

The Risk of Stroke Using CHA₂DS₂-VASC Score in Hemodialysis Patients at a Tertiary Hospital in Riyadh, Saudi Arabia

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Abstract

Introduction: Patients undergoing hemodialysis are at increased risk of stroke. However, less known about the impact of some of the stroke risk factors, and the value of stroke risk scores in determining the risk in those patients. Our main goal. To assess the risk factors for stroke in hemodialysis patients and the use of the new CHA₂DS₂-VASC score for stroke assessment.

Methods: Single center, retrospective cohort study of 336 patients undergoing hemodialysis from June 24, 2018, to September 6, 2018, was recruited. Baseline demographics, clinical, and laboratory data were collected. We calculated the CHA₂DS₂-VASC score for stroke assessment in all patients and categorized them into high, moderate and low risk patients according to CHA₂DS₂-VASC score and subcategorized them to two groups atrial fibrillation (AFib) and Non- Atrial fibrillation (Non AFib) patients.

Results: 336 patients were included in our study; the majority of patients were at high risk with a CHA₂DS₂-VASC Score mean of 2.9± 1.5, although history of stroke was observed only in 15 patients (4.46%). According to CHA₂DS₂-VASC score, 280 patients were at high risk, 172 (51.19%) were high-risk patients on treatment (anticoagulant or antiplatelet) and 108(32.14%) patients were high risk patients not on treatment 48 were at moderate risk (14.28%) and 8 were at low risk (2.38 %). Patients were divided into subgroups as non-AFib and AFib. In non-AFib patients 320 (95.23%), high-risk patients 103 (32.18%) were not treated; high-risk patients with treatment are 162 (50.62%), moderate patients were 47 (14.68%), 8(2.5%) was in low risk. AFib patients were 16 with a mean CHA₂DS₂-VASC score of 4.4±1.1. Patients with AFib were all at high risk except 1 was at moderate risk (6.25%). There were 11 (68.75%) patients on treatment and 5 (31.25%) patients not on treatment. The risk factors for stroke that were statistically significant in increasing score risk for all patients were: age ≥ 65 (95% CI, -2.04– -1.29; p = 0.000), being female (95% CI, -1.36– -0.68; p = 0.000) hypertension (95% CI, -2.59– -1.37; p = 0.000), diabetes (95% CI, -2.10– -1.50; p = 0.000), CVD (95% CI, -2.07– -1.24; p=0.000), history of stroke or TIA (95% CI, -3.70– -2.03; p = 0.000), CHF or LVEF (95% CI, -2.28– -0.91; p = 0.000).

Conclusions: The risk of stroke in hemodialysis patients is significant according to the use of CHA₂DS₂-VASC score in Non-AFib hemodialysis patients shows supportive evidence of increased risk of stroke in those patients, which suggest the importance of close monitoring of patients with stroke risk factors by the nephrologist and the stroke team which will lead to the initiation of early prophylaxis in those patients.

Introduction

The global incidence of end-stage renal disease (ESRD) has been increasing steadily. Hemodialysis (HD) or peritoneal dialysis (PD) has been widely accepted for treatment in patients with ESRD [1]. The prevalence of end stage renal failure treated by dialysis is estimated to be 604 cases/PMP; total death was 1,726 (9%), while the incidence of treated end-stage renal disease is estimated at 163 cases/PMP [2]. According to The dialysis statistics prepared by the Saudi Center for Organ Transplantation (SCOT) at the end of 2017 showed a total of 19,659 dialysis patients, hemodialysis (HD) and the remaining 1,389 treat 18,270 of them by peritoneal dialysis (PD). Patients with end stage renal disease (ESRD) have markedly

advanced vascular disease when compared to the general population [3]. Cardiovascular disease (CVD) is the leading cause of death in these patients, accounting for 40%–50% of all-cause mortality. End-stage renal disease (ESRD), the worst stage of kidney function, presents a risk of stroke approximately 5 to 10 times greater than normal kidney function [4]. Previous studies in the US and Japan reported 2- to 10-fold increased risks of stroke in dialysis patients compared to the general population [1]. Studies in Saudi Arabia have provided a hospital-based crude annual incidence rate of stroke of 15.1 per 100,000 persons in Jizan, 29.8 per 100,000 persons in the Eastern province, and 43.8 per 100,000 persons in Riyadh [5]. Approximately 15% of all strokes are attributed to non-valvular atrial

fibrillation or atrial flutter (AF) [6]. In such patients, CHADS₂ and CHA₂DS₂-VASc have emerged as the dominant prediction tools to estimate a patient's risk of stroke or systemic thromboembolism [7, 8]. CHADS₂ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke/ TIA (transient ischemic attack) (double score)) and CHA₂DS₂-VASc (congestive heart failure, hypertension, age ≥75 years (double score), diabetes mellitus, previous stroke/TIA (double score), vascular disease, age 65–74 years, sex class (female)) [8]. Recently, CHADS₂ and CHA₂DS₂-VASc clinical tools have been reported to have predictive capacity for outcomes in patients without known AF, including the risk of death after stroke [9].

The purposes of the study were to evaluate the practicality of the CHA₂DS₂-VASc clinical tools for the prediction of stroke, in hemodialysis patients without a history of atrial fibrillation.

Participants and Methods

Ethics statement

The study protocol was approved by the Research Ethics Committee HP-01-R-079 of Prince sultan military medical city in (Riyadh, Saudi Arabia).

Participants

Patients were recruited from one dialysis center of a tertiary hospital (prince sultan military medical city) between June 24, 2018 and September 6, 2018. The inclusion criteria for this study were all adult patients above 18 years old who received maintenance hemodialysis for more than 6 months; the exclusion criteria were pediatric patients on hemodialysis and patients on hemodialysis for less than 6 months.

Study Protocol

This was a retrospective observational cohort study. Baseline demographic data included age (y), gender (male, female), Body mass index (kg/m²), weight (kg), Height (cm) Race (black, white), co morbidities such Arteriosclerotic heart disease (ASHD), congestive heart failure (CHF), Diabetes mellitus, Atrial fibrillation, hypertension, Peripheral vascular disease (PVD), other Cardiovascular disease (CVD) and the primary cause of ESRD, laboratory parameters, including Hemoglobin (g/L), Serum albumin (g/L), Albumin-corrected calcium (mmol/L), Serum phosphorus (mmol/L), Total cholesterol (mmol/L), Total triglycerides (mmol/L), HDL-C (mmol/L), LDL-C (mmol/L) serum, Medication usage data were also collected from the patients' files such as patient on aspirin, clopidigerl, statin, novel anticoagulant (enoxaparin), NSAID (diclofenac sodium, celecoxib and naproxen) and the period of hemodialysis and if the patient smoker or not.

Stroke risk score calculation

The CHA₂DS₂-VASc score shown in (Table1) were used to access the risk of stroke in hemodialysis patients, stroke Risk were calculated for each patient by assigning 1 point each for the presence of chronic heart failure, hypertension, diabetes, vascular disease, age 65–74 years, and female sex; and by assigning 2 points of age ≥75 years, prior stroke or transient ischemic attack (TIA) [10].

Table 1: CHA₂DS₂-VASc score

Risk Factor	Score
Chronic heart failure	1
Hypertension	1
Diabetes	1
Vascular disease	1
Age 65-74 years	1
Female sex	1
Age ≥ 75years	2
Prior stroke or transient ischemic attack (TIA)	2

Patients were categorized according to the CHA₂DS₂-VASc score into low, moderate and high-risk patients. If the patient score a 0 score indicates low risk patient and may not require anticoagulation or antiplatelet therapy; and if the patient score 1 which indicate a moderate risk and should consider antiplatelet or anticoagulation, and if the score is 2 or greater this indicates a high risk and should otherwise be an anticoagulation candidate.

Statistical Analysis

A statistical analysis was performed using the Statistical package for the social sciences (SPSS) Software for Mac Book version 23.0 (IBM corporation, Armonk, New York, US). The analysis included a description of the sample involved in the study. The mean, SD, minimum and maximum for continues data were identified. The number and percentage of non-parametric data were also used. The analysis included knowing the association between CHA₂DS₂-VASc score and different laboratory parameters and medications, where P value was considered significant when the difference between groups was ≤ 0.05.

Results

Data from 336 eligible patients were analyzed. We found that the majority of patients are at a high risk with a CHA₂DS₂-VASc score mean of 2.9+ 1.5, although history of stroke was observed only in 15 patients (4.46%). Patients were subcategorized to three groups according to CHA₂DS₂-VASc score to: 280 patients at high risk (83.33%), 48 patients at moderate risk (14.29%) and 8 patients at low risk (2.38%).

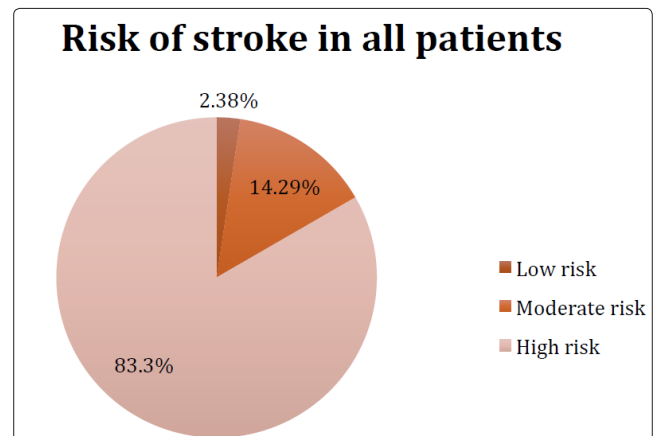


Figure 1

Patients were Divided to Subgroups as non---Atrial fibrillation and Atrial fibrillation. In non---Atrial fibrillation Patients 320 (95.23%), 162 (61%) of high---risk patients were On treatment (anticoagulant Or antiplatelet) while 103 (38%) were not. Atrial fibrillation Patients were 16 patients with a mean CHA₂DS₂-VASc score of 4.4±1.1. All patients were at high risk except 1 was at moderate risk. There were 11 (68.75%) on treatment and 5 (31.25%) not on treatment.

The mean age was 59.3 ± 16.9 and (45%) was female. For the race, 83% were white and 14% were black. Only (6.5%) were smokers. The mean height (cm) was 155.6 ± 29.12. The mean weight (kg) was 68.5±23.26 with a BMI (kg/m²) around 26.3 ± 8.5. The most common Co morbidities were Hypertension (91.6%) and DM (58%), CHF or LVEF (6.8%) and ASHD (3.57%). CVD was presented in (19%) of patients and PVD was (1.4%) (Table 2).

Table 2

Variables	Total (n=336)	P-value
Demographics		
Age (Y) (>65)	59.2 ± 17.1 (43.75%)	0.000
Gender (F%)	152 (45%)	0.000
Race (W)	279 (83%)	0.155
BMI (kg/m ²)	26.3 ± 8.5	0.528
Weight (Kg)	68.5±23.26	0.032
Height (cm)	155.6± 29.12	0.528
Smoker	22 (6.5%)	0.009
Comorbidities Diabetes mellitus	195 (58%)	0.000
Hypertension	308 (91.6%)	0.000
CVD	64 (19%)	0.000
CHF of LVEF	23 (6.8%)	0.001
Atrial fibrillation	16 (4.7%)	0.000
Stroke or TIA	15 (4.46%)	0.000
ASHD	12 (3.57%)	0.004
PVD	5 (1.4%)	0.58
Etiology of ESRD Chronic glomerulonephritis	5 (1.4%)	0.264
Diabetic nephropathy	164 (48%)	0.000
Hypertension	233 (69.3%)	0.626
Laboratory Variables Hemoglobin (g/L)	11.1 ± 1.6	0.263
Serum Albumin (g/L)	39.4 ± 5.9	0.000
Albumin corrected calcium (mmol/L)	2.1 ± 0.34	0.010
Serum Phosphorus (mmol/L)	1.5 ± 4.4	0.670
Total Triglyceride (mmol/L)	1.7 ± 1.1	0.092
Total Cholesterol (mmol/L)	3.6 ± 1.12	0.057
HDL-C (mmol/L)	1 ± 0.53	0.909
LDL-C (mmol/L)	2.09 ± 0.87	0.195
Medications Aspirin	157 (46.7%)	0.00
Clopidogrel	57 (17%)	0.74
Novel anticoagulant	6 (1.78%)	0.818
NSAID	152 (45.2%)	0.16

Statins	171 (50.89%)	0.00
CHAD ₂ vasc ₂ score	2.9 ± 1.5	

An independent-sample t-test was conducted to compare different variables with CHA₂DS₂-VASc scores. The risk factors for stroke that were statistically different in increasing score risk for all patients were: age > 65 (95% CI, -2.04 – -1.29; p = 0.000), being female (95% CI, -1.36– -0.68; p = 0.000) hypertension (95% CI, -2.59– -1.37; p = 0.000), diabetes (95% CI, -2.10– -1.50; p = 0.000), CVD (95% CI, -2.07– -1.24; p=0.000), history of stroke or TIA (95% CI, -3.70– -2.03; p = 0.000), CHF or LVEF (95% CI, -2.28– -0.91; p = 0.000). Figure 2 shows the risk factors for stroke.

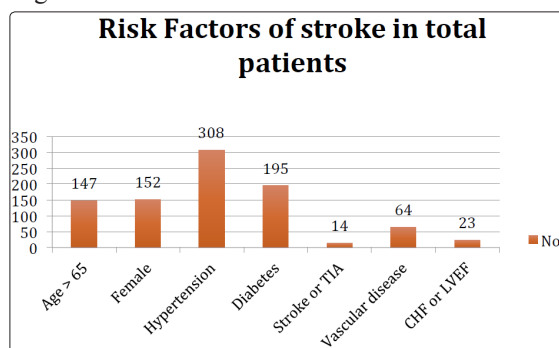


Figure 2

In terms of medications, 157 (46.7%) of patients were on aspirin, 57 (17%) were on clopidogrel, 6 (1.78%) were on novel anticoagulant, 152 (45.2%) were on NSAID (diclofenac sodium, celecoxib and naproxen) and 171 (50.89%) were on statins. Aspirin (95% CI, -0.99– -0.33; p = 0.000) and Statins (95% CI, -0.92– -0.26; p = 0.000) were associated with significant increase of risk score. There was no significant difference with clopidogrel (95% CI, -0.85– 0.40; p = 0.74) and NSAID (95% CI, -0.57– 0.10; p=0.16).

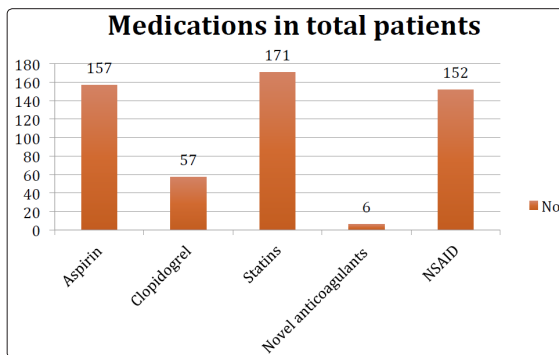


Figure 3

A Pearson Correlation Coefficient was computed to assess the relationships between different laboratory variables, age, weight and the total CHA₂DS₂-VASc scores. There was a strong negative correlation between total CHA₂DS₂-VASc score and serum albumin (r= -0.206, p= 0.000, n= 336) and a strong positive correlation between total CHA₂DS₂-VASc score and albumin corrected calcium (r= 0.141, p=0.010, n= 336) which both found to be statically significant. The correlation between total CHA₂DS₂-VASc score and age was positive and significant (r=0.641, p= 0.011, n=336) and between total CHA₂DS₂-VASc score and weight was negative and significant (r= -0.139, p=0.032, n=336).

Discussion

This is a retrospective, observational cohort single center study, which offers a detailed evaluation of the prevalence, clinical characters, and risk factors of stroke in hemodialysis patients. This is the first study in Saudi Arabia designed to assess the risk of stroke among ESRD patients undergoing hemodialysis by using the stroke risk assessment CHA₂DS₂-VASc score and to determine the practicality of CHA₂DS₂-VASc score for predicting stroke in hemodialysis patients without a history of atrial fibrillation. The main findings of this study were that the majority of hemodialysis patients have high incidence of developing stroke using CHA₂DS₂-VASc score especially in non-atrial fibrillation patients; the stroke risk factors were age, being female, hypertension, Diabetes mellitus, and history of stroke or TIA.

In clinical practice, the CHA₂DS₂-VASc score is useful in guiding antithrombotic therapy for atrial fibrillation, with patients having a high score benefiting from anticoagulation therapy. Hemodialysis (HD) patients are at a higher risk of serious bleeding due to several factors including uremic platelet dysfunction, anemia, and heparin use during dialysis. Therefore, in dialysis patient's clinical assessment scoring system such as CHA₂DS₂-VASc score may help physicians to identify patients at a higher risk for unfavorable events, and establish pre-emptive monitoring programs in order to decrease disease severity and negative outcomes instead of guiding therapy [10].

In the Middle East to our knowledge there is no similar study for the assessment of stroke risk in hemodialysis patients. Patients in our study with a previous history of stroke in total group's atrial fibrillation and non-atrial fibrillation patients were 15 (4.46%) of 44.6/1,000 patients. These findings are comparable to a study done by Junzhou Fu et al in a study of 590 patients undergoing hemodialysis (HD; n = 285) or peritoneal dialysis (PD; n = 305) they found the 62 strokes occurred during 1258 total patient-years of follow-up. Stroke occurred at a rate of 49.2/1,000 patient-years with predominance in HD patients compared with PD patients (74.0 vs. 31.8/1,000 patient-years). The cumulative hazard of developing stroke was significantly higher in HD patients (hazard ratio [HR], 1.75; 95% confidence interval [CI], 1.15–3.62; p = 0.046) after adjusting for potential confounders. HD patients had an increased risk of ischemic stroke (HR, 2.62; 95% CI, 1.56–4.58; p = 0.002). The risk of hemorrhagic stroke was not significantly different between PD and HD patients. On multivariate Cox analysis, risk factors of stroke in both HD and PD patients were older age, diabetes, and cardiovascular disease. Other independent risk factors of stroke were lower albumin-corrected calcium in HD patients and higher triglycerides in PD patients. In this study we found that patients on HD with a previous history of stroke [1].

Our study data shows that patients on hemodialysis with a high risk using CHA₂DS₂-VASc risk score assessment especially in patients with no history of atrial fibrillation the importance of initiation of anti thrombotic therapy. The study has some limitations mainly related to the nature of the study which is retrospective, single center study and relatively done in a small group of population. We recommend the carrying out multicenter prospective to further assess the risk of stroke using CHA₂DS₂-VASc risk score assessment.

Conclusion

The risk of stroke in hemodialysis patients is significant according to the use of CHA₂DS₂-VASc score in Non-AFib hemodialysis

patients shows supportive evidence of increased risk of stroke in those patients, which suggest the importance of close monitoring of patients with stroke risk factors by the nephrologists and the stroke team which will lead to the initiation of early prophylaxis in those patients.

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