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Prognosis of Midlife Stroke

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Abstract

Goals—To characterize stroke outcomes in a midlife population-based stroke cohort, and to describe comorbidities, quality of care, and risk of recurrence in this age group.

Materials and Methods—Ischemic strokes (IS) were identified from the population-based Brain Attack Surveillance in Corpus Christi Project (2000–2012). Data were from medical records and patient interviews. Ninety-day outcomes (functional, neurologic, cognitive, quality of life (QOL)), prevalence of comorbidities, quality of care, and 1-year recurrence were estimated for those 45–64 (midlife) and compared with those ≥65 using sex and race-ethnicity adjusted regression models.

Findings—Of 4,858 IS, 33% were in midlife. On average, the midlife group reported some difficulty with function, favorable neurologic and cognitive outcomes, and moderate QOL scores at 90 days. All outcomes except QOL were better in the midlife group. Prevalence of comorbidities in midlife was: hypertension 74%, diabetes 51%, hyperlipidemia 34%, heart disease 26%, prior stroke/TIA 23%, smoking 37%, excess alcohol 10%, atrial fibrillation 4%. Median BMI was 30 (IQR:26–35). Diabetes, smoking, and alcohol were more prevalent and BMI higher in the midlife group. Quality of stroke care did not differ by age. One-year recurrence in midlife was 8% (95% CI:5%–9%) and did not differ by age.

Conclusions—While 90-day outcomes were more favorable than in the elderly, midlife stroke survivors faced some disability and did not experience better QOL despite better outcomes. Additional research should identify targets to optimize secondary stroke prevention and improve outcomes in midlife stroke survivors, an understudied group with great potential disability and economic impact.

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Keywords

stroke; epidemiology; outcomes research; treatment; middle-aged

Introduction

While overall declines in stroke incidence have been observed in the United States (US), incidence in the midlife is unchanged or increasing in some sub-populations.[1–3] Coupled with the well documented declines in stroke mortality, particularly among those less than 65 years of age, [4, 5] these data suggest that a growing number of people will live longer with the consequences of stroke. Individuals who experience stroke in the midlife face unique challenges, such as issues surrounding return to work, lost earnings, need for long-term healthcare services, and psychosocial struggles.[6–8] Survivors of stroke in the midlife also face a longer exposure window for recurrent strokes, which are associated with increased mortality and worse functional outcome.[9–11] As the population of midlife stroke survivors grows, the US will face new stroke secondary prevention, treatment and recovery challenges. To guide these efforts, we sought to characterize stroke outcomes in a midlife population-based stroke cohort, and to describe the factors that may drive outcomes, including comorbidities, quality of stroke care, and risk of recurrence, in this age group. For comparison, outcomes in the midlife group were compared with those greater than or equal to 65 years of age.

Materials and Methods

Study Population

Data for this project are from the Brain Attack Surveillance in Corpus Christi (BASIC) Project. BASIC is a population-based stroke surveillance study conducted in Nueces County, Texas, a bi-ethnic, non-immigrant community. Surveillance includes identification of all strokes in the county among residents greater than 45 years of age. Detailed methods regarding stroke ascertainment have been previously published.[3, 12] Briefly, active and passive surveillance methods are used to identify possible strokes; all possible strokes then undergo validation by a stroke fellowship trained physician. For this analysis, only ischemic strokes were included and limited to one event per person. Data for this project are for the time period January 2000 through June 2012. Time periods varied based on the specific outcome as detailed below.

Demographics, Comorbidities and Behavioral Factors at Stroke Onset

Comorbidities and behavioral factors at stroke onset, including hypertension, diabetes, previous stroke/TIA, coronary artery disease, high cholesterol, atrial fibrillation, smoking, and excessive alcohol, were ascertained from medical records for the complete study time period; BMI was ascertained beginning in 2005. We have previously shown good agreement between information form medical records and self-report in this community.[12] In addition, age, sex, race-ethnicity, insurance status, and initial stroke severity, as measured by the National Institutes of Health Stroke Scale (NIHSS), were ascertained from the medical records.

Quality of Stroke Care

Quality of stroke care was assessed as adherence to seven stroke performance measures as defined by the 2009 Joint Commission and was measured for the time period February 2009 to June 2012. Measures included: patient given tissue plasminogen activator (tPA) among those who arrive within 2 hours, receipt of deep vein thrombosis (DVT) prophylaxis at 48 hours, receipt of antithrombotic at 48 hours, patient evaluated for rehabilitation, patient discharged on a cholesterol medication, patient discharged on an antithrombotic, and patients with atrial fibrillation discharged on anticoagulation. Data to assess quality of care were collected from medical records, and we have previously reported good reliability for ascertaining these measures.[13] A composite score representing the number of achieved performance measures over all patient-appropriate measures was also calculated for each patient.

Ninety Day Stroke Outcomes

Neurologic, functional, cognitive and quality of life (QOL) outcomes were ascertained at approximately 90 days post-stroke in a subset of patients who agreed to participate in the interview portion of the BASIC study. Outcome interviews were added in November 2008, and thus this portion of the analysis is limited to the time period from November 2008 to June 2012. Outcomes were ascertained via an in-person interview, the methods of which have been previously published.[14] If a patient was unable to respond, a proxy interview was conducted. Neurologic outcome was measured by the National Institutes of Health Stroke Scale (NIHSS) administered by a trained study coordinator. Functional outcome was measured using a series of self-reported questions assessing Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). Question responses were given on a Likert scale; responses were then averaged to come up with an ADL/IADL score for the patient ranging from 1 to 4 (higher scores represent worse functional outcome). Cognitive outcome was assessed using the Modified Minimental Examination (3MSE), which results in a score ranging from 0 to 100 (higher scores represent better cognitive function). QOL was assessed using the short-form Stroke Specific Quality of Life (SS-QOL) scale, which has been validated in our population.[15] The SS-QOL ranges from 1 to 5 (higher scores represent better quality of life). Proxies provided information on the functional and QOL outcomes but did not provide information on cognitive outcomes, and thus patients requiring a proxy were excluded from analysis of the cognitive endpoint (see online supplement).

Stroke Recurrence and All-Cause Mortality

Recurrent events were ascertained through BASIC surveillance and included any stroke (ischemic or intracerebral hemorrhage) identified after the first ischemic stroke. All-cause mortality was ascertained from the Texas Department of Health and Human Services and linked to BASIC data using first and last name, date of birth, sex, race-ethnicity and residential address information. Both recurrence and mortality were ascertained for the entire study time period. For the recurrence endpoint, cases were censored at death or the end of follow-up. For mortality, cases were censored at the end of follow up.

Statistical Analysis

Descriptive statistics were calculated for all variables by age group (45–64 years (midlife group) versus ≥65 years). Binary comorbidities and individual quality measures were summarized with frequencies and percents; continuous variables were summarized with medians and interquartile ranges (IQR); time-to-event variables were summarized as the estimated one-year probability of the event with associated 95% confidence intervals. To assess differences by age group, we fitted various models unadjusted and adjusted for sex and race-ethnicity (outcome models were additionally adjusted for years of education); logistic regression models were fitted for binary comorbidities; linear regression models with robust standard errors were fitted for continuous variables; proportional hazard models were fitted for time-to-event variables; generalized estimating equations (GEE) with a log link function were fitted for the binary quality outcomes and GEE with the identity link function for the overall composite quality measure. Robust standard errors for the quality indicator models were additionally corrected for the small number of hospital clusters.[16] Adjustment for hospital clustering was not performed for the tPA and anticoagulant for atrial fibrillation quality indicators due to small numbers of eligible patients, and thus Poisson regression models with robust standard errors were fitted for these two quality indicators. Statistical analysis was performed in SAS 9.3.

This study was approved by the Internal Review Boards of the University of Michigan and the two local hospital systems.

Results

A total of 4,858 ischemic strokes were identified during the study period, of which one-third were in those 45–64 years of age (n=1,618). Table 1 includes sociodemographics characteristics by age group. The midlife age group was comprised of a greater proportion of men and Mexican Americans than the older age group. Nearly 19% of stroke cases 45–64 years of age did not have medical insurance compared with less than 1% of those ≥ 65 years. The proportion of patients receiving thrombolytic therapy (not considering eligibility) was 7.7% in stroke cases 45–64 years of age and 9.8% in those age ≥ 65).

Ninety-day Stroke Outcomes

Table 2 includes data on 90-day stroke outcomes. During the time period when 90-day outcomes were collected, there were 891 ischemic strokes. Of the 891, 126 died before 90 days, 65 could not be located for interview and 74 refused the outcome interview, leaving 626 eligible for the 90-day interview. Final sample sizes were 599 for neurologic and functional outcome and 497 for cognitive outcome. Among cases who survived to 90 days, with the exception of cognitive outcome, participation was slightly higher for the older age group (80–81%) compared with the midlife group (75–76%). For cognitive outcome, participation was lower in the older age group compared with the midlife group due to the additional exclusion of cases requiring a proxy and those with language dysfunction, which was more common in older cases. QOL was not ascertained until a later time point resulting in a smaller sample size for this outcome. Among those 45–64 years of age, median ADL/IADL score was 1.98 (IQR: 1.27–2.73); a score of 2 represents “some difficulty” performing

ADL/IADL tasks. Median NIHSS (range 0–44, higher scores worse neurologic outcome) in those 45–64 years was 2 (IQR: 0–4), median 3MSE score (range 0–100, higher scores better cognitive function) was 92 (IQR: 85–96), and median SS-QOL (range 1–5, higher scores better quality of life) was 3.33 (IQR: 2.58–4.29). All 90-day outcomes were significantly better in those 45–64 years compared with those ≥65 years after adjusting for sex and race-ethnicity, with the exception of QOL where no difference was noted. Additional adjustment for education had little impact on the associations.

Comorbidities and Behavioral Factors at Stroke Onset

Table 3 displays the prevalence of comorbidities at stroke onset in those 45–64 years as well as the comparison of similar data in those ≥65 years. The most prevalent comorbidity among stroke cases 45–64 years was hypertension at 74%, followed by diabetes 51%, current smoking 37%, hyperlipidemia 34%, coronary artery disease 26%, history of stroke/TIA 23%, excessive alcohol consumption 10%, and atrial fibrillation 4%. Prevalence of diabetes, current smoking and excessive alcohol consumption were significantly higher in those 45–64 years compared with those ≥65 after adjusting for sex and race-ethnicity. Median BMI in those 45–64 years was 29.8 (IQR 25.8–35.0) compared with a median of 26.2 (IQR 23.0–29.8) in those ≥65, a difference which was statistically significant in the adjusted model. Initial stroke severity did not differ by age group (median NIHSS was 4 (IQR: 2–7) for those 45–64 years and 4 (IQR: 2–9) for those ≥65 years).

Stroke Quality of Care

Table 4 displays the seven stroke quality performance measures by age group. Among those 45–64, adherence to the performance measure was greatest for antithrombotic therapy at the end of hospital day 2 (95.2%) followed by assessed for rehabilitation (94.8%), discharged on antithrombotic therapy (89.7%), cholesterol lowering medication at discharge (84.2%) and DVT prophylaxis at the end of hospital day 2 (80.8%). Adherence was considerably lower for anticoagulant at discharge for those with atrial fibrillation (60.0%) and thrombolytic therapy (58.3%). No differences in adherence were noted between the two age groups with the exception of discharged on antithrombotic therapy which had a higher prevalence in those 45–64 years after accounting for hospital clustering, sex, race-ethnicity and education. The composite measure (number of achieved performance measures over all patient-appropriate measures) had a median of 1.0 (IQR: 0.8–1.0) in those 45–64 years and did not differ by age.

Stroke Recurrence and Mortality

Among those 45–64 years of age, the probability of stroke recurrence at one year was 8% (95% CI: 6%–9%) and the probability of death from any cause at one year was 10% (95% CI: 8%–11%). Stroke recurrence did not differ significantly between the two age groups (HR=0.89, 95% CI: 0.76–1.05). Stroke cases ages 45–64 had lower one year post-stroke mortality compared with those ≥65 years after adjusting for sex and race-ethnicity (see online supplement).

Discussion

In our population-based study, those with stroke in the midlife, on average, experienced favorable neurologic and cognitive outcomes but reported some difficulty with ADLs/IADLs and moderate QOL scores. We noted a high prevalence of comorbidities at stroke onset in the midlife group, in particular, hypertension and diabetes were present in 74% and 51%, respectively. Prevalence of behavioral risk factors, including current smoking and excessive alcohol intake, were also high at 37% and 10%, respectively. Median BMI in this age group was 29.8 suggesting 50% of people with stroke in the midlife are obese.

Our finding that the younger age group faced functional limitations is consistent with a case series of midlife stroke survivors from the Netherlands that found that 32% had a modified Rankin score greater than two an average of 9 years after stroke.[17] This finding is especially relevant given that the midlife group is still of working age and may face challenges to accessing rehabilitation due to lack of insurance or being under insured relative to the older, Medicare eligible age group.[18] The high prevalence of obesity and severe obesity might also pose challenges to rehabilitation in the midlife cohort as increasing BMI may be associated with decreased rehabilitation effectiveness and longer rehabilitation stays.[19, 20] Optimizing post-stroke recovery in the one-third of stroke survivors who are middle aged is a priority given the social, financial and psychological consequences of post-stroke disability.

Despite younger age and better neurologic, functional and cognitive outcomes among midlife stroke survivors, there was no difference in QOL between the age groups. This finding might reflect unique challenges faced by the midlife stroke survivors, such as the social, family and financial ramifications of stroke, that likely differentially influence QOL in younger stroke patients.[21] For example, we previously reported that only 40% of stroke survivors in this population return to work.[7] Some midlife stroke survivors report guilt over their disability and the impact on their spouse and family.[21] Others discuss the impact on their sexual relationships.[22] Additional contributions from comorbidities that are associated with age and lower QOL, such as post-stroke depression, could also be confounding the age association.[23] More detailed study of the impact of stroke on QOL in midlife stroke patients is needed.

Our findings have implications for secondary stroke prevention and stroke-related outcomes given that the majority of middle aged stroke survivors had hypertension and/or diabetes. Reductions in blood pressure lead to lower rates of recurrent stroke and heart disease and thus improved outcomes.[24, 25] Unlike hypertension, where the functional and cognitive ramifications are often indirect, diabetes can have a direct impact on function in the form of diabetic neuropathy and autonomic dysfunction, in addition to the indirect impact on post-stroke disability.[26, 27] One-year recurrence in the midlife cohort was not trivial at 8% highlighting the importance of effective treatment of post-stroke hypertension and diabetes. In addition to comorbidities, sociodemographic factors were distributed differently by age group. In contrast to the older age group, the midlife group included a greater proportion of men and those of Mexican American ethnicity. Of note, almost 20% of middle-aged stroke survivors did not have medical insurance suggesting that there may be challenges to accessing secondary stroke prevention and post-acute care in this growing population. Strategies that reach high risk individuals and deliver proven treatments are needed to prevent recurrent stroke and improve post-stroke functional and cognitive outcomes during midlife.

Quality of stroke care is critical to secondary prevention and recovery. The quality of stroke care received in our midlife cohort did not differ by age group. Of note, tPA treatment was 58% in eligible ischemic stroke patients in the midlife group, which is somewhat lower than contemporary estimates of tPA treatment among eligible patients in the Get With the Guidelines Stroke Hospitals.[28] This suggests that there are opportunities to improve stroke treatment in this population, which is critical given that midlife stroke patients face a greater number of years of stroke related disability. However, increases in tPA treatment are unlikely to have a large impact on population-level disability among midlife stroke survivors given the small proportion of patients who are eligible for tPA.[28] Anticoagulation at discharge for patients with atrial fibrillation was 60% in the midlife age group which was lower, although not statistically significant, than the older age group. This estimate is also considerably lower than estimates of anticoagulation for atrial fibrillation in the Get With the Guidelines Stroke Hospitals.[29] Reasons for lower adherence to this quality indicator should be investigated as treatment with anticoagulants is important for preventing cardioembolic strokes which tend to be more severe and have poorer outcomes than other stroke types.[30] Of note, sample size for both tPA and anticoagulant for atrial fibrillation was small given the number of patients eligible for these indicators and therefore these results should be interpreted with caution.

Our study has limitations. BASIC by design excludes stroke in individuals below 45 years of age, and thus our definition of midlife was focused on those 45–64. Additional research is needed to understand outcomes in those with stroke younger than 45 years of age. Stroke survivors with language and/or cognitive deficits requiring a proxy were excluded from cognitive outcomes, which differentially impacted those in the older age group and likely contributed to an underestimation of age-related differences in this outcome. We did not have information on stroke subtype. However, we did have data on initial stroke severity, which did not differ by age group, suggesting that the observed poorer outcomes in the older age group are not likely driven by older patients with atrial fibrillation having more severe strokes. Measures of comorbidity control were not available and would be important in planning secondary prevention initiatives. Given the design of BASIC, we present data for stroke cases only. An important next step would be to compare these outcomes with those in a non-stroke population to better understand the impact of stroke in the midlife.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Summary

This study provides a description of the salient features of stroke in the midlife. While outcomes were more favorable in the midlife stroke group than the elderly, midlife stroke survivors still faced some degree of disability and did not experience better QOL despite their better outcomes. Strategies aimed at effectively treating hypertension and diabetes, which were highly prevalent comorbidities, and improving the quality of stroke care, could reduce recurrent stroke and improve outcomes in midlife stroke survivors, an understudied group with great potential disability and economic impact.

Table 1

Sociodemographic Characteristics in Midlife Stroke Patients Aged 45–64 and Comparisons with Stroke Patients Age ≥ 65.

	Age 45–64 (N=1,618)	Age ≥ 65 (N=3,240)
	No. (%)	**No. (%)**
Age (median (IQR)	56.8 (52.2, 60.9)	78.3 (72.4, 84.7)
Female	682 (42)	1840 (56)
Race-ethnicity		
Non-Hispanic White	495 (31)	1538 (47)
Mexican American	1002 (62)	1556 (48)
African American	121 (7)	146 (5)
No insurance	306 (19)	28 (1)

Table 2

Ninety Day Stroke Outcomes in Midlife Stroke Patients Aged 45–64 and Comparisons with Stroke Patients Age ≥ 65.

	Age 45–64 Median (IQR)	Age ≥ 65 Median (IQR)	Unadjusted Diff (95% CI)	Adjusted* Diff (95% CI)†	Adjusted** Diff (95% CI)†
Functional outcome: ADL/IADL Score (Range 1–4, higher worse)	1.98 (1.27, 2.73)	2.77 (1.64, 3.68)	−0.60 (−0.77, −0.42)	−0.60 (−0.77, −0.43)	−0.53 (−0.71, −0.36)
Neurologic outcome: NIHSS (Range 0–42, higher worse)	2 (0, 4)	3 (1, 7)	−0.89 (−1.40, −0.38)	−1.17 (−1.73, −0.62)	−0.84 (−1.34, −0.35)
Cognitive outcome: 3MSE (Range 0–100, higher better)	92 (85, 96)	85 (70, 94)	6.90 (4.71, 9.08)	7.46 (5.31, 9.60)	5.71 (3.83, 7.59)
Quality of life: SS-QOL (Range 1–5, higher better)	3.33 (2.58, 4.29)	3.33 (2.33, 4.25)	0.10 (−0.14, 0.35)	0.13 (−0.12, 0.38)	0.06 (−0.19, 0.32)

*Adjusted for sex and ethnicity

**Adjusted for sex, ethnicity and educational attainment

**Adjusted for sex, ethnicity, education

†Estimates from linear regression with robust standard errors adjusted for sex and ethnicity

ADL/IADL activities of daily living/instrumental activities of daily living, NIHSS National Institutes of Health Stroke Scale, 3MSE Modified Minimental State Examination, SS-QOL short form Stroke-Specific Quality of Life

NOTE: ADL/IADL sample size for age 45–65 (N=260) and age ≥65 (N=339); NIHSS sample size for age 45–65 (N=262) and age ≥65 (N=337); 3MSE sample size for age 45–65 (N=247) and age ≥65 (N=250); SS-QOL collected from May 1, 2010; sample size for ages 45–64 (N=148) and age ≥65 (N=181).

Table 3

Prevalence of Comorbidities and Behavioral Factors in Midlife Stroke Patients Aged 45–64 and Comparisons with Stroke Patients Age ≥ 65.

	Age 45–64 (N=1,618)	Age ≥ 65 (N=3,240)	Unadjusted	Adjusted
Comorbidity/Behavioral Factor	**No. (%)**	**No. (%)**	**OR (95% CI)**	**OR (95% CI)***
Hypertension	1,199 (74)	2,568 (79)	0.75 (0.66, 0.87)	0.72 (0.62, 0.83)
Diabetes	832 (51)	1,187 (37)	1.84 (1.63, 2.07)	1.62 (1.42, 1.84)
Coronary artery disease/myocardial infarction	418 (26)	1,230 (38)	0.57 (0.50, 0.65)	0.53 (0.46, 0.61)
Atrial fibrillation	71 (4)	641 (20)	0.19 (0.14, 0.24)	0.21 (0.16, 0.28)
High cholesterol	548 (34)	1,082 (33)	1.02 (0.90, 1.16)	1.01 (0.89, 1.15)
History of stroke/transient ischemic attack	378 (23)	1,064 (33)	0.62 (0.55, 0.72)	0.62 (0.54, 0.71)
Current smoker	605 (37)	365 (11)	4.69 (4.00, 5.44)	4.69 (4.02, 5.47)
Excessive alcohol	163 (10)	128 (4)	2.73 (2.15, 3.47)	2.31 (1.80, 2.96)

*Estimates from logistic regression adjusted for sex and race-ethnicity

Note: Models were not run for insurance status due to the small number of people without insurance in the older age group.

Table 4

Adherence to Stroke Quality Performance Measures in Midlife Stroke Patients Aged 45-64 and Comparisons with Stroke Patients Age ≥ 65.

	Ages 45-64			Age ≥ 65			Adjusted for hospital clustering	Adjusted for sex, race-ethnicity and hospital clustering
Performance Measure	**No. eligible**	**No. received**	**%**	**No. eligible**	**No. received**	**%**	**RR (95% CI)***	**RR (95% CI)***
Deep vein thrombosis prophylaxis at end of hospital day 2	198	160	81	375	279	78	1.03 (0.89, 1.20)	1.03 (0.88, 1.20)
Discharged on antithrombotic therapy	321	288	90	409	340	83	1.08 (1.06, 1.10)	1.07 (1.05, 1.10)
Anticoagulant at discharge for patients with atrial fibrillation	25	15	60	112	80	71	0.84 (0.60, 1.18)	0.84 (0.60, 1.18)
Thrombolytic therapy	36	21	58	60	37	62	0.95 (0.67, 1.33)	0.97 (0.69, 1.36)
Antithrombotic at end of hospital day 2	289	275	95	430	397	92	1.03 (0.99, 1.08)	1.03 (0.97, 1.09)
Cholesterol lowering medication at discharge	241	203	84	315	244	78	1.09 (0.89, 1.33)	1.06 (0.85, 1.32)
Assessed for rehabilitation	290	275	95	390	377	97	0.98 (0.94, 1.03)	0.99 (0.91, 1.06)

*Estimates from GEE with a small number of cluster adjustment method.