The Efficacy of 3-mg Warfarin Initiating Dose in Adult Thai Patients, Who Required Long-Term Anticoagulant Therapy

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Background: *Warfarin anticoagulation is the standard treatment for patients with thromboembolic diseases. Prior studies recommended commencing warfarin with the initial doses between 5 mg and 10 mg for the first 1 or 2 days. However, lower warfarin loading dose is advised for the elderly and patients with co-morbid diseases. Moreover, warfarin requirement is also affected by several genetic factors, which differ among various ethnic populations. Currently, the optimal initiating dose of warfarin in Thai patients is unknown. However, based on the observation of the clinical practice at Siriraj hospital, a lower starting dose (3 mg/day) of warfarin was commonly given to patients who required long-term anticoagulant therapy.*
Objective: *To investigate the efficacy and safety of 3-mg warfarin initiating dose.*
Material and Method*: A retrospective study of inpatients who received warfarin 3 mg/day for the first two days of oral anticoagulation therapy with the target INR of 2.0-3.0 at Siriraj hospital from January 2004-December 2007 was performed. The efficacy of 3-mg warfarin loading dose was determined by assessing the proportion of patients who achieved the target INR of 2.0-3.0 between day 3 and day 5 of warfarin treatment.*
Results: *Total of 164 patients was included in the study. Eighty-six patients (52.4%) were males. The mean age was 55.1 $\pm$ 16.8 years (range 16-88 years). The mean body weight and serum albumin were 61.5 $\pm$ 12.2 kg and 3.7 $\pm$ 0.7 g/dl, respectively. Prosthetic heart valve replacement was the most common indication for warfarin anticoagulation therapy (36%), followed by deep vein thrombosis (32.3%). The mean cumulative weekly dose of warfarin was 22.3 $\pm$ 5.8 mg. The median time to therapeutic INR (2.0-3.0) was 6 days. Forty-seven patients (29%) achieved therapeutic INR between day 3 and day 5 of warfarin treatment. Time to therapeutic INR was not affected by age, gender, body weight, serum albumin, or concomitant medication use. Interestingly, patients who received warfarin due to prosthetic heart valve replacement were more likely to achieve therapeutic INR between day 3 and day 5 when compared to those with other indications with adjusted OR 16.25 (95% CI 5.13-51.44, $p < 0.001$). Bleeding complication was rare (0.6%) and was not associated with excessive anticoagulation.*
Conclusion: *3-mg warfarin initiating dose appeared to be safe in adult Thai patients. However, the efficacy of 3-mg starting dose as determined by the proportion of patients who achieved the target INR between day 3 and day 5 of warfarin treatment was relatively less efficient when compared with that previously reported with a 5-mg loading dose. Further randomized, prospective study is required to examine the efficacy of 3-mg versus higher warfarin starting dose in Thai patients.*

Keywords: *Warfarin initiating dose, Warfarin loading dose, Efficacy, Time to therapeutic INR*

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Oral anticoagulation with vitamin K antagonist is the standard treatment indicated in patients who develop thromboembolic diseases and in patients who are at high risk for systemic thromboembolic complications. The common indications included mechanical heart valve replacement, atrial fibrillation and deep vein thrombosis. Among the currently available vitamin K antagonists (VKAs), warfarin is the most frequently prescribed VKAs worldwide. In general, warfarin is initiated with a loading dose for one to two days, then the subsequent doses are adjusted according to the international normalized ratio

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(INR). With the proper starting dose, the time required to achieve the target INR could be curtailed and the bleeding risk from excessive anticoagulation could be minimized. Prior studies have demonstrated the efficacy and safety of 5-mg and 10-mg warfarin loading dose for the first two days during the initiation of oral anticoagulant therapy[1-3]. Currently, the American College of Chest Physicians (ACCP) recommends initiating warfarin with doses between 5 mg and 10 mg for the first 1 or 2 days. Nonetheless, a lower warfarin starting dose is advised for patients with various co-morbid conditions, who may have increased warfarin sensitivity, for example, in the elderly or malnourished patients, in patients who have congestive heart failure or liver disease and in patients who are taking medication known to interfere with warfarin metabolism[4].

In addition, warfarin dose requirement is also modified by the individual's genetic factors, particularly the cytochrome P4502C9 (CYP2C9) and the vitamin K epoxide reductase complex subunit 1 (VKORC1) polymorphisms, which have been shown to significantly affect warfarin metabolism, as well as warfarin sensitivity and probably explain the difference in warfarin dose requirement among diverse ethnic populations[4-7]. Earlier investigations have demonstrated that the Asians require a considerably lower warfarin maintenance dose, comparing with the Caucasians[8-10]. Thus, it is conceivable that the appropriate warfarin loading dose in the Asians may be different from that required by the western population. Currently, the optimal initiating dose suitable for the Asian residents has not been established. Based on the observation of our hospital's clinical practice, we found that most patients who required long-term anticoagulant therapy received a lower warfarin starting dose (3 mg/day) than that recommended by the ACCP. As a result, we conducted a retrospective study to investigate the efficacy and safety of 3-mg warfarin loading dose in Thai patients.

Material and Method

Medical records of patients receiving warfarin anticoagulation during the hospitalization at Siriraj hospital from January 2004 to December 2007 were reviewed. All patients who received warfarin 3 mg/day for the first two days of oral anticoagulant therapy with the target INR of 2.0-3.0 were included in the study. Patients were excluded if they were younger than age of 15, if there was no baseline INR performed prior to the initiation of warfarin, if the baseline INR was greater than 1.5 or if there was no INR result between day 3 and day 5 of warfarin therapy (the first day of warfarin treatment was designated as day 1). The efficacy of 3-mg warfarin loading dose was determined by assessing the proportion of patients who achieved the target INR of 2.0-3.0 between day 3 and day 5. Time to therapeutic INR was defined as the duration in days since the initiation of the first dose of warfarin, which the patients required to attain the target INR (2.0-3.0). The study was approved by the institution review board.

Statistical analysis

Subject characteristics were described using descriptive statistics, including means, standard deviation, median, minimum and maximum, frequencies and percentage. The normality of the distribution of the variables was examined with the Kolmogorov-Smirnov or the Shapiro-wilk test. For continuous variables, Student t-test and Mann-Whitney U test were used as appropriate. For dichotomous variables, Chi-square and Fisher exact test were used as appropriate. Logistic regression analysis was applied to explore factors associated with the achievement of the therapeutic INR. Variables, which were found to be significant in univariate analysis, were further entered into a multivariate model. For all tests performed, a two-tailed p-value < 0.05 was considered as statistical significance. The statistical software SPSS, version 13.0 was used for all the analyses performed.

Results

One hundred sixty-four patients met the inclusion criteria and were included in the study. Eighty-six patients (52.4%) were males. The mean age was 55.1 ± 16.8 years. The mean body weight and serum albumin were 61.5 ± 12.2 kg and 3.7 ± 0.7 g/dl, respectively. Seventeen patients (10.4%) had serum albumin less than 3 g/dl. The indications for warfarin anticoagulant therapy were prosthetic heart valve replacement in 59 patients (36%), deep vein thrombosis in 53 patients (32.3%), arterial thrombosis in 28 patients (17.1%), atrial fibrillation in 22 patients (13.4%) and ischemic stroke in 2 patients (1.2%). Among the enrolled patients, four (2.4%) had liver diseases, twenty-eight (17.1%) had congestive heart failure, eleven (6.7%) had malignancy and nine (5.5%) had prior history of bleeding. Regarding the concomitant heparin treatment, 50 patients (30.5%) received unfractionated heparin and 42 patients (25.6%) received low-molecular-weight heparin. The median duration of heparin therapy was 5 days. The mean cumulative weekly dose of warfarin was 22.3 ± 5.8 mg.

The median time to therapeutic INR was 6 days. There were fifty-seven patients (34.8%) who received at least one concomitant medication that may potentiate warfarin effect, including amiodarone (4.9%), metronidazole (0.6%), omeprazole (27.4%) and propanolol (9.1%). Eleven of these patients received two concurrent medications and one patient received three concurrent medications with warfarin (Table 1).

Forty-seven patients (29%) achieved the target INR of 2.0-3.0 between day 3 and day 5 of the warfarin therapy. However, the frequency of the INR checking of each patient was varied, depending on the attending physicians' discretion (Table 2). Moreover, some patients reached the target INR more than once between day 3 and day 5 of the treatment. For those patients, the first day that the target range attained was recorded as the time to therapeutic INR and the number of patients who accomplished the therapeutic INR was calculated accordingly. The proportion of patients achieving the therapeutic INR between day 3 and day 5 of warfarin treatment was shown in Table 2.

Age, gender, body weight, serum albumin, underlying disease, or concomitant medication use was not associated with time to therapeutic INR (Table 1 and 3). Interestingly, patients who received warfarin therapy due to prosthetic heart valve replacement were more likely to achieve therapeutic INR between day 3 and day 5 when compared to those with other indications with adjusted OR 16.25 (95% CI 5.13-51.44, $p < 0.001$) (Table 3). In addition, patients who achieved the target INR between day 3 and day 5 of warfarin treatment had INR checked more frequently with the mean number of INR tests of 2.7 ± 0.6, comparing with 1.7 ± 0.8 in those who did not accomplish therapeutic range between day 3 and day 5 of the treatment ($p < 0.001$). Lastly, the mean cumulative weekly dose of warfarin in patients who achieved the target INR was significantly lower than that of the patients who did not achieve the target range. (18.1 ± 4.6 mg vs. 24 ± 5.4 mg, $p < 0.001$)

Bleeding complication was rare. Only one patient developed lower gastrointestinal bleeding, which occurred on day 7 of warfarin therapy. At the time, the INR was 2.25. The colonoscopic findings revealed multiple colonic ulcers, which were suspected to be the principal cause of bleeding.

Discussion

In general, the initiation of oral anticoagulation usually begins with the concomitant use of warfarin and unfractionated or low-molecular-weight heparin until achieving the therapeutic INR, then heparin is discontinued. Previous studies demonstrated the efficacy of 5-mg and 10-mg warfarin loading dose for the first two days of the initiation of warfarin treatment in patients whose target INR was 2.0-3.0[1,3]. The usefulness of the lower warfarin loading dose (5-mg) was shown in the randomized, controlled study conducted by Crowther M et al, which enrolled 53 patients who required long-term anticoagulant therapy with warfarin. In this study, patients were randomized to receive a warfarin loading dose of 5-mg or 10-mg for the first two consecutive days. The primary end point was the proportion of patients who achieved the target INR (2.0-3.0) on day 3-4 or day 4-5 of the treatment. Intriguingly, those who received lower warfarin loading dose (5-mg) reached the primary end point in a larger proportion than those who received the higher warfarin loading dose (10-mg) (66% vs. 24%, $p < 0.003$)[1]. On the contrary, Kovacs MJ et al demonstrated the superior efficacy of 10-mg warfarin initiating dose in another randomized, controlled study, which included 201 patients diagnosed with deep vein thrombosis receiving 10-mg or 5-mg warfarin loading dose on two successive days in an outpatient setting. The primary outcome was the time required to accomplish the therapeutic INR (> 1.9). Comparing with the patients who received 5-mg warfarin loading dose, those in the 10-mg group attained the target INRs 1.4 days earlier than those in the 5-mg group (4.2 day vs. 5.6 days $p < 0.001$)[3]. Hence, warfarin starting dose between 5- and 10- mg per day given on the first 1 or 2 days of warfarin treatment is uniformly accepted in current medical practice and is recommended by the ACCP to be used as the initiating dose for most individuals who require long-term anticoagulant therapy with subsequent dose adjustment based on the INR results[4].

Nonetheless, several factors influencing the warfarin metabolism and response to warfarin, including patient's co-morbid conditions, concurrent medication use and hereditary factors, for instance the CYP2C9 and VKORC1 polymorphisms, also play a pivotal role in individual's warfarin dose requirement. As previously reported, the maintenance dose of warfarin required by patients from Asian ethinicity is generally lower than that required by other ethnic origins[10]. Thus, it is plausible that there might be the parallel effect on the initial dose requirement in the Asian population as well. In addition, the results from prior warfarin loading dose studies performed in the western population may not be entirely applicable to Thai patients and such recommendations should be

Table 1. Characteristics of patients enrolled in the study and patients who achieved the target INR of 2.0-3.0 between day 3 and day 5 of warfarin treatment.

	Total n = 164	Patients who achieved the target INR n = 47	Patients who did not achieve the target INR n = 117	p-value
Male (%)	86 (52.4)	27 (57.4)	59 (50.4)	0.52
Mean age, years (± SD)	55.1 (± 16.8)	53.8 (± 14.6)	55.6 (± 17.6)	0.50
Mean body weight, kg (± SD)	61.5 (± 12.2)	59.8 (± 12.0)	62.2 (± 12.2)	0.32
Mean serum albumin, g/dl (± SD)	3.7 (± 0.7)	3.9 (±0.6)	3.7 (± 0.7)	0.07#
Underlying disease				
Liver disease (%)	4 (2.4)	0 (0)	4 (3.4)	0.58##
Congestive heart failure (%)	28 (17.1)	11 (23.4)	17 (14.5)	0.26
Malignancy (%)	11 (6.7)	4 (8.5)	7 (6.0)	0.51##
Prior history of bleeding (%)	9 (5.5)	1 (2.1)	8 (6.8)	0.45##
Indication for oral anticoagulation therapy				
Prosthetic heart valve replacement (%)	59 (36.0)	31 (66.0)	28 (23.9)	< 0.001*
Deep vein thrombosis (%)	53 (32.3)	6 (12.8)	47 (40.2)	0.001*
Arterial thrombosis (%)	28 (17.1)	8 (17.0)	20 (17.1)	> 0.99
Atrial fibrillation (%)	22 (13.4)	2 (4.3)	20 (17.1)	0.05
Ischemic stroke (%)	2 (1.2)	0 (0)	2 (1.7)	> 0.99##
Heparin treatment				
Unfractionated heparin (%)	50 (30.5)	10 (21.3)	40 (34.2)	0.15
Low-molecular weight heparin (%)	42 (25.6)	5 (10.6)	37 (31.6)	0.01*
Warfarin treatment				
Mean cumulative weekly dose, mg (± SD)	22.3 (± 5.8)	18.1 (± 4.6)	24.0 (± 5.4)	< 0.001#
Median time to therapeutic INR (2.0-3.0), day (range)	6.0 (3-13)	4.0 (3-10)	7.0 (4-13)	< 0.001#
Concurrent medication use				
Drugs potentiate warfarin effect (% of patients)	57 (34.8)	15 (31.9)	42 (35.9)	0.76
Drugs inhibit warfarin effect (% of patients)	1 (0.6)	0 (0)	1 (0.9)	> 0.99##

*p-value < 0.05, significance, #Mann-Whitney U test, ##Fisher exact test

Table 2. The INR response between day 3 and day 5 of warfarin treatment

INR	Number of patients (%)		
	Day 3	Day 4	Day 5
<2.0	78 (83.9)	105 (75.5)	51 (52.0)
2.0-3.0	12 (12.9)	24 (17.3)	32 (32.7)
>3.0	3 (3.2)	10 (7.2)	15 (15.3)
Total number of patients	93 (100)	139 (100)	98 (100)

followed with caution.

Presently, there is no available data from the randomized, controlled trials concerning the effective and safe loading dose in the Asian population. In the current study, the safety of 3-mg warfarin initiating dose was demonstrated. Further more, the median time to therapeutic INR attained with 3-mg initiating dose (6 days) was quite comparable to that obtained after taking 5-mg warfarin loading dose as shown in the preceding study by Kovacs MJ et al, in which the median time to therapeutic INR was 5.6 days[3]. However, the proportion of patients who achieved the therapeutic

Table 3. Factors associated with time to therapeutic range

	Patients who achieved therapeutic INR n = 47 (%)	Patients who did not achieve therapeutic INR n = 117 (%)	Univariate		Multivariate	
			Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age > 60 years	14 (29.8)	48 (41.0)	0.61 (0.29-1.26)	0.18	1.46 (0.45-4.77)	0.53
Male gender	27 (57.4)	59 (50.4)	1.33 (0.67-2.63)	0.42	2.08 (0.75-5.78)	0.16
Body weight < 50 kg	9 (19.1)	15 (12.8)	1.55 (0.61-3.94)	0.36	3.42 (0.97-12.04)	0.06
Serum albumin < 3.0 g/dl	4 (8.5)	13 (11.1)	0.74 (0.23-2.39)	0.61	1.48 (0.13-16.24)	0.75
Prosthetic heart valve replacement	31 (65.9)	28 (23.9)	6.16 (2.94-12.90)	<0.001*	16.25 (5.13-51.44)	<0.001*
Concomitant potentiating medication use	15 (31.9)	42 (35.9)	0.84 (0.41-1.72)	0.63	0.40 (0.15-1.08)	0.07

*p-value < 0.05; significance

INR with 3-mg initiating dose between day 3 and day 5 in this study (29%) appeared to be lower than that previously reported by Crowther M et al[1], who reported that 66% of the studied patients receiving 5-mg warfarin loading dose achieved the target INR of 2.0-3.0 on day 3-4 or day 4-5. Nevertheless, the efficacy of 3-mg warfarin loading dose may be underestimated in this retrospective study since many patients did not have the INR results during the study endpoint date (between day 3 to day 5 of warfarin therapy), for example, patients whose INR results were approaching the target range on day 3 or day 4 did not have the repeat tests on the following days. Therefore, it was possible that the proportion of the patients who accomplished the therapeutic INR could have been higher if the INR had been checked on the subsequent days.

Interestingly, prosthetic heart valve replacement as the indication for oral anticoagulation was the only factor associated with time to accomplish therapeutic INR from univariate and multivariate analysis (Table 3). The mean number of INR tests in this group was significantly more frequent than that performed on patients who received warfarin for other indications [2.9 vs. 1.5, 95% CI 1.27-1.56, p < 0.001]. It was probable that the close monitoring of warfarin anticoagulant effect by regular INR tests may lead to appropriate warfarin dose adjustment, which may have an effect on the duration to attain the target INR.

On the other hand, several limitations had to be considered. Due to the retrospective nature of the study, some of the important data was not available in a homogenous fashion, including the INR results on the study endpoint dates, which may be responsible for the lower proportion of patients fulfilling the therapeutic range. In addition, the number of the enrolled subjects was relatively small.

In conclusion, 3-mg warfarin initiating dose appeared to be safe in adult Thai patients. However, the efficacy of 3-mg starting dose as determined by the proportion of patients who achieved the target INR between day 3 and day 5 of warfarin treatment was relatively less efficient when compared with that previously reported with a 5-mg loading dose[1]. Nonetheless, the median time to achieve the therapeutic INR with 3-mg initiating dose was fairly similar to that demonstrated earlier in another study using 5-mg initiating dose[3]. Due to several limitations of the current study, further prospective investigations comparing 3-mg warfarin initiating dose with different warfarin starting doses in a randomized fashion would be helpful in establishing the optimal warfarin management in Thai population.

Potential conflicts of interest

None.

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การศึกษาประสิทธิภาพของยาวอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวันในผู้ป่วยไทย ที่ได้รับยาต้านการแข็งตัวของเลือด ในระยะยาว

บุณฑริกา สุวรรณวิบูลย์, ปิยะนุช คงทิม, ยิ่งยง ชินธรรมมิตร์, ธีระ ฤชุตระกูล, วันชัย วนะชิวนาวิน

ภูมิหลัง: *วอร์ฟารินเป็นยาต้านการแข็งตัวของเลือดชนิดรับประทานที่ใช้อย่างแพร่หลายในเวชปฏิบัติ ผลการศึกษาในต่างประเทศพบว่าการให้วอร์ฟารินในขนาดยาเริ่มต้นที่ 5 มิลลิกรัม ต่อวัน และ 10 มิลลิกรัม ต่อวันใน 1 ถึง 2 วันแรกของการรักษาเป็นขนาดยาเริ่มต้นที่มีประสิทธิภาพดี อย่างไรก็ตามเป็นที่ทราบแล้วว่ามีหลายปัจจัยที่มีผลต่อขนาดยาวอร์ฟารินที่ผู้ป่วยแต่ละรายต้องการ เช่น อายุ โรคร่วม และ ปัจจัยทางพันธุกรรมที่มีผลต่อเมตาบอลิสซึมของวอร์ฟาริน ซึ่งมีความแตกต่างกันไปในประชากรแต่ละเชื้อชาติ เป็นต้น ปัจจุบันขนาดยาวอร์ฟารินที่เหมาะสมในการเริ่มการรักษาด้วยยาต้านการแข็งตัวของเลือดในผู้ป่วยไทยยังไม่เป็นที่ทราบแน่ชัด อย่างไรก็ตามจากการสังเกตของคณะผู้วิจัยพบว่าวอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวันเป็นขนาดยาเริ่มต้นที่ใช้บ่อยในโรงพยาบาลศิริราช*

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพและความปลอดภัยของการใช้วอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวัน*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาแบบ retrospective โดยการทบทวนเวชระเบียนของผู้ป่วยในที่ได้รับการรักษาในโรงพยาบาลศิริราช ในช่วงเดือนมกราคม พ.ศ. 2547 ถึง ธันวาคม พ.ศ. 2550 โดยคัดเลือกเฉพาะผู้ป่วยที่ได้รับยาวอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวันเป็นเวลาสองวันติดต่อกัน และมีระดับ INR ที่ต้องการ อยู่ระหว่าง 2.0-3.0 ประสิทธิภาพของยาวอร์ฟารินได้รับการประเมิน โดยการวิเคราะห์อัตราส่วน จำนวนผู้ป่วยที่มีระดับ INR อยู่ระหว่าง 2.0-3.0 ในระหว่างวันที่ 3 ถึงวันที่ 5 ของการรักษาเปรียบเทียบกับจำนวน ผู้ป่วยทั้งหมด*

ผลการศึกษา: *ในจำนวนผู้ป่วยที่เข้าร่วมการศึกษาทั้งหมด 164 คน, 86 คน (52.4%) เป็นผู้ป่วยชาย อายุเฉลี่ย 55.1 $\pm$ 16.8 ปี ค่าเฉลี่ยของน้ำหนักตัวและระดับอัลบูมินในซีรัมเท่ากับ 61.5 $\pm$ 12.2 กิโลกรัม และ 3.7 $\pm$ 0.7 กรัมต่อเดซิลิตร ตามลำดับ ข้อบ่งชี้ในการใช้ยาวอร์ฟารินที่พบบ่อยที่สุด ได้แก่ การผ่าตัดเปลี่ยนลิ้นหัวใจเทียม คิดเป็นร้อยละ 36 รองลงมาคือ ภาวะลิ่มเลือดอุดตันในหลอดเลือดดำ คิดเป็นร้อยละ 32.3 ค่าเฉลี่ยของขนาดยาวอร์ฟาริน ต่อสัปดาห์เท่ากับ 22.3 $\pm$ 5.8 มิลลิกรัม และระยะเวลาเฉลี่ยที่ผู้ป่วยเข้าถึงระดับ INR ที่ต้องการ (2.0-3.0) คือ 6 วัน มีผู้ป่วยจำนวน 47 คน (29%) ที่มีระดับ INR อยู่ระหว่าง 2.0-3.0 ในระหว่างวันที่ 3 และวันที่ 5 ของการรักษาด้วยวอร์ฟาริน อายุ, เพศ, น้ำหนักตัว, ระดับอัลบูมินในซีรัม หรือยาที่ใช้ร่วมกับวอร์ฟาริน ไม่มีผลต่อระยะเวลาที่ผู้ป่วยใช้ในการเข้าถึงระดับ INR ที่เป็นเป้าหมายของการรักษา (2.0-3.0) อย่างไรก็ตามพบว่าผู้ป่วยที่ได้รับการผ่าตัดเปลี่ยนลิ้นหัวใจเทียม มีโอกาสที่สูงกว่าในการเข้าถึงระดับ INR 2.0-3.0 ในระหว่างวันที่ 3 และวันที่ 5 ของการรักษา เมื่อเทียบกับผู้ป่วยที่ได้รับวอร์ฟารินด้วยข้อบ่งชี้อื่น (adjusted OR 16.25, 95% CI 5.13-51.44, $p < 0.001$) ภาวะเลือดออกผิดปกติพบในผู้ป่วย 1 ราย ซึ่งไม่สัมพันธ์กับระดับ INR ที่สูงกว่าปกติ*

สรุป: *การใช้ยาวอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวันน่าจะมีความปลอดภัยในผู้ป่วยไทย อย่างไรก็ตามพบว่าประสิทธิภาพของวอร์ฟารินในขนาดเริ่มต้นดังกล่าวโดยการดูอัตราส่วนของผู้ป่วยที่เข้าถึงระดับ INR 2.0-3.0 ระหว่างวันที่ 3 และวันที่ 5 ของการรักษายังไม่ดีเท่าที่ควรเมื่อเปรียบเทียบกับผลการศึกษา ในต่างประเทศที่ใช้วอร์ฟารินในขนาดเริ่มต้นที่ 5 มิลลิกรัมต่อวัน การศึกษาแบบสุ่มเพื่อประเมินประสิทธิภาพ ของการใช้วอร์ฟารินในขนาดเริ่มต้นที่ 3 มิลลิกรัมต่อวันเปรียบเทียบกับขนาดยาเริ่มต้นที่สูงกว่าน่าจะมีประโยชน์ ในการช่วยวางแนวทางการรักษาผู้ป่วยไทยด้วยยาวอร์ฟารินให้มีความเหมาะสมมากยิ่งขึ้นในอนาคต*