original article

Health outcomes after acute ischemic stroke: retrospective and survival analysis from Oman

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Citation: Al Alawi AM, Al Busaidi I, Al Shibli E, Al-Senaidi A, Al-Manwari S, Al Busaidi I, et al. Health outcomes after acute ischemic stroke: retrospective and survival analysis from Oman. Ann Saudi Med 2022; 42(4): 269-275. DOI: 10.5144/0256-4947.2022.269

Received: October 28, 2021

Accepted: February 4, 2022

Published: August 4, 2022

Funding: None.

BACKGROUND: Stroke mortality and related functional disability have been declining over the last two decades, but stroke continues to represent the second leading cause of cardiovascular death worldwide and the number one cause for acquired long-term disability.

OBJECTIVES: Assess short- and long-term health outcomes after acute ischemic stroke and analyze factors associated with poor survival and functional outcomes.

DESIGN: Retrospective and survival analysis

SETTING: Inpatient unit at a tertiary care referral hospital.

PATIENTS AND METHODS: All patients admitted with acute ischemic stroke from 1 January 2017 to 31 August 2018 were included in the study. Functional status was assessed using the modified Rankin Scale (mRS). Other demographic and clinical variables were obtained from medical records. Data were analyzed by multivariable logistic regression, Cox proportional hazards, and the Kaplan-Meier method. Long-term follow-up data, including mortality and mRS was collected by follow-up phone call.

MAIN OUTCOME MEASURES: Functional dependency and factors associated with mortality.

SAMPLE SIZE AND CHARACTERISTICS: 110 with mean age of 67.0 (14.7) years; 59 patients (53.6%) were males.

RESULTS: Hypertension (75.5%), diabetes mellitus (54.6%), and dyslipidemia (29.1%) were common. Sixty-five patients (59.1%) had mRS >2 upon discharge including 18 patients (16.4%) who died during the hospital stay. The cumulative mortality rate was 25.4% (28/110) at 12 months and 30.0% (33/110) at 24 months. Twenty-nine stroke survivors (29/70, 41.4%) remained physically dependent (mRS >2) at the end of follow-up. Old age, atrial fibrillation, history of prior stroke, chronic kidney disease, and peripheral arterial disease were associated with increased mortality and functional dependence.

CONCLUSIONS: Patients in Oman with acute ischemic stroke tend to have a high comorbidity burden, and their functional dependency and mortality are higher compared to patients from developed countries. Therefore, evidence-based measures such as establishing stroke units are essential to improve the health outcomes of patients with acute ischemic stroke.

LIMITATIONS: Retrospective at single center.

CONFLICT OF INTEREST: None.

Stroke mortality and related functional disability have been declining over the last two decades due to advances in the management of acute ischemic stroke.[1,2] Such advances include but are not limited to thrombolytic therapy, mechanical thrombectomy, acute stroke units, and post-stroke rehabilitation programs, which have been shown to reduce both mortality and functional disability.[2,3] However, stroke continues to represent the second leading cause of cardiovascular death worldwide and the number one cause for acquired long-term disability, resulting in a global annual economic burden.[4] Around 25-50% of stroke survivors continue to have a severe functional disability.[5] Furthermore, comorbidity is prevalent in patients with ischemic stroke. Comorbidity is associated with increased mortality and morbidity.[6,7] Old age, pre-stroke functional dependency, atrial fibrillation, and high comorbidity are associated with worse post-stroke survival rate and functional independence.[7]

In the Middle Eastern countries, including Oman, studies addressing health outcomes after ischemic stroke are sparse;[8-10] hence studying ischemic stroke health outcomes and analyzing factors associated with poor outcomes are essential elements of the healthcare quality improvement process. We aimed to assess short- and long-term health outcomes after acute ischemic stroke. Also, we analyzed factors associated with poor survival and functional outcomes.

PATIENTS AND METHODS

The study was a retrospective study with a survival analysis that included all patients admitted to Sultan Qaboos University Hospital (SQUH) with acute ischemic stroke (within seven days of the onset of the symptoms) from 1 January 2017 to 31 August 2018. Functional status was assessed using the modified Rankin Scale (mRS), and functional dependency was defined as mRS >2.[11] As relevant determinants of prognosis in ischemic stroke, the following variables were collected from the medical records: age, sex, treatment, atrial fibrillation (AF), ischemic heart disease, smoking status, hypertension, hyperlipidaemia, chronic kidney disease (CKD), diabetes mellitus, previous stroke, length of hospitalization, and mRS on discharge. In addition, long-term follow-up data, including mortality and mRS was done through a phone follow-up call in November 2020. The study was approved by the Medical Research Ethics Committee (MREC) of the College of Medicine and Health Sciences at Sultan Qaboos University (MERC. No.1949)

Categorical variables are reported as number and percentage. Continuous variables are expressed as mean and standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed data. Continuous variables between the two groups were compared using the t test for normally distributed variables or Wilcoxon rank-sum for non-normally distributed variables. The Fisher exact test was used to assess the association between categorical variables (due to the small sample size). Relevant clinical characteristics with *P* values <.25 were included in a multivariable logistic regression to identify independent predictors associated with severity of mRS (on discharge and follow up). Multivariable Cox proportional hazards regression was performed to identify variables related to mortality. In addition, long-term mortality outcome was analyzed as time-to-event using the Kaplan–Meier method and by using log-rank tests for comparisons. Hazard and odds ratios were calculated with 95% confidence intervals (CIs). Two-sided *P* values <.05 were considered to be statistically significant. Statistical calculations were performed using the Stata v. 16.1 software package (StataCorp LLC, USA).

RESULTS

One hundred ten patients were admitted with ischemic stroke during the study period (**Table 1**). The mean age was 67.0 (14.7) years, and 59 patients (53.6%) were males. Hypertension (75.5%), diabetes mellitus (54.6%), dyslipidemia (29.1%) were common. Only eight patients (7.3%) were treated with thrombolytic therapy, and 82 patients (74.6%) were discharged on aspirin and clopidogrel. The median length of hospitalization was 7 days (IQR: 5-11). Sixty-five patients (59.1%) had mRS >2 upon discharge including 18 patients (16.4%) who died during the index admission. Twenty-two patients died after discharge (20%). Multivariate logistic regression showed that old age (*P*=.002), AF (*P*<.001), and previous stroke (*P*=.013) were associated with an increased risk of functional dependency on discharge (mRS>2). The mean follow-up duration was 25.4 (1.3) months. There were 66 patients (60.0%) who had mRS>2 on the follow-up date, including 22 patients (20%) who died during the follow-up period.

The cumulative mortality rate was 25% at 12 months and 30% at 24 months (**Figure 1**). After excluding overall death (n=40), 41.4% of stroke survivors (29/70) remain physically dependent (mRS >2). Old age (*P*<.001), atrial fibrillation (AF) (*P*<.001), history of prior stroke (*P*<.001) were more common in patients who had an ischemic stroke resulting in functional dependency (mRS >2). Patients with functional dependency on discharge (mRS >2) had increased mortality (*P*<.001) and poor functional outcome during the

follow-up period (*P*<.001). Also, old age (*P*=.02), AF (*P*<.001), and previous stroke (*P*=.02), were associated with poor functional outcome (mRS>2) on follow up.

Forty patients died during the index admission or the follow-up period, and the reported underlying cause of deaths were ischemic stroke (n=28), sepsis (n=4), ischemic heart disease (n=3), malignancy (n=2), diabetes mellitus (n=1) and unknown causes (n=2). In addition, the log rank test in the Cox regression showed that mRS>2 (*P*=.002), AF (*P*<.0001), chronic kidney disease (CKD) (*P*=.07), peripheral arterial disease (*P*=.017) were associated with increased mortality (**Figure 2**).

DISCUSSION

This study provides important data on the health outcomes of patients who suffered from acute ischemic stroke in this region of the world. The mean age of the patients with acute ischemic stroke was 67 years, 16.4% of the patients died during the index admission, 20% died during follow up, and 41.4% of stroke survivors remained physically dependent (mRS >2). Old age, AF, CKD, physical dependency on discharge (mRS >2), peripheral artery disease, and previous stroke were associated with poor health outcomes in patients with acute ischemic stroke.

Most of the patients were males (53.6%), which is similar to the findings of previous studies. This could be explained by the protective effect of estrogen in females and the higher prevalence of cardiovascular risk factors on males including smoking, and hypertension.[12,13] Also, the patients in our cohort had a high burden of comorbidities, with the most common being hypertension (75.5%), followed by diabe-

Table 1. Baseline characteristics, treatment and health outcomes of patients admitted with acute ischemic stroke.

	Total cohort (n=110)	mRS (≤2) (n=45)	mRS (>2) (n=65)	*P*
Age (years)	67.0 (14.7)	60.1 (13.9)	71.8 (13.4)	**<.001**
Male	59 (53.6)	23 (51.1)	36 (55.4)	.700
Hypertension	83 (75.5)	31 (68.9)	52 (80.0)	.183
Smoking	18 (16.4)	11 (16.9)	7 (15.6)	.183
Diabetes mellitus	60 (54.6)	25 (55.6)	35 (53.9)	.859
Dyslipidemia	32 (29.1)	13 (28.9)	19 (29.2)	.969
Atrial fibrillation	14 (12.7)	0	14 (21.5)	**<.001**
Ischemic heart disease	24 (21.8)	7 (15.7)	17 (26.2)	.217
Chronic kidney disease	19 (17.3)	6 (13.3)	13 (20.0)	.450
Peripheral Arterial disease	4 (3.6)	1 (2.2)	3 (4.6)	.510
Prior stroke	27 (24.5)	4 (8.9)	23 (35.4)	**<.001**
Thrombolytic therapy	8 (7.3)	3 (6.7)	5 (7.7)	.839
Aspirin or clopidogrel	25 (22.7)	12 (26.7)	13 (20.0)	.701
Aspirin and clopidogrel	82 (74.6)	32 (71.1)	50 (77.0)	.701
Anticoagulant alone	19 (17.3)	5 (11.1)	14 (21.5)	.380
Antiplatelet + anticoagulant	4 (3.6)	2 (3.1)	2 (3.1)	
Median length of hospitalization (days)	7 (5-11)	7 (5-9)	7 (5-12)	.8644
Median follow up (months)	29.3 (23.9)	34.0 (10.5)	25.4 (25.8)	**<.001**
mRS on discharge	3.3 (2.1)	1.1 (0.8)	4.9 (0.9)	**<.001**
mRS on follow up	3.4 (2.9)	1 (0-3)	4.6 (4.9)	**<.001**
Mortality	40 (36.4)	4 (8.9)	36 (55.38)	**<.001**

Data are n (%) or mean (standard deviation) for age, or median (interquartile range) for length of hospitalization and follow-up time. mRS: modified Rankin Scale; IQR: interquartile range.

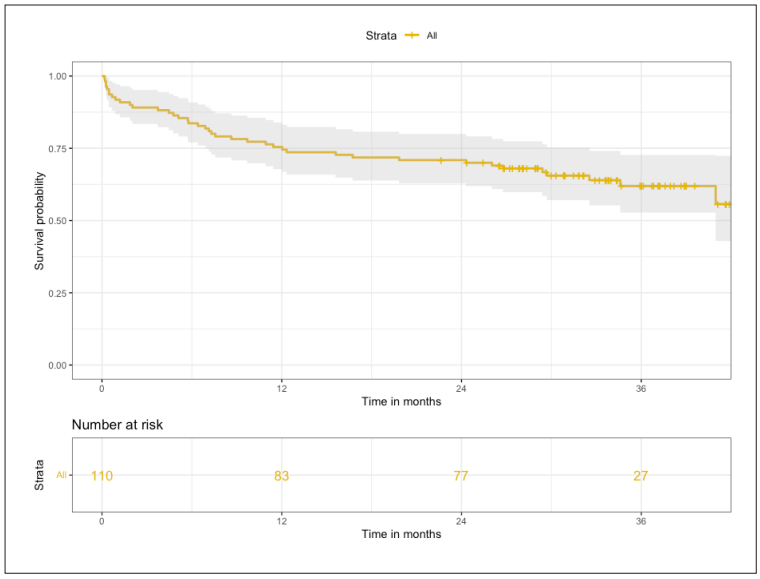

Figure 1. Kaplan-Meier survival analysis for patients with acute ischemic stroke (n=110).

tes mellitus (54.6%) and dyslipidemia (29.1%). These findings are similar to findings of previous studies in the Middle East, including studies in Saudi Arabia.[14-18] Hypertension is the most prevalent and modifiable risk factor for stroke and is associated with worsened outcomes.[19] In general, a high comorbidity burden is associated with the complexity of clinical management, poor health outcomes and increased health care cost. In patients with stroke, an increased morbidity index is associated with increased mortality; however, there are very few studies to assess the impact of comorbidity in other stroke outcomes.[1,20,21]

Only 7.3% of patients received thrombolytic therapy, similar to the reported figures in some developing countries.[22] A recent study from Saudi Arabia showed that only 8.6% of patients with acute ischemic stroke received thrombolytic therapy.[23] In contrast, some studies from Europe showed that more than 20% of patients received thrombolytic therapy for acute ischemic stroke.[24] Thrombolytic therapy is associated with improved health outcomes in patients with acute ischemic stroke.[25,26] The low percentage of patients who received thrombolytic therapy could be explained by delayed presentation to the hospital due to several factors, including the poor awareness of stroke symptoms among patients at increased risk.[8,22]

Also, endovascular thrombectomy has become a standard treatment for patients with large vessel occlusion related acute ischemic stroke. However, this is not readily available in our center.[27] The majority of the patients were prescribed dual antiplatelets, which reflects adherence to the current recommendation of acute ischemic stroke management.[28]

Eighteen patients (16.4%) died during hospitalization; the reported in-hospital mortality rate after acute stroke ranged between 1.8-41% in developing countries and 0-22.0% in developed countries.[22,29-32] A study from Japan reported a 30-day mortality rate of 9.8% after acute ischemic stroke.[33] Also, a study from Saudi Arabia reported an inpatient mortality rate of 9.7% after acute ischemic stroke.[34] This variation in the inpatient mortality rate for stroke is primarily due to delayed presentation, poor access to essential medications and other health care facilities in countries with poor health systems.[29,35]

The median follow-up duration was 29.3 (23.9) months. Another 22 patients died during the follow-up period. The cumulative mortality rate was 25% at 12 months and 30% at 24 months which is lower than the mortality rate in some of the developing countries but slightly higher than the reported rate in some developed countries.[36-38]

AF was associated with increased stroke severity and higher mortality, which is similar to findings of previous studies.[39-41] The Framingham study analyzed stroke severity in AF; the 30-day mortality was greater in AF strokes than non-AF strokes (25% vs 14%). In addition, the AF group had poor survival and more risk of recurrence of stroke in the one-year follow up; hence the use of anticoagulation is crucial.[42,43]

Also, severe disability on discharge (mRS >2), old age, chronic kidney disease, peripheral arterial disease were associated with increased mortality in this study. Similarly, previous studies identified old age, smoking, female sex, dyslipidemia dementia, chronic kidney disease, AF, diabetes mellitus, peripheral artery disease, chronic heart disease and malignancy as factors associated with increased stroke mortality.[32,37,44] Most patients died due to the sequel of ischemic stroke (e.g. aspiration pneumonia, infected pressure ulcer) or due to ischemic heart disease. This finding is similar to the findings of previous studies.[45] Appropriate management of cardiovascular risk factors (e.g. hypertension and diabetes) and prevention of aspiration pneumonia are important measures to improve the survival of patients with ischemic stroke.[22]

Around 41% of stroke survivors remained physically dependent (mRS>2). The reported incidence of physical dependence among stroke survivors varies between 15-30% in the USA to 45% in China.[46] We found that old age, previous stroke, AF, and high mRS>2 at discharge were associated with an increased functional disability during the follow-up period.

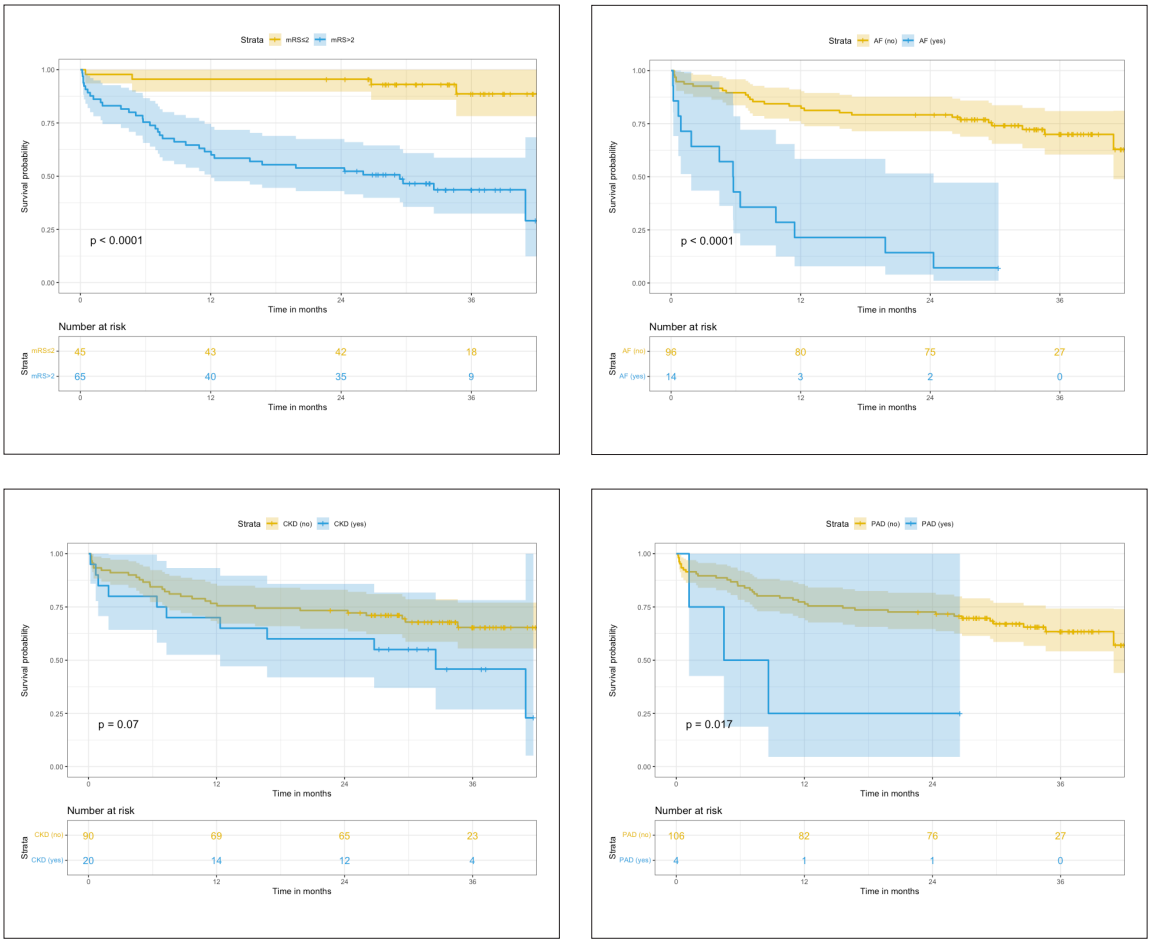

Figure 2. Kaplan-Meier survival analysis for patients with acute ischemic stroke by modified Rankin scale (mRS), atrial fibrillation (AF), chronic kidney disease (CKD) and peripheral arterial disease (PAD).

Our study has several limitations; first, it was a retrospective, single center and hospital-based. Some important data were not collected, including Glasgow coma scale, socioeconomic status and The National Institutes of Health Stroke Scale score. However, the study, being the first of its kind in the region, provides important data that can be used to improve care for patients with stroke.

This study suggests that stroke mortality rate and physical dependence post-stroke in this part of the world are higher than reported numbers from developed countries. There are very few studies addressing the stroke outcomes in the Middle East region. Increasing public awareness of risk factors of stroke, symptoms of stroke and establishment of emergency transportation services are key factors to increase the rate of thrombolysis and hence improving stroke health outcomes.[8,22,35] In addition, establishing a stroke unit, access to endovascular intervention, and well-structured multi-disciplinary rehabilitation service are essential elements to optimize the care for patients with acute ischemic stroke.[22] Our study findings should provide insights to health care managers and stakeholders to plan the necessary changes like allocating health care resources and implementing the necessary improvement in the current health care settings.

In conclusion, our study is one of the few studies reporting short- and long-term outcomes in patients with acute ischemic stroke from our region. The patients with acute ischemic stroke tend to have a high comorbidity burden, and their functional dependency and mortality were higher compared to patients from developed countries. Therefore, important measures including increasing public awareness of stroke, improving emergency transportation services, establishing stroke units and optimizing multi-disciplinary rehabilitation services are important elements to improve

the health outcomes of patients with acute ischemic stroke. Our study findings should provide insights to health care managers and stakeholders to plan the necessary changes like allocating health care resources and implementing the necessary improvement in the current health care settings.

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