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10.4103/bc.bc_33_18

Utilization and safety of extracranial–intracranial bypass surgery in symptomatic steno-occlusive disorders

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Abstract:

OBJECTIVE: The objective of this study was to investigate patterns of utilization and safety of extracranial–intracranial (EC-IC) bypass in patients with symptomatic cerebrovascular steno-occlusive disorders.

METHODS: Patients with one of the steno-occlusive conditions (defined as symptomatic intracranial stenosis, extracranial stenosis, and moyamoya disease) were identified using all nonfederal hospitalizations in New York (2005–2014) and Florida (2005–2015). EC-IC bypass surgery was defined using the corresponding procedure codes. Patients were included if there was a prior history of ischemic stroke or transient ischemic attack. Patients were excluded for any preceding diagnosis of cerebral hemorrhage, aneurysm, or trauma. The primary outcome was perioperative ischemic stroke, cerebral hemorrhage, or mortality occurring within 30 days of surgery. We also determined yearly trends for the volume of EC-IC bypass procedures in the study period.

RESULTS: Among 346 patients with steno-occlusive disease treated with EC-IC bypass, median age was 52.5 years and 52.5% were female. Rates of EC-IC bypass surgery procedure increased until 2011 and then decreased coinciding with the publication of the Carotid Occlusion Surgery Study trial. Thirty-day event rates of stroke, hemorrhage, or death decreased in patients treated with EC-IC bypass (odds ratio: 0.2, confidence interval: 0.0.4–0.99; $P = 0.03$) over the 10-year study period.

CONCLUSIONS: Overall utilization of EC-IC bypass procedure is relatively low, whereas the 30-day complication rates for patients with steno-occlusive conditions appear to be relatively low and improving. Further research is needed to confirm these findings and to determine the subset of patients who would most likely benefit from this intervention.

Keywords:

Cerebrovascular steno-occlusive disease, extracranial–intracranial bypass, perioperative, stroke

Introduction

The extracranial–intracranial (EC-IC) bypass surgery trial published in 1985 found no benefit for surgical bypass of carotid or middle cerebral steno-occlusive lesions with 12% 30-day morbidity and mortality and high bypass patency rates (96%).^[1] The Japanese EC-IC Bypass Trial reported some benefits for the surgical cohort with a statistically lower stroke

recurrence rate than the medical arm^[2] although perioperative outcomes were not specified. The Carotid Occlusion Surgery Study (COSS) was published in 2011 with a conclusion that EC-IC bypass did not benefit symptomatic carotid occlusion patients with hemodynamic cerebral ischemia as defined by the study through positron emission tomography imaging. Thirty-day rates of perioperative morbidity and mortality for the surgical cohort were 14.4% in this trial.^[3] Since then, the safety and efficacy of the procedure have been debated in the literature. More recent studies have

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How to cite this article: Saber H, Rajah G, Palla M, Sheth SA. Utilization and safety of extracranial–intracranial bypass surgery in symptomatic steno-occlusive disorders. *Brain Circ* 2019;5:32-5.

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Submission: 24-11-2018
 Revised: 26-02-2019
 Accepted: 13-03-2019

reported the efficacy of the procedure for steno-occlusion in carefully selected patient populations.^[4] Yeo *et al.* carefully selected patients using HMPAO single-photon emission computed tomography and found 13% ischemic event rates versus 45% event rates for the medical arm at a mean of 34 months, suggesting that surgical bypass in the right steno-occlusion candidate can be beneficial.^[5] EC-IC bypass in moyamoya disease is a less contested topic where a large meta-analysis of 47 studies in adult moyamoya patients noted that direct bypass was associated with lower rates of hemorrhage, recurrent ischemic stroke, and better outcomes.^[6]

The current trends on the utilization of the EC-IC bypass surgery in cerebrovascular steno-occlusive disorders are unclear. Furthermore, “real-world” population-level rates of perioperative stroke, hemorrhage, and mortality have not been well established following this procedure. We sought to examine the overall utilization of the EC-IC bypass procedure in two large and ethnically diverse states over a 10-year period. We also aimed to determine if the population-level rates of perioperative complications are comparable to those noted in published literature.

Methods

Study design

We performed an observational cohort analysis, using administrative claims data from the Healthcare Cost and Utilization Project State Inpatient Databases on all discharges from nonfederal acute care hospitals in New York (2005–2014) and Florida (2005–2015). We chose the state inpatient data because they contain longitudinal follow-up data for individual patients by a unique linkage variable; thus, a patient can be tracked prospectively. In addition, Florida and New York were chosen because they are large demographically and socioeconomically diverse states containing a considerable proportion of the US population.

This analysis complied with the Reporting of Studies Conducted Using Observational Routinely Collected Health Data guidelines for administrative claims data.^[7]

Demographic and procedural data

Diagnoses and procedures were identified using International Classification of Diseases (ICD-9) codes and derived from prior relevant literature for consistency and comparison.^[8] Symptomatic Intracranial atherosclerotic disease (ICD-9: 437.0), symptomatic occlusion or stenosis of the carotid artery (ICD-9: 433.10 and 433.11), and moyamoya disease (ICD-9: 437.5) were defined with the accompanying codes for ischemic stroke or transient ischemic attack (TIA). Ischemic stroke was defined using previously validated techniques by ICD-9 codes 433.x1, 434.x1, or 436 in any hospital discharge

diagnosis code position without a primary hospital discharge diagnosis code for rehabilitation (V57) or any accompanying codes for trauma (800–804 or 850–854), intracerebral hemorrhage (430 or 431), or subarachnoid hemorrhage (430).^[8,9]

TIA was defined as ICD-9 codes 435.x or V1254. EC-IC bypass surgery was defined as 39.28 with an accompanying code for steno-occlusive conditions as defined above.

Outcome and covariates

Patients entered the cohort at the time of their first hospitalization for one of the steno-occlusive conditions or EC-IC bypass. We analyzed trends for first-time EC-IC bypass performed for the symptomatic steno-occlusive conditions in this time period. The primary endpoint was a composite of immediate postprocedural and 30-day hospital admission for any ischemic stroke, cerebral hemorrhage, or mortality. Demographic characteristics (age, sex, and ethnicity), stroke risk factors (hypertension, diabetes, atrial fibrillation, coronary artery disease, congestive heart failure, and chronic kidney disease), and a composite score of comorbidities using the Charlson index were ascertained.^[10,11]

Statistical analysis

Crude rates for the prevalence of each treatment strategy were reported with 95% confidence intervals. Multivariate regression models were adjusted for covariates described below and used to identify the predictors of the primary endpoint. The Charlson index was used as covariates in the multivariate model, and additional covariates for smoking, age (by tertile), and race were added as these are risk factors known to be associated with steno-occlusive conditions and not represented explicitly in the Charlson index.^[10] Statistical analyses were performed using STATA 14 (College Station, TX) and GraphPad Prism 7.0 (La Jolla, CA) software.

Results

Patient population

Among the 346 individuals who underwent EC-IC bypass, median age was 52.5 years (interquartile range [IQR]: 41–62) and 57.23% were female. Overall, 33.5% of the included patients had diabetes and 67.6% carried a diagnosis of hypertension. The Charlson morbidity index was 3 (IQR: 2–5). Table 1 shows the baseline characteristics in the cohort.

Extracranial–intracranial utilization

The national trends for utilization over the study period in the state inpatient data and the volume of

first-time EC-IC bypass surgery for cerebrovascular steno-occlusive diseases increased steadily until 2011 and then declined, as shown in Figure 1.

Thirty-day outcomes

Overall, the 30-day rate of stroke, hemorrhage, or death in the entire cohort was 5.49% for patients with symptomatic cerebrovascular steno-occlusive conditions who were treated with EC-IC bypass. The overall combined event rate for a given year ranged from 2.8% to 16.6% in the study period. After adjusting for Charlson index, age, and race, there was a statistically significant decline in the likelihood of 30-day combined outcome for the EC-IC bypass (odds ratio: 0.2, CI: 0.04–0.99; $P = 0.03$) over the 10-year study period. Figure 2 shows the change over time for the combined outcome.

Discussion

In this cohort study over a 10-year time period, we observed an initial increase in utilization of EC-IC bypass (2005–2010), followed by a decrease in 2011, coinciding with the publication of the COSS trial.^[3] Overall rates of 30-day stroke, hemorrhage, and mortality in our cohort were relatively low (range: 2.8%–16.6%) and within the range of event rates reported in prior randomized trials.^[12] Over the study period, this rate appeared to be decreasing.

The decline in EC-IC bypass utilization in 2011 may be related to the release of clinical trial findings during the study period. The COSS trial was performed to assess the effectiveness of the EC-IC bypass surgery in reducing subsequent stroke in patients with symptomatic atherosclerotic internal carotid artery occlusion and hemodynamic cerebral ischemia.^[3] The authors

concluded that EC-IC bypass surgery did not reduce the risk of recurrent ipsilateral ischemic stroke at 2 years as compared to medical therapy alone. It should be noted that the 30-day morbidity and mortality was 15% in this trial, which was comparable to the rate of 12% reported from the EC-IC Bypass Trial.^[1] The COSS trial was halted for futility despite only a 6% rate (3% per year) of recurrent ipsilateral stroke in the surgical arm for the remainder of the 2-year follow-up after the 30-day period versus the 23% rate of combined endpoint in the medical arm. Although our perioperative event rates may not be directly comparable to the rates from randomized trials given the variations in patient selection and outcome ascertainment, a declining trend in overall perioperative morbidity and mortality may suggest a signal for the effectiveness of this procedure for improving long-term outcomes in well-selected groups of patients in future trials.

Several factors may affect the risk of perioperative events following EC-IC bypass. Importantly, hemodynamic fragility has been shown to be a major contributing factor in the development of postoperative complications.^[13] Recently, Rice *et al.* reported a series of 126 patients who

Table 1: Baseline characteristics of the included patients following extracranial–intracranial bypass

Characteristics	EC-IC bypass
<i>n</i>	346
Age, median (IQR)	52.5 (41-62)
Female, <i>n</i> (%)	198 (57.2)
Diabetes, <i>n</i> (%)	116 (33.5)
Hypertension, <i>n</i> (%)	234 (67.6)
PVD, <i>n</i> (%)	33 (9.5)
Renal failure, <i>n</i> (%)	11 (3.2)
Charlson index, median (IQR)	3 (2-5)

EC-IC: Extracranial–intracranial, IQR: Interquartile range, PVD: Peripheral vascular disease

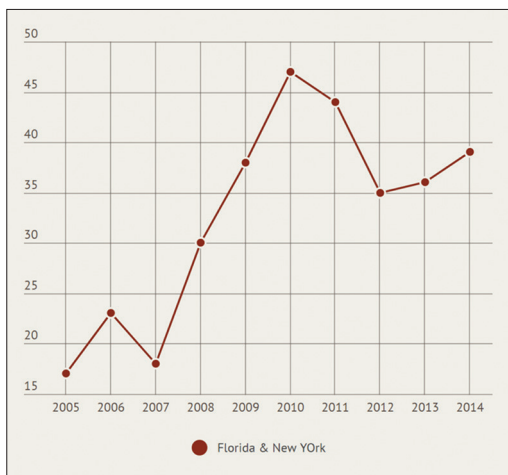


Figure 1: Extracranial–intracranial bypass surgery utilization trend for cerebrovascular steno-occlusive disorders using Florida and New York State Inpatient Databases

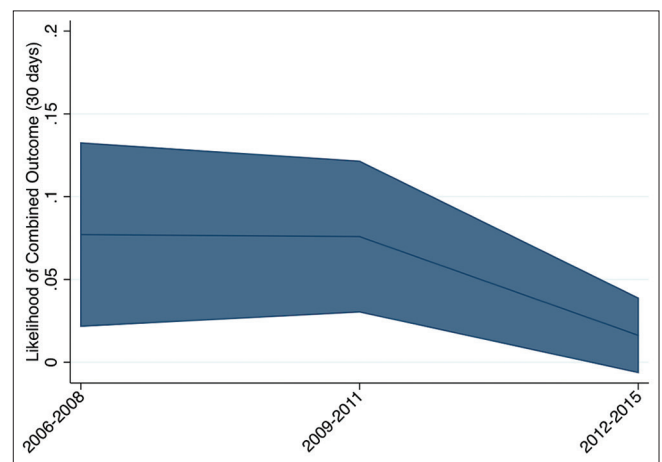


Figure 2: Trends in 30-day risk of death, stroke, or hemorrhage following extracranial–intracranial bypass surgery using Florida and New York State Inpatient Databases

underwent EC-IC bypass for ischemic stroke or recent TIA and found that in those patients undergoing the procedure within 7 days of their event, the perioperative stroke rate was 31%, as compared to 11.5% for those undergoing surgery at >7 days.^[14] Thus, future studies with better identification of the optimal timing of the procedure may contribute to improvements in perioperative outcomes.

EC-IC bypass may also be beneficial in other steno-occlusive conditions such as acute ischemic stroke.^[15] Horiuchi *et al.* described 58 patients undergoing urgent revascularization via superficial temporal artery–middle cerebral artery bypass with 69% of patients having neurological improvement.^[16] Our population-level findings of a relatively acceptable perioperative morbidity risk following EC-IC bypass would support this intervention as a viable treatment option in future trials for patients who fail first-line endovascular thrombectomy. Similar lines of reasoning may be used to propose this procedure as a safe option in future trials that aim to assess changes in cognitive outcomes following cerebral revascularization in moyamoya disease.

Our study has several limitations, many of which are inherent to administrative databases and nonrandomized cohort data. We cannot make direct comparisons between EC-IC bypass and other procedures or conservative therapies in the absence of a randomized design, as the features of the patients' presentation and imaging that drive the decision to select a treatment strategy cannot be obtained from administrative data. In addition, we cannot determine specific clinical characteristics including site of vascular occlusion. While the validity of our findings relies largely on the correct procedural coding, our large state-level analysis provides unique insights into the "real world" milieu of EC-IC bypass surgery and their utilization, especially given the fact that this type of information cannot be obtained from trials or registries. Future studies are needed in the optimization of EC-IC bypass indications and outcomes for steno-occlusive diseases.

Conclusion

The overall utilization of the EC-IC bypass procedure is low. Further research is needed to confirm these findings and to determine the subset of patients who would most likely benefit from this intervention.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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