Stroke in Patients with Atrial Fibrillation.

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Abstract:

Background: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting 0.5% of the adult population, its prevalence increases with age affecting 6% of the population older than 65 years. It is associated with 5- 6 % per year risk of embolic stroke.

Patients & Methods: Between January 2007 and September 2007, 80 patients with stroke and AF were studied for types & risk factor of stroke, causes of AF & whether apirin or warfarin were used properly.

Result: Stroke in AF patients was more common in females (55%) than males (45%) and sixty five percent of the patients were above 65 years, the mean age was 66.4 years. Hypertension (58.7%) and coronary artery disease (27.5%) were the most common causes of AF. 40% of the patients had 3 or more risk factors for stroke. 65% of the patients were at high and very high risk of stroke. Most common types of stroke were: cerebral infarction 83.7% & cerebral hemorrhage 10%.Among patients who were warfarin eligible, 80.7% were not given this medication.

Conclusions: The majority of stroke patients with AF were elderly and more than half were females. Hypertension and coronary artery disease were found in a significant number of them. Warfarin was not used by the majority of the eligible patients.

Key words: Atrial fibrillation, Stroke. Warfarin.

Introduction:

The prevalence of AF is 0.5% in the adults [1], increases markedly with age affecting 6% of the population older than 65years of age, and increases up to 9% at the age of 80-89 years, with the majority (70%) of peoples with AF aged 65-85 years [2].

Because of ineffective mechanical function of the atria during fibrillation, stasis of the blood may occur especially in the atrial appendages and results in thrombus formation and predisposes to stroke and other forms of systemic embolism [3]. Stroke is an important complication of AF that increases its risk six folds and 20-30% of acute stroke are cardioembolic in origin [4].

Stroke is defined as abrupt onset of a neurological deficit that is attributable to a focal vascular cause [5].

Stroke is broadly classified as either ischemic or hemorrhagic. There are two main classifications of ischemic stroke, thrombosis and embolism that account for about 75% of all strokes [6].

In stroke patients with AF, 10.4% have cerebral hemorrhage and 89.6% have infarction while in stroke patients without AF 16.2% have cerebral hemorrhage and 83.8% have infarction [7].

Not all patients with AF have the same risks for stroke and this had led to the idea of risk stratification. It is well established that the antithrombotic therapy confer thromboprophylaxis in patients with AF who are at risk of thromboembolism [8].

Any patient with high or very high risk of stroke should be treated by warfarin [1]. Moderate risk group's patients can be treated by warfarin or aspirin [1]. Ischemic stroke patients with AF are at high risk of stroke recurrence and patients with non valvular AF who have an ischemic stroke have 10-20% risk of another one within the next 1-2 year [9, 10], this can be greatly reduced by long term anticoagulation soon after the presenting event [9].

Several large studies showed that treatment with warfarin (target INR 2-3) reduces the risk of stroke by two thirds but with an annual risk of bleeding of about 1-1.5 % whereas treatment with aspirin reduces the risk of stroke by only one fifth [1]. Warfarin is indicated in patients at a high or a very high risk of stroke [1]. Patients at a moderate risk of stroke may be treated with warfarin or aspirin after discussing the balance of risk and benefit with the patients while patients at a low risk can be treated by aspirin [1]. The risk of stroke in patients with no risk factors is too low for warfarin to be beneficial [11].

Patients &Methods:

This study included 80 stroke patients with AF (36 males & 44 females), the age range was 35-80 years, and mean age was 66.4 years, admitted to the medical department of Sulaimaniya General Hospital between January 2007 to October 2007. The inclusion criteria included all stroke patients with AF admitted during that period.

Clinical diagnosis of stroke was confirmed by CT scan and AF by ECG. The patients were studied for the causes of AF, the risk factors and types of stroke, the prophylactic medications (aspirin or warfarin) which were taken by the patients who were at risk of stroke and the reasons for not using them properly.

The patients were divided into two groups according to their age:

Group 1 (< 65 years) and Group 2 (≥ 65 years).

Regarding the risk stratification the patients were classified into four groups [1] :

1. Very high risk group: included patients with previous stroke or TIA.
2. High risk group: included patients more than 65 years with one other risk factor.
3. Moderate risk group: included patients more than 65 years with no other risk factors or those less than 65 with other risk factors.
4. Low risk group: included patients less than 65 years and no other risk factors.

The risk factors for stroke are [11]:

1. Age more than 75 years
2. Previous stroke or TIA
3. Hypertension (systolic BP >160 mmHg)
4. Diabetes mellitus.
5. Mitral stenosis
6. Heart failure
7. Echo risk features (left ventricular hypertrophy, hypokinesia, akinesia).

The following data were obtained from each patient by direct interview:

1. Age
2. Gender
3. History of cigarette smoking
4. Alcohol intake
5. Family history of Stroke
6. Taking oral contraceptive pills by female patients
7. Medical history (hypertension, heart failure, diabetes mellitus, coronary artery disease, valvular heart disease or hyperthyroidism)
8. Previous history of stroke or TIA
9. Types of the prophylactic medications (aspirin or warfarin) which were taken by the patients before the occurrence of stroke
10. Causes for not taking the medications by the patients which included:

a. Asymptomatic patient (not diagnosed previously).
b. Medications not prescribed by the physicians.
c. Non compliance.
d. Contraindications to medications.
e. Drug interactions.

Physical examination included: assessment of the pulse rate and rhythm, peripheral pulses (normal, diminished, any bruit), blood pressure (normal, high, or low blood pressure), cardiac examination, chest examination, thyroid examination (normal, signs of hyperthyroidism) and neurological examination. The patients were subjected to the following Investigations:

Hemoglobin level, ECG, blood glucose, serum electrolytes, chest x-ray, lipid profile, Echocardiography, CT scan of the head & thyroid function tests (T3, T4 and TSH).

Categorical variables were tested by Chi- square and p values < 0.05 were considered significant.

Results:

Age & gender distribution

The results were obtained from 80 stroke patients with AF. 36 males (45%) and 44 females (55%). The age range was 35 to 80 years, mean age (66.4) years. 52 patients (65 %) were Above 65 while 28 patients (35%) were < 65 years (P value <0.001) so there is significant Difference between the two age groups as in Table1**.**

Causes of AF:

The most common causes of AF in stroke patients were hypertension 47 patients (58.7%) And coronary artery disease (CAD) 22 patients (27.5%). Other causes included mitral valve Disease in 10 patients (12.5%), alcoholism in three patients (3.7 %), hyperthyroidism in 3 Patients (3.7%) and dilated cardiomyopathy in 2 patients (2.5%) as in Table 2.

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Table 1. Age groups of stroke patients with AF

Age group (year)	Male No. (%)	Female No. (%)	Total No. (%)
<65	15 (18.7)	13 (16.3)	28 (35)
≥65	21 (26.3)	31 (38.7)	52 (65)
Total N. (%)	36 (45)	44 (55)	80 (100)

P value < 0.001.

Table 2. Causes of AF in stroke patients

Causes of AF	Male No. (%)	Female No. (%)	Total No. (%)
Hypertension	23 (28.7)	24 (30)	47 (58.7)
CAD*	10 (12.5)	12 (15)	22 (27.5)
MVD**	2 (2.5)	8 (10)	10 (12.5)
Hyperthyroidism	1(1.2)	2 (2.5)	3 (3.7)
Alcoholism	3 (3.7)	0 (0)	3 (3.7)
DCMP***	1(1.25)	1 (1.25)	2 (2.5)
Idiopathic	5 (6.3)	8 (10)	13 (16.3)

***CAD: Coronary artery disease.**
****MVD: Mitral valve disease.**
*****DCMP: Dilated cardiomyopathy.**

Risk factors for stroke

The majority of the patients had more than one risk factors for stroke which included:

Fifty two patients, 65%, (age ≥ 65 years), 47 patients, 58.7%, (hypertension), 22 patients, twenty seven point five percent (heart failure), 21 patients, 26.2%, (diabetes mellitus), 10 patients, 12.5%, mitral valve disease and 25 patients, 31.3%, echocardiographic risk features as in **Table 3.**

Twenty two patients (27.5%) had previous stroke or TIA. 32 patients (40%) had three or more risk factors, 23 patients (28.7%) had two, 18 patients (22.5%) had only one while 7 patients (8.7%) had no risk factor as in **Table 4.**

Table 3. Risk factors for stroke in AF patients

Risk factors	Male No. (%)	Female No. (%)	Total No. (%)
Age > 65	21 (26.3)	31 (38.7)	52 (65)
Hypertension	23 (28.7)	24 (30)	47 (58.7)
Heart failure	8 (10)	14 (17.5)	22 (27.5)
Diabetes mellitus	8 (10)	13 (16.3)	21 (26.3)
Dyslipidemia	6 (7.5)	7 (8.7)	13 (16.2)
MVD*	2 (2.5)	8 (10)	10 (12.5)
Previous stroke	8 (10)	14 (17.5)	22 (27.5)
Echo. risk features	10 (12.5)	15 (18.7)	25 (31.2)

*MVD: Mitral valve disease.

Table 4. Distribution of patients according to No. of risk factors

No. of risk factors	Male No. (%)	Female No. (%)	Total No. (%)
3 and more	13 (16.3)	19 (23.7)	32 (40)
2	9 (11.3)	14 (17.5)	23 (28.7)
1	11 (13.7)	7 (8.8)	18 (22.5)
0	3 (3.7)	4 (5)	7 (8.8)
Total No. (%)	36 (45)	44 (55)	80 (100)

Risk stratification

Twenty two patients (27.5%) were considered to be a very high risk group because they had previous stroke or TIA, 30 patients (37.5%) high risk group because they were older than 65years and had one other risk factor, 21 patients (26.2%) moderate risk group, they were older than 65 years with no other risk factor or less than 65 years with risk factors & 7patients (8.75%) low risk group because the age was less than 65 years & had no risk factors as in **Figure 1.**

Types of stroke

Stroke was complete in 72 patients (91.7% of the males and 88.7% of the females), evolving in 5 patients (5.6 % of the males & 6.8% of the females), while 3 patients had TIA (2.7% of the males and 4.5% of the females). Statistically there is no significant difference between males and females in terms of types of stroke (Chi x2 = 0.2, P Value=0.9). **Figure 2**

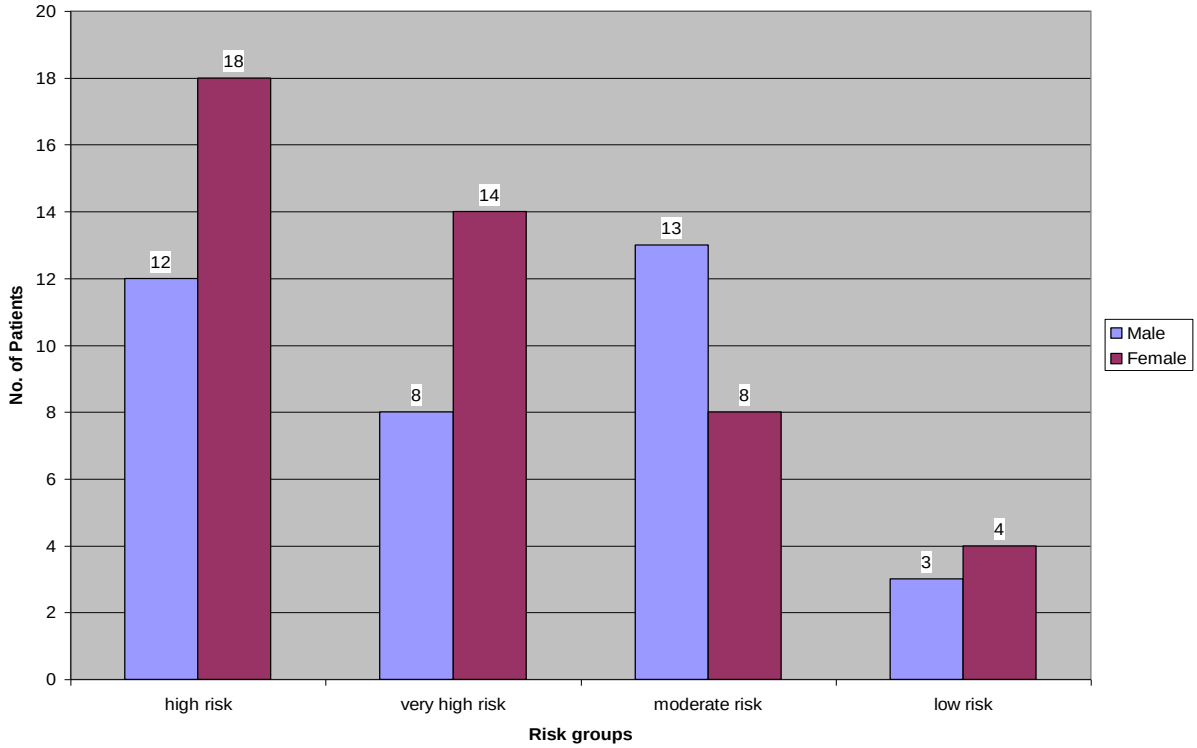

Figure 1. Classification of patients according to the risk groups

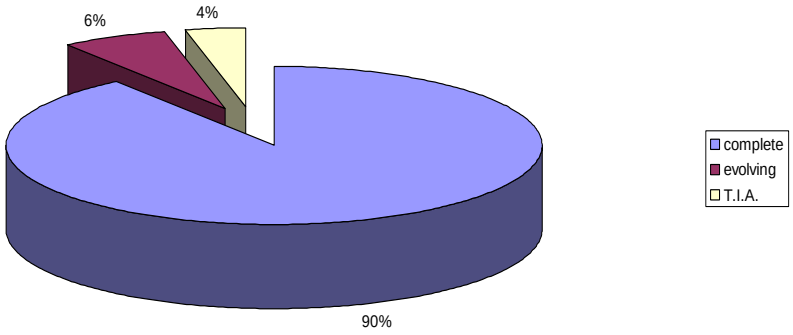

Figure 2 .Types of stroke in AF patients

Results of brain CT scan

The results were: Cerebral infarction in 67 patients (83.7%), cerebral hemorrhage in 8 patients (10%), cerebral infarction with hemorrhagic conversion in 1 patient (1.25%) & normal CT in four patients (5%) as in **Figure 3.**

Prophylactic Medications of AF Patients with Stroke:

Only 35 patients (43.7%) used anticoagulants or antiplatelets before the occurrence of stroke while 45 patients (56.3 %) did not use them, those patients who were using antiplatelets or anticoagulants, 21 patients (60%) used the drugs regularly and 14 patients (40%) used them irregularly. Aspirin was taken by 23 patients (28.7%) and warfarin by 12 patients (15%). In very high risk group patients (22 patients, 27.5%), only 16 patients (72.7%) used medications (aspirin 9and warfarin 7 patients) while 6 patients (27.3%) did not take medications.

In high risk group patients (30 patients, 37.5%), 11 patients (36.7%) used medications (aspirin 8 and warfarin 3 patients) while 19 patients (63.3%) had no medications previously. In moderate risk group patients (21 patient, 26.2%) 7 patients (33.3%) used medications (aspirin 5 and warfarin 2 patients) and 14 patients (66.7%) had no medications as in **Table 5.**

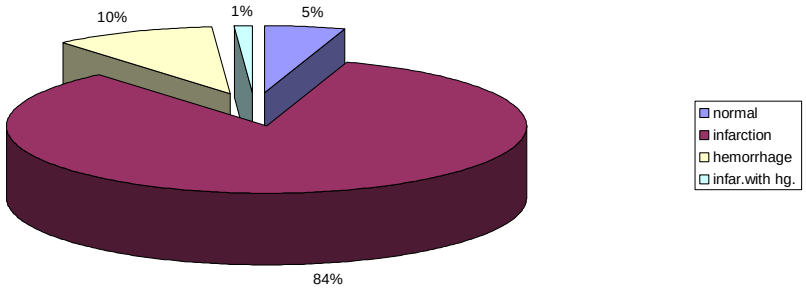

Figure 3. Results of CT scan in stroke patients with AF.

Table 5. Medications intake according to risk groups

Risk groups	No. of patients (%)	Patients using medications Aspirin No. (%)	Warfarin No. (%)	Total No. (%)	Not using medications No. (%)
Very high	22 (27.5*)	9 (40.9**)	7 (31.8)	16 (72.7)	6 (27.3)
High	30 (37.5)	8 (26.7)	3 (10)	11(36.7)	19 (63.3)
Moderate	21 (26.2)	5 (23.8)	2 (9.5)	7 (33.3)	14 (66.7)
Low	7 (8.8)	1 (14.3)	0 (0)	1 (14.3)	6 (85.7)
Total	80 (100)	23 (28.7*)	12 (15)	35 (43.7)	45 (56.3)

*Percentage from total number of patients (80).
** Percentage from the number of patients in the risk group.

Causes of not Using Prophylactic Medications:

Among 45 patients (56.3%) with risk factors for stroke who were not using aspirin or warfarin previously, 18 patients (40%) were asymptomatic (not diagnosed previously).

In 14 patients 31.1% medications were not prescribed by the physicians, 8 patients (17.8%) had bad compliance with medications, 3 patients (6.7%) had contraindications (recent GIT) bleeding, chronic liver disease and uncontrolled HT) and 2 patients (4.4%) had drug interactions with aspirin or warfarin (cimetidine and NSAID) as in **Figure 4.**

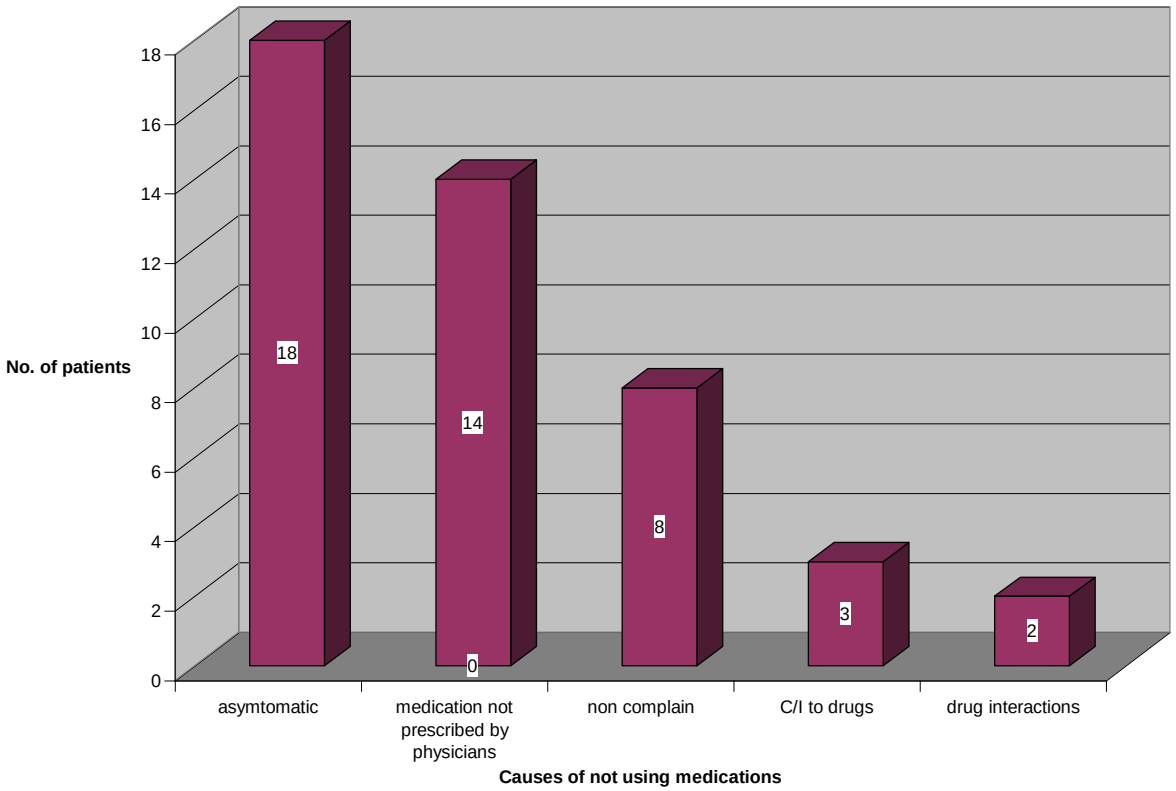

Figure 4. Causes of not using medications

Discussion:

Age and gender distribution:

This study of stroke patients with AF showed that females (55%) were more affected than males (45%). Most of the patients (65%) were more than 65 years old. These finding are consistent with other studies as that of Steger et al [12], Marini et al [2], Benjamin et al [13], Candelise et al [7] and McCormic et al [14].These results can be explained by the fact that elderly patients with AF had three or more risk factors for stroke so they were more liable to be affected, also the propensity of elderly for stroke may be related to a higher prevalence of comorbid conditions and to dual factors of age and chronicity [15].

Risk factors for stroke:

Because (65%) of our patients were old age and had other co-morbidities so most of them had one or more risk factors for stroke (previous stroke, age >65, hypertension, heart failure, diabetes mellitus, mitral valve disease, and echocardiographic risk features). 40% had 3 or more risk factors for stroke, 28.7% had two risk factors and 22.5% had one risk factor, these findings were in accordance with that of Steger et

al [12], who found that AF patients had more often 3 or more risk factors for stroke.

Risk stratification

In this study, most of the patients were at high and very high risk for stroke and the number of patients in the very high risk group was less than that of patients in high risk group, probably because of increased mortality after the first stroke. These findings were different from those of Brass et al [16], who found that most of stroke patients with AF were at moderate to high risk for stroke. Further studies are needed to see the exact difference.

Results of CT scan of the brain

High percentage of cerebral infarction (83%) was found in this study because AF is the most common cause of cerebral embolism [17], as stasis of blood in the atria result in thrombus formation and predispose to stroke. (3.7%) had normal CT scan because some of the patients had TIA and possibly the CT scan of some of patients was done early and needed to be repeated later. Eight patients (10%) had cerebral hemorrhage, one of them was on warfarin before the occurrence of stroke and the others were very old and possibly they had other causes of

cerebral hemorrhage like hypertension, these results were in accordance with that of Candelise et al. who found that 10.4% of AF patients with stroke had cerebral hemorrhage [7]. While Steger et al. found that 8% of AF patients with stroke had cerebral hemorrhage and eighty eight percent had ischemic infarction [12].

The use of warfarin or aspirin in AF Patients with Stroke:

Although the majority of the patients in this study were eligible for anticoagulants or antiplatelets, only 43.7% took these medications before the occurrence of stroke and 56.3% had no medications. Aspirin was taken by 28.7% and warfarin by 15% of the patients, these results were in contrast to that of Connolly J. [11] who showed that 25-50% of patients with AF with or without risk factors for stroke are actually given warfarin and Scott et al. [18] who found that 40% of AF patients with stroke used warfarin alone, 28% used aspirin, 5% used both and 27% had no medications. In very high and high risk group patients (65%) who were eligible for warfarin, only 19.3% were on warfarin before the stroke occurrence, 32.7% were on aspirin and 48% had no medications, this means that 80.7% of patients who were warfarin eligible were actually not using it. This is because a significant number of these patients used aspirin because of the underlying CAD (27.5%) and probably warfarin was not prescribed by the physicians, because of difficulty in patient's follow up and the related investigation (INR) was not available regularly. These results were some what different from that of Somerfield et al [10], who showed that in very high risk group patients 24% were taking warfarin, 58% were taking aspirin and 18% had no antithrombotic therapy.

Causes of non use of Medications:

Somerfield et al [10] found that the most common reasons for not commencing warfarin in AF patients with stroke were severe disability and frailty (32%), high risk of falls (30%) and limited life expectancy (10%), other causes included GIT bleeding (8%), risk of intracerebral hemorrhage (5%) and previous adverse events on warfarin (2%), while in this study the most common causes for not using medications by AF patients as a secondary stroke prevention were the following:

1. Asymptomatic patients (40%)
2. Medications were not prescribed by the physicians (31.1%)
3. Non compliance (17.8%)
4. Contraindications to medications (recent GIT bleeding, chronic liver disease and uncontrolled HT) (6.7%)
5. Drug interactions (cimetidine and NSAID) (4.4%)

Conclusions:

Sixty five percent of Stroke patients with AF were above 65 years, 65% were at high or very

High risk of stroke. Females (55%) were more affected than males (45%). Hypertension

(58.7%) and coronary artery disease (27.5%) were the most common causes of AF.

Cerebral infarction (83.7%) was the most common type of stroke and warfarin was not used

In (80.7%) of the eligible patients.

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