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Long-Term Outcomes for Low Income Patients Who Received Endovascular Therapy for Large Vessel Occlusion Stroke: Hospital Readmissions and Mortality

A Study Proposal Utilizing the New York State Medicaid Claims Data

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please keep me informed about publication

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Background and Problem

Stroke is the fifth leading cause of death in the United States and the leading cause of disability. Its costs amount to $34 billion each year including the cost of health care services, medicines to treat stroke, and missed days of work (CDC, 2017). Ischemic strokes due to large vessel occlusion (LVO) compared with non-LVO strokes are larger in infarct size, have more severe presenting deficits, and are associated with a 4.5-fold increased odds of death and a 3-fold reduction in odds of a good outcome (Malhotra, Gornbein & Saver, 2017). A 2007 study of Medicare beneficiaries found that more than half of ischemic stroke survivors died or were readmitted at least once during the first year after discharge (Bravata, Ho, Meehan, Brass & Concato).

Significance and Innovation

In 2015, an emergency endovascular clot removal treatment, thrombectomy, became the standard of care (Berkhemer, et al., 2015) for its role in reducing disability after a devastating LVO stroke. With successful reperfusion therapy, significantly higher levels of functional outcomes have been observed and have revolutionized stroke care. While procedural costs of endovascular therapy (EVT) are initially higher that standard medical management, EVT results in downstream savings in stroke care because of better outcomes. Researchers have estimated cost effective values of $16,001, $12,120 and $9386 per quality adjusted life year gained with EVT (Ganesalingam et al., 2015).

Strokes caused by LVO can be treated in as late as 24 hours after onset at hospitals who offer acute EVT. Because the initial positive trials demonstrating the efficacy of EVT are fairly recent, an investigation on longer-term outcomes can help clinicians, stroke teams and acute care facilities better understand the resonant effects of EVT on outcomes after hospitalization. Additionally, studying a Medicaid population offers unique insight on the recovery trajectory of disadvantaged patients who may be at higher risk of complications and mortality (Seifi, Elliott, Elsehety, 2016; Marshall et al., 2015). Typically, individuals eligible for Medicaid are required to be within the poverty income level of about $12,140 per year and are considered low socioeconomic status. Data studying the effects of socioeconomic status after stroke thrombectomy are limited, however researchers who studied race, insurance status, income, gender and age found lower utilization rates of endovascular therapy in uninsured patients, Medicare patients and black patients (Brinjikji, Rabinstein & McDonald, 2014). d Cloft

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The purpose of this study is to evaluate the question: what are the long-term outcomes (readmission and mortality) of large vessel occlusion strokes after endovascular treatment for a low-income population? Conducting these 6-month analyses may complement the current literature and its available RCTs with real world data beyond 90 days, and determine if ~~our real-world~~ findings differ from published outcomes in controlled studies. An additional aim of this research is to study readmission types, characteristics, intervals, and frequencies for low-income patients who were treated with emergent endovascular therapy for LVO stroke.

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Scientific Premise

Traditional statistical methods have been prevalent in readmission analyses, but data science approaches have gained popularity in the last decade. A 2018 meta-analysis on 77 hospital readmission studies found that 68% of researchers utilized regression techniques, 13% used survival analyses and 18% used machine learning techniques (Artetxe, Beristain & Grana, 2018). Recent studies have utilized regression models and survival analyses in evaluating and predicting

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outcomes after surviving stroke. Ramchand and colleagues (2018) estimated 30- and 90-day readmission rates using National Readmission Data survey, weighting methods, and HCUP single-level Clinical Classification Software. Using descriptive statistics, they examined patient, clinical and hospital characteristics and constructed weighted unconditional logistic regression models to estimate the odds of all-cause non-elective readmissions. These investigators found that non-elective readmission rates in patients who underwent thrombectomy were 12.5% at 30 days and 20.7% at 90 days with leading diagnoses of sepsis and recurrent stroke.

Nouh and colleagues (2017) also measured 30-day inpatient readmissions after stroke for patients readmitted to the same facility and excluded elective surgeries, palliative care and hospice. They then utilized multivariate logistic regression and other analytic tests to explore certain relationships.

Mortality rates after endovascular therapy within 3-6 months were only available from one study that reviewed LVO versus non-LVO strokes. They found that 26.2% of patients died within 3-6 months of their LVO stroke versus 1.3% of patients who had non-LVO stroke; they estimated LVO strokes accounted for 95.6% of all post-stroke mortality (Malhotra, Gornbein & Saver, 2017). In a 2013 prospective cohort study (FUTURE) on young stroke and TIA patients, long-term (20-year) mortality was measured with standard mortality ratio and survival analyses. Theses researchers found that observed mortality exceeded expected mortality in all stroke types. Kaplan Meier analyses were studied on case fatality 30 days after stroke or TIA, and Cox proportional hazards models were constructed to measure any associations of age, gender thrombolytic therapy and stroke subtype on mortality. The investigators divided age into three groups and compared Kaplan-Meier curves between age and gender categories and found that even 20 years after stroke for patients aged 18 through 50, patients are at significantly high risk of death. These data were collected and published prior to the mainstream adoption of endovascular treatment into stroke clinical practice guidelines, and long-term survival analyses on mortality after EVT would lend important knowledge to the evolving field.

Conceptual Framework

This research study's conceptual framework is composed of the independent variables or the predictors influencing the outcomes or responses which are the dependent variables. A primary objective is to estimate and predict outcomes after endovascular treatment for large vessel stroke. Independent variables represent demographic, disease-related and social factors that may influence outcomes. Demographic variables such as age and gender (GND), disease-related factors such as disease rank (DSRK) and major comorbidities, and behavioral health issues such as substance abuse, depression, anxiety, and low income were also studied for their potential influence on outcomes. Lastly, inpatient length of stay (LOS) and rates of hemorrhagic transformation (HT) after stroke were other independent variables added for their relevancy in stroke outcomes.

Two dependent variables or responses were studied in relation to the independent variables. The primary outcome studied was timing of unplanned readmission, or "survival" without readmission after EVT treatment. Both emergency room visits and inpatient readmissions were studied separately but combined within our overall analysis. Readmission rates were reported at 30, 90 and 180 days post initial EVT inpatient discharge. The second dependent variable, or outcome, was rate of mortality within the year of EVT treatment. A model depicting this conceptual framework can be found on Appendix A, Model of Conceptual Framework of long-term outcomes for low income patients who received endovascular therapy for LVO stroke: hospital readmissions and mortality.

Data Registry

Background

The research-related data analyzed were payment claims for a two and a quarter year period, 2016, 2017, and through March 2018. These data were collected by the New York State Medicaid program who received the data directly from ~~hospitals~~ insurers with standardized clinical and demographic information electronically housed within the Medicaid Data Warehouse. Claims from the Western New York region were obtained, which is comprised of 17 counties. The target population were all patients ages 18 years and older who underwent endovascular therapy for large vessel stroke. For the purpose of quantifying treatment and utilization rates, 2017 ischemic stroke volumes were measured for the medical and surgical subgroups.

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You mean the number of cases
volume here is confusing

Key registry items were codes of the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10). Important pertinent data for the initial identification of the EVT event were the surgical-ICD 10 codes. There are Current Procedural Terminology (CPT) codes and surgical ICD-10 codes. Initial attempts to filter the treatment population by CPT code of 61645 (Percutaneous arterial transluminal mechanical thrombectomy and/or infusion for thrombolysis, intracranial, any method…) was unsuccessful in identifying EVT treated patients within the claims database. However, the surgical ICD-10 codes were immediately retrievable within the "procedure code" fields. These codes are defined as: removal of thrombus. The code 03C_3ZZ has the middle space designated for an alphabetic letter that specifies the artery from which the thrombus was removed. The code 03CG3ZZ represents Extirpation of Matter from Intracranial Artery, Percutaneous Approach. The middle letter changes from "H" thru "N" to describe the cerebral or precerebral artery that was treated. The codes 03CP3ZZ and O3CQ3ZZ represent to thrombus removal from either the right or left vertebral arteries respectively, as we included posterior circulation strokes in our analyses unlike the published RCTs.

The ICD-10 medical diagnoses codes confirmed ischemic stroke for cases with documented EVT codes. These ICD-10 codes were defined within the I63.xx series starting with I63.30 (cerebral infarction due to thrombosis of unspecified cerebral artery) followed with additional codes that specified a cerebral artery. In addition, the ICD-10 code category I63.4xx (cerebral infarction due to embolism of unspecified cerebral artery) specifies the mechanism (embolism) of the stroke and is followed by the specific vessel occlusion. Primary ICD-10 codes along with other diagnosis codes 1 through 5 were reviewed to characterize concurrent problem, to categorize reasons for readmissions, and to identify any behavioral health issues such as depression, anxiety, tobacco and alcohol abuse, and substance abuse.

Temporal data were necessary in studying hospital readmissions after stroke. Admit dates, service dates and discharge dates associated with their corresponding ICD-10 codes were requested in order to create the survival analysis. The EVT encounter discharge date served as the unique starting point for analysis for each patient, and subsequent encounters within 6 months represented readmissions. The Medicaid claims classification types (inpatient [IP], emergency room [ER] or outpatient [OP]) were needed to select the visits needed for analysis. Lastly, a flag that indicated patient death was needed for calculating mortality rates.

Cleaning and transforming the data

Claims data obtained for 2016-March 2018 surgical stroke treatment were reviewed in detail. These amounted to 1984 claims for "surgical" ischemic stroke patients. Initial cleansing of the data was performed by removing non-EVT surgical procedures such as tracheostomies, intra-arterial lines and feeding tube insertions. Duplicate claims were further removed, resulting in 1071 claims. Additional cleansing of the data involved removing claims outside of our temporal window-- encounters that were beyond 180 days from the EVT were excluded, as were encounters that predated the EVT stroke hospitalization. And claims other than ER or IP visits were removed. Ninety-eight claims were then retained. ED-to-inpatient versus ED only visits were then filtered for duplicates, and a total of 70 claims were retained for analysis. Characterization of each encounter was performed by translating and categorizing primary and diagnosis codes 1 thru 5. The 70 claims were then merged with demographic, complexedex disease ranking and the mortality data. These claims included 30 patients who were treated for LVO stroke with EVT and 40 unique readmissions encounters within 6 months. Appendix B, Flow Chart on Data Cleansing provides a visual on the process of cleaning and transforming the data as described.

what is the unit of analysis

cases or claims

cases

claims

encounters

We identified the EVT encounter as the "Primary" encounter and utilized each unique discharge date as our starting point for readmission intervals. Formulas were created in Excel to flag encounters falling within 1-180 days after EVT stroke discharge and only those claims were retained for analysis. Patients were then grouped into two categories: those who were readmitted within 180 days, and those who survived without readmission at 180 days. Descriptive analyses using Chi-squared tests were run to compare variables that were significantly associated with unplanned readmission versus no readmission such as demographic factors, disease factors and behavioral factors. Binary data coding – 1, for any positive result and a 0 for another negative result – was used when possible.

Volumes and treatment rates were analyzed by filtering ischemic stroke encounters and procedure codes for intravenous thrombolysis or EVT using the 2017 data available in the raw claims. Raw claims reviewed included 2033 claims for 2017 ICD-10 ischemic stroke codes patients

(I63.xx). This was further filtered to identify the acute inpatient ischemic stroke encounters which totaled 726 claims. Of those, 697 were medically managed. Twenty-nine of these medically managed patients were treated with intravenous tPA (tissue plasminogen activator) as evidenced by CPT code 3E03317, and 28 patients were treated with EVT.

I'm confused after reading this section — clarify & be careful to define terms claims encounters patients

Descriptive statistics

Descriptive statistics on demographic data, treatment rates, readmission frequencies, readmission types, readmission diagnoses and mortality rates were run and compared to available rates published in the medical literature. Nearly 40% of the population studied were considered "young" or under the age of 50, there were slightly more male than females who underwent endovascular therapy for large vessel occlusion stroke. Utilization of endovascular therapy for acute ischemic stroke occurred in 3.8% of patients in 2017.

Readmissions

Readmissions were defined as any unplanned admission to the emergency department only or inpatient readmissions. 17.6% of all patients who received EVT were readmitted within six months of discharge from their stroke hospitalization. Lower inpatient readmission rates were observed at 30 days when compared to rates published in a 2018 study measuring readmissions after EVT for 22 states utilizing the national readmission database (10.7% versus 12.5%), but 90-day readmissions were similar (20% versus 20.7%) (Ramchand et al., 2018). Inpatient readmission rates at 180 days are not available in the medical literature, but we observed a rate of 25%. Rates of ED-only readmissions are not available in the literature, but were studied in this analysis separately and overall. The median frequency of readmissions per patient was one, and reasons for readmission were diverse. Compared with published 90-day recurrent stroke rate of 9.9%, we observed a lower rate of 7.1% at 180 days.

Chi-squared analyses were run to determine significant demographic, disease-related and other factors and their relationship to readmission. Chronic disease classification and frailty were statistically significant variables for patients who were readmitted (p=0.0026, p=0.0084). Higher disease rank, smoking, hypertension and behavioral disorders were most often observed in patients who were readmitted. Some patients who were readmitted had comorbidities of coronary artery disease, congestive heart failure, diabetes mellitus, lipid disorders and cancer, whereas patients who were not readmitted did not have these conditions. Fewer young patients were readmitted, but this was not statistically significant. Appendix C details factors that were associated with readmission versus non-readmission.

need to define

Mortality

A slight mortality benefit was observed with EVT-treated patients compared to rates published in randomized controlled trials (RCTs). Overall unadjusted mortality rate for all EVT patients was 13.3%. Four patient deaths were observed, two of which were in-hospital deaths. In-hospital deaths were associated with brain compression, coma, COPD and hemispheric stroke (carotid occlusion), and conditions associated with death within one year included multi-organ failure, sepsis and cancer. This was compared with mortality rate of 15.3% at half of the time-span we measured (90 days) as published in a 2016 meta-analysis of EVT patients enrolled in 5 international RCTs – 18.9% of deaths were observed in LVO strokes who did not receive EVT (Goyal et al., 2016).

Of note, our study population and analyses captured all large vessel strokes including posterior, or vertebra-basilar artery strokes which were excluded in RCTs. Additional outcomes studied included rates of hemorrhagic transformation that can manifest as a fatal complication of EVT. In this analysis, three patients (10%) of patients had intracerebral hemorrhage coded alongside their ischemic stroke diagnosis. In this population, hemorrhagic was not associated with death, but it was associated with readmission and the highest readmission recurrences. Lastly, median length of stay for EVT inpatient stroke encounters was 6 days.

Creating an analytic database

Data were cleansed and analyzed using Microsoft Excel version 2016 with Analysis TookPak. After data were filtered and transformed as described above, earliest dates of any ED or inpatient readmissions were used for the survival analysis. The population for analysis was first selected by surgical ICD-10 codes, and temporal data including the discharge date of EVT hospital encounter, and the earliest admit date of ED and IP admissions were needed for a survival readmission analysis. Readmission days were calculated per each individual's discharge date by utilizing Excel's inbuilt functionality to subtract the earliest admit dates from the primary discharge date. This was done at intervals of 30,90 and 180 day intervals.

Proposed data science approach

As recent RCTs had unanimously affirmed that higher level of 90-day functional outcomes were achieved with EVT versus standard care for large vessel stroke, we sought to analyze longer-term outcomes by measuring the intervals of unplanned readmissions using a survival analysis. Survival analyses aim to model time to event data (Reddy & Li, 2015), and by measuring ED or inpatient encounters following the hospital discharge we can estimate the likelihood of an EVT-treated patient's risk of readmission at a given time point. With nonparametric data, a Kaplan-Meier curve was selected which uses the actual length of time observed to estimate the interval of time and risk of readmission, or survival probability for our population. Appendix D represents the Kaplan Meier analysis on readmissions up to 6 months after EVT stroke treatment. A survival analysis on stroke treatment readmissions has the benefit of shedding insight on continuing vulnerabilities stroke survivors face over time and can inform interventions to improve transitions of care and reduce readmissions.

Survival analysis findings

Our Kaplan-Meier analysis shows that the predicted rate of surviving after EVT stroke treatment without unplanned ED or inpatient admission is 82.7% at 30 days, 58.6% at 90 days and 41.3% at 180 days.

Lessons learned

It was through trial and error that appropriate data definitions were tried and selected. We learned that while a CPT code was not successful in filtering our main population of interest, surgical ICD-10 codes were. An attempt to search for large vessel stroke subtypes within the ischemic stroke category would have benefitted from starting with a broader search of ICD-10 stroke codes. We learned that ICD "Z" codes representing social disorders were not utilized within the first five diagnoses of our patient encounters. And our initial attempt to search for pharmaceutical codes by GPI for anticoagulants and thrombolytics were unsuccessful, therefore medication adherence was not analyzed. Initially we expected a sizeable volume of atrial fibrillation or atrial flutter diagnoses but found few of these codes with our cleansed data. We then learned that conducting this ICD-10 code search in all claims predating stroke hospitalization yielded more findings, as they were not always visible within the first five diagnoses.

Through the process we learned that data cleansing, data prep and data transformation are very time-consuming and requires critical thinking at each step of the process. Team work and communication were essential, and a balance of content and analysis expertise is needed in order to generate sound data. Importantly, the experience empowered our team of nurses, nurse practitioners and computer science experts to utilize a data science approach in addition to traditional statistical methods to analyze and generate important knowledge for nurses, physicians, healthcare providers, administrators, stroke systems of care and payers.

In order to strengthen the analysis, we would refine our Kaplan-Meier analysis to analyze ED versus inpatient readmissions, separately, and we could utilize evaluation metrics to assess the overall performance of the prediction model such as a Brier score. Outpatient utilization could also be studied in regards to unplanned readmissions. Overall the data suggest that our group of Medicaid patients who underwent EVT had comparable outcomes to those published in RCTs, with slightly lower rates of 30-day readmission and overall mortality. As a pilot study, these findings are underpowered in volume, and a larger data set would be needed to produce more generalizable data, especially considering some outliers were present. Further analysis could inform targeted readmission programs and support efforts to ensure that the low-income population is afforded consideration for EVT if eligible within existing and evolving stroke systems of care. Ultimately such data science and prediction modeling methods could inform and help improve care and resources for low-income stroke survivors.

I think the question of comparing survival with those who didn't get EVT is appropriate.

I would list as a next step in this paper

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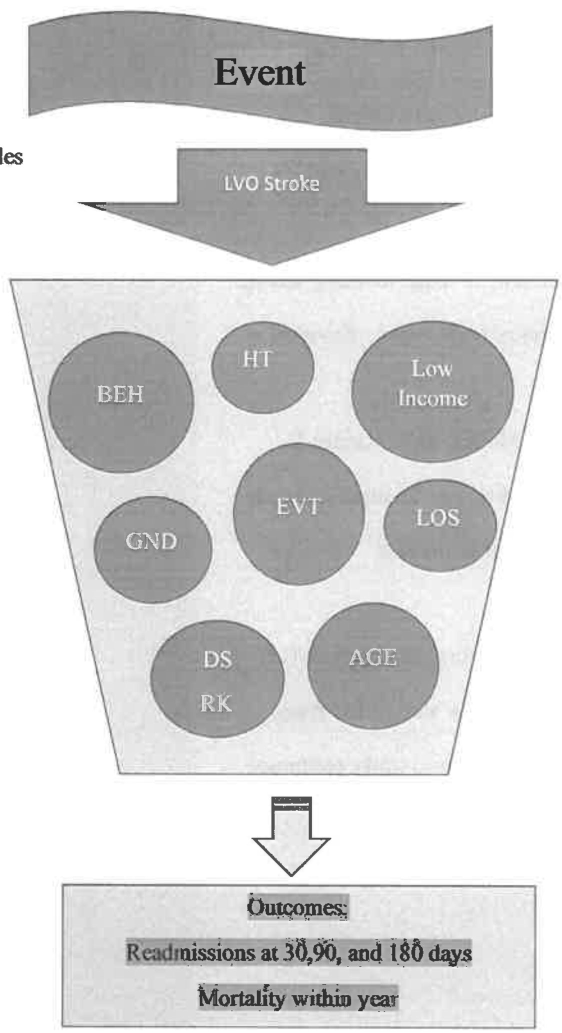
Appendix A

Model of Conceptual Framework of long-term outcomes for low income patients who received endovascular therapy for LVO stroke: Hospital readmissions and mortality.

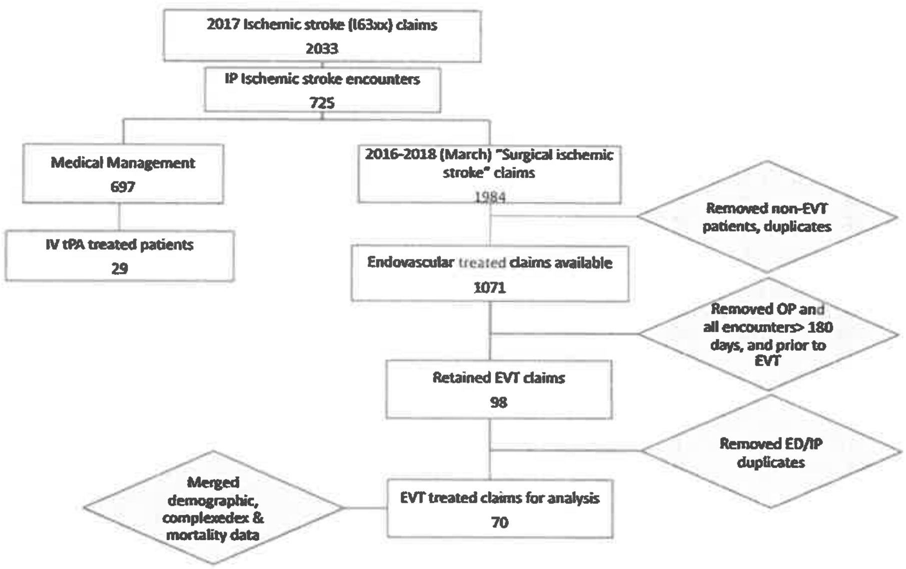
Independent Variables
(Predictors)



Dependent
Variables
(Responses)

Appendix B

Flowchart on data cleansing



Appendix C

Factors associated with readmission versus non-readmission

	Readmitted (n=17)	Not Readmitted (n=11)	*p*-value
Age < 50	35%	45%	0.5908
Male gender	59%	58%	0.8232
MIP (mean)	10	8	
ICH	3	0	0.1403
Death	2	0	0.2377
LOS (mean)	6	9	
Disease rank (mean)	9	1	
Afibflutter	3	2	0.9712
ARF	1	3	0.1142
CKD	0	1	0.2055
CHF	3	0	0.1403
CAD	3	0	0.1403
DM	3	0	0.1403
COPD	1	2	0.3041
Behavioral	4	0	0.0822
Anxiety	3	0	0.1403
Depression	2	0	0.2377
Asthhma	1	1	0.7474
Obesity	1	0	0.4127
HTN	7	1	0.0664
LD	3	0	0.1403
Smoking	6	1	0.1179
Cancer	1	0	0.4127
Frailty	6	0	**0.0262**
Chronic	10	1	**0.0085**

Appendix D

Survival analysis on readmissions after EVT stroke treatment