Patients with stroke and psychiatric comorbidities have lower carotid revascularization rates

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Abstract

Objective

We investigated whether mental illness is associated with lower rates of carotid endarterectomy (CEA)/carotid artery stenting (CAS) after stroke due to carotid stenosis.

Methods

In this retrospective cross-sectional study, ischemic stroke cases due to carotid stenosis were identified in the 2007–2014 Nationwide (National) Inpatient Sample. Psychiatric conditions were identified by secondary ICD-9-CM diagnosis codes for schizophrenia/psychoses, bipolar disorder, depression, anxiety, or substance use disorders. Using logistic regression, we tested the association between psychiatric conditions and CEA/CAS, controlling for demographic, clinical, and hospital factors.

Results

Among 37,474 included stroke cases, 6,922 (18.5%) had a psychiatric comorbidity. The presence of any psychiatric condition was associated with lower odds of CEA/CAS (adjusted odds ratio [OR] 0.84, 95% confidence interval [CI] 0.78–0.90). Schizophrenia/psychoses (OR 0.72, 95% CI 0.55–0.93), depression (OR 0.83, 95% CI 0.75–0.91), and substance use disorders (OR 0.73, 95% CI 0.65–0.83) were each associated with lower odds of CEA/CAS. The association of mental illness and CEA/CAS was dose-dependent: compared to patients without mental illness, patients with multiple psychiatric comorbidities (OR 0.74, 95% CI 0.62–0.87) had lower odds of CEA/CAS than those with only one psychiatric comorbidity (OR 0.86, 95% CI 0.79–0.92; *p* value for trend <0.001).

Conclusion

The odds of carotid revascularization after stroke is lower in patients with mental illness, particularly those with schizophrenia/psychoses, depression, substance use disorders, and multiple psychiatric diagnoses.

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Glossary

APR-DRG = All Patient Refined–Diagnosis-Related Group; **CAS** = carotid artery stenting; **CCI** = Charlson Comorbidity Index; **CEA** = carotid endarterectomy; **CI** = confidence interval; **ICD-9-CM** = *International Classification of Diseases, Ninth Revision, Clinical Modification*; **NIS** = Nationwide Inpatient Sample; **OR** = odds ratio.

Acute ischemic stroke is a leading cause of morbidity and mortality in the United States,¹ and an estimated 20% to 30% of ischemic strokes can be attributed to extracranial carotid artery disease.² Revascularization with carotid endarterectomy (CEA) or carotid artery stenting (CAS) decreases future stroke risk in patients with stroke due to carotid stenosis.^{3–5} However, carotid revascularization is underutilized in certain patients: racial minorities are less likely to receive CEA/CAS both for symptomatic⁶ and for asymptomatic⁷ carotid artery disease compared to white patients, and women are less likely to receive carotid revascularization after acute ischemic stroke compared to men.⁸

Mental illness is prevalent in the United States, as an estimated 18.3% of adults have had a psychiatric condition, and 7.5% of adolescents and adults have had a substance use disorder over a 1-year period.⁹ Patients with psychiatric comorbidities experience inequities in treatment for a range of medical conditions,¹⁰ including cardio- and cerebrovascular disease, which are major causes of mortality in patients with mental illness.^{11,12} Patients with acute myocardial infarctions and comorbid psychiatric conditions are not only less likely to undergo cardiac catheterization or revascularization^{13–15} than those without psychiatric conditions but are also more likely to die within a year.^{13,16} Ischemic stroke patients with schizophrenia or other psychoses are significantly less likely to receive cerebrovascular arteriography and more likely to die within a year compared to those without psychiatric conditions.¹³ Similarly, stroke patients with any comorbid psychiatric condition are less likely to receive IV thrombolysis,¹⁷ and patients with depression, anxiety, or multiple psychiatric diagnoses are more likely to be rehospitalized or die within 6 months of a stroke.¹⁸

At present, it is unclear whether a history of mental illness is associated with differences in CEA/CAS use in patients with stroke due to carotid artery disease. In the present study, we aimed to determine whether the presence of psychiatric comorbidities is associated with lower odds of carotid revascularization with CEA/CAS in a representative sample of US adult stroke patients. Identifying differences in carotid revascularization in such patients may inform interventions aimed at promoting equal stroke care for all patients.

Methods

Data source

Data were obtained from the Nationwide Inpatient Sample (NIS), the largest all-payer inpatient database in the United

States (hcup-us.ahrq.gov). The NIS was renamed the National Inpatient Sample after its redesign in 2012. NIS captures information on demographics, hospital characteristics, diagnoses, procedures, comorbidities, and case severity measures on several million hospital discharges each year. All diagnoses and procedures are recorded using ICD-9-CM codes.

Standard protocol approvals, registrations, and patient consents

Because NIS data are publicly available and contain no personal identifying information, this study was exempt from institutional review board approval.

Case selection

We identified adult cases with a primary diagnosis of acute ischemic stroke due to carotid artery disease between 2007 and 2014 using ICD-9-CM codes 433.11 (occlusion and stenosis of carotid artery with cerebral infarction) and 433.31 (occlusion and stenosis of multiple and bilateral precerebral arteries with cerebral infarction). Records of patients enrolled in a clinical trial were excluded. Records of those transferred to another hospital were excluded, while incoming hospital transfers were included, to prevent double counting of 2 admissions pertaining to the same patient. Records missing information on age, sex, race/ethnicity, income, key hospital characteristics, and/or insurance status were also excluded.

Primary exposure and outcome of interest

The primary exposure of interest was the presence of comorbid psychiatric conditions, as identified by secondary ICD-9-CM diagnosis codes for schizophrenia or other psychoses, bipolar disorder, depression, anxiety, or substance use disorders, as described previously (data available from Dryad, table e-1, doi.org/10.5061/dryad.6hq8p8j).^{17,19,20} Diagnoses of depression and bipolar disorder were mutually exclusive; individuals with secondary diagnoses of both depression and bipolar disorder were categorized as having only bipolar disorder. The outcome was carotid revascularization with either CEA or CAS, as identified by ICD-9-CM procedure codes 38.12 and 00.63, respectively.

Comorbidity and severity adjustment

Comorbidities were measured using a Charlson Comorbidity Index (CCI) that has been modified specifically for use in ischemic stroke and validated for such patient populations.²¹ The modified CCI is a weighted average of 16 comorbidities, as identified by ICD-9-CM codes; from this score, patients were then categorized as having a CCI of 0, 1, 2, 3, 4, or >4. Case severity was determined using the All Patient Refined–Diagnosis-Related Groups (APR-DRGs), a 4-point ordinal

Figure 1 Flow diagram indicating case selection

scale (minor, moderate, major, and extreme) derived from age, primary and secondary diagnoses, and procedures.²² The APR-DRG algorithm is a validated indicator of case severity, and is frequently used in studies relating to stroke.²³

Statistical analysis

Demographic, clinical, and hospital characteristics were compared between those with and without psychiatric conditions using χ^2 for categorical variables and Wilcoxon rank sum tests for continuous variables. Logistic regression analyses were used to test the association between receiving CEA/CAS and presence of a psychiatric comorbidity. All models accounted for the sampling design of the NIS and were adjusted for patient demographics (age, sex, race/ethnicity, primary expected payer, and estimated median household income in the patient's zip code), hospital characteristics (region, location, teaching status, bed size), admission year, and clinical characteristics (modified CCI, APR-DRG severity subclass, IV thrombolysis, diabetes mellitus, coronary artery disease, hypertension, hypercholesterolemia, atrial fibrillation, valvular disease, peripheral vascular disorders, renal failure, coagulopathy, anemia, and thrombocytopenia). In addition, we analyzed the association between each psychiatric diagnosis and CEA/CAS use separately, controlling for the other psychiatric comorbidities.

Potential interactions between psychiatric comorbidity and race/ethnicity, and between psychiatric comorbidity and sex,

were explored. To reduce potential bias as a result of missing data, we performed sensitivity analyses after multiple imputation of missing values of the race and income variables. Statistical analyses were conducted using Stata version 15 (StataCorp LLC, College Station, TX). Statistically significant results were defined as $p < 0.05$, and 95% confidence intervals (CIs) are reported.

Data availability

NIS data are publicly available at hcup-us.ahrq.gov.

Results

Sample characteristics

In total, 37,474 cases of ischemic stroke due to carotid artery disease met inclusion criteria (figure 1), of which 6,922 (18.5%) had any of the 5 psychiatric comorbidities of interest. The median age of patients without any psychiatric comorbidity was 72 years (interquartile range 62–81), and the median age of those with psychiatric comorbidities was 66 years (interquartile range 56–75; <0.001). Other demographic, clinical, and hospital characteristics of the study population, stratified by the presence of psychiatric conditions, are presented in table 1.

Comorbid mental illness is associated with lower odds of carotid revascularization

Carotid revascularization with either CEA or CAS was performed in a total of 22.3% of stroke patients without

Table 1 Baseline characteristics of the study population stratified by presence of any comorbid psychiatric condition (n = 37,474)

Characteristic	No psychiatric comorbidity (n = 30,552)	Psychiatric comorbidity (n = 6,922)	p Value
Age, y, median (IQR)	72 (62–81)	66 (56–75)	<0.001
Female	13,206 (43.2)	3,215 (46.5)	<0.001
Race/ethnicity			<0.001
White	23,468 (76.8)	5,502 (79.5)	
Black	3,407 (11.2)	797 (11.5)	
Hispanic	2,020 (6.6)	380 (5.5)	
Asian or Pacific Islander	718 (2.4)	66 (1.0)	
Other	939 (3.1)	177 (2.6)	
Primary expected payer			<0.001
Private insurance	6,297 (20.6)	1,404 (20.3)	
Medicare	20,377 (66.7)	3,904 (56.4)	
Medicaid	1,758 (5.8)	813 (11.8)	
Self-pay	1,325 (4.3)	531 (7.7)	
No charge/other	795 (2.6)	270 (3.9)	
Median household income in patient zip code			<0.001
Quartile 1	8,720 (28.5)	2,128 (30.7)	
Quartile 2	8,167 (26.7)	1,838 (26.6)	
Quartile 3	7,364 (24.1)	1,721 (24.9)	
Quartile 4	6,301 (20.6)	1,235 (17.8)	
Hospital region			<0.001
Northeast	5,718 (18.7)	1,178 (17.0)	
Midwest	5,574 (18.2)	1,459 (21.1)	
South	13,405 (43.9)	3,071 (44.4)	
West	5,855 (19.2)	1,214 (17.5)	
Hospital location/teaching status			0.005
Rural	2,460 (8.1)	546 (7.9)	
Urban non-teaching	12,400 (40.6)	2,673 (38.6)	
Urban teaching	15,692 (51.4)	3,703 (53.5)	
Hospital bed size			0.224
Small	2,969 (9.7)	703 (10.2)	
Medium	7,589 (24.8)	1,763 (25.5)	
Large	19,994 (65.4)	4,456 (64.4)	
Modified CCI			0.066
0	10,709 (35.1)	2,455 (35.5)	
1	10,565 (34.6)	2,279 (32.9)	
2	5,503 (18.0)	1,260 (18.2)	
3	2,321 (7.6)	580 (8.4)	

Continued

Table 1 Baseline characteristics of the study population stratified by presence of any comorbid psychiatric condition (n = 37,474) (continued)

Characteristic	No psychiatric comorbidity (n = 30,552)	Psychiatric comorbidity (n = 6,922)	p Value
4	800 (2.6)	188 (2.7)	
>4	654 (2.1)	160 (2.3)	
Diabetes mellitus	10,958 (35.9)	2,146 (31.0)	<0.001
Coronary artery disease	9,231 (30.2)	1,858 (26.8)	<0.001
Hypertension	25,242 (82.6)	5,709 (82.5)	0.776
Hypercholesterolemia	18,137 (59.4)	4,199 (60.7)	0.047
Atrial fibrillation	4,893 (16.0)	789 (11.4)	<0.001
Valvular disease	2,782 (9.1)	524 (7.6)	<0.001
Peripheral vascular disease	4,953 (16.2)	1,207 (17.4)	0.013
Renal failure	4,039 (13.2)	721 (10.4)	<0.001
Coagulopathy	795 (2.6)	203 (2.9)	0.123
Anemia	3,764 (12.3)	920 (13.3)	0.027
Thrombocytopenia	654 (2.1)	172 (2.5)	0.078
IV thrombolysis	1,760 (5.8)	394 (5.7)	0.825
APR-DRG severity			0.017
Minor	2,302 (7.5)	513 (7.4)	
Moderate	13,050 (42.7)	2,854 (41.2)	
Major	12,257 (40.1)	2,920 (42.2)	
Extreme	2,943 (9.6)	635 (9.2)	

Abbreviations: APR-DRG = All Patient Refined–Diagnosis-Related Group; CCI = Charlson Comorbidity Index; IQR = interquartile range. Data represent n (%) unless otherwise indicated.

psychiatric conditions (95% CI 21.6%–22.9%) and 21.3% of those with comorbid psychiatric conditions (95% CI 20.3%–22.4%; $p = 0.092$). In adjusted multivariable logistic regression, having any psychiatric comorbidity was associated with a 16% decrease in the odds of receiving CEA/CAS (odds ratio [OR] 0.84, 95% CI 0.78–0.90; table 2 and figure 2). This corresponds to an adjusted predicted probability of CEA/CAS of 0.201 (95% CI 0.191–0.210) in patients with, compared to 0.226 (95% CI 0.220–0.231) in patients without, psychiatric conditions (table 2). The magnitude of the association between mental illness and carotid revascularization remained virtually unchanged after multiple imputation of missing values for race and income (OR 0.83, 95% CI 0.78–0.89; table 3).

Presence of any psychiatric comorbidity was associated with lower odds of carotid revascularization in men (OR 0.78, 95% CI 0.71–0.86) but not women (OR 0.92, 95% CI 0.82–1.02; p value for interaction <0.001). There were no significant interactions between psychiatric comorbidity and minority race/ethnicity (p value for interaction = 1.000).

Schizophrenia, depression, substance use disorders, and multiple psychiatric diagnoses are associated with lower odds of carotid revascularization.

When analyzing psychiatric diagnosis separately, stroke patients with schizophrenia or other psychoses (OR 0.72, 95% CI 0.55–0.93), depression (OR 0.83, 95% CI 0.75–0.91), and substance use disorders (OR 0.73, 95% CI 0.65–0.83) each had significantly lower odds of CEA/CAS (table 2 and figure 2) compared to those without any psychiatric conditions. Strength and direction of these associations did not substantially change after multiple imputation of missing values for race and income (table 3). The adjusted associations between carotid revascularization and bipolar disorder, and anxiety did not reach statistical significance (table 2 and figure 2).

The number of psychiatric comorbidities was inversely related to the odds of carotid revascularization: the presence of only one psychiatric comorbidity was associated with 14% lower odds of CEA/CAS (OR 0.86, 95% CI 0.79–0.92; table 2 and figure 2), while the presence of more than one comorbidity

Table 2 Adjusted ORs and predicted probabilities of carotid endarterectomy/carotid artery stenting stratified by psychiatric comorbidity status in the study population (n = 37,474)

Exposure	No. (%)	Adjusted OR (95% CI)	Adjusted probability (95% CI)
Psychiatric comorbidities			
No psychiatric condition	30,552 (81.5)	1.0 (reference)	0.226 (0.220–0.231)
Any psychiatric condition	6,922 (18.5)	0.84 (0.78–0.90)	0.201 (0.191–0.210)
Schizophrenia/psychoses	440 (1.2)	0.72 (0.55–0.93)	0.177 (0.144–0.209)
Bipolar disorder	324 (0.9)	0.79 (0.58–1.06)	0.190 (0.151–0.230)
Depression	3,104 (8.3)	0.83 (0.75–0.91)	0.197 (0.184–0.210)
Anxiety	1,878 (5.0)	1.12 (0.99–1.27)	0.237 (0.218–0.255)
Substance use disorders	2,278 (6.1)	0.73 (0.65–0.83)	0.181 (0.165–0.196)
No. of psychiatric comorbidities			
No psychiatric comorbidity	30,648 (81.5)	1.0 (reference)	0.226 (0.220–0.231)
Only 1 comorbidity	5,890 (15.7)	0.86 (0.79–0.92)	0.204 (0.194–0.214)
More than 1 comorbidity	1,032 (2.8)	0.74 (0.62–0.87)	0.184 (0.163–0.205)

Abbreviations: CI = confidence interval; OR = odds ratio.

Categories for individual psychiatric diagnoses are not mutually exclusive. All ORs are compared to those without any psychiatric conditions.

was associated with 26% lower odds of CEA/CAS (OR 0.74, 95% CI 0.62–0.87), compared to those without any psychiatric conditions (p value for trend <0.001).

Discussion

In this study, we show that the odds of carotid revascularization with either CEA or CAS after stroke due to carotid stenosis is significantly lower in patients with comorbid psychiatric conditions. Among individual psychiatric diagnoses, depression, schizophrenia, and substance use disorders were each associated with significantly lower odds of CEA/CAS. These findings are consistent with previous studies showing that Medicare patients with mental illness are less likely to undergo coronary angioplasty, coronary artery bypass surgery, and pacemaker insertion.^{24,25} Patients with depression, schizophrenia, and substance use disorders had significantly decreased odds of CEA/CAS, consistent with worse outcomes and higher disability burden typically associated with these conditions in other health care settings.^{26–29}

Our data indicate that stroke patients with multiple psychiatric diagnoses have lower odds of CEA/CAS compared to those with only one psychiatric comorbidity, suggesting that stroke patients with a greater burden of psychiatric conditions are most vulnerable to treatment differences. This is in line with previous findings that patients with multiple psychiatric comorbidities, especially comorbid substance abuse, have a more severe course of illness, increased barriers to treatment access, and overall worse outcomes.^{26,28,30} Furthermore, the

presence of multiple psychiatric comorbidities is associated with higher rates of rehospitalization or death within 6 months of a stroke.¹⁸ Although our study did not evaluate long-term outcomes, the differences in stroke care demonstrated in the present and a recent study¹⁷ may be contributing to worse outcomes in stroke patients with psychiatric conditions.^{13,18,31}

Figure 2 Adjusted multivariable logistic regression models for carotid endarterectomy/carotid artery stenting use in stroke patients with psychiatric comorbidities, relative to those without any psychiatric conditions

CI = confidence interval; ref = reference.

Table 3 Sensitivity analysis: Adjusted ORs and CIs of carotid endarterectomy/carotid artery stenting stratified by psychiatric comorbidity status after multiple imputation of missing values for race and income (n = 44,105)

Exposure	Adjusted OR (95% CI)
Psychiatric comorbidities	
No psychiatric condition	1.0 (reference)
Any psychiatric condition	0.83 (0.78–0.89)
Schizophrenia/psychoses	0.77 (0.61–0.99)
Bipolar disorder	0.84 (0.64–1.10)
Depression	0.81 (0.74–0.89)
Anxiety	1.13 (1.01–1.27)
Substance use disorders	0.72 (0.64–0.80)
No. of psychiatric comorbidities	
No psychiatric comorbidity	1.0 (reference)
Only 1 comorbidity	0.85 (0.79–0.91)
More than 1 comorbidity	0.75 (0.64–0.88)

Abbreviations: CI = confidence interval; OR = odds ratio. Categories for individual psychiatric diagnoses are not mutually exclusive. All ORs are compared to those without any psychiatric conditions.

Although we were not able to investigate the reasons for the observed treatment differences, a combination of patient and provider factors are likely to have a role. Patients with psychiatric conditions might be more likely to refuse or defer carotid revascularization, and patients with mental illness may have inadequate social support and therefore fewer people in their lives advocating for them to receive appropriate stroke treatment.³² Providers may be more hesitant to perform an intervention on those with psychiatric conditions, as patients with psychiatric comorbidities, in general, have an increased risk of complications and greater mortality in the postoperative period.^{33–35} In addition, providers may have concerns surrounding issues of informed consent and postoperative compliance in those with psychiatric conditions.³⁶ Lastly, implicit biases may have a role, as several studies have shown that health care providers' implicit attitudes are associated with differences in treatment recommendations.³⁷ Stigma related to psychiatric conditions perceived to be more severe, such as depression, schizophrenia, and substance abuse, may contribute to the observed differences and may explain why the presence of anxiety was not associated with lower odds of CEA/CAS.^{38–41}

A better understanding of barriers to evidence-based stroke care in patients with psychiatric comorbidities is particularly critical because mental illness in and of itself confers an increased lifetime risk of stroke.^{42–44} Moreover, patients with psychiatric conditions represent a disproportionately high number of stroke patients under the age of 45,⁴⁵ even after accounting for

demographic and clinical factors. Thus, addressing treatment inequities in patients with psychiatric conditions is an important component of preventing long-term disability from stroke.

Our study has several limitations. The NIS does not include information on the degree of carotid stenosis, and we were unable to adjudicate clinical appropriateness of the treatment decisions regarding CEA/CAS. We captured patients who received CEA/CAS during the same admission as their stroke, and those who were initially discharged and later readmitted for CEA/CAS; however, since the unit of analysis in NIS is discharges rather than patients, it is possible that some patients who were discharged after the initial stroke event were later admitted for CEA/CAS to a hospital that was not part of the NIS sampling frame. Another limitation of our study is its use of an administrative dataset that is dependent on ICD-9-CM codes and inpatient discharge records. A validation study comparing depression defined by ICD-9-CM codes in hospital discharge records to depression diagnoses made by inpatient chart review showed that definitions from ICD-9-CM codes had very high specificity but only moderate sensitivity.⁴⁶ Our findings are not generalizable to patients with TIAs or asymptomatic carotid artery disease. TIAs were excluded because administrative datasets have limited reliability in identifying TIAs.⁴⁷ Asymptomatic carotid stenosis cases were excluded because these patients benefit from intensive medical therapy, and the added benefit of CEA/CAS in those patients is uncertain.⁴⁸ We were unable to address potential differences in CEA/CAS use for asymptomatic carotid disease in patients with vs without psychiatric comorbidities since the NIS only captures information on hospitalized patients and does not include patients who receive outpatient medical management for asymptomatic carotid disease. However, even if there were also lower use of CEA/CAS for asymptomatic carotid disease in patients with psychiatric comorbidities, this may not constitute an alarming health care disparity because of the aforementioned unclear benefit of CEA/CAS in asymptomatic carotid disease. Although the absolute adjusted decrease in CEA/CAS use for some psychiatric comorbidities (i.e., schizophrenia/psychosis or substance use) was as much as 4% to 5% compared to patients without psychiatric conditions, we acknowledge that the absolute difference in carotid revascularization for others, albeit statistically significant, was relatively small. Furthermore, frequently used clinical endpoints, such as long-term recurrent stroke risk or functional outcomes, were not available in NIS. Therefore, the effect of the disparity described herein on long-term clinical outcomes is not known.

Despite these limitations, our study suggests that patients with stroke due to carotid stenosis who have comorbid psychiatric conditions are significantly less likely to receive CEA/CAS. Understanding the underlying reasons for lower odds of carotid revascularization in such patients may be a step toward reducing disparities in stroke care and stroke care delivery.

Author contributions

Ms. Bongiorno and Dr. Faigle were involved in study design, statistical analysis, data interpretation, and writing of the

manuscript. Dr. Daumit and Dr. Gottesman were involved in data interpretation and critical revision of the manuscript.

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Disclosure

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