Differences in Reperfusion Therapy Utilization and Effectiveness in Pediatric vs. Young Adult Acute Ischemic Stroke: A Nationwide Cohort Study

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Introduction

Pediatric acute ischemic stroke (AIS), while sharing pathophysiologic features with adult stroke, presents unique challenges that require specialized management considerations. Unlike adult stroke, which is predominantly caused by atherothrombotic and cardioembolic mechanisms, pediatric stroke often results from congenital heart disease, genetic disorders, and inflammatory conditions. While the evidence base for acute reperfusion therapy (RT), such as intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT), is robust for adults, real-world utilization patterns and comparative effectiveness of these therapies between pediatric and young adult populations remain poorly characterized. In this nationwide retrospective study, we assessed population differences for pediatric versus young adult AIS patients in terms of baseline characteristics, reperfusion therapy utilization, and treatment effectiveness.

Methods

Study Design

This was a nationwide cohort study using the 2016 to 2022 Nationwide Readmissions Database. AIS patients aged 2 to 39 years were included. Patients with primary hemorrhagic stroke or traumatic brain injury were excluded. Patient demographics, comorbidities, and stroke characteristics were identified using ICD-10 diagnosis codes and procedure codes. Stroke location was categorized as middle cerebral artery, internal carotid artery, vertebral/basilar artery, or other territories. Stroke severity was assessed using NIH Stroke Scale (NIHSS) scores when available. Reperfusion treatments were identified using ICD-10 procedure codes for IVT and EVT. Large vessel occlusion (LVO) stroke was defined using validated algorithms incorporating stroke location and NIHSS scores >6.
The primary outcome was excellent functional outcome, defined as discharge to home with routine care.

Statistical Methods

Chi-square tests compared categorical variables between groups, and Wilcoxon rank-sum tests compared continuous variables. Multivariable logistic regression models assessed the association between reperfusion treatments and excellent outcomes, adjusting for confounders. Interaction terms between age group and treatment type tested for effect modification.

Results

Patient Characteristics

84,639 AIS patients between the ages 2-39 years were identified, of whom 3,603 were pediatric patients (less than 18 years old), and 81,036 were young adults (age 18 to 39). Overall, pediatric patients had significantly lower rates of traditional vascular risk factors such as hypertension (17.0% vs. 50.8%), hyperlipidemia (4.2% vs. 30.9%), diabetes (1.8% vs. 19.6%), atrial fibrillation (0.5% vs. 3.8%), and tobacco use (1.6% vs. 35.5%; all p<0.001); meanwhile, pediatric patients had higher rates of congenital heart disease (19.0% vs. 13.7%) and moyamoya disease (8.6% vs. 2.0%; p<0.001 for both; **Figure 1**).

RT utilization

Rate of IVT use was significantly lower for pediatric patients (6.8% vs. 17.9%, p<0.001), while the rate of EVT use among LVO patients was similar (34.5% vs. 45.3%, p=0.087).

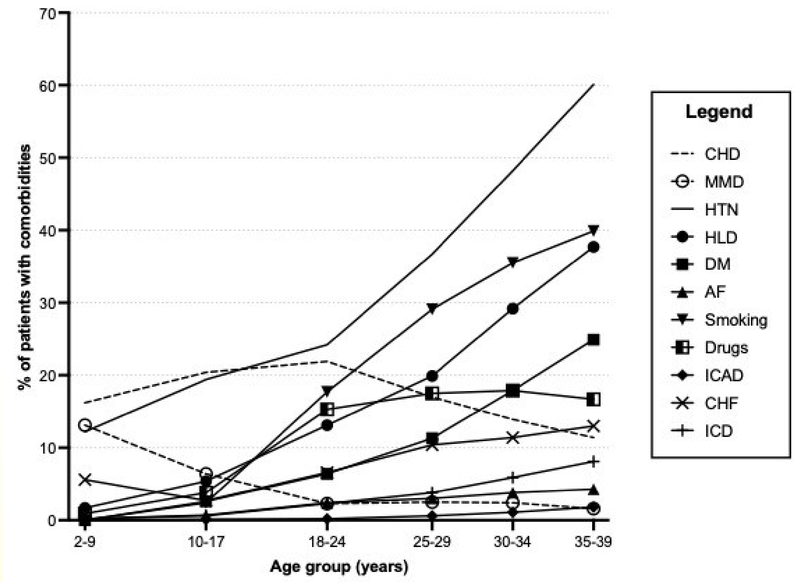

Figure 1: Rates of stroke risk factors across age groups. Abbreviations: CHD - congenital heart defect, MMD - moyamoya disease, HTN - hypertenion, HLD - hyperlipidemia, DM - diabetes mellitus, AF - atrial fibrillation or flutter, ICAD - intracranial atherosclerotic disease, CHF - congestive heart failure, ICD - ischemic cardiac disease.

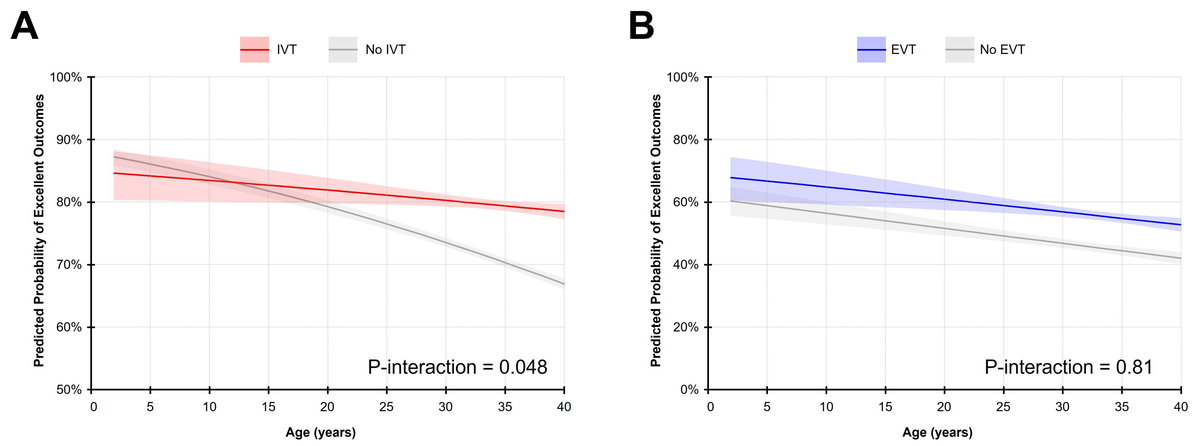

Figure 2: Predicted probabilities of achieving excellent discharge outcomes associated with acute stroke reperfusion treatments across the study age range (2 to 39 years). Predicted probabilities were calculated from logistic regression models adjusted for sex, NIH stroke scale, stroke location, treatment year, hospital type, concomitant reperfusion treatments, and potential contraindications for treatment (anticoagulant use, endocarditis, moyamoya disease). Interaction analyses between age (as a continuous variable) and treatment (IVT or EVT) were performed to assess for heterogeneity of treatment efficacy across the study age range. Confidence bands represent standard error. Predicted probabilities of excellent outcomes for IVT vs. no IVT among all ischemic stroke patients are presented in Panel A; a significant heterogeneity in treatment efficacy of IVT was observed (p-interaction 0.048), where IVT appears to be less effective in improving odds of excellent outcomes in younger patients. In contrast, among large vessel occlusion AIS patients (Panel B), EVT appeared to be beneficial across the study age range, without significant heterogeneity of treatment effect (p-interaction = 0.81). Abbreviations: IVT – intravenous thrombolysis, EVT – endovascular thrombectomy.

RT outcomes

IVT was associated with higher odds of excellent outcomes in young adults (OR 1.60 [95%CI 1.45-1.76], p<0.001) but not in pediatric patients (OR 0.78 [95%CI 0.20-3.03], p=0.71; interaction p=0.048; **Figure 2**). Among LVO patients, EVT had a similar magnitude of association with higher odds of excellent outcomes in both young adults (OR 1.56 [95%CI 1.35-1.79], p<0.001) and pediatric patients (OR 1.35 [0.39-4.63], p=0.63; interaction p=0.81; **Figure 2**)

Conclusions

1. **Baseline characteristics of AIS patients differed by age.**
2. **IVT use is lower among pediatric patients; EVT use is similar across age groups**
3. **IVT is associated with reduced efficacy in younger patients. Age did not moderate EVT's efficacy.**