Clinical Outcomes of Oral Anticoagulation and No Anticoagulation among End-Stage Renal Disease Patients on Maintenance Hemodialysis with Atrial Fibrillation: A Single-Center Prospective Cohort Study

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Abstract

Introduction. The delicate balance of risk versus benefit of oral anticoagulation in the general population is well established but the decision to use these agents in end-stage renal disease (ESRD) remains complex and difficult owing to the paucity of clinical trials and lack of substantial evidence in literature for its safe and effective use in the hemodialysis population. This study aims to determine the difference in clinical outcomes between oral anticoagulation and no anticoagulation therapy among ESRD patients on maintenance hemodialysis with atrial fibrillation.

Methods. This is a prospective, single-center, observational study conducted in Perpetual Succour Hospital that included all ESRD patients on maintenance hemodialysis for at least 3 months with atrial fibrillation. Out of the 188 identified patients, only 69 patients were included in the study and were grouped according to how the cardiac dysrhythmia was approached either with oral anticoagulation or no use of oral anticoagulation. Basic demographic information were obtained as well as the etiology of ESRD, CHA_2DS_2-VASc Score and the HAS-BLED Score. Lastly, patients were prospectively followed for a period of 12 months and were then assessed for new onset of thromboembolic events, hemorrhagic events, calciphylaxis and all-cause mortality.

Results. At enrollment, 59 (85.5%) patients were identified to have no oral anticoagulation therapy and 10 (14.5%) were already receiving oral anticoagulation. Ischemic strokes were more prevalent among patients who were on oral anticoagulant (80%, $p < 0.0001$). Patient outcomes differ significantly in terms of intracranial hemorrhage (30%, $p = 0.0004$) and gastrointestinal bleeding (50%, $p < 0.00001$) which were noted among patients on oral anticoagulation. In relation to over-all mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis, there was no significant difference between the two groups.

Conclusion. This study suggests that the use of oral anticoagulation did not prevent ischemic strokes in ESRD patients on maintenance hemodialysis with atrial fibrillation and its use was associated with increased risk for intracranial hemorrhage and gastrointestinal bleeding. There was no significant difference in relation to all-cause mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis between the two study groups.

Keywords: End-Stage Renal Disease, Atrial fibrillation, oral anticoagulation

Introduction

In the not-so distant past, kidney failure was considered to be a death sentence until the resourceful spirit of Dr. Willem Kolff during the World War II found a way to make a machine that would do the work of the kidneys using a "washing machine", sausage skins, orange juice cans and other common items to make a device that could clear and remove toxins from the blood. Progress has been made over the past six decades in the world of kidney medicine, however it still remains as a challenge for clinicians around the world since it is coupled with an increasing incidence of dysrhythmia that results in a cardiac mortality as high as 41% in the first year of hemodialysis.

Atrial fibrillation occurs more frequently among patients with end-stage renal disease (ESRD) with a varied

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prevalence of 9 to 25%, this being 10 to 20-fold higher than the general population. Dialysis patients not only have higher prevalence of atrial fibrillation, but also are at greater risk of heart failure, hypertension and diabetes that enhances stroke risk and serious bleeding in the setting of atrial fibrillation.[1]

Large observational studies have confirmed the benefit of oral anticoagulation therapy for stroke prevention in atrial fibrillation but it is noteworthy that patients on maintenance hemodialysis have been excluded from randomized trials, and such patients might have multiple risk factors for stroke and thus, high CHA_2DS_2VASc score.[6] With regards to stroke risk stratification approaches in atrial fibrillation, patients with severe renal impairment have been excluded and in this way, the benefit of oral anticoagulation in patients with atrial fibrillation with normal renal function cannot be extrapolated to patients with atrial fibrillation and ESRD.[5]

Many patients with ESRD and atrial fibrillation will have a risk profile for thromboembolic episodes leading to systemic anticoagulation, with warfarin as the traditional mainstay of therapy for this indication.[2] However, the balance between efficacy and safety of warfarin use among this group of patients is not clear. At best, warfarin offers protection from cardiovascular events when studied in large retrospective studies without increasing bleeding. Other reports, including aggregate data from meta-analyses, warfarin use in ESRD patients with atrial fibrillation offers no reduction in mortality, ischemic events, or stroke but instead, increases major bleeding.[7] Likewise, warfarin use has also been reported to cause the rare effect of calcific uremic arteriopathy in patients with ESRD, that adds to the increasing morbidity and mortality by 50%.[8]

These prevailing data provide a setting to seek out safer alternatives. Non-vitamin K oral anticoagulants (NOACs) in observational studies are preferred to warfarin in some hemodialysis patients because of ease of administration, comparable or improved efficacy, and lower incidence of intracranial hemorrhage and fatal bleeds. In contrast, other observational studies reported that patients on NOACs had significantly higher risk of complications compared with warfarin users.[4] However, the data on the efficacy of oral anticoagulants on thromboembolic risk in ESRD patients are extremely conflicting and there is no clear evidence that warfarin is associated with a reduced incidence of cerebrovascular events in HD patients. On the contrary, there seems to be a clear association between vitamin K inhibitors and the risk of bleeding.

There may be convincing as well as opposing arguments regarding the use of anticoagulants in ESRD patients with atrial fibrillation, but without well-conducted clinical trials, it is definitely impossible to consider the use of anticoagulation in this special group of population.

Research Question

Is there a difference in clinical outcomes between oral anticoagulation and no anticoagulation among End-Stage Renal Disease patients on maintenance hemodialysis with atrial fibrillation in Perpetual Succour Hospital?

Definition of Terms

End-Stage Renal Disease. End-stage renal disease is a condition of individuals with Chronic Kidney Disease, who require renal replacement therapy to sustain life.

Atrial fibrillation. Atrial fibrillation is an irregular heart rhythm that is confirmed with electrocardiographic findings of absent P waves, presence of fibrillatory waves and/or irregularly irregular QRS complexes.

Oral anticoagulants. Anticoagulants are agents used to treat and prevent further embolic events. They can be either vitamin K antagonists such as warfarin or a NOAC (non-vitamin K antagonist oral anticoagulants) like dabigatran, rivaroxaban and apixaban.

Systemic thromboembolism. Thromboembolism encompasses two interrelated conditions that are part of the same spectrum, deep venous thrombosis (DVT) and pulmonary embolism (PE) due to a thrombus formation.

Ischemic Stroke. Ischemic stroke is characterized by a neurologic deficit or an alteration in level of consciousness that is confirmed with a noncontrast computed tomography (CT) scan findings of either of the following, hypodensity, loss of gray-white matter, cortical swelling or effacement of sulci.

Intracranial hemorrhage. Intracranial hemorrhage is a pathological accumulation of blood within the intracranial spaces characterized by a marked hyperdensity on noncontrast computed tomography (CT) scan.

Gastrointestinal hemorrhage. Gastrointestinal hemorrhage refers to all forms of bleeding in the gastrointestinal tract, from the mouth to the rectum. Symptoms may include vomiting of red blood, vomiting black blood, bloody stool, or black stool.

Calciphylaxis. Calciphylaxis is a clinical diagnosis of vascular calcification and cutaneous necrosis in an ESRD patient with hypercalcemia, hyperphosphatemia and hyperparathyroidism.

CHA_2DS_2-VASc Score. The CHA_2DS_2-VASc score is a risk stratification schema that determines the one risk of an ischemic stroke in patients with atrial fibrillation. The acronym, CHA_2DS_2-VASc stands for C- Congestive Heart Failure; H- Hypertension; A2-Age >=75 years; D-Diabetes Mellitus; S2- Prior Stroke or Transient Ischemic Attack; V- Vascular Disease; A- Age 64-74 years and Sc-Sex Category (i.e. female sex).

HAS-BLED Score. HAS-BLED is a scoring system developed to assess 1-year risk of major bleeding in patients with atrial fibrillation. A calculated HAS-BLED score is between 0 to 9 and based on seven parameters with a weighted value of 0-2. HAS-BLED mnemonic stands for H- Hypertension; A- Abnormal renal and liver

function; S- Stroke; B- Bleeding; L- Labile INR; E- Elderly and D- Drugs or alcohol.

Significance of the Study. The delicate balance of risk versus benefit of using oral anticoagulants in the general population is well established but the decision to use these agents in end-stage renal disease remains complex and difficult owing to the paucity of clinical trials and lack of substantial evidence in literature for its safe and effective use in the hemodialysis population. Moreover, little is known regarding the epidemiology of atrial fibrillation among dialysis patients in the Philippines.

This, in turn, will provide local data regarding the incidence of atrial fibrillation in hemodialysis patients as well as clinical information based on the epidemiological data derived from our own patient population that will be incorporated in the clinical judgment regarding anticoagulation benefits and risks in our care plan.

Considering the current lack of randomized studies that can hardly be carried out in this setting, the researcher believed that prospective studies using a statistical approach, in order to simulate estimation of a randomized controlled trial, may contribute in giving information about a correct therapeutic approach when treating these complex patients.

General Objective. To determine the difference in clinical outcomes between oral anticoagulation and no anticoagulation therapy among End-Stage Renal Disease patients on maintenance hemodialysis with atrial fibrillation in Perpetual Succour Hospital.

Specific Objectives.

1 To provide local data on the prevalence of atrial fibrillation in ESRD receiving maintenance hemodialysis and frequency of oral anticoagulation therapy and no anticoagulation in this group of patients.
2 To compare the clinical outcomes for a period of 12 months in between groups in terms of ischemic stroke, systemic thromboembolism, intracranial hemorrhage, gastrointestinal bleeding and all-cause mortality.
3 To investigate the association between anticoagulation therapy and mortality for different CHA2DS2-VASc scores in a cohort of end-stage renal disease patients receiving dialysis treatment.
4 To assess the association between oral anticoagulation therapy and bleeding risks using the HAS-BLED scoring system in this special subgroup of patients.

Scope and Limitations of the Study. The aim of this study is to compare the use of oral anticoagulation and non-use among end-stage renal disease patients with atrial fibrillation receiving maintenance hemodialysis in Perpetual Succour Hospital for a period of 12 months. The outcomes measured were ischemic stroke, acute coronary syndrome, peripheral arterial occlusive disease, intracranial hemorrhage, gastrointestinal bleeding, calciphylaxis and all-cause mortality.

A limitation is the fact that this was not a randomized study. The comparison between oral anticoagulant use and non-use in an observational design makes confounding-by-indication as the most important limitation.

Methods

Study Design and Setting. In this prospective, single-center, observational cohort study conducted in a tertiary hospital in Cebu City, Cebu, all patients with End-Stage Renal Failure on hemodialysis at Perpetual Succour Hospital were reviewed for eligibility. All subjects with atrial fibrillation and on maintenance hemodialysis for at least 3 months were recruited.

Study Population and Data Collection

Inclusion Criteria. All diagnosed End-Stage Renal Disease patients with atrial fibrillation on maintenance hemodialysis for at least 3 months were included in the study.

Exclusion Criteria.

1 Those who died within the observation period of 12 months
2 Atrial fibrillation with reversible causes
3 Active bleeding in the previous 6 months
4 Severe hepatic impairment
5 Any type of stroke within 3 months prior to baseline
6 Underwent kidney transplant

Data Collection. First, all patients with ESRD receiving maintenance hemodialysis for at least 3 months at Perpetual Succour Hospital with atrial fibrillation from May 2017 up until October 1, 2018 were identified and observed for at least 1 year. All patients provided written informed consent prior to participation. Out of 188 patients on hemodialysis, there were 74 noted patients with atrial fibrillation as confirmed by 12-Lead electrocardiography. During the study period, five (5) subjects were excluded during the eligibility screening due to death prior to completion of the study.

As shown in *Figure 1*, patients were assigned into two groups as to how cardiac dysrhythmia was approached: Oral Anticoagulation Group and No Anticoagulation Group

Information collection was completed which included the demographics such as age, sex and co-morbidities. Moreover, identification of clinically relevant factors were accomplished which included:

1 Cause of ESRD: Diabetes, Hypertension, Glomerulonephritis, Obstructive uropathy and other causes
2 Anticoagulant used during dialysis; Low molecular weight heparin, Unfractionated Heparin
3 Maintenance medications: Beta blockers, Calcium channel blockers, Amiodarone, Digoxin, ACEI, ARBs, Diuretics and Statins
4 Antiplatelet use: Aspirin, Clopidogrel and other anti-platelets

5 Hemodialysis access used: IJ catheter, Permanent catheter, AV fistula and AV graft
6 CHA_2DS_2-VASc Score
7 HAS-BLED Score
8 Lastly, patients were prospectively followed for a period of 12 months and assessed for new onset of the following:
9 Thromboembolic Events: Ischemic stroke, myocardial infarction, peripheral arterial occlusive disease
10 Hemorrhagic Events: Intracranial hemorrhage and gastrointestinal bleeding
11 All-cause mortality and Calciphylaxis
12 Statement of Confidentiality

The data gathering of the study did not include the patient's name, any marks or personal information, description to preserve the patient's privacy. Other information that reflected the patient's financial status, or may lead to social stigmatism or discrimination were not included. The researcher guaranteed that strict standards were observed in this paper. In addition, the researcher did not seek any financial support from any pharmaceutical companies and did not provide any financial assistance to the participants in the study.

Institutional Approval. The study was approved by the Institution Ethics and Review board (Level III).

Sample Size Determination. The Perpetual Succour Hospital had 188 hemodialysis patients as of May 2017. A sample size of 69 was determined using conservative capture rate of 50% estimated at 95% confidence level with ± 9.41 margin of error.

Data Processing and Statistical Analysis. All data gathered were encoded in Microsoft Excel 2015. This study used frequency and percentage distribution in expressing categorical data. Likewise mean and standard deviations were utilized as well as indicators of continuous information. In comparing average age between the two groups, Z-test for two sample means and Z-test for two sample proportions were utilized. Any associated p-value less than 0.05 alpha were considered significant. Minitab Version 18 was used in processing the data for accuracy purposes of all computations.

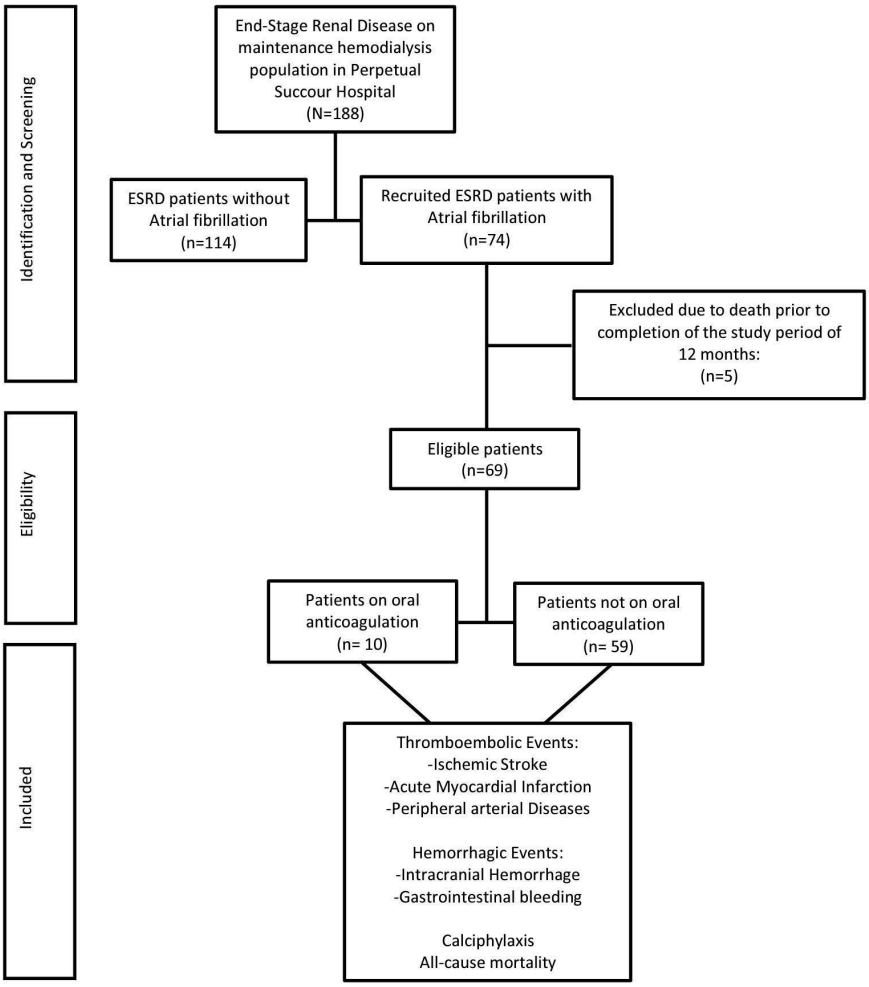

Figure 1. Flow diagram illustrating the details on how the study population were obtained.

Results

Study Population. A total of 188 patients were receiving maintenance hemodialysis at Perpetual Succour Hospital from May 2017 until October 2018, of which 74 (39.4%) individuals had a documented atrial fibrillation. *Table I* shows the demographic profile of the study population.

A diagnosis of atrial fibrillation was recorded in 74 individuals but the study was carried out in a cohort of 69 hemodialysis patients after 5 subjects were excluded due to death prior to the completion of the study period. The mean ages of the patients in the two groups registered to be significantly different as manifested by the *p=0.008* of the z-test of two sample means. As shown in *Table I*, 14.5% (n=10) were identified to be treated with oral anticoagulation and 85.5% (n=59) had no oral anticoagulation therapy.

There was no significant difference recorded in the proportion of both genders

Table I. Baseline demographic features of the study population.

Characteristics	With Anticoagulant (n=10, %)	No Anticoagulant (n= 59, %)	Total (n=69)	p-value (z-test)
Age (in years)	59.89 ± 8.45]	69.12 ± 10.29]	69	0.008[a*]
Gender				
Male	8[80%]	37[63%]	45	0.2891[b]
Female	2[20%]	22[37%]	24	0.2891[b]
Cause of ESRD				
Diabetes	9[90%]	40[68%]	49	<0.001*
Hypertension	2[20%]	8[14%]	10	0.59
Glomerulonephritis	1[10%]	7[12%]	8	0.87
Obstructive Uropathy	0	2[3%]	2	0.5552
Comorbidities				
Hypertension	2[20%]	7[12%]	9	0.48
HPN+ DM	5[50%]	41[69%]	46	0.23
HPN+ DM+ COPD	2[20%]	3[5%]	5	0.93
HPN+ DM+ BA	1[10%]	2[3%]	3	0.34
Malignancy	0	1[2%]	1	0.68
Hematologic Diseases	0	2[3%]	2	0.56
Liver Disease	0	3[5%]	3	0.47
Past Medical History				
CVD Infarct	6[60%]	15[25%]	21	0.027*
CVD Bleed	1[10%]	1[2%]	2	0.15
TIA	1[10%]	2[3%]	3	0.34
History of ACS	8[80%]	34[58%]	42	0.18
GI Bleed	3[30%]	1[2%]	4	0.004*
None	2[20%]	18[31%]	20	< .0001*

Abbreviations: ESRD- End-stage renal disease; HPN- Hypertension; DM- Diabetes mellitus; COPD- Chronic Obstructive Pulmonary Disease; BA- Bronchial Asthma; CVD- Cerebrovascular Disease; TIA- Transient Ischemic Attack; GI- Gastrointestinal; ACS- Acute Coronary Syndrome; AVF- Arteriovenous fistula; AVG- Arteriovenous Graft; IJ- Intrajugular

[a] *two-tailed z-test for two sample means*

[b] *two-tailed z-test for two sample proportions*

reflecting that the males and females were statistically distributed evenly (*p-= 0.2891*) in this study. Being diabetic was more prominent as a cause of ESRD in both groups, with 90% of them on oral anticoagulation as compared to the 68% from the other group (*p-< 0.001*). Incidence of hypertension, glomerulonephritis and obstructive uropathy were found to be statistically the same between the two study groups.

Verified from the two-tailed z-test for two sample proportions that all $p > 0.05$, this implies that the two groups have statistically the same incidence of comorbidities. Additionally, there were significant differences noted from the past medical history between the patient groups. In fact, a greater proportion of patients who took anticoagulants had histories of CVD Infarct (60%, $p = 0.03$) and GI bleeding (30%, $p = 0.0004$). But significantly, most of the patients (31%, $p < 0.0001$) who had no pertinent past medical history came from the group with no anticoagulation treatment.

Medication Profile of the study population. The decision to use rate or rhythm control and anticoagulation in the management of atrial fibrillation requires an integrated consideration to avoid risk of complications and minimize symptoms. Antiplatelet therapy with Clopidogrel was significant among patients not on oral anticoagulants (61% versus 10%, $p = 0.002$). None of the patients were receiving both Aspirin as well as an oral anticoagulant in this study. Similarly, the use of digoxin (40% and 7%, $p = 0.002$) and statins (80% and 41%, $p = 0.0208$) were among the medications taken by patients in the group treated with oral anticoagulation. The use of anticoagulants (Regular Heparin and LMWH) during hemodialysis sessions did not differ between groups and were evenly distributed statistically with a $p = 0.76$. Use of beta blockers, calcium channel blockers and amiodarone use did not differ significantly in between groups as shown in *Table II*.

Risk prediction scores for thrombotic and hemorrhagic events among ESRD patients. Validated predictive scores such as CHA_2DS_2-VASc and HAS-BLED exist to aid in identifying patients who will benefit most and who are at risk of hemorrhagic complications. *Table III* illustrates that none of the enrolled subjects had CHA_2DS_2-VASc score of 0 and 1. Thirteen (18.8%) had a score of 3 while the majority of the subjects, 53 (76.8%) had a score of more than 3. A user-friendly HAS-BLED scoring was used to assess one year risk for major bleeding. None of the patients included had a score of 0. High risk for bleeding (HAS-BLED score > 3) was noticeable in both groups with a frequency of 46 (66.67%). The patients in both groups had no statistical difference in terms of their distribution.

Clinical Outcomes. Patients with ESRD coupled with atrial fibrillation are at greater risk for stroke however, it remains unclear whether oral anticoagulant therapy

Table II. Antiplatelet therapy and other medication profile of the study population.

Variables	With Anticoagulant (n=10, %)	No Anticoagulant (n= 59, %)	Total (n=69)	p-value (z-test)
Oral Anticoagulant				
Warfarin	6[60%]	0	6	< 0.0001*
NOAC	8[80%]	0	8	< 0.0001*
None	0	59[100%]	59	< 0.0001*
Antiplatelet				
Aspirin	0	4[7%]	4	0.40
Clopidogrel	1[10%]	36[61%]	37	0.002*
Others	1[10%]	7[12%]	8	0.87
None	1[10%]	15[25%]	16	0.28
Medications				
Beta Blockers	7[70%]	45[76%]	52	0.67
Calcium-Channel Blockers	7[70%]	45[76%]	52	0.67
Amiodarone	4[40%]	10[17%]	14	0.09
Digoxin	4[40%]	4[7%]	8	0.002*
ACEI	0	3[5%]	3	0.010*
ARBS	5[50%]	45[76%]	50	0.09
Diuretics	0	0	0	n.a
Statins	8[80%]	24[41%]	32	0.0208*
Anticoagulant during HD				
Regular Heparin	1[10%]	8[14%]	9	0.76
LMWH	9[90%]	51[86%]	60	0.76
Access used				
AVF	9[90%]	45[76%]	54	0.332
AVG	0	1[2%]	1	0.680
Permanent Catheter	1[10%]	7[12%]	8	0.87
IJ Catheter	1[10%]	5[8%]	6	0.8729

Abbreviations: NOAC- non-vitamin K oral anticoagulants; ACEI- Angiotension converting enzyme inhibitor; ARBS- Angiotenson receptor II blockers; LMWH- Low molecular weight Heparin; HD- Hemodialysis.
[a] *two-tailed z-test for two sample means*
[b] *two-tailed z-test for two sample proportions*
[*] *Significant at 0.05 level of significance*

Table III. CHA_2DS_2-VASc and HAS-BLED Score profiles of the study population.

Variables	With Anticoagulant (n=10, %)	No Anticoagulant (n= 59, %)	Total (n=69)	p-value (z-test)
CHA_2DS_2-VASc Score				
0	0	0	0	n.a
1	0	0	0	n.a
2	1[10%]	2[3%]	3	0.34
3	1[10%]	12[20%]	13	0.44
≥4	8[80%]	45[76%]	53	0.79
HAS-BLED Score				
1	0	0	0	n.a
2	1[10%]	8[14%]	9	0.74
3	0	14[24%]	14	0.08
3	9[90%]	37[63%]	46	0.09

[a] *two-tailed z-test for two sample means*
[b] *two-tailed z-test for two sample proportions*
[*] *Significant at 0.05 level of significance*

decreases this risk. *Table IV* compares the outcomes of the two study groups. There were recorded significant differences in ischemic strokes, which was more prevalent in patients on oral anticoagulation (80%, $p < 0.0001$). Likewise, patients differed significantly in terms of the intracranial hemorrhage (30%, $p = 0.0004$) and gastrointestinal bleeding (50%, $p = 0.00001$) which were more noticeable among patients receiving oral anticoagulation therapy. In relation to acute myocardial infarction (40% versus 56%, p = 0.35), peripheral arterial occlusive disease (30% versus 34%, $p = 0.81$)) and calciphylaxis (40% versus 14%, $p = 0.4136$), there were no sufficient evidence to show significant difference between two groups. Of the 69 subjects enrolled in the study, 30 (43%) patients died. Mortality was high in patients on oral anticoagulant but not statistically

Table IV. Comparison of Clinical Outcomes between patients on oral anticoagulation and no anticoagulation among End-stage renal disease patients on maintenance hemodialysis with atrial fibrillation.

Clinical Outcomes	With Anticoagulant (n=10, %)	No anticoagulant (n= 59, %)	Total (n=69)	p-value
Thromboembolic Events				
Ischemic Strokes	8 (80%)	8 (14%)	16	< 0.00001
Acute Myocardial Infarction	4 (40%)	33 (56%)	37	0.3500
Peripheral Arterial Disease	3 (30%)	20 (34%)	23	0.8100
Hemorrhagic Events				
Intracranial Hemorrhage	3 (30%)	1 (2%)	4	0.0004
Gastrointestinal Bleeding	5 (50%)	3 (5%)	8	<.00001
Calciphylaxis	4 (40%)	8 (14%)	12	0.4136
Death	5 (50%)	25 (42%)	30	0.6500

two-tailed z-test for two sample proportions
**Significant at 0.05 level of significance*

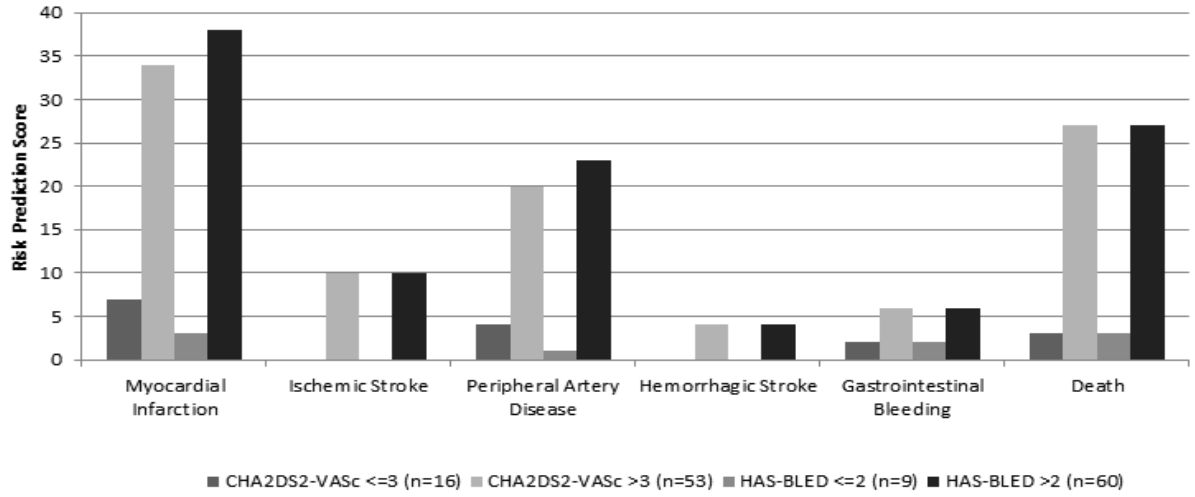

Figure 2. Risk prediction scores for thrombotic and hemorrhagic events of the study population.

significant (50% versus 42%, p = 0.65). Majority of deaths in this study were not due to stroke and were often non-cardiac, as previously observed in other populations of atrial fibrillation patients with and without ESRD.

Figure 2 shows that high CHA_2DS_2-VASc and HAS-BLED scores identify patients at higher thromboembolic and hemorrhagic risk, confirming that these scores, even in subjects with ESRD may provide consistent data.

Discussion

Incidence of Atrial Fibrillation among ESRD Patients. Perpetual Succour Hospital is a tertiary institution in Cebu City that had a total of 188 ESRD patients receiving maintenance hemodialysis since May 2017 with 74 (39.3%) patients documented to have atrial fibrillation which is higher compared to the reported incidence of 3.8% to 27% as accounted by Konigsbrugge et al., on his research article.[10] This large variability in prevalence may be associated with age included in the study and may be from hemodialysis procedure itself, which can lead to changes in electrolytes and in cardiac dimensions, as well as volume resulting in atrial fibrillation development. Thus, the prevalence of atrial fibrillation in dialysis patients may depend upon hemodialysis-specific patient characteristics and treatment modalities.

Risk prediction scores for thrombotic and hemorrhagic events among ESRD patients. Elevated calculated risk predictive thromboembolic (CHA_2DS_2VASc) and hemorrhagic (HAS-BLED) scores were statistically identical in both groups. Most of the variables of the CHA_2DS_2VASc scoring such as hypertension, diabetes, advanced age or congestive heart failure are highly prevalent in dialysis populations, raising the score 2 points or higher in the majority. Equally, these patients carry a significantly increased risk of bleeding due to uremic platelet dysfunction, altered vessel architecture and impaired nitric oxide metabolism and thus, elevated HAS-BLED scores. At least two of the score components,

such as hypertension and advanced age, are highly prevalent in this special population and the third variable, namely CKD, is present by definition.

Clinical Outcomes. This study was designed specifically to determine the difference in the clinical outcomes between oral anticoagulation and no oral anticoagulation therapy among ESRD patients on maintenance hemodialysis with chronic atrial fibrillation. Of the 69 patients included in the study, there were only 10 (14.5%) on oral anticoagulation. This research suggested that oral anticoagulation therapy in patients on hemodialysis with atrial fibrillation significantly increased the risk of ischemic stroke and hemorrhagic events such as intracranial and gastrointestinal bleeding. Few high quality observational studies have attempted to clarify the role of oral anticoagulants in the dialysis population. Wakasugi suggested in a prospective cohort study that warfarin use is not associated with a significant reduction in ischemic stroke events.[9] This was complemented by Genovesi in his observational cohort study that the dialysis population presents both with thromboembolic and bleeding risk.[3] Lastly, McCullough and Keskar corresponded that risks of warfarin use in ESRD outweighs the benefits as it increases risk for bleeding in a population who are inherently vitamin K-deficient from malnutrition, chronic illness and out-of-range INR levels.[4,6]

Key to the high incidence of stroke in patients with ESRD is the coincidence of many of the known risk factors that includes hypertension and diabetes. In the same way, the process of hemodialysis itself contributes to the chronic inflammatory milieu and recent evidence has shown that inflammatory process greatly increases the risk of stroke. Similarly, this vulnerable population uniquely has increased risk for thromboembolism and a paradoxical increased risk of bleeding from chronic inflammatory state. These results highlighted the need to identify effective interventions that go beyond anticoagulation to reduce unlikely events in the ESRD population with atrial fibrillation.

Conclusion

This study suggests that the use of oral anticoagulation did not prevent ischemic strokes in ESRD patients on maintenance hemodialysis with atrial fibrillation and its use was associated with increased risk for intracranial hemorrhage and gastrointestinal bleeding. There was no significant difference in relation to all-cause mortality, acute myocardial infarction, peripheral arterial occlusive disease and calciphylaxis between the two study groups.

Recommendations

In managing a cohort of ESRD patients with atrial fibrillation, one must consider that this susceptible group of individuals are at high risk for both thrombosis and bleeding, and that any administered oral anticoagulant may further predispose them for hemorrhagic events. Prospective studies and randomized trials are greatly needed to provide clinicians additional knowledge concerning how to address hemodialysis patients with atrial fibrillation to prevent thromboembolic events of arrhythmia as well as avoiding hemorrhagic complications related to oral anticoagulation therapy.

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