Extracranial Systemic Embolic Events in a Nationally Representative Discharge Database

A Thesis Submitted to the Faculty of the Graduate School of the University of Minnesota by

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In Partial Fulfillment of the Requirements for the Degree of Masters of Science

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December 2020

Acknowledgements

The research project reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health Award Number UL1TR000114 and 5KL2TR113. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Abstract

Introduction: Systemic emboli affect the brain and extracranial sites resulting in ischemic events with high morbidity and mortality. Extracranial systemic embolic events (ESEEs) frequently affect aortic, iliac, mesenteric, kidney, upper and lower extremity sites. The understanding of factors associated with ESEEs is limited, but atrial fibrillation is likely a major ESEE risk factor.

Methods: A retrospective cross-sectional study was completed using the largest publicly available all-payer inpatient care database, the National Inpatient Sample (NIS). All adult NIS discharges were included and atrial fibrillation and ESEE subgroups identified for analysis. Descriptive statistics, multivariable logistic and linear regression were used to assess the association between ESEEs and atrial fibrillation. Other outcomes included inpatient mortality, length of stay and total hospital charges.

Results: Hospital discharges with ESEEs had higher inpatient mortality (10.3% vs 2.2%), longer length of stay (6 days vs 3 days) and higher total charges ($86,888 vs $30,737) than non-ESEE discharges. The discharges with concurrent atrial fibrillation were more likely to experience ESEEs, with the majority of events involving lower limbs, mesentery and kidneys. After adjustment for demographic, geographic and institutional factors, ESEEs remained associated with increased mortality, higher total hospital charges and longer length of stay.

Discussion: ESEEs with concurrent atrial fibrillation were associated with high inpatient mortality, total hospital charges and longer length of stay. Overall, among all NIS discharges, the most frequent ESEE sites were the lower extremity, mesentery and iliac regions.

Table of Contents

Acknowledgements	i
Abstract	ii
Table of Contents	iii
List of Tables	iv
List of Figures	v
Introduction and Background	1
Methods	4
Results	6
Discussion	9
Tables	11
Figures	25
Bibliography	28
Appendix	31

List of Tables

Table	Page Number
Table 1: Discharge Characteristics and Outcomes by ESEE Status	12
Table 2: Characteristics of Discharges with and without Atrial Fibrillation	13
Table 3: Discharge Outcomes by Atrial Fibrillation Status	15
Table 4: Discharge Characteristics Grouped by Atrial Fibrillation and ESEE Status	16
Table 5: Discharge Outcomes by Atrial Fibrillation and ESEE Status	18
Table 6: ESEE Discharge Characteristics by Event Location	19
Table 7: Logistic Regression for Mortality by ESEE Location	20
Table 8: Multivariable Logistic Regression of Inpatient Mortality	21
Table 9: Multivariable Linear Regression Log10 of Length of Stay	22
Table 10: Multivariable Linear Regression Log10 Total Charges	23
Table 11: 20 Most Frequent Locations of Multisite ESEEs	24

List of Figures

Figure Number	Page Number
Figure 1: ESEEs by Atrial Fibrillation Status	26
Figure 2: Counts of Concurrent ESEE events	27

Introduction and Background

Thromboembolic events associated with atrial fibrillation are a major source of morbidity and mortality.[1] When atrial fibrillation limits effective blood outflow from the heart, blood stasis facilitates clot formation which can become emboli if propelled into the circulatory system. The emboli can travel throughout the body and disrupt arterial blood flow. Much of the prior research has focused on understanding cerebral emboli due to the high stroke morbidity and mortality including long-term disability.[2] Though substantial efforts have been undertaken to understand cerebral emboli and the associated issues with cerebrovascular accidents, extracranial emboli are much less well categorized and understood despite high associated morbidity and mortality.[3]

Atrial Fibrillation and ESEE

Atrial fibrillation has been noted to be associated with systemic embolic events (SEE) to both the brain and extracranial sites and is a growing clinical concern. The atrial fibrillation incidence rate has increased between 2006 and 2018 from 4.74 to 6.82 cases per 1000 person-years and increases with age.[4,5] There are a number of risk factors for atrial fibrillation such as rheumatic heart disease, obesity, smoking, heart failure, diabetes, cardiovascular disease, left ventricular hypertrophy, and hyperthyroidism.[6-9] Atrial fibrillation increases the risk of cardioembolic events and may be difficult to diagnose due to subclinical presentation. For those with stroke and transient ischemic attacks, subclinical atrial fibrillation may be a key risk factor and may require extended evaluation efforts for diagnosis. With extended monitoring, a diagnosis of atrial fibrillation is made in up to 11% of cases.[10-12]

Types of Systemic Embolic Events

Systemic embolic emboli can affect both the brain and extracranial sites, leading to end organ damage and ischemia. Prior studies have noted that approximately 9 in 10 systemic emboli affect the brain vasculature and the remaining 1 in 10 affect extracranial sites [3,13], however certain specific patient subgroups may have higher extracranial event risk such as those with cardiac valve disease [14] and higher rates of events have been noted with increasing age.[15]

ESEEs have been noted in prior studies to affect locations including mesenteric, renal, splenic, aortic, iliac (pelvic), upper and lower extremities [3,14,16-19]. The ESEEs have high associated mortality with 23.4-25% of individuals dying within 30 days.[3,13]

A SEE can cause disruption of blood supply by lodging in end arterial locations leading to catastrophic functional loss or mortality. Since the emboli may fragment or be present in multiple emboli, they can impact multiple sites simultaneously, creating diagnostic and treatment challenges. Emboli to the limbs can present with sensory loss, loss of motor function and cooling

of the affected limb[20]. Peripheral emboli affecting the limbs have been associated with cardiac procedures, atrial fibrillation, and myocardial infarctions with the emboli being frequently noted in lower extremities.[21] Emboli which affect limbs can lead to loss of limb function and mortality and typically affect the lower extremities more often (67%) versus 33% in the lower extremities.[22] Prior interventional studies have noted the emboli were of cardiac origin in 82% of cases.[22,23]

The mesenteric arteries can be impacted by SEE, though the diagnosis is often more difficult to accurately and quickly ascertain as the symptoms may overlap with other disorders. Typical symptoms include abdominal pain out of proportion to physical findings and may also include gut emptying and vomiting with later peritoneal signs.[24] SEE from a cardiac source embolus tend to enter the superior mesenteric artery due to the size and angle of the artery from its point of origin from the aorta. [24] Mesenteric ischemic events have been reported to have a high risk of mortality with up to 50% mortality associated with the events.[24] Prior population studies have identified rates of acute thrombo-embolic occlusion of the superior mesenteric artery of 5.3 per 100,000 persons per year with 95% of individuals having a history of atrial fibrillation.[25] Risk factors for acute mesenteric occlusion include cardiac disease including atrial fibrillation, recent myocardial infarction, and congestive heart failure. Other risk factors include previous arterial emboli, hypercoagulable states and hypovolemic shock.[24] Acute mesenteric ischemic events have been attributed to emboli from the left atria in atrial fibrillation, but also can come from other sources.[26] More recent studies of revascularization for acute arterial mesenteric ischemia have shown about 50% being embolic and 40-50% being thrombotic with mortality rates of 38% for those with embolic events.[24,27,28]

SEE can also affect the renal system as the emboli can affect renal blood flow leading to flank pain, abdominal pain, nausea and vomiting along with biochemical markers for infection, ischemia and reduction in kidney function.[29] Prior autopsy studies have noted that 0.5 to 1.4% had renal infarctions present with nearly 75% of individuals having bilateral renal involvement and simultaneous emboli noted in other sites such as the brain, spleen and lungs.[30] Renal infarction has been noted to be associated with an elevated thromboembolic risk in more than 80% of cases.[31]

Risk Factors for ESEE

Among patients with ESEE, a high percentage have been noted to have atrial fibrillation and associated arterial embolism risk factors including increased patient age, female sex and atherosclerotic coronary disease.[32,33] In patients who were on therapy with oral anticoagulants for SEE prevention, a prior meta-analysis noted that patient age ≥75 years, female sex, a prior history of stroke or transient ischemic attack, renal impairment, prior aspirin use, Asian race,

CHADS2 score >=3 and naïve vitamin-K antagonist status were noted to be associated with a higher risk of stroke.[34] In prior research studies, peripheral arterial emboli have been noted to be associated with atrial fibrillation and post-myocardial thrombus as well as less common sources such as tumors and septic emboli.[35]

Thromboembolic Events and Event Prevention

A better understanding of the risk factors associated with ESEEs is essential in order to identify and target effective primary and secondary prevention. If high risk patients can be proactively identified using known risk factors and characteristics, enhanced patient monitoring of these patients for cardiac arrhythmias can facilitate early identification of atrial fibrillation and allow for appropriate clinical treatment and follow-up for embolic event prevention.[36-38] The current understanding on SEE is limited primarily to secondary analyses of existing clinical trial data with limited capacity to identify optimal diagnostic, treatment and prevention strategies.

Methods

The primary aim of the study was to identify and assess the factors associated with ESEE among hospital discharges including the presence of concurrent atrial fibrillation. The study used de-identified data from the NIS database and was deemed exempt from review by the University of Minnesota Institutional Review Board.

Data Source

The study utilized the 2017 National Inpatient Sample (NIS) database from the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS database provides the largest publically accessible all-payer inpatient healthcare dataset in the United States. It contains hospital discharge data that represents a 20% stratified sample of discharges from 4584 US community hospitals, excluding rehabilitation and long-term care hospitals, from 48 states.[39] The NIS has approximately 7 million un-weighted discharges per year and approximately 35 million weighted national discharges per year. The 2017 NIS has one primary diagnosis and up to 39 secondary discharge diagnoses for each inpatient discharge. The NIS contains discharge data along with a unique record number, but does not have a specific unique patient identifier. Further information about the database is available on the HCUP website.[39]

Study Population

Individual discharges were included from the NIS database and weights were applied based on the discharge weight information provided by the NIS. A total of 35,798,453 weighted admissions were included in the data set. Weighted information is provided in the NIS to represent inpatient discharges from 4584 hospitals in the U.S., excluding rehabilitation and long-term acute-care hospitals.[39]

The entire NIS population for 2017 was initially included in the study with exclusion of discharges with ages less than 18. From the adult discharge data, two specific subgroups were identified for analysis including those with atrial fibrillation and those with extracranial systemic embolic events. Discharges with atrial fibrillation were identified based on the International Classification of Diseases, Tenth Edition Clinical Modification (ICD-10-CM) diagnostic codes in any position using those previously identified in other studies for atrial fibrillation (I48.x) using hospital discharge codes.[40-44]

Extracranial events were identified using (ICD-10-CM) codes in any position using previously published code sets which were supplemented with additional codes after a focused clinical

review of pertinent ICD10 codes of events noted in prior ESEE studies.[13,16,40,45] The mesenteric and renal events were also identified using text search and review of available ICD10 diagnostic codes to supplement and update the codes and disease categories used in the prior published studies. The "other location" events included ICD10 codes which were events in either "unspecified" or "other" arteries[40]. "Multiple location" ESEEs were those which had simultaneous events in multiple ESEE location categories. The extracranial events were grouped by event location including aortic, upper extremity, lower extremity, iliac, mesenteric, renal, other locations and multiple location events. The list of ESEE ICD10 codes is in Appendix A.

Clinical Comorbidities

Clinical comorbidities were identified using the Elixhauser-based comorbidity system. Comorbidities were identified using the software mappings and included in the analysis and aggregated weighted scores were calculated based on previously published weights for specific disease categories.[46] The Elixhauser mapping was completed using the v2020.1 (beta version) of Elixhauser Comorbidity Software for ICD-10-CM which was downloaded from the Health Care Utilization Project (HCUP) website. Inpatient ischemic strokes were identified using ICD10 codes where ischemic stroke was a primary diagnosis using a previously established code set.[47,48]

Statistical Analysis

Means are presented as mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Chi-square analysis was used for between group comparisons of categorical variables. T-tests were used where normally distributed continuous outcome variables were available. Kruskall-Wallis tests were used for non-parametric tests for continuous variables with non-normal distributions. Multivariable logistic regression was used to analyze inpatient mortality outcomes. Both length of stay and total charge outcome variables had substantial skewness toward higher values, thus multivariable linear regression was used for the assessment of length of stay and total charge outcomes after log base 10 transformation of the outcome variables to approximate normality. P-values of less than 0.05 were considered significant for the study. Statistical analysis was completed using SAS Version 9.4.

Results

The 2017 NIS data set has 7,159,694 hospital discharges with a total of 35,798,453 weighted admissions in the data set. The hospitalizations were removed for those under age 18 leaving a weighted total of 30,420,907 hospital discharges in the dataset.

In Table 1, all the eligible discharges were grouped by ESEE status with statistically significant differences between groups for atrial fibrillation, women, age, Elixhauser score, inpatient mortality, length of stay and total charges. The outcomes from the ESEE discharges had higher comorbidity scores, inpatient mortality, length of stay and total charges.

The characteristics of discharges with and without atrial fibrillation are summarized in Table 2. Hospital discharges with atrial fibrillation, as compared to those without atrial fibrillation, had a lower proportion of women, fewer elective admissions, and older age. They also had a greater proportion of Medicare coverage and was less racially diverse.

The atrial fibrillation discharges also had a higher percentage of congestive heart failure, valvular heart disease, peripheral vascular disease, chronic pulmonary disease, diabetes with chronic complications, hypothyroidism, renal failure, coagulopathy, deficiency anemias, fluid and electrolyte disorders and hypertension.

In Table 3, the atrial fibrillation discharges had a longer length of stay, higher total charges, more ischemic strokes and higher inpatient mortality than non-atrial fibrillation discharges. The atrial fibrillation discharges had more discharges to higher levels of care including transfers to other care facilities and home health care. Atrial fibrillation discharges had higher percentages of all ESEEs of each type with upper extremity, lower extremity, mesentery and kidney ESEEs being more than 50% higher in atrial fibrillation discharges than non-atrial fibrillation discharges.

In Table 4, discharge data is summarized among those with and without atrial fibrillation present during the discharge and further divided among those discharges with and without ESEEs. Among both the atrial fibrillation and non-atrial fibrillation discharges with ESEEs, both groups received more care in larger hospitals and in more urban/teaching settings. In both the atrial fibrillation and non-atrial fibrillation groups with ESEEs, there are lower percentages of discharges with hypothyroidism, diabetes without chronic conditions, obesity and depression. The discharges with ESEEs have higher Elixhauser scores with notably higher peripheral vascular disease, coagulopathy, weight loss and fluid/electrolyte disorders comorbidity percentages. Among the subset without atrial fibrillation, ESEEs discharges are older, have more chronic pulmonary disease, diabetes with chronic conditions, renal failure and hypertension.

In both the atrial fibrillation and non-atrial fibrillation discharges in Table 5, the presence of ESEEs was associated with longer lengths of stay, higher total charges, increased inpatient mortality, and more transfers of care to other facilities.

In Figure 1, all ESEEs are included in a donut chart to show the distribution of events. Among discharges with concurrent atrial fibrillation (outer ring) a higher percentage of extracranial events occurred in the lower extremity, upper extremity and mesentery as compared to non-atrial fibrillation discharges. For discharges without atrial fibrillation, the percentage of extracranial events was higher in the iliac region, abdominal aorta, and the “other” sites as well as among those with multiple site events.

Table 6 shows the ESEEs discharge characteristics with key characteristics by location of ESEE stratified by presence of concurrent atrial fibrillation. For discharges with atrial fibrillation as compared to those without atrial fibrillation, there was a higher percent of ischemic stroke related admissions, higher age, higher comorbidity scores and higher inpatient mortality in each ESEE site category. The inpatient mortality was highest for mesenteric and multiple location categories in both groups.

Table 7 shows the unadjusted odds ratios from the logistic regression of inpatient mortality by ESEE site. The odds ratios are compared to no ESEEs at each respective site. The unadjusted logistic regression results for mortality showed that mesenteric ESEE had the highest odds ratio for mortality 13.9 (13.5-14.4), followed by multiple site events 7.1 (6.7-7.6) and kidney at 4.2 (3.9-4.5). All the locations had a mortality odds ratio of greater than two. The relative odds ratios are also shown for visual comparison.

Table 8 shows the multivariable logistic regression results for inpatient mortality controlling for age, income data, hospital characteristics, Elixhauser clinical comorbidities, insurance information, race and seasonal factors to adjust the model. The odds ratios for mortality are shown for select parameters. The odds ratios for mortality are higher for each ESEE site with the highest values at the mesenteric and multiple location event sites. The presence of atrial fibrillation is associated with a higher inpatient mortality as are several comorbidity factors with metastatic cancer, pulmonary circulation disease and fluid and electrolyte disorders having the highest odds ratios for mortality. Reduced odds ratios for mortality are found among women, obesity, blood loss anemia, depression and psychosis related discharges.

Multivariable regression was completed for the log base 10 of the length to stay in Table 9 with transformed log estimated to provide the percent change in length of stay. Length of stay was more than 50% longer among lower extremity, mesenteric, kidney and multiple location discharges.

Multivariable regression was completed for the log-transformed total charges in Table 10. Each of the ESEE types was associated with an increase in total hospital charges with a relatively moderate effect of atrial fibrillation. The results showed the total charges were more than 90% higher among lower extremity, iliac, mesenteric and multiple location discharges.

For the discharges for which an ESEE was diagnosed, the largest proportion of events affected a single site as noted in figure 2. However, there were a substantial number of discharges with ESEEs at multiple locations affecting up to five locations during the discharge.

Table 11 has the data on multiple site ESEEs. For the discharges with multiple concurrent ESEEs, the most frequent combination was the lower extremity and iliac location with the abdominal aortic-iliac and abdominal aortic-lower extremity locations being the 2nd and 3rd most frequent. The most frequent three site combination is the abdominal aortic-lower extremity-iliac combination which is also 6th most frequent multiple ESEE overall.

Discussion

Hospital discharges with ESEEs had higher inpatient mortality (10.3% vs 2.2%), longer length of stay (6 days vs 3 days) and higher total charges ($86,888 vs $30,737) than non-ESEE discharges. The absolute number of ESEEs was higher in the non-atrial fibrillation patients (83,135 or 0.32% of non-atrial fibrillation discharges) but the percentage of discharges having ESEEs were higher among concurrent atrial fibrillation discharges (26,905 or 0.59% of atrial fibrillation discharges).

In models adjusting for demographic, geographic and institutional factors, ESEEs are associated with increased mortality in comparison to those without ESEEs. The subset with atrial fibrillation have a higher mortality than those without atrial fibrillation. In models of total charges, ESEEs are associated with higher total charges with the multiple location, lower extremity and mesenteric events having the highest total charges. Similar findings were noted with length of stay with multiple location, mesenteric and lower extremity events having longer lengths of stay.

A significant number of discharges (9.4%) with ESEEs affected multiple sites during the hospital discharge. These multiple site ESEEs more frequently affected the lower extremity, iliac and abdominal aortic locations with combinations of these three sites comprising more than 50% of the multiple event discharges.

The high mortality, long length of stay and high total charges are consistent with prior findings among hospitalizations for atrial fibrillation, however, there is limited prior literature on non-atrial fibrillation associated ESEEs. The increased prevalence of ESEE with age among atrial fibrillation discharges is similar to prior findings reporting increased event rates with each decade over age 60.[15]

In this study, the ratio of the relative distribution of ESEEs to the upper and lower extremities was approximately 4 lower extremity events to every 1 upper extremity event. These numbers are higher than prior studies which noted ratios of about 2 to 1.[22] Though prior studies have indicated that up to 80% of ESEE were cardioembolic in origin, the numbers may be lower in this study since the majority of events occurred in subjects without atrial fibrillation.[22,23] This may be due to the limitations of the NIS data which covers a single admission timeframe, but may require additional exploration in a broader data set to look for presence of subclinical atrial fibrillation.[10-12]

Limitations. There are several limitations to this study. The data in the NIS are retrospective observational data limited to the inpatient setting. The data in the database are limited to hospital discharge data and does not link to prior hospitalizations or outpatient clinical care data. As a result, it is possible that discharges classified as non-atrial fibrillation may have a prior history of

atrial arrhythmias including atrial fibrillation creating the potential for misclassification and resulting confounding.

The data set is based at the discharge level rather than being at an individual person-level data. This provides a means to provide appropriate sampling for the dataset, but an individual may appear multiple times in the data set which may create potential bias, however, since the data in the study covers only one year and the NIS weights were used this bias should be minimized.

Another data limitation is the lack of available data on mortality post-hospitalization. Typical outcomes associated with hospitalization may include measures such as 30 day mortality or 1 year mortality after an event, however, this follow-up data is not available in the NIS data to provide such comparisons and likely understates hospitalization-related mortality.

The use of administrative data has limitations due to the quality of administrative data which may not be at the same level as other high quality curated research databases. Prior research has noted that the administrative data may miss more cases than a departmental procedural database which may result in this study potentially missing cases [49]. Similarly, ICD10 administrative codes have limitations especially with regard to granularity as in the case of the "unspecified" and "other" categories which are not clear as to their site of involvement as noted in Appendix A.

Conclusion: ESEEs have a relatively high cost, mortality and resource use clinical event. Atrial fibrillation is associated with increased risk of ESEEs and worse outcomes. Other factors associated with ESEEs include age, peripheral vascular disease, coagulopathy, weight loss and fluid and electrolyte disorders. ESEEs are lower in diabetes without chronic conditions, hypothyroidism, obesity and depression. A significant number of the ESEEs occur in multiple event discharges with the lower extremity, iliac and abdominal aortic sites being involved in more than 50% of these multiple site ESEEs. Future work is needed to better understand each ESEE type and to better understand the factors associated these ESEEs in order to better target potential screening and interventional research.

Tables

Table 1: Discharge Characteristics and Outcomes by ESEE Status			
Discharge Characteristics			
	Non-ESEE Discharges (N=30310867)	**ESEE Discharges (N=110040)**	**P-Value**
Ischemic Stroke	2.10%	2.10%	0.2
Atrial Fibrillation	15.1%	24.5%	<.01
Women	57.80%	47.40%	<.01
Age (Years)	57.92 (57.90-57.94)	64.55 (64.34-64.75)	<.01
Elixhauser Score	4.76 (4.75-4.77)	10.16 (10.02-10.29)	<.01
Discharge Outcomes by ESEE Status			
Died	2.20%	10.30%	<.01
Length of Stay (days)	3 (2-5)	6 (3-11)	<.01
Total Charges ($US)	30737 (16471-59104)	86888 (43779-171979)	<.01

Table 2: Characteristics of Discharges with and without Atrial Fibrillation		
Characteristic	**No Atrial Fibrillation (N = 25829494)**	**Atrial Fibrillation (N=4591413)**
Age Distribution		
Age 18-30	15.9%	0.3%
31-40	13.2%	0.7%
41-50	10.6%	2.4%
51-60	16.5%	8.6%
61-70	18.6%	20.2%
71-80	14.3%	29.8%
81 and over	11.0%	38.0%
Primary Payor		
Medicare	41.9%	80.6%
Medicaid	21.0%	4.9%
Private insurance	29.4%	11.7%
Self-pay	4.4%	1.1%
No charge	0.4%	0.1%
Other	3.0%	1.7%
Racial Categories		
White	64.9%	80.7%
Black	16.3%	9.2%
Hispanic	12.0%	5.8%
Asian or Pacific Islander	2.9%	2.0%
Native American	0.7%	0.4%
Other	3.2%	2.0%
Household Median Income		
$1-43,999	31.1%	26.9%
$44,000-55,999	26.5%	27.1%
$56,000-73,999	23.2%	24.6%
$74,000+	19.1%	21.4%
Bed Size of Hospital		
Small	20.1%	19.9%
Medium	29.5%	30.0%
Large	50.4%	50.1%
Hospital Location/Teaching status		
Rural	9.1%	9.9%
Urban Nonteaching	22.9%	23.9%
Urban Teaching	68.0%	66.2%
Region of hospital		
Northeast	18.5%	20.0%

Midwest	22.1%	24.3%
South	39.6%	37.9%
West	19.8%	17.7%
Control/ownership of hospital		
Government, nonfederal	11.8%	9.7%
Private, Not-for-Profit	73.1%	76.8%
Private, Investor Owned	15.0%	13.6%
Women	59.6%	47.3%
Elective Admission	25.5%	13.4%
Weekend Admission	20.3%	22.0%
Age (years) (SD)	54.9 (44.7)	75.0 (26.5)
Elixhauser Comorbidity Information		
Elixhauser Total Score (SD)	3.9 (18.6)	9.5 (21.7)
Congestive heart failure	7.2%	27.4%
Valvular disease	2.7%	10.4%
Pulmonary circulation disease	0.7%	1.0%
Peripheral vascular disease	4.6%	10.8%
Paralysis	3.0%	4.5%
Other neurological disorders	8.1%	10.8%
Chronic pulmonary disease	17.9%	29.8%
Diabetes w/o chronic complications	10.3%	13.2%
Diabetes w/ chronic complications	13.3%	23.2%
Hypothyroidism	11.2%	19.7%
Renal failure	11.9%	30.0%
Liver disease	4.3%	3.9%
Peptic ulcer Disease x bleeding	0.7%	1.0%
Acquired immune deficiency syndrome	0.3%	0.1%
Lymphoma	0.7%	1.2%
Metastatic cancer	2.3%	2.3%
Solid tumor w/out metastasis	2.0%	2.9%
Rheumatoid arthritis/collagen vasc	2.8%	3.8%
Coagulopathy	5.3%	9.5%
Obesity	15.3%	18.5%
Weight loss	5.5%	8.3%
Fluid and electrolyte disorders	24.7%	37.2%
Chronic blood loss anemia	3.1%	1.3%
Deficiency Anemias	16.6%	24.4%
Alcohol abuse	4.9%	3.2%
Drug abuse	5.2%	1.7%
Psychoses	4.1%	2.3%
Depression	12.5%	12.4%
Hypertension	45.8%	62.9%
All Results are statistically significantly different at p<0.05		

Table 3: Discharge Outcomes by Atrial Fibrillation Status		
	No Atrial Fibrillation	**Atrial Fibrillation**
Length of stay (days)	3 (2-5)	4 (2-7)
Total charges ($US)	29710 (15965-56835)	38022 (20264-75516)
Ischemic Stroke (Concurrent)	1.8%	3.4%
Disposition of Patient		
Routine	67.3%	41.8%
Transfer to Short-Term Hospital	1.9%	2.7%
Transfer Other: SNF, ICF, other	14.1%	29.0%
Home Health Care	13.2%	20.9%
Against Medical Advice	1.7%	0.7%
Died	1.8%	4.8%
ESEEs (Combined)	0.322%	0.586%
Extracranial Embolic Events by Site		
Aortic	0.031%	0.038%
Upper Extremity	0.018%	0.053%
Lower Extremity	0.081%	0.190%
Iliac	0.040%	0.044%
Mesentery	0.055%	0.105%
Kidney	0.033%	0.061%
Other Location	0.036%	0.055%
Multiple Locations	0.028%	0.041%
All Results are statistically significant at p<0.05		

Table 4: Discharge Characteristics Grouped by Atrial Fibrillation and ESEE Status						
Discharge Characteristics	**NonAfib Non-ESEE N=25746359**	**NonAfib ESEE N=83135**	**P-value**	**Afib Non-ESEE N=4564508**	**Afib ESEE N=26905**	**P-value**
Age Distribution						
Age 18-30	15.9%	4.1%	<.001	0.3%	0.4%	<.001
31-40	13.2%	5.9%		0.7%	0.9%	
41-50	10.6%	11.5%		2.4%	2.7%	
51-60	16.5%	23.6%		8.6%	9.0%	
61-70	18.5%	26.5%		20.2%	21.3%	
71-80	14.3%	18.2%		29.8%	28.7%	
81 and over	11.0%	10.2%		38.0%	37.1%	
Primary Payor						
Medicare	41.9%	50.4%	<.001	80.6%	78.7%	<.001
Medicaid	21.0%	17.0%		4.9%	5.9%	
Private insurance	29.4%	25.2%		11.7%	11.8%	
Self-pay	4.4%	4.1%		1.1%	1.6%	
No charge	0.4%	0.5%		0.1%	0.1%	
Other	3.0%	2.9%		1.7%	1.9%	
Racial Categories						
White	64.8%	71.1%	<.001	80.7%	79.9%	0.001
Black	16.3%	15.1%		9.2%	9.5%	
Hispanic	12.1%	8.8%		5.8%	5.8%	
Asian or Pacific Islander	2.9%	1.7%		2.0%	2.2%	
Native American	0.7%	0.7%		0.4%	0.4%	
Other	3.2%	2.6%		2.0%	2.2%	
Median Income						
$1-43,999	31.1%	32.9%	<.001	26.9%	28.0%	<.001
$44,000-55,999	26.5%	27.5%		27.1%	26.3%	
$56,000-73,999	23.2%	22.8%		24.6%	24.4%	
$74,000+	19.2%	16.8%		21.4%	21.3%	
Bed Size of Hospital						
Small	20.2%	13.7%	<.001	20.0%	15.1%	<.001
Medium	29.5%	26.7%		30.0%	27.0%	
Large	50.3%	59.6%		50.0%	57.9%	
Hospital Location/Teaching Status						
Rural	9.2%	5.2%	<.001	9.9%	4.9%	<.001
Urban Nonteaching	22.9%	17.5%		23.9%	18.7%	
Urban Teaching	68.0%	77.3%		66.1%	76.4%	
Region of Hospital						
Northeast	18.5%	17.2%	<.001	20.0%	19.4%	<.001
Midwest	22.1%	22.7%		24.3%	24.6%	

South	39.6%	40.1%		37.9%	36.9%	
West	19.8%	19.9%		17.7%	19.1%	
Control/Ownership of Hospital						
Government, nonfederal	11.8%	12.7%	<.001	9.7%	10.0%	<.001
Private, Not-for-Profit	73.1%	75.2%		76.8%	78.6%	
Private, Investor Owned	15.1%	12.2%		13.6%	11.4%	
Women	59.6%	46.5%	<.001	47.2%	50.2%	<.001
Elective Admission	25.6%	20.8%	<.001	13.4%	13.5%	0.63
Weekend Admission	20.3%	19.8%	<.001	21.9%	22.4%	0.09
Age (Years)	54.9	61.4	<.001	75.0	74.4	<.001
Elixhauser Comorbidity Information						
Elixhauser Aggregate Score	3.9	9.3	<.001	9.4	12.8	<.001
Congestive heart failure	7.2%	8.9%	<.001	27.4%	22.4%	<.001
Valvular disease	2.6%	4.0%	<.001	10.4%	8.8%	<.001
Pulmonary circulatory dsx	0.7%	2.5%	<.001	1.0%	1.7%	<.001
Peripheral vascular dsx	4.4%	52.3%	<.001	10.5%	50.9%	<.001
Paralysis	3.0%	4.5%	<.001	4.5%	7.0%	<.001
Other neurologic dsx	8.1%	7.8%	<.001	10.8%	10.4%	0.014
Chronic pulmonary dsx	17.9%	25.3%	<.001	29.8%	29.1%	0.016
Diabetes w/o comp.	10.3%	8.4%	<.001	13.2%	8.4%	<.001
Diabetes w/ complications	13.3%	20.1%	<.001	23.2%	24.2%	<.001
Hypothyroidism	11.2%	9.9%	<.001	19.7%	16.3%	<.001
Renal failure	11.9%	16.8%	<.001	30.0%	29.1%	0.002
Liver disease	4.3%	6.0%	<.001	3.9%	5.1%	<.001
Peptic ulcer x bleeding	0.7%	1.5%	<.001	1.0%	1.9%	<.001
Acquired Immune Def Syndrome	0.3%	0.3%	0.085	0.1%	0.1%	0.048
Lymphoma	0.7%	0.6%	0.049	1.2%	0.7%	<.001
Metastatic cancer	2.3%	3.2%	<.001	2.3%	2.2%	0.44
Solid tumor w/out mets	2.0%	2.8%	<.001	2.9%	3.2%	0.002
Rheum arth/collagen vas	2.8%	3.5%	<.001	3.8%	3.5%	0.038
Coagulopathy	5.3%	12.5%	<.001	9.5%	16.3%	<.001
Obesity	15.3%	13.5%	<.001	18.6%	13.9%	<.001
Weight loss	5.5%	13.1%	<.001	8.3%	14.3%	<.001
Fluid/electrolyte disorders	24.6%	37.9%	<.001	37.1%	45.5%	<.001
Chronic blood loss anemia	3.1%	1.4%	<.001	1.3%	1.7%	<.001
Deficiency Anemias	16.6%	20.0%	<.001	24.4%	22.7%	<.001
Alcohol abuse	4.9%	5.2%	<.001	3.2%	3.6%	<.001
Drug abuse	5.2%	5.3%	0.18	1.7%	2.0%	<.001
Psychoses	4.1%	3.3%	<.001	2.3%	1.8%	<.001
Depression	12.5%	11.3%	<.001	12.4%	9.0%	<.001
Hypertension	45.7%	59.6%	<.001	62.9%	63.4%	0.088

Table 5: Discharge Outcomes by Atrial Fibrillation and ESEE Status						
Hospital Discharge Outcomes	**NonAfib Non-ESEE N=25746359**	**NonAfib ESEE N=83135**	**P-value**	**Afib Non-ESEE N=4564508**	**Afib ESEE N=26905**	**P-value**
Length of stay (days)	3.0	6.0	<.001	4.0	6.0	<.001
Total charges ($US)	29629	86144	<.001	37860	89535	<.001
Stroke during Hospitalization	1.8%	1.9%	0.30	3.4%	2.9%	<.001
Disposition of Patient						
Routine	67.4%	49.0%	<.001	41.8%	29.4%	<.001
Transfer to Short-Term Hospital	1.9%	3.5%		2.7%	3.5%	
Transfer Other: SNF, ICF, other	14.1%	20.9%		29.0%	34.4%	
Home Health Care	13.2%	16.6%		21.0%	17.7%	
Against Medical Advice	1.7%	1.1%		0.7%	0.5%	
Died	1.8%	8.9%		4.8%	14.6%	
Discharge Alive, Destination Unknown	<0.1%	***		<0.1%	***	
*** Results which have represent cell sizes <10 and cannot be included due to NIS data use requirements						

Table 6: ESEE Discharge Characteristics by Event Location									
ESEE Discharges with Concurrent Atrial Fibrillation (N=26905)									
ESEE Location	**N**	**% Group**	**Stroke Dx**	**% Women**	**Age (SD)**	**Elix. Score (SD)**	**Died Inpt**	**Length of Stay (IQR)**	**Total Charges, $ (IQR)**
Aortic	1750	6.5%	5.4%	49.4%	73.9 (24.7)	13.7 (23.4)	12.3%	6 (3-11)	85397 (41392-152835)
Upper Extremity	2415	9.0%	2.7%	59.0%	76.5 (28.7)	10.7 (23.8)	8.3%	5 (3-10)	61837 (33054-138364)
Lower Extremity	8715	32.4%	2.2%	48.5%	76.2 (25.3)	11.7 (22.1)	8.7%	6 (4-11)	96308 (54683-173356)
Iliac	2020	7.5%	***	43.1%	72.8 (25.0)	11.8 (21.5)	8.7%	6 (3-12)	98980 (54988-193853)
Mesentery	4805	17.9%	***	53.8%	75.6 (24.0)	16.4 (23.7)	33.3%	9 (4-16)	119525 (57419-240258)
Kidney	2780	10.3%	4.0%	46.2%	70.1 (30.2)	12.5 (23.9)	9.9%	6 (3-10)	48799 (26812-133046)
Other Location	2545	9.5%	8.1%	47.9%	71.9 (29.5)	11.7 (23.3)	10.8%	6 (3-12)	76534 (30410-165069)
Multiple Locations	1875	7.0%	***	54.7%	72.0 (32.6)	13.8 (22.0)	22.1%	7 (4-13)	112363 (54525-231890)
ESEE Discharges without Concurrent Atrial Fibrillation (N=83135)									
ESEE Location	**N**	**% Group**	**Stroke Dx**	**% Women**	**Age (SD)**	**Elix. Score (SD)**	**Died Inpt**	**Median LOS (IQR)**	**Median Charges (IQR)**
Aortic	7990	9.6%	4.8%	51.5%	63.7 (28.1)	8.9 (21.0)	6.1%	5 (3-9)	73037 (36948-135063)
Upper Extremity	4705	5.7%	2.2%	53.3%	57.9 (37.6)	8.8 (24.0)	7.9%	5 (3-10)	74398 (37430-165733)
Lower Extremity	20890	25.1%	1.0%	38.7%	63.2 (31.1)	8.4 (20.8)	5.1%	5 (3-10)	99214 (56100-178328)
Iliac	10215	12.3%	1.1%	41.2%	63.7 (28.3)	7.7 (19.7)	3.9%	4 (2-9)	85313 (46175-158144)
Mesentery	14275	17.2%	***	55.8%	63.6 (35.9)	11.2 (23.5)	20.8%	7 (3-13)	85390 (42913-179467)
Kidney	8575	10.3%	2.9%	46.2%	54.3 (38.3)	9.8 (23.1)	8.3%	5 (3-10)	58340 (29726-141159)
Other Location	9260	11.1%	3.8%	48.2%	58.7 (36.2)	9.7 (23.6)	6.2%	6 (3-12)	75071 (35511-159212)
Multiple Locations	7225	8.7%	1.9%	46.8%	59.5 (31.0)	10.3 (22.9)	11.7%	7 (3-13)	116034 (60191-224724)

(SD) Standard Deviation (IQR) Interquartile Range

*** Results which have represent cell sizes <10 and cannot be included due to NIS data use requirements

Table 7: Logistic Regression for Mortality by ESEE Location				
ESEE Location	SEE #	Odds Ratio	95% Confidence Limits	
Aortic	1	3.5	3.2	3.7
Upper Extremity	2	3.9	3.5	4.2
Lower Extremity	3	2.9	2.8	3.0
Iliac	4	2.2	2.0	2.4
Mesentary	5	13.9	13.5	14.4
Kidney	6	4.2	3.9	4.5
Other Location	7	3.4	3.2	3.7
Multiple Locations	8	7.1	6.7	7.6

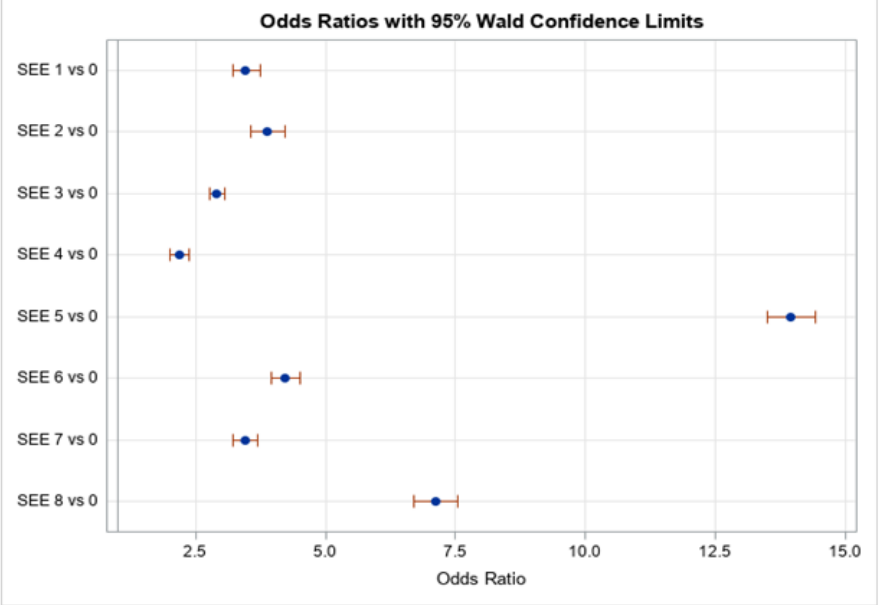

Table 8: Multivariable Logistic Regression of Inpatient Mortality			
ESEE Site	**Odds Ratio**	**95% Confidence Limits**	
Aortic	2.31	2.12	2.51
Upper Extremity	2.31	2.10	2.54
Lower Extremity	1.86	1.77	1.96
Iliac	1.74	1.59	1.90
Mesentery	7.53	7.25	7.83
Kidney	2.49	2.31	2.67
Other Location	2.13	1.97	2.30
Multiple Locations	4.33	4.04	4.64
Atrial Fibrillation	1.32	1.31	1.33
Women	0.89	0.89	0.89
Age	1.04	1.04	1.04
Congestive Heart Failure	1.82	1.80	1.83
Pulmonary circulation disease	2.84	2.80	2.89
Coagulopathy	2.52	2.51	2.54
Fluid and electrolyte disorders	2.70	2.68	2.71
Paralysis	1.61	1.59	1.63
Metastatic Cancer	2.97	2.94	3.00
Weight Loss	1.78	1.77	1.80
Obesity	0.81	0.80	0.81
Chronic blood loss anemia	0.67	0.66	0.69
Psychosis	0.83	0.82	0.84
Depression	0.70	0.70	0.71

Multivariable model adjusted for demographic and comorbidities with inpatient mortality odds ratios compared with no event at the respective ESEE site. P-values are all $p < 0.01$

Table 9: Multivariable Linear Regression Log10 of Length of Stay				
Variable	**% Change**	**Estimates**	**95% Confidence Limits**	
Aortic	34.9	0.13	0.08	0.17
Upper Extremity	47.9	0.17	0.12	0.23
Lower Extremity	66.0	0.22	0.19	0.25
Iliac	28.8	0.11	0.06	0.15
Mesentery	77.8	0.25	0.21	0.28
Kidney	58.5	0.2	0.15	0.24
Other Location	54.9	0.19	0.15	0.24
Multiple Locations	86.2	0.27	0.22	0.32
Atrial Fibrillation	14.8	0.06	0.06	0.06
ESEE results are relative to no ESEE event Adjusted for demographic, comorbidity and other factors P-values were all <0.001				

Table 10: Multivariable Linear Regression Log10 Total Charges				
Variable	**% Change**	**Estimates**	**95% Confidence Limits**	
Aortic	66.0	0.22	0.2	0.23
Upper Extremity	77.8	0.25	0.23	0.27
Lower Extremity	108.9	0.32	0.31	0.33
Iliac	99.5	0.3	0.29	0.32
Mesentery	108.9	0.32	0.3	0.33
Kidney	62.2	0.21	0.19	0.22
Other Location	73.8	0.24	0.22	0.25
Multiple Locations	134.4	0.37	0.36	0.39
Atrial fibrillation	5.9	0.025	0.024	0.026
ESEE results are relative to no ESEE event Adjusted for demographic, comorbidity and other factors P-values were all <0.001				

Table 11: Most Frequent Locations of Multisite ESEEs	
ESEE Combination Event	**Number Events**
Lower-Iliac	2490
AAA-Iliac	1160
AAA-Lower	705
Other-Kidney	625
AAA-Kidney	420
AAA-Lower-Iliac	350
Other-Iliac	290
Mesentery-Kidney	280
Other-Mesentery	275
Upper-Lower	255
Upper-Other	225
Lower-Kidney	200
Lower-Other	185
Iliac-Kidney	180
AAA-Other	160
AAA-Mesentery	140
AAA-Upper	120
Lower-Mesentery	120

Figures

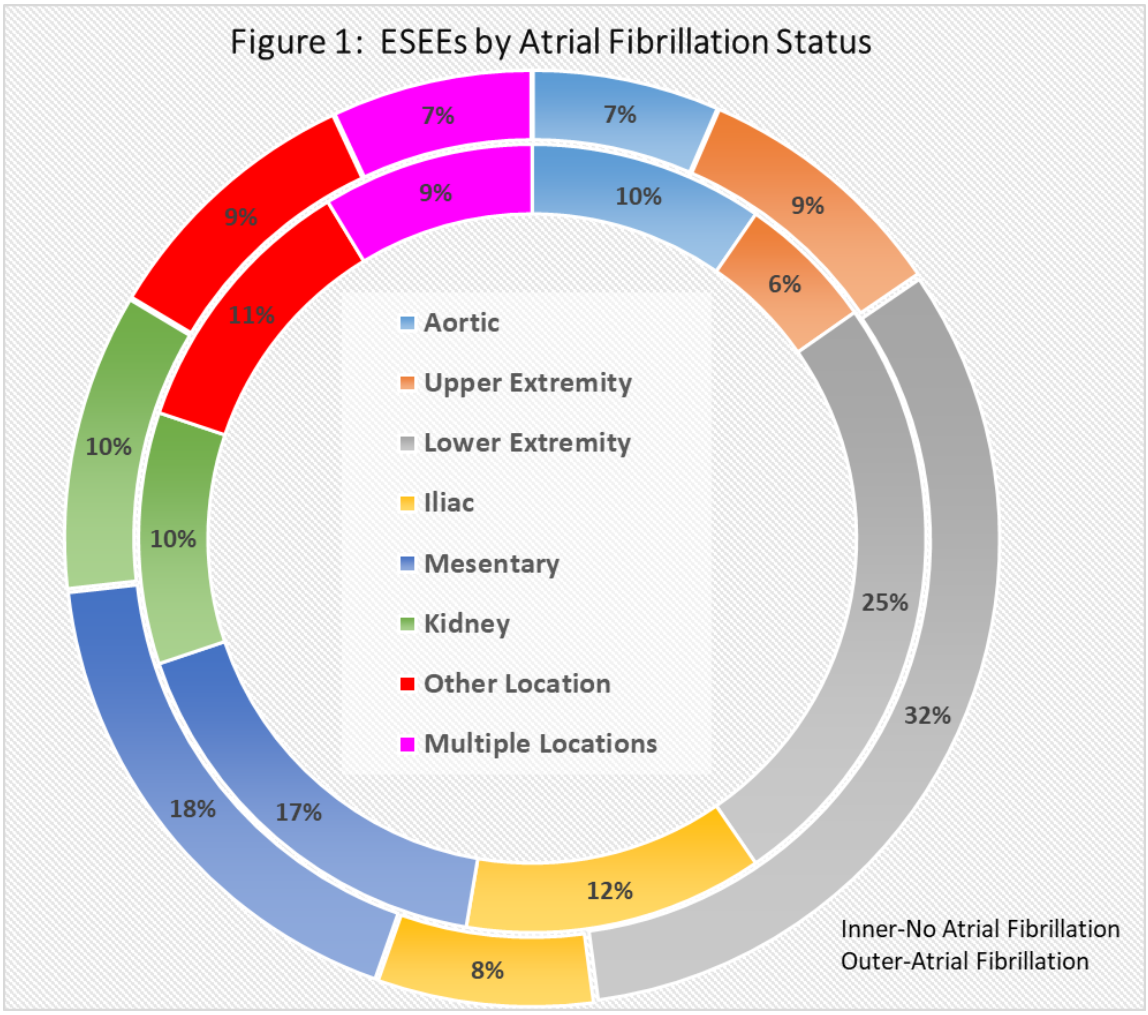
Figure 1: ESEEs by Atrial Fibrillation Status
7%
9%
6%
25%
32%
12%
8%
17%
18%
10%
10%
11%
9%
7%
10%
Aortic
Upper Extremity
Lower Extremity
Iliac
Mesentary
Kidney
Other Location
Multiple Locations
Inner-No Atrial Fibrillation
Outer-Atrial Fibrillation

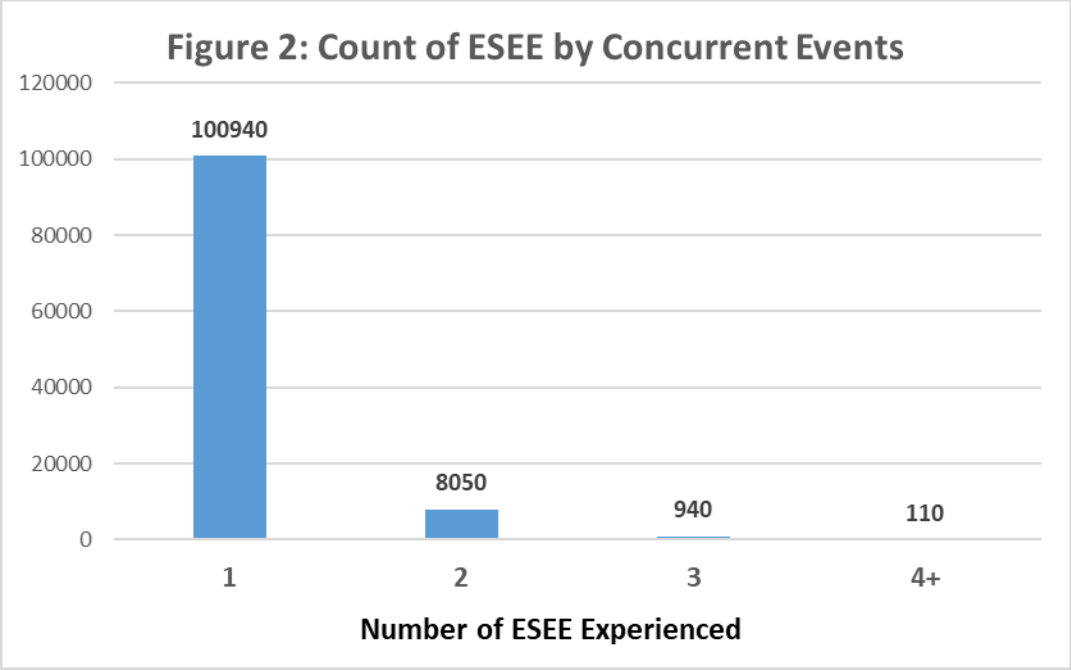
Figure 2: Count of ESEE by Concurrent Events
120000
100000
80000
60000
40000
20000
0
100940
8050
940
110
1
2
3
4+
Number of ESEE Experienced

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Appendix A: ICD10 Codes for Each ESEE Group

Group	ICD10 Code	ICD10 Code Description
AAA	I74	Arterial embolism and thrombosis
AAA	I740	Embolism and thrombosis of abdominal aorta
AAA	I7401	Saddle embolus of abdominal aorta
AAA	I7409	Other arterial embolism and thrombosis of abdominal aorta
AAA	I741	Embolism and thrombosis of other and unspecified parts of aorta
AAA	I7410	Embolism and thrombosis of unspecified parts of aorta
AAA	I7411	Embolism and thrombosis of thoracic aorta
AAA	I7419	Embolism and thrombosis of other parts of aorta
Upper	I742	Embolism and thrombosis of arteries of upper extremities
Lower	I743	Embolism and thrombosis of arteries of lower extremities
Other	I744	Embolism and thrombosis of arteries of extremities, unspecified
Iliac	I745	Embolism and thrombosis of iliac artery
Other	I748	Embolism and thrombosis of other arteries
Other	I749	Embolism and thrombosis of unspecified artery
Mesentery	K550	Acute vascular disorders of intestine
Mesentery	K5502	Acute infarction of small intestine
Mesentery	K55021	Focal (segmental) acute infarction of small intestine
Mesentery	K55022	Diffuse acute infarction of small intestine
Mesentery	K55.029	Acute infarction of small intestine, extent unspecified
Mesentery	K5504	Acute infarction of large intestine
Mesentery	K55041	Focal (segmental) acute infarction of large intestine
Mesentery	K55042	Diffuse acute infarction of large intestine
Mesentery	K55049	Acute infarction of large intestine, extent unspecified
Mesentery	K5506	Acute infarction of intestine, part unspecified
Mesentery	K55061	Focal (segmental) acute infarction of intestine, part unspecified
Mesentery	K55062	Diffuse acute infarction of intestine, part unspecified
Mesentery	K55069	Acute infarction of intestine, part and extent unspecified
Kidney	N280	Ischemia and infarction of kidney