37 480 USD versus $24 054; IQR, $18 803–29 338 USD and $30 934; IQR, $23 706–38 334 USD versus $24 240; IQR, $18 357–29 974 USD, respectively) (Table 2).

Associations With In-Hospital Complications

After multilevel modeling adjusting for age, sex, race, and relevant comorbidities, the risk of in-hospital MAE for the whole cohort was significantly increased by factoring age ≥80 years old (1.4-fold) as well as female sex (1.3-fold). The presence of congestive heart failure (odds ratio [OR], 1.32 [95% CI, 1.16–1.49]), diabetes (OR, 1.28 [95% CI, 1.13–1.45]), renal disease (OR, 2.38 [95% CI, 2.08–2.72]), weight loss (OR, 3.39 [95% CI, 1.79–6.43]), dementia (OR, 2.29, [95% CI, 1.72–3.04]), anemia (OR, 2.27, [95% CI, 1.98–2.60]), and dyslipidemia (OR, 1.16 [95% CI, 1.02–1.32]) had higher impact on the risk of MAE (Figure 5A). Among patients ≥80 years old, higher odds of in-hospital MAE were observed in women (1.61-fold), and individuals with

Table 1. Baseline Characteristics and In-Hospital Outcomes of the Study Population

Patient characteristics	All (n=6779)	≥80 y (n=2371)	<80 y (n=4408)	Adjusted *P* value*
Mean age, y	76.0±8.0	84.1±3.0	71.6±6.3	<0.001
Women	2830 (42)	1041 (43.9)	1789 (40.6)	0.01
Race‡				
White	5663 (86)	2037 (89)	3626 (85)	<0.001
Non-White†	908 (14)	264 (11)	644 (15)	
Type of admission§				
Elective	6175 (91)	205 (91)	379 (91)	0.95
Nonelective	584 (9)	2159 (9)	4016 (9)	
Median household income‖				
0–25th percentile	1353 (20)	423 (18)	930 (21)	0.01
26–50th percentile	1740 (26)	605 (26)	1135 (26)	
51–75th percentile	1864 (28)	672 (29)	1192 (27)	
76–100th percentile	1725 (26)	638 (27)	1087 (25)	
Patient location¶				
Urban	5688 (84)	2044 (86)	3644 (83)	<0.001
Rural	1082 (16)	324 (14)	758 (17)	
Hospital teaching status and location				
Rural	124 (1.8)	43 (1.8)	81 (1.8)	
Urban nonteaching	630 (9.3)	228 (9.6)	402 (9.1)	0.80
Urban teaching	6025 (89)	2100 (89)	3925 (89)	
Hospital bed-size				
Small	727 (11)	288 (12)	439 (10)	
Medium	1423 (21)	499 (21)	924 (21)	0.02
Large	4629 (68)	1584 (67)	3045 (69)	
Primary payer				
Medicare	6011 (89)	2246 (95)	3765 (86)	<0.001
Medicaid	81 (1.2)	<10 (0.3)	73 (1.7)	
Private insurance	547 (8.1)	78 (3.3)	469 (11)	
Other	126 (1.9)	34 (1.4)	92 (2.1)	
Comorbidities				
Smoking	2358 (35)	787 (33)	1571 (36)	0.04
Dyslipidemia	4058 (60)	1414 (60)	2644 (60)	0.78
Hypertension	5822 (86)	2025 (85)	3797 (86)	0.41
Diabetes	2357 (35)	660 (28)	1697 (38)	<0.001
Previous myocardial infarction	852 (13)	270 (11)	582 (13)	0.03
Previous CABG	1012 (15)	400 (17)	612 (14)	0.001
Congestive heart failure	2604 (38)	917 (39)	1677 (38)	0.39
Valvular disease	1441 (21)	638 (27)	803 (18)	<0.001
Previous cerebrovascular disease	1951 (29)	685 (29)	1266 (29)	0.88
Peripheral vascular disease	703 (10)	260 (11)	443 (10)	0.24
Renal disease	1553 (23)	574 (24)	979 (22)	0.06
Chronic pulmonary disease	1481 (22)	451 (19)	1030 (23)	<0.001
Obesity	1129 (17)	235 (9.9)	894 (20)	<0.001
Dementia	187 (2.8)	113 (4.8)	74 (1.7)	<0.001
Rheumatic disease	199 (2.9)	60 (2.5)	139 (3.2)	0.15
Liver disease	87 (2.6)	14 (1.3)	73 (3.3)	0.001
Hypothyroidism	1138 (16)	458 (19)	680 (15)	<0.001

(*Continued*)

Table 1. Continued

Patient characteristics	All (n=6779)	≥80 y (n=2371)	<80 y (n=4408)	Adjusted *P* value*
Depression	510 (7.5)	147 (6.2)	363 (8.2)	0.002
Cancer	160 (2.4)	65 (2.7)	95 (2.2)	0.13
Anemia	1130 (17)	406 (17)	724 (16)	0.46
Charlson Comorbidity Index	2.1±1.7	1.9±1.7	2.1±1.7	<0.001
0	1183 (18)	458 (19)	725 (16)	0.001
1	1857 (27)	672 (28)	1185 (27)	
2	1477 (22)	509 (22)	968 (22)	
≥3	2262 (33)	732 (31)	1530 (35)	
Elixhauser Comorbidity Score	9.8±5.9	9.9±5.7	9.6±5.9	0.03
≤0	84 (1.2)	21 (0.9)	63 (1.4)	0.05
1–5	2401 (36)	814 (4)	1587 (36)	
6–10	1418 (21)	489 (21)	929 (21)	
≥11	2876 (42)	1047 (44)	1829 (42)	
$CHADS_2$ score	2.8±1.3	3.1±1.2	2.6±1.3	<0.001
≥2	5726 (84)	2212 (93)	3514 (80)	<0.001
CHA_2DS_2-VASc score	4.3±1.5	4.7±1.4	4.0±1.5	<0.001
≥2	6629 (98)	2371 (100)	4258 (97)	<0.001
Year of procedure				
2015 (October–December)	114 (1.7)	30 (1.3)	84 (2.0)	0.01
2016 (January–December)	1017 (15)	340 (14)	677 (15)	
2017 (January–December)	2163 (32)	719 (30)	1444 (33)	
2018 (January–December)	3485 (51)	1282 (54)	2203 (50)	
In-hospital MAE	345 (5.1)	142 (6.0)	203 (4.6)	0.01
Bleeding complications	38 (0.6)	15 (0.6)	23 (0.5)	0.55
Cardiac complications	139 (2.1)	58 (2.4)	81 (1.8)	0.09
Vascular complications	30 (0.4)	14 (0.6)	16 (0.4)	0.18
Stroke	24 (0.4)	12 (0.5)	12 (0.3)	0.12
Acute kidney injury	161 (2.4)	60 (2.5)	101 (2.3)	0.53
Death	<10 (0.1)	<10 (0.3)	<10 (0.1)	0.05
Length of stay, d	1 (1–1)	1 (1–1)	1 (1–1)	0.23
Length of stay (d, range)	0–35	0–35	0–33	…
≤1 d	5811 (86)	2010 (85)	3801 (86)	0.10
>1 d	361 (14)	361 (15)	607 (14)	
Index admission cost#, USD	24 343 (18 588–30 166)	24 168 (18 886–29 753)	24 469 (18 487–30 381)	0.38

Values are expressed as mean±SD, median (interquartile range), or % unless otherwise noted. Exact counts (n) for variables with <10 patients are not detailed as per the Healthcare Cost and Utilization Project data use agreement. The rate of the overall incidence of cardiac tamponade (computed as cardiac complication) was 0.62% (0.76% among those ≥80 years old and 0.55% among those <80 years old). CABG indicates coronary artery bypass surgery; CHA_2DS_2-VASc, Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, prior Stroke or transient ischemic attack, Vascular disease (including previous myocardial infarction), Age 65 to 74 years, Sex category; MAE, major adverse event; and USD, United States dollar.

*Adjusted *P* values for each variable were computed from adjusting sampling design by discharge-level weights, cluster, and strata.

†Non-white race/ethnicity included Black, Hispanic, Asian/Pacific islander, Native Americans and "other" as per National Inpatient Sample (NIS) categorization.

‡Race was missing in 3.1%.

§Type of admission was missing in 0.3%.

‖Median household income was missing in 1.4%.

¶Urban location was defined as counties in metro areas of ≥50 000 population.

#Index admission cost was missing in 0.6%.

congestive heart failure (≈2-fold), diabetes (≈1.5-fold), renal disease (2.6-fold), anemia (≈2.7-fold), and dementia (≈5-fold), Figure 5B. In patients <80 years, higher risk of in-hospital MAEs were encountered among women (≈1.4-fold) as well as patients with diabetes (≈1.3-fold), renal disease (≈2.6-fold), anemia (≈2-fold), and dyslipidemia (1.2-fold) (Figure 5C).

In the whole cohort, the area under the receiver operating characteristic curves, Akaike information criterion, and Brier score were 0.91 (95% CI,

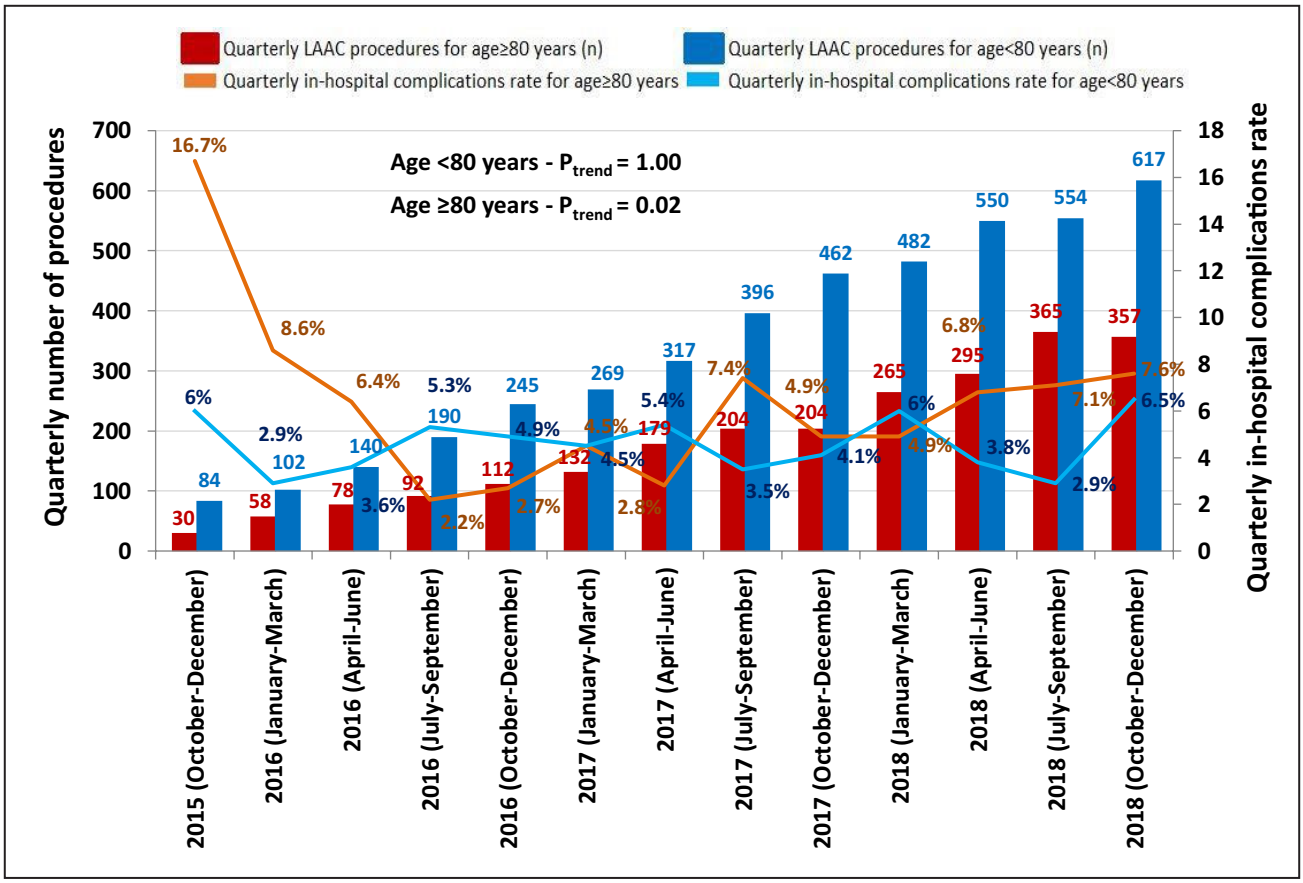


Figure 4. Temporal trends in left atrial appendage closure procedures performed quarterly and in-hospital complications from 2015 to 2018 according to age ≥80 years old and <80 years old.
Cochran-Armitage trend test shows statistically significant decrease in complication rates over time among ≥80 year-old patients. LAAC indicates left atrial appendage closure.

0.89–0.92), 10 473, and 0.057, respectively. In those ≥80 years old, the area under the receiver operating characteristic curves, Akaike information criterion, and Brier score were 0.95 (95% CI, 0.93–0.96), 3511, and 0.074, respectively; whereas these values were 0.94 (95% CI, 0.93–0.95), 5666, and 0.053, respectively, in those ≥80 years old, (Figure 5).

DISCUSSION

In this cohort of 6779 hospitalizations for LAAC, close to 1 in 3 patients were ≥80 years old and, therefore, represents one of the largest cohorts of patients ≥80 years of age who underwent LAAC. The overall cohort presented with high burden of comorbidities. Patients ≥80 years old experienced higher rates of in-hospital complications mainly driven by the numerically higher rate of cardiac complications and death among individuals ≥80 years old as compared with <80 years old. Women and the presence of heart failure, diabetes, renal disease, and anemia were factors commonly associated with in-hospital adverse events among both groups.

Contribution to Previous Studies

Studies have shown that among individuals ≥80 years of age, >80% of this population present with multiple comorbid conditions, and comorbidity burden is a strong predictor of poor outcomes.[14,15,19–23] One potential explanation for the differences in CCI and ECS (lower CCI in patients ≥80 years old while higher ECS as compared with <80 years old) would be the fact that the CCI captures about half the number of comorbidities than the ECS and, therefore, the differences in *P* values are likely driven by the difference in sample sizes.

Elderly patients are generally more fragile, and more prone to complications during interventional procedures; therefore, the benefit of LAAC may indeed be limited or at least questioned. Nonetheless, as above-stated, elderly patients show a combined increased risk of thromboembolic and

Table 2. Baseline Characteristics of the Study Population According to the Occurrence of In-Hospital MAE

Patients' characteristics	≥80 y (n=2371)			<80 y (n=4408)			Adjusted *P* value†	Adjusted *P* value‡
	With in-hospital MAE n=142	Without in-hospital MAE n=2229	Adjusted *P* value*	With in-hospital MAE n=203	Without in-hospital MAE n=4205	Adjusted *P* value*		
Mean age, y	84.1±2.8	84.1±3.0	0.87	71.2±7.0	71.6±6.2	0.47	<0.001	<0.001
Women	77 (54)	964 (43)	0.01	96 (47)	1693 (40)	0.05	0.22	0.02
Race‖								
White	119 (85)	1918 (89)	0.18	151 (77)	3475 (85)	0.001	0.06	<0.001
Non-White§	21 (15)	243 (11)		46 (23)	85 (15)			
Median household income¶								
0–25th percentile	26 (19)	397 (18)	0.63	41 (21)	889 (21)	0.99	0.84	0.01
26–50th percentile	35 (25)	570 (26)		50 (26)	1085 (26)			
51–75th percentile	45 (33)	627 (29)		55 (28)	1137 (28)			
76–100th percentile	32 (23)	606 (27)		49 (25)	1038 (25)			
Patient location#								
Urban	121 (86)	1923 (86)	0.97	163 (80)	3481 (83)	0.34	0.13	<0.001
Rural	19 (14)	305 (14)		40 (20)	718 (17)			
Hospital teaching status and location								
Rural	<10 (2.1)	40 (1.8)	0.58	<10 (1.5)	78 (1.9)	0.92	0.62	0.89
Urban nonteaching	17 (12)	211 (9.5)		19 (9.4)	383 (9.1)			
Urban teaching	122 (86)	1978 (89)		181 (89)	3744 (89)			
Hospital bed-size								
Small	20 (14)	268 (12)	0.52	15 (7.4)	424 (10)	0.44	0.10	0.04
Medium	25 (18)	474 (21)		45 (22)	879 (21)			
Large	97 (68)	1487 (67)		143 (70)	2902 (69)			
Primary payer								
Medicare	136 (96)	2110 (95)	0.77	176 (87)	3589 (86)	0.67	0.02	<0.001
Medicaid	<10 (0)	<10 (0.4)		<10 (2.5)	68 (1.6)			
Private insurance	<10 (3.5)	73 (3.3)		18 (8.9)	451 (11)			
Other	<10 (0.7)	33 (1.5)		<10 (2.0)	88 (2.1)			
Comorbidities								
Smoking	33 (23)	754 (34)	0.01	66 (33)	1505 (36)	0.34	0.07	0.12
Dyslipidemia	87 (61)	1327 (60)	0.68	137 (67)	2507 (60)	0.03	0.25	0.95
Hypertension	125 (88)	1900 (85)	0.36	183 (90)	3614 (86)	0.09	0.52	0.44
Diabetes	55 (39)	605 (27)	0.003	95 (47)	1602 (38)	0.01	0.14	<0.001

(*Continued*)

Table 2. Continued

Patients' characteristics	≥80 y (n=2371)			<80 y (n=4408)			Adjusted *P* value†	Adjusted *P* value‡
	With in-hospital MAE n=142	Without in-hospital MAE n=2229	Adjusted *P* value*	With in-hospital MAE n=203	Without in-hospital MAE n=4205	Adjusted *P* value*		
Previous myocardial infarction	20 (14)	250 (11)	0.30	26 (13)	556 (13)	0.86	0.73	0.02
Previous CABG	24 (17)	376 (17)	0.99	30 (15)	582 (14)	0.71	0.60	0.001
Congestive heart failure	72 (51)	855 (37)	0.003	99 (49)	1578 (38)	0.001	0.72	0.51
Valvular disease	42 (30)	596 (27)	0.46	42 (21)	761 (18)	0.35	0.06	<0.001
Previous cerebrovascular disease	45 (32)	640 (28)	0.45	52 (26)	1214 (29)	0.32	0.20	0.89
Peripheral vascular disease	21 (15)	239 (11)	0.13	25 (12)	418 (10)	0.27	0.50	0.33
Renal disease	59 (42)	515 (23)	<0.001	86 (42)	893 (21)	<0.001	0.88	0.09
Chronic pulmonary disease	33 (23)	418 (19)	0.19	52 (26)	978 (23)	0.44	0.61	<0.001
Obesity	19 (13)	216 (9.7)	0.15	47 (23)	847 (20)	0.30	0.02	<0.001
Dementia	13 (9.2)	100 (4.5)	0.01	<10 (2.5)	69 (1.6)	0.37	0.004	<0.001
Rheumatic disease	<10 (0.7)	59 (2.6)	0.15	<10 (3.4)	132 (3.1)	0.81	0.09	0.26
Liver disease	<10 (1.4)	26 (1.2)	0.80	<10 (3.0)	72 (3.5)	0.66	0.34	<0.001
Hypothyroidism	31 (22)	427 (19)	0.43	36 (18)	644 (15)	0.35	0.33	<0.001
Anemia	50 (35)	356 (16)	<0.001	68 (33)	656 (16)	<0.001	0.74	0.70
Depression	19 (13)	128 (5.7)	<0.001	13 (6.4)	350 (8.3)	0.33	0.03	<0.001
Cancer	<10 (2.8)	61 (2.7)	0.95	<10 (3.0)	89 (2.1)	0.42	0.93	0.12
Charlson comorbidity index	2.7±1.8	1.8±1.9	<0.001	2.7±2.0	2.1±1.7	<0.001	0.49	<0.001
0	15 (11)	443 (20)	<0.001	22 (11)	703 (17)	<0.001	0.68	0.001
1	38 (27)	634 (28)		43 (21)	1142 (27)			
2	23 (16)	486 (22)		38 (19)	930 (22)			
≥3	66 (46)	666 (30)		100 (49)	1430 (34)			
Elixhauser comorbidity score	11.6±6.2	9.9±5.6	0.001	11.9±6.6	9.5±5.9	<0.001	0.75	0.03
≤0	<10 (1.4)	19 (0.9)	0.004	<10 (2.0)	59 (1.4)	<0.001	0.88	0.06
1–5	29 (20)	785 (35)		44 (22)	1543 (37)			
6–10	34 (24)	455 (20)		42 (21)	887 (21)			
≥11	77 (54)	970 (44)		113 (56)	1716 (41)			
$CHADS_2$ score	3.4±1.3	3.1±1.2	0.004	2.8±1.3	2.6±1.3	0.06	<0.001	<0.001
≥2	132 (93)	2080 (93)	0.86	172 (85)	3342 (79)	0.07	0.02	<0.001
CHA_2DS_2-VASc score	5.2±1.5	4.7±1.4	0.001	4.3±1.5	4.0±1.5	0.01	<0.001	<0.001

(*Continued*)

Table 2. Continued

Patients' characteristics	≥80 y (n=2371)			<80 y (n=4408)				
	With in-hospital MAE n=142	Without in-hospital MAE n=2229	Adjusted *P* value*	With in-hospital MAE n=203	Without in-hospital MAE n=4205	Adjusted *P* value*	Adjusted *P* value†	Adjusted *P* value‡
≥2	142 (100)	2229 (100)	…	200 (99)	4058 (97)	0.12	0.15	<0.001
Length of stay, d	2 (1–5)	1 (1–1)	<0.001	3 (1–5)	1 (1–1)	<0.001	0.30	0.51
≤1 d	48 (34)	1962 (88)	<0.001	62 (31)	3739 (89)	<0.001	0.52	0.28
>1 d	94 (66)	267 (12)		141 (69)	466 (11)			
Index admission cost**, USD	28 727 (21 145–37 480)	24 054 (18 803–29 338)	<0.001	30 934 (23 706–38 334)	24 240 (18 357–29 974)	<0.001	0.13	0.48

Values are expressed as mean±SD, median (interquartile range), or n (%) unless otherwise noted. Exact counts (n) for variables with <10 patients are not detailed as per the Healthcare Cost and Utilization Project data use agreement. CABG indicates coronary artery bypass surgery; CHA_2DS_2-VASc, Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, prior Stroke or transient ischemic attack, Vascular disease (including previous myocardial infarction), Age 65 to 74 years, Sex category; MAE, major adverse event; and USD, United States dollar.

*Adjusted *P* values for each variable were computed from adjusting sampling design by discharge-level weights, cluster, and strata.

†Differences between ≥80 and <80 years with ‡ and without ‡ in-hospital MAE.

§Non-white race/ethnicity included Black, Hispanic, Asian/Pacific islander, Native Americans and "other" as per National Inpatient Sample (NIS) categorization.

‖Race was missing 3.0% in ≥80 years old cohort and 3.1% in <80 years old cohort.

¶Median household income was missing 1.4% in ≥80 years old cohort and 1.5% in <80 years old cohort.

#Urban location was defined as counties in metro areas of ≥50 000 population.

**Index admission cost was missing 0.6% in ≥80 years old cohort and 0.6% in <80 years old cohort.

bleeding events. Previous registry data showed similar periprocedural complications in patients <75 versus ≥75 years old, although older patients had a higher incidence of cardiac tamponade.[24] Another registry compared the safety and efficacy of LAAC in patients <85 versus ≥85 years old and revealed similar procedural success and no differences in procedure-related adverse events.[25] Of note, the sample size of elderly patients included in these 2 registries was indeed significantly smaller than ours (ie, 430 and 84 patients ≥75 and ≥85 years old, respectively).[24,25]

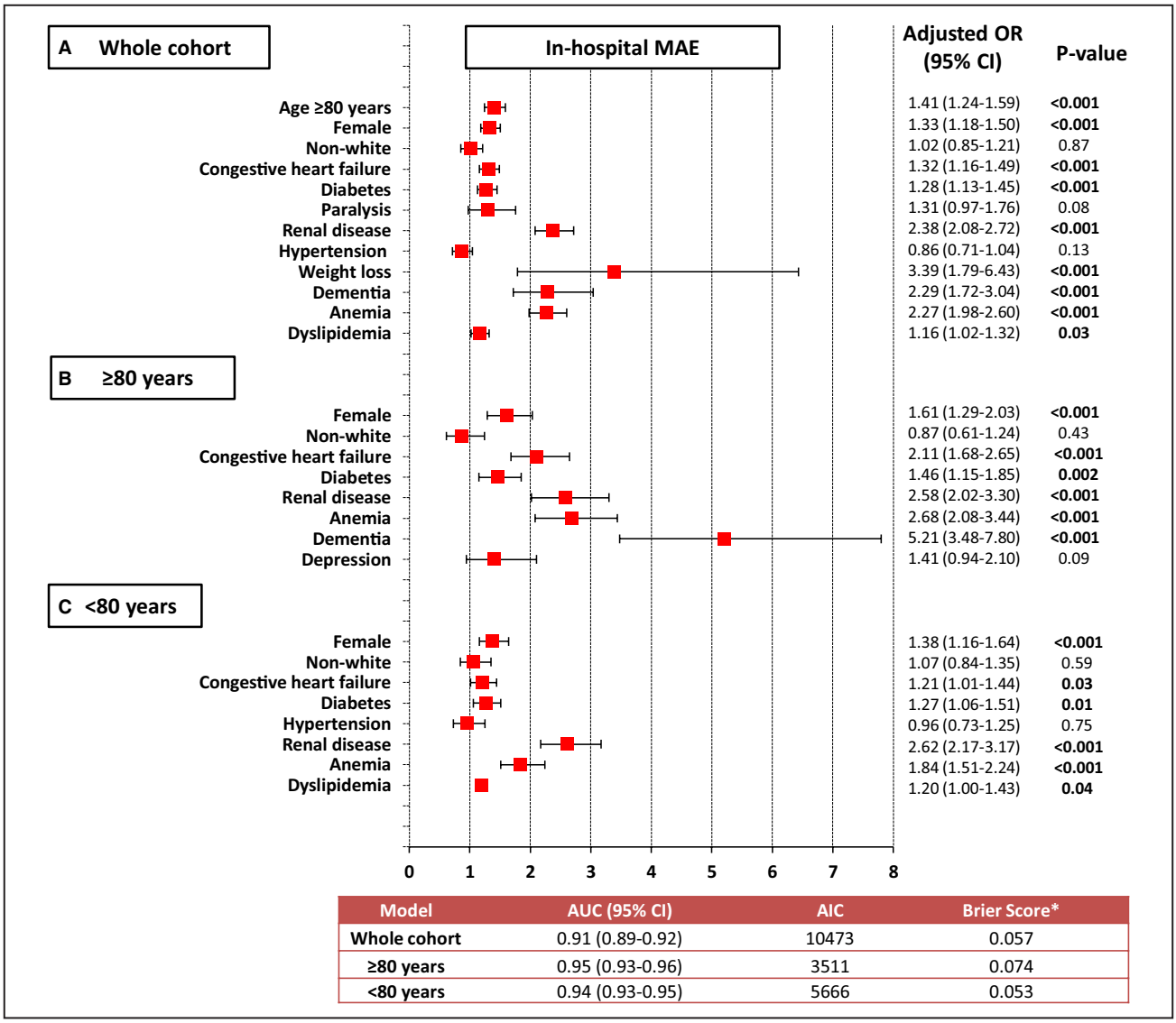
Our findings are relevant since elderly patients are often underrepresented in clinical trials and across a broad spectrum of health conditions, with marked disparities in the type of presentation, and clinical outcomes.[26,27] Moreover, our study presents national estimates in which one third of the patients (n=2371) were ≥80 years of age, and the overall number of patients who have undergone LAAC has increased over time, while the occurrence of in-hospital MAE appears to have improved.

Strengths and Limitations

The strength of our analysis lies in its large sample size, and that it is the first study to appraise the clinical impact of comorbidity burden in patients ≥80 years old undergoing LAAC. Nonetheless, this study presents with limitations. The main limitation lies in its retrospective nature and reliance on an administrative claims database, therefore, errors while coding may have occurred and thus affected the data gathering and the ability to adjust for unmeasured confounders. Even though the event rates after LAAC were relatively low and hence pooled for a composite end point, postprocedural MAE are not well adjudicated in NIS. Moreover, pharmacologic agents such as anticoagulation management were not available and remain a source for potential confounders in terms of bleeding or thromboembolic events. Finally, the impact of these findings on long-term follow-up remains unknown.

CONCLUSIONS

In this cohort-based study including a large number of patients ≥80 years old who underwent LAAC, the rates of in-hospital MAE were higher compared with patients <80 years. Women and those with heart failure, diabetes, renal disease, and anemia experienced higher rates of in-hospital adverse events in both groups. Furthermore, adequately powered research is needed to develop a risk stratification model to help with the clinical decision-making of patients undergoing LAAC.



Model	AUC (95% CI)	AIC	Brier Score*
Whole cohort	0.91 (0.89-0.92)	10473	0.057
≥80 years	0.95 (0.93-0.96)	3511	0.074
<80 years	0.94 (0.93-0.95)	5666	0.053

Figure 5. Multilevel multivariable logistic regression analyses of factors associated with in-hospital MAE.
A, Whole cohort, (**B**) ≥80 years old, and (**C**) <80 years old. AIC indicates Akaike's information criterion (lower values indicate better fit of the model); AUC, area under receiver operating characteristic curve; MAE, major adverse events; and OR, odds ratio. For continuous variables, the OR are per unit of increase in each of the predictive factors. *Lower values (close to 0) indicate better calibration of the model.

ARTICLE INFORMATION

Received June 7, 2021; accepted July 22, 2021.

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Acknowledgments

We are grateful to the Healthcare Cost and Utilization Project (HCUP) and the HCUP Data Partners for providing the data used in the analysis.

Sources of Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Sanjoy received partial funding for his MSc studies from a Lawson Health Research Institute Internal Research Fund (studentship award).

Disclosures

Dr Holmes is on the Advisory Board for Boston Scientific, unpaid. The remaining authors have no disclosures to report.

Supplementary Material

Tables S1–S3

REFERENCES

1. Freedman JE, Gersh BJ. Atrial fibrillation and stroke prevention in aging patients: what's good can be even better. *Circulation*. 2014;130:129–131. doi: 10.1161/CIRCULATIONAHA.114.010873
2. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285:2864–2870. doi: 10.1001/jama.285.22.2864
3. Lip GY, Lim HS. Atrial fibrillation and stroke prevention. *Lancet Neurol*. 2007;6:981–993. doi: 10.1016/S1474-4422(07)70264-8
4. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on Atrial Fibrillation. *Chest*. 2010;137:263–272. doi: 10.1378/chest.09-1584
5. Dang G, Jahangir I, Sra J, Tajik AJ, Jahangir A. Atrial fibrillation and stroke in elderly patients. *J Patient Cent Res Rev*. 2016;3:217–229. doi: 10.17294/2330-0698.1409
6. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener H-C, Heidbuchel H, Hendriks J, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace*. 2016;18:1609–1678. doi: 10.1093/europace/euw295
7. Andrade JG, Macle L, Nattel S, Verma A, Cairns J. Contemporary atrial fibrillation management: a comparison of the current AHA/ACC/HRS, CCS, and ESC guidelines. *Can J Cardiol*. 2017;33:965–976. doi: 10.1016/j.cjca.2017.06.002
8. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, Ellinor PT, Ezekowitz MD, Field ME, Furie KL, et al. AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. *Circulation*. 2019;140:e125–e151. doi: 10.1016/j.jacc.2019.01.011
9. Halperin JL, Hankey GJ, Wojdyla DM, Piccini JP, Lokhnygina Y, Patel MR, Breithardt G, Singer DE, Becker RC, Hacke W, et al. Efficacy and safety of rivaroxaban compared with warfarin among elderly patients with nonvalvular atrial fibrillation in the Rivaroxaban Once Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). *Circulation*. 2014;130:138–146. doi: 10.1161/CIRCULATIONAHA.113.005008
10. Guerriero F, Orlando V, Monetti VM, Colaccio FM, Sessa M, Scavone C, Capuano A, Menditto E. Predictors of new oral anticoagulant drug initiation as opposed to warfarin in elderly adults: a retrospective observational study in southern Italy. *Ther Clin Risk Manag*. 2018;14:1907–1914. doi: 10.2147/TCRM.S171346
11. Holmes DR Jr, Doshi SK, Kar S, Price MJ, Sanchez JM, Sievert H, Valderrabano M, Reddy VY. Left atrial appendage closure as an alternative to warfarin for stroke prevention in atrial fibrillation: a patient-level meta-analysis. *J Am Coll Cardiol*. 2015;65:2614–2623. doi: 10.1016/j.jacc.2015.04.025
12. Tzikas A, Shakir S, Gafoor S, Omran H, Berti S, Santoro G, Kefer J, Landmesser U, Nielsen-Kudsk JE, Cruz-Gonzalez I, et al. Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug. *EuroIntervention*. 2016;11:1170–1179. doi: 10.4244/EIJY15M01_06
13. Boersma LVA, Schmidt B, Betts TR, Sievert H, Tamburino C, Teiger E, Pokushalov E, Kische S, Schmitz T, Stein KM, et al. Implant success and safety of left atrial appendage closure with the watchman device: peri-procedural outcomes from the EWOLUTION registry. *Eur Heart J*. 2016;37:2465–2474. doi: 10.1093/eurheartj/ehv730
14. Bagur R, Martin GP, Nombela-Franco L, Doshi SN, George S, Toggweiler S, Sponga S, Cotton JM, Khogali SS, Ratib K, et al. Association of comorbid burden with clinical outcomes after transcatheter aortic valve implantation. *Heart*. 2018;104:2058–2066. doi: 10.1136/heartjnl-2018-313356
15. Sanjoy S, Choi YH, Holmes D, Herrman H, Terre J, Alraies C, Ando T, Tzemos N, Mamas M, Bagur R. Comorbidity burden in patients undergoing left atrial appendage closure. *Heart*. 2021;107:1246–1253. doi: 10.1136/heartjnl-2020-317741
16. Healthcare Cost Utilization Project. *Overview of the National (Nationwide) Inpatient Sample (NIS)*. Agency for Healthcare Research and Quality. Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed March 9, 2021
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383. doi: 10.1016/0021-9681(87)90171-8
18. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36:8–27. doi: 10.1097/00005650-199801000-00004
19. Velu JF, Haas SD, Van Mourik MS, Koch KT, Vis MM, Henriques JP, Van Den Brink RB, Boekholdt SM, Piek JJ, Bouma BJ, et al. Elixhauser comorbidity score is the best risk score in predicting survival after MitraClip implantation. *Struct Heart*. 2018;2:53–57. doi: 10.1080/24748706.2017.1404172
20. George S, Kwok CS, Martin GP, Babu A, Shufflebotham A, Nolan J, Ratib K, Bagur R, Gunning M, Mamas M. The influence of the Charlson Comorbidity Index on procedural characteristics, VARC-2 endpoints and 30-day mortality among patients who undergo transcatheter aortic valve implantation. *Heart Lung Circ*. 2019;28:1827–1834. doi: 10.1016/j.hlc.2018.11.006
21. Borovac JA, Kwok CS, Mohamed MO, Fischman DL, Savage M, Alraies C, Kalra A, Nolan J, Zaman A, Ahmed J, et al. The predictive value of CHA2DS2-VASC score on in-hospital death and adverse periprocedural events among patients with the acute coronary syndrome and atrial fibrillation who undergo percutaneous coronary intervention: a 10-year National Inpatient Sample (NIS) analysis. *Cardiovasc Revasc Med*. 2020:S1553-8389(20)30472-3 [epub ahead of print]. doi: 10.1016/j.carrev.2020.08.003. Available at: https://pubmed.ncbi.nlm.nih.gov/32828675/. Accessed August 17, 2021
22. Kwok CS, Achenbach S, Curzen N, Fischman DL, Savage M, Bagur R, Kontopantelis E, Martin GP, Steg PG, Mamas MA. Relation of frailty to outcomes in percutaneous coronary intervention. *Cardiovasc Revasc Med*. 2020;21:811–818. doi: 10.1016/j.carrev.2019.11.009
23. Sparrow R, Sanjoy S, Choi YH, Elgendy IY, Jneid H, Villablanca PA, Holmes DR, Pershad A, Alraies C, Sposato LA, et al. Racial, ethnic and socioeconomic disparities in patients undergoing left atrial appendage closure. *Heart*. 2021 Apr 1 [epub ahead of print]. doi: 10.1136/heartjnl-2020-318650. Available at: https://pubmed.ncbi.nlm.nih.gov/33795381/. Accessed August 17, 2021
24. Freixa X, Gafoor S, Regueiro A, Cruz-Gonzalez I, Shakir S, Omran H, Berti S, Santoro G, Kefer J, Landmesser U, et al. Comparison of efficacy and safety of left atrial appendage occlusion in patients aged <75 to >/= 75 years. *Am J Cardiol*. 2016;117:84–90. doi: 10.1016/j.amjcard.2015.10.024
25. Cruz-Gonzalez I, Ince H, Kische S, Schmitz T, Schmidt B, Gori T, Foley D, de Potter T, Tschishow W, Vireca E, et al. Left atrial appendage occlusion in patients older than 85 years. Safety and efficacy in the EWOLUTION registry. *Rev Esp Cardiol (Engl Ed)*. 2020;73:21–27. doi: 10.1016/j.rec.2019.02.008
26. Herrera AP, Snipes SA, King DW, Torres-Vigil I, Goldberg DS, Weinberg AD. Disparate inclusion of older adults in clinical trials: priorities and opportunities for policy and practice change. *Am J Public Health*. 2010;100(suppl 1):S105–S112. doi: 10.2105/AJPH.2009.162982
27. Tahhan AS, Vaduganathan M, Greene SJ, Alrohaibani A, Raad M, Gafeer M, Mehran R, Fonarow GC, Douglas PS, Bhatt DL, et al. Enrollment of older patients, women, and racial/ethnic minority groups in contemporary acute coronary syndrome clinical trials: a systematic review. *JAMA Cardiol*. 2020;5:714–722. doi: 10.1001/jamacardio.2020.0359

SUPPLEMENTAL MATERIAL

Table S1. Charlson Comorbidity Index and ICD-10-CM codes.

Comorbidity	Points	ICD 10-CM codes
Myocardial infarction	1	I25.2
Congestive heart failure	1	I09.81, I25.5, I42.0, I42.5 - I42.9, I43.x, I50.x
Peripheral vascular disease	1	I70.x, I71.x, I72.x, I73.1, I73.8, I73.9, I77.1, I77.7, I79.0, I79.1, I79.8, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular disease	1	I69.x, Z86.73
Dementia	1	F01.5, F02.8, F03.9, G30.x, G31.1, G31.8, G31.9
Chronic pulmonary disease	1	I27.8, I27.9, J40.x - J47.x, J60.x - J67.x, J68.4, J70.1, J70.3, J84, J96.1
Rheumatic disease	1	L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0 - M31.3, M32.x - M35.x, M45.x, M46.5, M46.1, M46.8, M46.9, M48.8, M49.8
Peptic ulcer disease	1	K25.5, K25.7, K25.9, K26.5, K26.7, K26.9, K27.5, K27.7, K27.9, K28.5, K28.7, K28.9
Mild liver disease	1	B18.x, K70.0 - K70.3, K70.9, K71.3 - K71.5, K71.7, K73.x, K74.x, K76.0, K76.0, K76.4, K76.8, K76.9, Z94.4
Diabetes without chronic complication	1	E08.9, E09.9, E10.9, E11.9, E13.9
Diabetes with chronic complication	2	E08.2-E08.8, E09.x, E10.2 - E10.8, E11.2 - E11.8, E12.2 - E12.8, E13.2 - E13.8
Hemiplegia	2	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0 - G83.5, G83.8, G83.9, I69.x, R53.2
Renal disease	2	I12.0, I13.1, N18.x, N19.x, N25.0, Z49.0 - Z49.2
Cancer	2	C00.x - C26.x, C30.x - C34.x, C37.x - C41.x, C43.x, C45.x - C58.x, C60.x - C76.x, C81.x - C85.x, C88.x, C90.x - C96.x
Moderate or severe liver disease	3	I85.0, I86.4, K72.1, K72.9, K76.5, K76.6, K76.7
Metastatic solid tumor	6	C77.x - C80.x, R18.0
AIDS	6	B20

ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification. AIDS: acquired immune deficiency syndrome.

Table S2. Elixhauser Classification System and ICD-10-CM codes.

Comorbidity	Points	ICD-10-CM codes
Congestive heart failure	7	I09.81, I25.5, I42.0, I42.5 - I42.9, I43.x, I50.x
Cardiac arrhythmias	5	I44.1 - I44.3, I45.6, I45.9, I47.x - I49.x, R00.0, R00.1, R00.8, Z95.0
Valvular disease	-1	A52.0, I05.x - I08.x, I09.1, I09.8, I34.x - I39.x, Q23.0 - Q23.3, Z95.2 - Z95.4
Pulmonary circulation disorders	4	I26.x, I27.x, I28.0, I28.8, I28.9
Peripheral vascular disorders	2	I70.x, I71.x, I72.x, I73.1, I73.8, I73.9, I77.1, I77.7, I79.0, I79.1, I79.8, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Hypertension	0	I10.x, I11.x - I13.x, I15.x
Paralysis	7	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0 - G83.5, G83.8, G83.9, I69.x, R53.2
Neurodegenerative disorders	6	E75.0, E75.1, E75.2, E75.4, F84.2, G10.x - G13.x, G20.x - G21.x, G24.0, G24.2, G24.8, G25.4, G25.5, G30.0, G31.0, G31.1, G31.2, G31.8, G31.9, G32.8, G35.x - G37.x, G80.3
Chronic pulmonary disease	3	I27.8, I27.9, J40.x - J47.x, J60.x - J67.x, J68.4, J70.1, J70.3, J84, J96.1
Diabetes, uncomplicated	0	E08.9, E09.9, E10.9, E11.9, E13.9
Diabetes, complicated	0	E08.2-E08.8, E09.x, E10.2 - E10.8, E11.2 - E11.8, E12.2 - E12.8, E13.2 - E13.8
Hypothyroidism	0	E00.x - E03.x
Renal failure	5	I12.0, I13.1, N18.x, N25.0, Z49.0, Z49.3, Z91.1, Z99.2
Liver disease	11	B18.x, I85.x, K70.x, K71.1, K71.3 - K71.5, K71.7, K72.x - K74.x, K75.4, K75.8, K76.0, K76.2 - K76.9, Z94.4
Peptic ulcer disease, no bleeding	0	K25.5, K25.7, K25.9, K26.5, K26.7, K26.9, K27.5, K27.7, K27.9, K28.5, K28.7, K28.9
AIDS/HIV	0	B20
Lymphoma	9	C81.x - C86.x, C88.x, C90.0, C90.2, C90.3, C96.x, D47.Z9
Metastatic cancer	12	C77.x - C80.x, R18.0
Solid tumor without metastasis	4	C00.x - C26.x, C30.x - C34.x, C37.x - C41.x, C43.x, C45.x - C58.x, C60.x - C76.x, D03.1-D03.9, E31.2
Rheumatoid arthritis/collagen, vascular disease	0	L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0 - M31.3, M32.x - M35.x, M45.x, M46.5, M46.1, M46.8, M46.9, M48.8, M49.8
Coagulopathy	3	D66 - D68.x, D69.1, D69.3 - D69.6

Obesity	-4	E66.x, Z68.3, Z68.4, Z68.5
Weight loss	6	E40.x - E46.x, R63.4, R63.6
Fluid and electrolytes disorders	5	E22.2
Blood loss anemia	-2	D50.0
Deficiency anemia	-2	D501, D50.8, D50.9, D51.x - D53.x, D63.1, D63.8
Alcohol misuse	0	F10, E52, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51.x, Z71.4
Drug abuse	-7	F11.x - F16.x, F18.x, F19.x, Z71.5
Psychosis	0	F20.x, F22.x - F25.x, F28.x, F29.x, F30.1, F30.2, F31.2, F31.6, F44.8
Depression	-3	F20.4, F31.3 - F31.5, F32.x, F33.x, F34.1, F41.2, F43.2

ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification. AIDS/HIV: acquired immune deficiency syndrome and human immunodeficiency virus infection.

Table S3. 10-CM codes for in-hospital major adverse events.

Adverse Events	ICD-10-CM codes
Post procedural hemorrhage	D7821, D7822, D7831, D7832, E89810, E89811, E89820, E89821, G9751, G9752, G9761, G9762, H59311, H59312, H59313, H59319, H59321, H59322, H59323, H59329, H59331, H59332, H59333, H59339, H59341, H59342, H59343, H59349, H9541, H9542, H9551, H9552, I97610, I97611, I97618, I9762, I97620, I97621, I97630, I97631, I97638, J95830, J95831, J95860, J95861, K91840, K91841, K91870, K91871, L7621, L7631, M96830, M96840, N99820, N99821, N99840, N9984
Cardiac complications	I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I214, I219, I21A1, I21A9, I220, I221, I222, I228, I229, I469, I97710, I97790, I9788, I9789, I312, I314, I442, 0W9D30Z, 0W9D3ZX, 0W9D3ZZ, 0W9D40Z, 0W9D4ZX, 0W9D4ZZ, 02HK3JZ, 02HK3MZ, 02HL3JZ, 02HL3MZ, 02H63JZ, 02H73JZ, 02HK3JZ, 02HL3JZ, 5A1213Z, 5A1223Z, 0JH60PZ, 0JH60PZ, 0JH63PZ, 0JH63PZ, 0JH80PZ, 0JH80PZ, 0JH83PZ, 0JH83PZ, 0JH604Z, 0JH634Z, 0JH804Z, 0JH834Z, 0JH605Z, 0JH635Z, 0JH805Z, 0JH835Z, 0JH606Z, 0JH636Z, 0JH806Z, 0JH836Z, T8111XA, 028D0ZZ, 02QD0ZZ, 02890ZZ, 02Q90ZZ, 02QF0ZZ, 02QG0ZZ, 02QH0ZZ, 02QJ0ZZ, 02BK0ZZ, 02NK0ZZ, 02NL0ZZ, 02QF0ZZ, 02QA0ZZ, 02B50ZZ, 02RM0JZ, 02U50JZ, 02UM0JZ, 02U50JZ, 02RM0JZ, 02UM0JZ, 02QF0ZZ, 02QG0ZZ, 02QH0ZZ, 02QJ0ZZ, 02U50JZ, 02UM0JZ, 02RM07Z, 02RM0KZ, 02U507Z, 02U508Z, 02U50KZ, 02UM07Z, 02UM0KZ, 02U507Z, 02U508Z, 02U50KZ, 02RM07Z, 02RM0KZ, 02UM07Z ,02RK07Z, 02RK0KZ, 02RL07Z, 02RL0KZ, 02U607Z, 02U608Z, 02U707Z, 02U708Z, 02U70KZ, 02UK0KZ, 02UL0KZ, 02Q50ZZ, 02QM0ZZ, 02Q50ZZ, 02QM0ZZ, 02QB0ZZ, 02QC0ZZ, 02U50JZ, 021609P, 021609Q, 021609R, 02160AP, 02160AQ, 02160AR, 02160JP, 02160JQ, 02160JR, 02160KP, 02160KQ, 02160KR, 02160ZP, 02160ZQ, 02160ZR, 02W50JZ, 02WF07Z, 02WF08Z, 02WF0JZ, 02WF0KZ, 02WG07Z, 02WG08Z, 02WG0JZ, 02WG0KZ, 02WH07Z, 02WH08Z, 02WH0JZ, 02WH0KZ, 02WJ07Z, 02WJ08Z, 02WJ0JZ, 02WJ0KZ, 02WM0JZ, 02Q50ZZ, 02QM0ZZ, 021K0Z5, 021L0Z5, 02B60ZZ, 02B70ZZ, 02BK0ZZ, 02BL0ZZ, 02B60ZZ, 02B70ZZ, 02BK0ZZ, 02BL0ZZ
Post-procedural stroke or transient ischemic attack	I6322, I63139, I63239, I63019, I63119, I63219, I6359, I6359, I6320, I6330, I6340, I6350, I6300, I63011, I63012, I63019, I6302, I63031, I63032, I63039, I6309, I6320, I63211, I63212, I63219, I63549, I6359, I638, I639, H3400, H3401, H3402, H3403, H3410, H3411, H3412, H3413, H34211, H34212, H34213, H34219, H34231, H34232, H34233, H34239, G450, G451, G458, G459, G9781, G9781, G9782, I97811, I97821
Vascular complications	T1490, D7811, D7811, D7812, E3611, E3612, G9748, G9749, H59219, H59229, H9531, H9532, I9751, I9752, J957, J9572, K9171, K9172, L7611, L7612, M96820, M96821, N9971, N9972, T888XXA, S15009A, S15309A, S15209A, S158XXA, S090XX, S158XXA, S159XXA, S2500XA, S25109A, S2520XA, S25309A, S25409, S25409A, S25509A, S25809A, S2590XA, S3500XA, S3510XA, S35299A, S35219A, S35229A, S35239A, S35339A, S35349A, S35319A, S35329A, S358X9A, S35403A, S35406A, S35516A, S35513A, S35533A, S35536A, S3559XA, S358X9A, S3590XA, S45809A, S45009A, S45209A, S45109A, S55109A, S65109A, S55009A, S65009A, S65209A, S65309A, S65409A, S65509A, S45809A, S55809A, S65809A, S45909A, S55909A, S65909A, S75009A, S75109A, S75209A, S85309A, S85409A, S85009A, S85509A, S85109A, S85139A, S85809A, S85169A, S95109A, S75809A, S95809A, S75909A, S85909A, S95902A
Acute kidney injury	N170, N171, N172, N178, N179, N990, R34

ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification.