Evaluation of Oral Anticoagulant Use in Atrial Fibrillation Patients

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Abstract Oral anticoagulant (OAC) is used for thromboembolic prevention in atrial fibrillation (AF) patients. This study aim to observe the use of OAC in AF patients in a tertiary Hospital. We enrolled all patients with complete data of medical record. The data of the use of OAC in AF patients is taken from patients that was hospitalized in Cardiology ward during January 2015-August 2016. Patients were given OAC during hospitalization. Sixty three patients with atrial fibrillation were analysed in this study. Incidence of valvular disease was higher than non-valvular atrial fibrillation (65% vs 35% patients). Most of the patients was women (67.4%). Warfarin as oral anticoagulant for thromboembolic prevention was still more popular than dabigatran (61.8% vs 34.2%). Almost of patients had low HAS-BLED score. The intrahospital bleeding occured in 6% of all patients given warfarin. Warfarin is still used as a mainstay therapy in AF patients for thromboembolic prevention. Bleeding rate due to warfarin use for hospitalized patients was rare.

Keywords: anticoagulants, bleeding, warfarin

1. Introduction

Atrial fibrillation (AF) is the most common cardiac rhythm disorder worldwide [1]. Prevalence AF at Harapan Kita Hospital, Indonesia in 2009 was 9.8% [2]. Fifteen percent of AF patients will be had stroke[2-4]. In patients with AF at higher risk for thromboembolism, the use of oral anticoagulant such as warfarin (a vitamin K antagonist) or the newer anticoagulants could reduce morbidity and mortality [1]. In the other side, oral anticoagulant use carries a risk of bleeding, especially vitamin K antagonist [1]. Warfarin is the most common OAC that prescribed for AF patients [2,4]. New oral anticoagulant (NOAC) especially dabigatran is more frequently use for non-valvular AF but it is not coveraged by National Health Insurance for atrial fibrillation. Due to controversial use of NOAC in thromboembolism prevention, we need to evaluate the benefit and risk of oral anticoagulant in atrial fibrillation.

2. Methods

This study was a retrospective study from medical record of AF patients. All patients admitted to cardiology ward/intensive cardiovascular care unit (ICCU) with atrial fibrillation as primer or secondary diagnosis. Admission date of patients should be on January 2015 until August 2016. Inclusion criteria were patients above 18 years old), receiving OACs in hospital either warfarin or dabigatran. Exclusion criteria were uncompleted medical record. Sixty-seven patients were included in the study. CHA_2DS_2 Vasc and HAS-BLED score of all patients were calculated at pre-admission.

The use of anticoagulant for non-valvular AF should consider stroke and bleeding risk [5]. Recent guidelines for non-valvular AF (NVAF) recommend the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age [>75 years], diabetes, stroke/transient ischemic attack, vascular disease, age [65–74 years], sex category [female]) for stroke risk stratification [6,7]. HAS-BLED score (hypertension, abnormal renal or liver function, stroke history, bleeding history, labile international normalized ratio, age >65 years, drugs, or alcohol) was recommended for bleeding risk stratification [6].

Patients with CHA_2DS_2 Vasc score $\geq$ 2 had higher stroke risk and recommend anticoagulant. If CHA_2DS_2 Vasc score = 1 may use antithrombotic therapy with oral anticoagulant or antiplatelet. If CHA_2DS_2 Vasc score = 0, antithrombotic therapy was not recommended. HAS-BLED score $\geq$ 3 should be monitored regularly because high risk of bleeding [6].

This study described the use of oral anticoagulant for stroke prevention in patients with AF, including warfarin and dabigatran. Among patients treated with anticoagulant therapy, we also examined whether these patients were treated with an antiplatelet agent. Treatment with an antiplatelet agent was defined as prescription of aspirin and clopidogrel.

Statistic analysis

Baseline characteristic data were analysed as with SPSS version 17.0. Normally distributed continuous variables are expressed as means and standard deviations, whereas categorical variables are expressed as proportions.

Ethical consideration

This study was approved for ethical clearance from Ethical Committee of Faculty of Medicine, Andalas University.

3. Results

A total of 62 patients were included in the study. Baseline characteristics among patients are shown in Table 1. Female patients outnumbered males (44 vs. 23). Fifty-six percent patients were 40-64 years old. Body Mass Index (BMI) mean was 22.3 $\pm$ 3 kg/m2. More than half AF patients was non-valvular. Heart failure and hypertension were the common AF risk factors in our patients. Sixty-one percent of patients (41 of 67) received warfarin.

Table 1. Baseline characteristics of atrial fibrillation patients

Characteristics	Total (n=67)	Percentage (%)
Sex		
Male	23/67	34.3
Female	44/67	65.7
Age (years)	53.5+13.4	
< 40	13/67	19.4
40-64	38/67	56.7
≥ 65	16/67	23.9
Valvular disease		
Yes	22/67	32.8
No	45/67	67.2
Comorbidities		
Chronic Heart Failure	34/67	50.7
Hypertension	30/67	44.8
Diabetes Mellitus	3/67	4.5
Dyslipidemia	5/67	7.5
Smoker	12/67	17.9
Body Mass Index*	22.3 ± 3	
Underweight	5/67	7.5
Normal	38/67	56.7
Overweight	17/67	25.4
Obese I	5/67	7.5
Obese II	2/67	3.0
Anticoagulant		
Warfarin	41	61.2
Dabigatran	26	38.8

*BMI classification for ASIANs from WHO

HAS-BLED score of patients were varied. Half of patients with warfarin therapy had HAS-BLED score = 0 or no bleeding risk. Bleeding risk of patient was low-moderate. Figure 1 shows 3/4 patients with high bleeding risk (HAS-BLED ≥ 3) still received warfarin. Bleeding occur only in one patient.
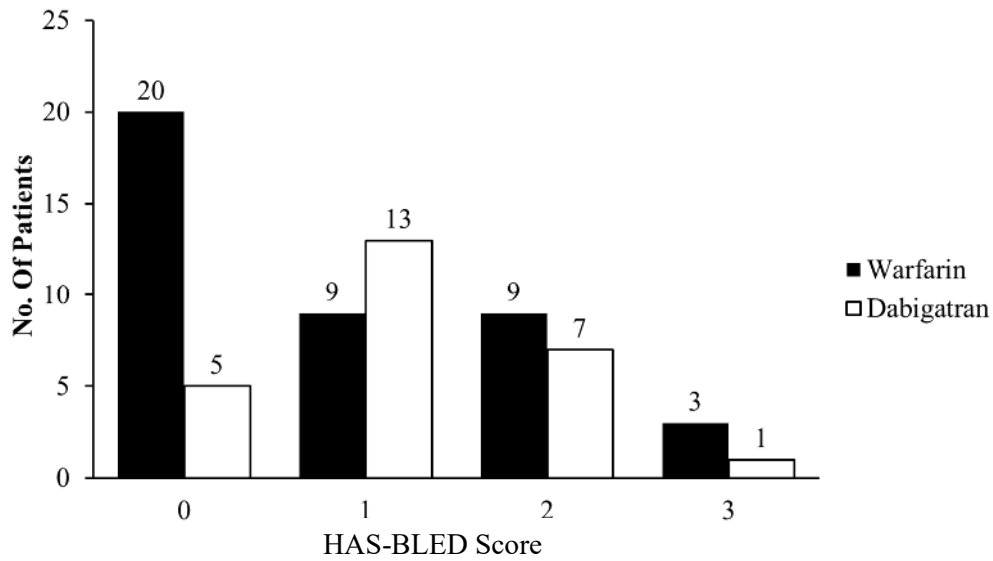
Figure 1. HAS-BLED score between warfarin and dabigatran group

Intrahospital bleeding occured only 4 of 67 patients. All of these patients received warfarin. Hypertension and older age increased bleeding risk in warfarin and dabigatran group (Table 2). Among 4 patients with intrahospital bleeding, 2 patients used concomitant low dose aspirin (Table 3). Bleeding still occur although the international normalised ratio (INR) was in target range for prevention thromboembolism.

Table 2. Bleeding risk between warfarin and dabigatran group

	Warfarin group (n=41)	Dabigatran group (n=23)
Intrahospital bleeding event	4	0
HAS-BLED score		
Hypertension	11	15
Abnormal liver/renal	5	2
function	3	0
Stroke history	3	2
Bleeding history	0	0
Labile INR	6	10
Age > 65	6	2
Drug / alcohol		

Table 3. Clinical condition of patients with intrahospital bleeding

Patient	Sex	Age	INR	HAS-BLED score	Abnormal renal / liver function	Warfarin dose	Concomitant drug
1	Female	52	2.5	0	No	4 mg	No
2	e	82	0.97	3	Yes	5 mg	Aspirin low dose
3	Male	46	2.52	1	No	5 mg	Aspirin low dose
4	Male Female e	36	1.49	2	No	2.5 mg	No

From subgroup analysis of non-valvular AF, 40% patients had high risk of stroke (CHA_2DS_2 Vasc score ≥ 2) (Figure 2). About 5/45 patients with low stroke risk and do not need anticoagulant.
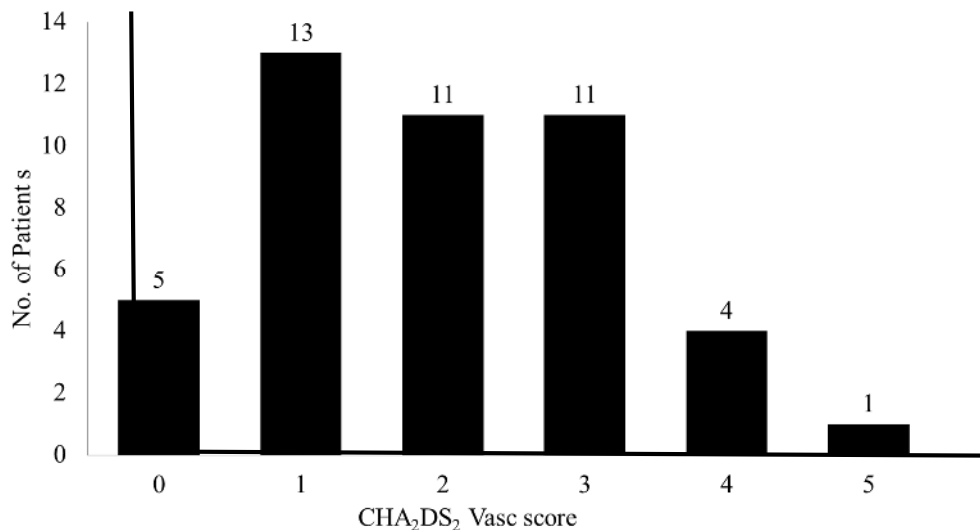
Figure 2. CHA_2DS_2 Vasc score distribution among non-valvular AF (n=45)

4.   Discussion

This study found that female AF patient was higher than male. Its differ from Worldwide Epidemiology of Atrial Fibrillation and developing nations epidemiology which male outnumbered female[8,9]. The proportion of valvular and non-valvular AF showed that non-valvular AF was more common than valvular. Martinez et al also found the increasing incidence of non-valvular AF in UK in a decade.

The common risk factors for AF were advancing age, male sex, diabetes mellitus, hypertension, valvular disease, myocardial infarction, heart failure, obesity, elevated inflammatory marker concentrations, and PR-interval prolongation, as recently reviewed elsewhere [10]. From Farmingham Study, independent risk factors for AF were men gender,

diabetes, hypertension, congestive heart failure, and valve disease [11]. Hypertension, valvular disease, and heart failure are the main risk factors for AF in our patients.

Al-Turaiki et al. revealed that most of the patients were at moderate (63.3%) to high (27.7%) risk of bleeding [12]. In this study, bleeding risk of patients was low-moderate. Risk of intrahospital bleeding in warfarin group was higher than dabigatran. Bleeding risk may increase by concomitant use of antiplatelet drugs, advancing age, and abnormal renal/liver function, eventhough the INR at first admission was below 3.0. Sarawate et al. report first INR on admission (INR >3.0) was associated with intrahospital bleeding (OR-adjusted [95%CI], 1.72 [1.02–2.90]) [13].

The CHA_2DS_2- VASc score was calculated for non-valvular AF patients. The CHA_2DS_2- VASc score includes categories of 0 = low risk, 1 = intermediate risk, and ≥ 2 as high risk. About 40% non-valvular AF patients were high risk for stroke. Al-Turaiki et al found that 92% patients were high risk for stroke [12]. In this study, 40 % patient high risk for stroke.

Many risk factors associated with the risk of bleeding in warfarin therapy such as older age [14]. One of patient (52 y.o) in warfarin therapy, with HAS-BLED score 0, still get bleeding. The annual rate of extracranial bleeding of warfarin therapy for patients under 60 years old is 0.28 [15].

5.   Conclusions

Non-valvular atrial fibrillation is higher than valvular. Intrahospital bleeding occur in warfarin group, even the risk of bleeding in this patients is low. There are multifactorial risk factor for bleeding in patient who received warfarin, such as age, renal dysfunction, the use of aspirin low dose, warfarin dose and INR level. The use of warfarin as oral anticoagulant for non-valvular patient still recommended, but the therapeutic level plasma of warfarin should be monitored.

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