EVALUATION OF WARFARIN ORAL USED BY INTERNATIONAL NORMALIZED RATIO VALUE AND DETERMINATION FREQUENCY TO CARDIOVASCULAR PATIENT AT HAJI ADAM MALIK GENERAL HOSPITAL, MEDAN, INDONESIA

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INTRODUCTION

The bleeding is the common problem in cardiovascular disease. The two types of bleeding in cardiovascular are ischemic and hemorrhage. The bleeding event was caused by a disorder or manipulating (mechanic or pharmacologic) in the treatment of the disease [1]. The pharmacologic manipulation associated with clinically significant side effects from medicines and supplements [2,3].

The bleeding is related to the anticoagulant group by minor and major bleeding. The minor bleeding such as in the nose, pharynx, urinary tract, soft tissue, and joint space. The major bleeding such as in cerebrovascular (intracranial) and gastrointestinal (40–60%) systems that may occur in the retroperitoneal region and intraocular. Intracranial hemorrhage is a fatal hemorrhage associated with warfarin therapy. Although the incidence is estimated to range from 0.3% to 2%, 60% of sufferers experience death from the incidence value [4].

Heparin is a parenteral anticoagulant that acts as indirect thrombin inhibitor and is extensively used for treatment and prophylaxis of several thromboembolic conditions in clinical practice. Heparin is a heterogeneous mixture of sulfated mucopolysaccharides whose biologic activity is dependent on the endogenous anticoagulant antithrombin. Common use oral anticoagulant is warfarin [5].

The 50% of the bleeding that occurs is major bleeding. The bleeding associated with warfarin causes morbidity due to transfusion and hospitalization. An average of 1 in 10 major hemorrhages causes death and 1 in 12 patients will experience bleeding after reuse of warfarin [6]. During the development of research on major bleeding related to warfarin, the mortality rate reached 9.5–13.4% [7,8]. An examination of the international normalized ratio (INR) in patients receiving warfarin therapy is needed to monitor the chances of bleeding [9,10].

Based on high mortality rate due to bleeding because of warfarin usage, evaluation of warfarin based on INR value and relation with bleeding number of patient needs to be evaluated. In this study, patients of cardiovascular disease who received warfarin were grouped by frequency of the determination of INR values.

METHODS

Ethical clearance

The study was approved by Health Research Ethical Committee, Medical Faculty of University of Sumatera Utara/Haji Adam Malik General Hospital with an ethical clearance number of 368/TGL/KEPK FK USU-RSUP HAM/2017.

Study design

The study design in this research was case-control study. The data were collected by retrospective method for evaluation of clinical condition and identify study participants based on their case status in medical record. This study was compared and analyzing statistical associations between exposure and outcomes [11].
Time and location
This study was conducted at Haji Adam Malik Hospital from May to September 2017, and the data used in study were taken from 2016s data.

Population and sample
The population was all of the cardiovascular patients’ medical record in Haji Adam Malik Hospital, Medan, Indonesia. The sample was collected by simple random sampling method from the medical record in 2016 year period. The simple random sampling method used the Slovin formula for count the number of sample from all of the population. The Slovin formula is:

\[ n = \frac{N \times e^2}{n - N} \]

n: The number of sample, N: The number of population, e: The number of deviation or error (10%).

The collected sample was grouped by the type of determination frequency of INR value; there are no measurements, once in year period, unregularly, thrice a year, and every month.

Statistical analysis
Statistical analysis was conducted using analysis of variant method to identify significantly different between all groups and conclude the relationship of determination frequency of INR value and warfarin used. In this study, the independent variable was determination frequency and dependent variable was INR value for the evaluation of coagulant or bleeding status in patients.

RESULT
Characteristic of patients demography
The number of patients by sex can be viewed in Table 1.

| Sex   | n (%) |
|-------|-------|
| Male  | 47 (52.22) |
| Female| 43 (47.78) |

| Ages (years) | n (%) |
|--------------|-------|
| 20–30        | 7 (7.78) |
| 31–40        | 20 (22.22) |
| 41–50        | 15 (16.67) |
| 51–60        | 23 (25.56) |
| >60          | 25 (27.78) |

The number of patients by age can be viewed in Table 2.

Table 1: The number of patients by sex

Table 2: The number of patients by age

INR monitoring in patients with low thrombotic risk is done daily until INR 2–3 is reached if it is stable enough to examine 4–6 weeks. While for patients with high thrombotic risk, an initial examination is done every 3 days until the INR value reaches 2, then every week to INR 2–3, if the INR has stabilized then it should be checked once every 4–6 weeks [14-16].

Evidence suggests that stroke prevention by warfarin is effective when the time in therapeutic range (TTR) is either >70%. TTR is the proportion of time when INR 2–3 is achieved compared to overall duration of warfarin consumption. Therefore, continuous dose regulatory efforts should be made to obtain target values of INR 2–3. The difficulty of using warfarin in Indonesia is the unavailability of the INR inspection facility in peripheral areas. In this regard, it should also be noted that genetic factors in Indonesian ethnicity are related to the sensitivity of individuals to warfarin [17].

CONCLUSION
The examination of INR values is an important factor in the evaluation of coagulant and bleeding events in the treatment of cardiovascular disease using anticoagulant therapy such as warfarin with periodic checks; health workers can monitor the use of drug doses to achieve a better quality of life for patients.

CONFLICTS OF INTERESTS
Declared none.

AUTHORS CONTRIBUTION
The first author has carried out the research. Second and third authors have provided study conception, the design of work and critical revision.

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