Evaluation of Patients with High National Institutes of Health Stroke Scale as Thrombectomy Candidates Using the Kentucky Appalachian Stroke Registry

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Keywords

Stroke · National Institutes of Health Stroke Scale · Rural health · Thrombectomy

Abstract

Introduction: Mechanical thrombectomy has become standard of care for emergent large vessel occlusive stroke. Estimates of incidence for thrombectomy eligibility vary significantly. National Institutes of Health Stroke Scale (NIHSS) of 10 or greater is highly predictive of large vessel occlusion. Using our Kentucky Appalachian Stroke Registry (KApSR), we evaluated temporal trends in stroke admissions with NIHSS ≥ 10 to determine patient characteristics among that group along with effects and needs in thrombectomy utilization. **Methods:** Using the KApSR database that captures patients throughout the Appalachian region in our stroke network, we evaluated patients admitted with ischemic stroke with NIHSS ≥ 10 . We recorded demographics, comorbidities, treatment (thrombectomy, decompressive craniectomy),

and county of origin. Change in NIHSS from admission to discharge was used as an indicator of inpatient outcome. **Results:** Between 2010 and 2016, 1,510 patients were admitted with NIHSS ≥ 10 . 87.2% had high blood pressure, 69.6% had dyslipidemia, and 41.7% used tobacco. There were significant sex differences in the types of patients presenting with NIHSS ≥ 10 with females being older on average and having more atrial fibrillation and obesity. There was an increase in thrombectomy utilization from 2010 to 2016, but only 7.5% of the potentially eligible patients underwent the procedure. In comparison to the period 2010–2014, the 2015–2016 period had higher rates of obesity and tobacco abuse. **Conclusion:** Among patients with significant burden of ischemic stroke, the most common coexisting medical condition was high blood pressure. Patients who underwent thrombectomy had significantly better inpatient clinical improvement. These data support the need to maximize utilization of thrombectomy along with need to devote increased resources on modifiable stroke risk factors.

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Introduction

Ischemic stroke accounts for approximately 87% of stroke [1], with emergent large vessel occlusions (ELVO) representing 28–46% [2]. The presence of ELVO has been shown in various studies to increase odds of death by 4.5 fold and to cause a 3-fold reduction of good outcome in affected populations [2]. The goal of current therapeutic strategies is recanalization of the occlusion before irreversible damage has occurred. Intravenous tissue plasminogen activator (IV-tPA) given up to 4.5 h after onset of symptoms has been the only standard of care for acute ischemic strokes in the past [3], even though in cases of proximal vessel occlusion it only results in early reperfusion in 13–50% of cases [4]. More recently, endovascular mechanical thrombectomy (MT) has become a standard of care procedure with established benefits shown in multiple clinical trials [4–7]. More recently, with the use of perfusion-based imaging and automated software, this time window has been extended up to 24 h in a selected patient population with target mismatch [8, 9]. Estimates of incidence for thrombectomy eligibility vary significantly across the nation. The National Institutes of Health Stroke Scale (NIHSS) is a validated tool to assess stroke severity and scores ≥ 10 have been associated with positive predictive value of 97% in carotid and 96% in vertebral-basilar occlusions [10].

High stroke incidence and stroke risk factor burden in West Virginia and rural Kentucky have led to development of the Kentucky Appalachian Stroke Registry (KApSR) to collect demographic and clinical data in real time from stroke patients' electronic health records and to utilize this information for quality of care and research [11]. The aim of this study was to evaluate temporal trends in regional stroke admissions with NIHSS ≥ 10 to determine epidemiologic effects and needs in thrombectomy utilization using the KApSR.

Methods

Using the previously described KApSR methodology [11], a snapshot database was created for cross-sectional analysis of patients over 18 years of age, admitted from January 1, 2010, to December 31, 2016, to the University Hospital with acute ischemic stroke or transient ischemic attack. These patients were studied retrospectively, and the patients with NIHSS ≥ 10 recorded on admission were selected for further analysis. This was based on the hypothesis that the patients with NIHSS ≥ 10 have a very high likelihood of having a proximal vessel occlusion and are potential thrombectomy candidates. Demographic characteristics were obtained and studied. We also analyzed whether these patients re-

ceived intravenous thrombolytic, underwent thrombectomy, or underwent decompressive hemicraniectomy during their hospitalization. Change in NIHSS from admission to discharge was measured as an indicator of inpatient outcome [12]. The data were also analyzed for gender differences. Finally, we analyzed subgroups of epochs before (2010–2014) and after (2015–2016) AHA/ASA guidelines recommended thrombectomy as a standard for ELVO [13].

Summary statistics and analyses were performed on PC – SAS version 9.1, and $p \leq 0.05$ was considered significant. Proportion was compared using chi-square statistics, and means were compared using 2 sample t tests. The research protocol was approved by our Institutional Review Board, which waived informed consent for study subjects due to the retrospective nature of the study.

Results

Population Characteristics and Risk Factors

In total, 1,510 adult patients had NIHSS ≥ 10 recorded at presentation between 2010 and 2016 and were selected for analysis. Table 1 provides the demographic, comorbidity, and treatment details for the cohort. The mean age of patients was 68.15 ± 14.65 with average NIHSS on admission of 17.58 ± 6.24 . The most common comorbidity was hypertension (87.2% of patients), followed by dyslipidemia (69.6%), tobacco use (41.7%), and coronary artery disease (CAD; 41.1%). Females were, on average, 5 years older and were significantly more likely to have atrial fibrillation (AF) and obesity. Conversely, males used tobacco more frequently and were more likely to have CAD. Figure 1 illustrates significant differences in patients admitted with NIHSS ≥ 10 between the 2 time periods 2010–2014 and 2015–2016. Patients admitted in the later epoch had lower rates of CAD (44.1 vs. 34.9%; $p < 0.001$) and dyslipidemia (71.7 vs. 65.3%; $p = 0.01$). However, comparing time epochs, patients in the later cohort were younger (68.8 vs. 66.9 years; $p = 0.02$), had higher rates of tobacco use (38.5 vs. 48.0%; $p < 0.001$), and had higher rates of obesity (8.9 vs. 18.7%; $p < 0.001$).

Treatments Administered

Among 1,510 patients, 308 patients (20.4%) with NIHSS ≥ 10 on admission underwent treatment with intravenous thrombolysis between 2010 and 2016. Thrombectomy was performed in 113 patients (7.5%) only with no significant difference between sexes in terms of utilization. Annual utilization of thrombectomy was plotted and showed an increase over time from 0.8% in 2010 to 9.4% in 2016 (Fig. 2). On comparison between the 2010–2014 and 2015–2016 periods, it was found that patients in

Fig. 1. Comparison between 2010–2014 and 2015–2016 with significant differences.

Table 1. Population demographics with comparisons between the male and female patient population

Variable	Total (n = 1,510)	Male (n = 715)	Female (n = 795)	p value
Age, years	68.15±14.65	65.39±14.09	70.64±14.81	<0.001
NIHSS at time of admission	17.58±6.24	17.22±6.06	17.90±6.38	0.0319
NIHSS at time of discharge	13.46±9.00	13.13±9.09	13.77±8.91	0.1657
Improvement in NIHSS (NIHSS at time of discharge – NIHSS at time of admission)	–4.11±7.80	–4.09±7.85	–4.13±7.75	0.9135
History of hypertension (yes/no)	1,316/194 (87.2/12.8)	612/103 (85.6/14.4)	704/91 (88.6/11.4)	0.1013
History of AF (yes/no)	539/971 (35.7/64.3)	222/493 (31.0/69.0)	317/478 (39.9/60.1)	<0.001
History of prior stroke (yes/no)	202/1,308 (13.4/86.6)	87/628 (12.2/87.8)	115/680 (14.5/85.5)	0.2173
History of CAD (yes/no)	620/890 (41.1/58.9)	319/396 (44.6/55.4)	301/494 (37.9/62.1)	0.0090
Tobacco use (yes/no)	629/881 (41.7/58.3)	369/346 (51.6/48.4)	260/535 (32.7/67.3)	<0.001
Obesity (yes/no)	184/1,326 (12.2/87.8)	70/645 (9.8/90.2)	114/681 (14.3/85.7)	0.0088
History of dyslipidemia (yes/no)	1,051/459 (69.6/30.4)	508/207 (71.0/29.0)	543/252 (68.3/31.7)	0.2702
History of carotid stenosis (yes/no)	144/1,366 (9.5/90.5)	79/636 (11.0/89.0)	65/730 (8.2/91.8)	0.0703
History of heart failure (yes/no)	338/1,172 (22.4/77.6)	155/560 (21.7/78.3)	183/612 (23.0/77.0)	0.5740
History of PVD (yes/no)	74/1,436 (4.9/95.1)	41/674 (5.7/94.3)	33/762 (4.2/95.8)	0.1924
Prosthetic heart valve (yes/no)	24/1,486 (1.6/98.4)	10/705 (1.4/98.6)	14/781 (1.8/98.2)	0.7217
TPA administered (yes/no)	308/1,202 (20.4/79.6)	135/580 (18.9/81.1)	173/622 (21.8/78.2)	0.1859
Thrombectomy performed (yes/no)	113/1,397 (7.5/92.5)	61/654 (8.5/91.5)	52/743 (6.5/93.5)	0.1707
Decompressive craniotomy performed (yes/no)	14/1,496 (0.9/99.1)	8/707 (1.1/98.9)	6/789 (0.8/99.2)	0.6396

NIHSS, National Institutes of Health Stroke Scale; AF, atrial fibrillation; CAD, coronary artery disease; TPA, tissue plasminogen activator; PVD, peripheral vascular disease.

the later epoch were almost twice as likely to get a thrombectomy (12.2 vs. 5.2%; $p < 0.001$) along with increase in decompressive craniectomy (2.4 vs. 0.2%; $p < 0.001$). The percentage use of tPA declined in the later time period (from 25.8 to 9.6%; $p < 0.001$).

Outcome Measures

Comparison of the mean NIHSS score change from admission to discharge between those who underwent MT and those who did not show a significant difference (-5.78 ± 9.09 vs. -3.98 ± 7.67 ; $p = 0.04$) with the biggest

Fig. 2. The figure shows number of thrombectomies performed per year since 2010. The annual rate of MT significantly increased from 2010 to 2016 with maximum increase from 2014 to 2015.

Table 2. Inpatient NIHSS outcomes and length of stay in patients that underwent thrombectomy as compared to the patients that did not undergo the procedure

	Thrombectomy group	No thrombectomy group	p value
NIHSS score change (n = 1,510)	-5.78±9.09	-3.98±7.67	0.04
NIHSS score change in year 2010–2014 (n = 1,008)	-5.00±9.17	-3.97±7.74	0.43
NIHSS score change in year 2015–2016 (n = 502)	-6.44±9.04	-3.99±7.53	0.047
LOS (n = 1,510)	14.75±36.42	10.14±14.30	0.18
LOS in year 2010–2014 (n = 1,008)	13.52±24.36	10.10±12.41	0.32
LOS in year 2015–2016 (n = 502)	15.80±44.38	10.23±17.76	0.34

NIHSS, National Institutes of Health Stroke Scale; MTY, mechanical thrombectomy yes; MTN, mechanical thrombectomy no; LOS, length of stay.

difference noted in year 2015–2016 (NIHSS decrease of 6.4 in thrombectomy patients vs. 4.0 in nonthrombectomy patients; $p = 0.05$). The “No Thrombectomy” group had a slightly but not significantly shorter length of stay. Analysis of LOS and NIHSS change by sex showed a significant difference in mean LOS, with males having longer LOS (14.55 vs. 10.2; $p = 0.0054$; Table 2).

Discussion

We analyzed the temporal trends in thrombectomy at a regional stroke center serving a primarily rural US population. Our Comprehensive Stroke Center receives thrombectomy patients from central Kentucky, northern Tennessee, and western West Virginia. As such, many of

our patients originate from the Appalachian region, where stroke represents a major health disparity. Rural cohorts in regions such as Appalachia have been shown to have higher rates of stroke, even after accounting for comorbidities and other risk factors [14]. Furthermore, unlike large urban environments, central Kentucky has only 2 Comprehensive Stroke Centers (with only 4 in the entire state). Treatment of severe stroke, therefore, tends to be centralized in the 2 largest cities (Louisville for western Kentucky and Lexington for central and eastern Kentucky). In that setting, we aimed to understand the patient population presenting with high NIH stroke scales, which represents patients most likely to have an Emergent Large Vessel Occlusion. Despite the growing evidence supporting MT, only 7.5% of the patients that presented to our hospital with NIHSS ≥ 10 underwent thrombectomy, highlighting the need for additional edu-

cation and collaboration with referring hospitals and emergency medical service providers; this is particularly important, as the window for thrombectomy has been expanded to 24 h [9].

As shown by our data, the burden of comorbidities suffered by patients in the rural Kentucky and broader Appalachian region with acute ischemic stroke is significant. Even though AF is one of the main causes of vessel occlusion, the incidence of AF in our patient population was low as compared to hypertension, dyslipidemia, and tobacco abuse. This stresses the need to devote more resources toward management of these chronic medical conditions. Furthermore, we showed significant differences in the rates and types of comorbidities among men and women in our region. While men had higher rates of CAD and tobacco use, women had higher rates of AF and obesity. These findings are consistent with some other published studies evaluating sex differences in stroke [15–17]. Tobacco use, CAD, AF, and obesity are all linked to increased inflammation, which is a major factor in stroke susceptibility [18–21]. Interestingly, the behaviors or pathologies associated with inflammation linked to stroke differ between the sexes. These represent important sex-specific modifiable risk factors, which should be targets for public policy intervention regarding stroke prevention.

In addition to sex-based differences in high-NIHSS stroke incidence, we also noted changing characteristics among the patients in 2 sequential epochs. While overall rates of CAD and dyslipidemia decreased from 2011–2014 to 2015–2016 among the cohort, rates of obesity and tobacco usage increased. Elevated body mass index in particular has been linked to increased stroke mortality in younger patients [22]. As stated above, obesity and tobacco use are both associated with inflammation [20]. Since inflammation is prothrombotic [23], obesity, and tobacco use among younger people could be synergistic in decreasing the age of onset for stroke. This reflects the growing and important role that obesity has in the rural population as a modifiable stroke risk factor. Most importantly, the mean age of patients presenting with NIHSS of 10 or more was lower in the later cohort. This is concerning, since it reflects an epidemiologic shift toward younger age severe stroke incidence in our region.

There are several limitations to our study. First, the retrospective nature limits the ability to perform well-controlled and designed comparisons. Second, our analysis reflects patients presenting with NIHSS ≥ 10 specifically rather than confirmed ELVO. While the 2 have been

shown to be closely associated, they are not the same. This limitation of data extrapolation through this methodology is that individual patients cannot be evaluated in terms of protected health information. Therefore, there are variables we could not incorporate. For example, the rate of tPA usage in this population went down from the earlier to later epoch. However, this is likely explained by expanded indications for transfer of ELVO patients for thrombectomy. If more patients arrived at our institution in the >4.5 h window, then the number of tPA-eligible patients with high NIHSS would be lower as a result. Finally, while our goal was to provide a region-specific analysis of patients with severe ischemic stroke, extrapolation of our results to another geographic region may not be valid.

Conclusions

Estimates of thrombectomy eligibility and utilization differ across geographic regions. In Appalachia, evaluation of the patients with severe NIH stroke scales suggests gross underutilization of MT. As the age of stroke patients in the region is decreasing, the need for additional resources to treat severe stroke as a community burden is intensifying. In creating prevention and treatment policies, we should consider notable sex differences in known risk factors, and use that information to design-specific strategies to reduce severe ischemic stroke incidence, and to rapidly treat it with thrombectomy when appropriate.

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Statement of Ethics

The research protocol was approved by our Institutional Review Board.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

P.G.: study design, interpretation of data, manuscript writing, and approval of final manuscript. M.R.D. and J.F.F.: study design, interpretation of the data, and critical revision of the manuscript

for intellectual content. K.P., P.K., M.W., and G.J.B.: critical revision of the manuscript for intellectual content and approval of final manuscript. R.J.K.: interpretation of the data, statistical analysis, and critical revision of the manuscript for intellectual content. K.E.: acquisition of data and approval of final manuscript.

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