



Comparison Between Given Prophylaxis and Non-Prophylaxis of Deep Vein Thrombosis in Traumatic Brain Injury Patients In Tropical Climate

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Abstract: Deep Vein Trombosis (DVT) is one of the extracranial complications after TBI. Prophylaxis DVT using on TBI reduce incidence and mortality. Climate variants of an area affect the risk of DVT. UV ray increasing synthesis of vitamin D and lowering risk of thrombus fomation. A systematic review and meta-analysis we performed according PRISMA guidelines. A through literature search was conducted on PubMed, Scopus, and Cochrane database. Total 3 publications match study criteria with 178 samples, without 144 samples and 34 samples with prophylaxis. The overall incidence is 5% (0-6.8%), without 6.25% (5.3-6.8%) and with prophylaxis 0%. No reported complications and 100% survival rate. The incidence of DVT in TBI in tropical climate is low on average 5% (0-6.8%). There was no difference in the outcome of DVT in TBI in tropical climate which given and without DVT prophylaxis. Asian races ethnic protective factor and UV ray exposure may contributed to the low of incidence rate. Prevention of DVT is still recommended for the use of prophylaxis, mechanical compression and early mobilization in cases of TBI to prevent the occurrence of DVT.

Keyword : DVT Prophylaxis, TBI, Tropic

I. INTRODUCTION

Traumatic brain injury is the leading cause of death ¹.WHO predicts at 2030, brain injury will be the leading cause of disability and death worldwide. Complications that can occur after brain injury is deep vein thrombosis (DVT), it is a clots formation in the veins, especially in the lower extremities. DVT can be dangerously and deathly ². The incidence of DVT after trauma around 6% - 58% ³.

Climate variant is threat element of DVT, feasible mechanisms are climate-related hypersensitivity, haemostatic abnormalities and lack of activity during winter ⁴. Cold climate disturbing coagulation cascade and peripheral vasoconstriction, It makes vasoconstrictive tone of the arteries and veins, increasing risk of DVT. Tropical climate exposed to sunlight and UV makes increases vitamin D synthesis that is related to upregulation of thrombomodulin and downregulation of tissue factor ^{5,6}.

II. RESEARCH METHODOLOGY

2.1 Eligibility Criteria

Study used were fully accessible literature, clinical trials, prospective, retrospective, and observational cohorts on only English literature and the literature published less than 20 years who diagnosed with TBI in tropical region, and measured for whether have DVT or not. The DVT prophylaxis status recorded. Reviews, unpublished articles, letter to editor, abstracts, study not written in English were excluded from the study

Type of outcome measures

Clinical outcome, measured with :

- Incidence of DVT
- Morbidity after given prophylaxis DVT
- Mortality

2.2 Search Methods and Identification of Studies

1. Information Sources

The following databases were searched in July 2012 for primary studies: PubMed/Medline, Google scholar, Research Gate, and Cochrane. The limitations of the literature used are, literature only in English, literature published less than 20 years, fully accessible literature after filtering, and not case report literature or systematic review.

2. Search Protocol

Study question was formed from the PICO. Authors used the following search keywords to search all trials registers and databases: ("Traumatic Brain Injury" OR "TBI" OR "Traumatic Head Injury" OR "Brain Injury") AND ("Deep vein thrombosis" OR "DVT") AND ("DVT Prophylaxis" OR "Thrombosis Prophylaxis")

Study selection and analysis

Study were reviewed to identify clinical trials, prospective, retrospective, and observational cohorts with or without comparison groups reporting on the prophylaxis and non-prophylaxis of DVT in TBI patients. Three investigators (AW, AHB, TA) independently reviewed the study meeting our inclusion criteria; only literature in English, literature published less than 20 years, fully accessible literature, and literature with the following design: clinical trials, prospective, retrospective, and observational cohorts.

3. Data Extraction and Management

For eligible studies, three review authors (AW, AHB, TA) independently extracted data using the data extraction form on characteristics of patients and interventions, study quality, and outcomes of interventions.⁷ For measured outcomes of (DVT incidence and DVT risk), we extracted the incidence of DVT in both of the experimental and control group (with its 95% confidence interval (CI) as reported by the study authors. We extracted the incidence of DVT in each group for pooled incidence risk analysis for DVT incidence. For DVT risk, dichotomous data of incidence in each arm for risk ratio outcome. Two review authors (AW, AM) entered all data into the Review Manager (RevMan) software version 5.4.⁸

4. Assessment of study quality and risk of bias in included studies

Review authors independently assessed risk of bias for each included study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions for non-randomized studies, called as Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) for non-randomized studies and Risk of Bias 2 (RoB 2) for randomized studies⁷. Any disagreement was resolved by discussion or by involving third assessor. We summarized judgements in 'Risk of bias' tables along with the characteristics of the included studies and interpreted the results of meta-analyses in light of the overall 'Risk of bias' assessment^{9,10}.

5. Measures of treatment effect

We presented the results of the generic inverse variance data as pooled incidence rate with 95% confidence intervals (CI) for DVT incidence. For DVT risk, we presented the results of the dichotomous data as risk ratio with 95% confidence intervals (CI) to combine trials that measured the same outcome and same comparison. Meta-analysis was planned if the data were appropriate for pooling. Summary of estimates was presented as mean difference for the outcomes. Consequently, both fixed-effects and random-effects meta-analyses were used, although the latter was prespecified in the protocol. If pooling was inappropriate, a narrative synthesis was implemented. The definitions of CI, heterogeneity, and P value are conventional (CI 95%; $I^2 < 40\%$: unimportant; 30%–60%: moderate; 50%–90%: substantial, 75%–100%: considerable; P value < 0.05 : significant; P value for interaction < 0.1 : significant).¹¹ Review Manager 5.4 was used for meta-analysis⁸.

III. RESULTS

Search literature on journal databases boldly. The databases of bold journals used in the search include Medline/PubMed (12 journals), Google Scholar (333 journals), Research Gate (15 journals) and Cochrane (1 journal) with a total of 361 literatures obtained. After the duplication, obtained 99 duplications. Followed by a search for titles, abstracts and research locations obtained 14 filtered literature. Followed by full text, 11 literatures were excluded because 1 literature is a case report, 8 literatures does not describe tropical climate, 2 literatures not clear described incident rate. There were 3 literatures that met the criteria. The search process and result are presented in PRISMA flowchart in Figure 1.

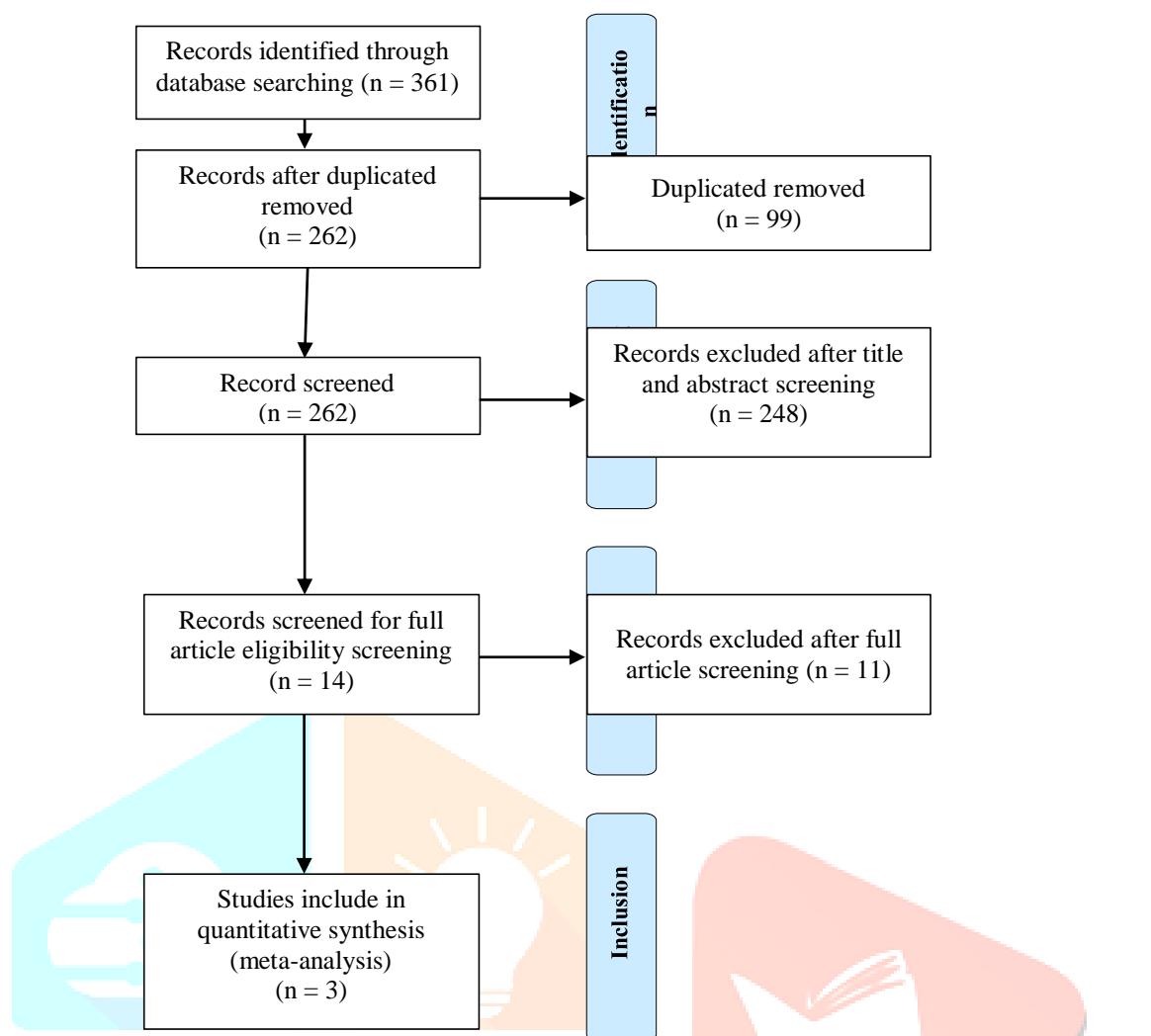


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines flowchart.

Literature Characteristics

Three literatures meet inclusion criteria, shown in table 1. Existing literature was obtained from 2009 to 2016. All literature was non-randomized clinical trial studies, a study without prophylaxis and two studies reporting prophylactic use. In general, there were a total of 178 TBI patients in this study with 9 patients experiencing DVT, 5% incidence rate.

Table 1 Characteristics of the Literature Included in the Systematic Review

No	Author	Title	Type of Prophylaxis	City or Country	Climate
1	Chua, 2009	Deep Venous Thrombosis in Asian Traumatic Brain Injury Patients During Rehabilitation: Prevalence and Risk Factors	without	Singapore	Tropic
2	Behera, 2009	Incidence of Deep Vein Thrombosis in Neurointensive Care Unit Patients—Does Prophylaxis Modality Make Any Difference?	UFH	Karnataka / India	Tropic
3	George, 2016	The incidence of deep venous thrombosis in high-risk Indian neurosurgical patients: Need for early chemoprophylaxis?	without	Tamil Nadu/ India	Tropic

Risk of Bias Analysis

The result of bias risk assessment of studies involved measured by ROBINS-I for non-randomized studies. The result showed in Figure 2 and Figure 3 below.

	Confounding Bias	Selection Bias	Intervention Bias	Missing Data Bias	Outcome Bias	Selective Reporting Bias	Overall Risk Bias
Behera 2009	?	+	+	+	+	?	+
Chua 2009	+	-	+	+	+	?	?
George 2016	+	+	+	-	+	?	?

Figure 2 Risk assessment of bias using ROBINS-I for non-RCT studies.

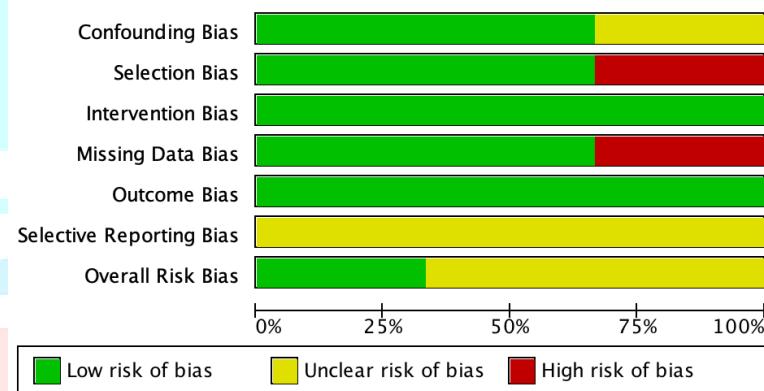


Figure 3 Proportion of the results of a risk assessment of bias using ROBINS-I for non-RCT studies based on an assessment for each risk of bias.

DVT Prophylaxis in TBI Patients Tropical Climate

A journal reported group of patients using DVT prophylaxis shown in table 2 below.

Table 2 Characteristics of literature with DVT prophylaxis

No	Author	Number of Sample	Number of DVT	Incidence rate	Complication	Survival rate
1	Behera, 2009	34	0	0	Mortality 0%	100%
	Total	34	0	0		

A literature reported the incidence of DVT in patients given prophylaxis with incidence 0%. The total number of patients obtained was 34 patients, with 0 patients experiencing DVT. Survival rates reported is 100% and no complication related given prophylaxis ¹².

Without DVT Prophylaxis in TBI Patients Tropical Climate

Two literatures reports a group of TBI patients without DVT prophylaxis, shown in table 3 below.

Table 3 Characteristics of the literature without DVT prophylaxis

No	Author	Number of Sample	Number of DVT	Incidence rate	Complication	Survival rate
1	Chua, 2009	56	3	5.3	mortality 0%	100%
2	George, 2016	88	6	6.8	mortality 0%	100%
	Total	144	9	6.25		

Two literatures reported the incidence of DVT in patients without prophylaxis, the prevalence of 5.3 - 6.8%. The total number of patients obtained was 144 patients, with 9 patients experiencing DVT. The crude incidence of DVT in this group of TBI patients without prophylaxis was 6.25% ^{13,14}. Two literatures reported survival rates and mortality, all survival rates is 100% and 0% mortality associated DVT ¹³⁻¹⁵.

Forest plot pooled analysis of the incidence of DVT in patients without prophylaxis, found that DVT occurred in 6% of patients (95% CI, 0.02– 0.10) Between studies on this pooled analysis is homogenous ($I^2 = 0\%$). The results of the analysis can be seen in forest plot (Figure 5) below.

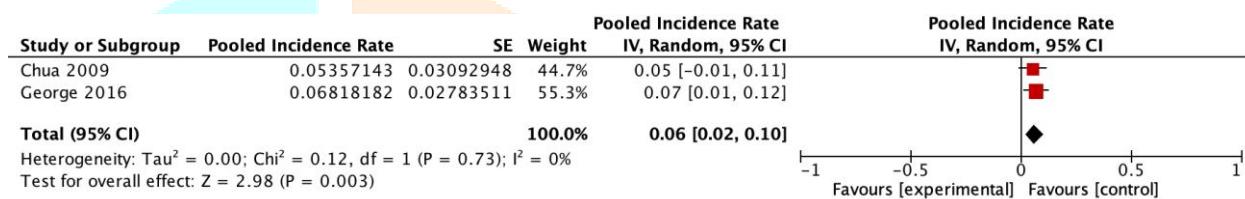


Figure 5. Pooled-analysis of the incidence of DVT in TBI patients not receiving prophylaxis in tropical.

IV. DISCUSSION

Demographics

The 3 literatures study resulted in a total of 178 patients, with 144 patients in the group without DVT prophylaxis and 34 patients in the group with DVT prophylaxis. A total of 9 patients had DVT in both groups, with 0 patient in the non-prophylactic group and 9 patients in the prophylactic group. The incidence rate of DVT in TBI patients in this study is 5%. This figure is lower than the average incidence of DVT in major trauma patients 6-58% and from cold climate 24-60% ^{2,16}.

Confounding Factors

Therefore, there are several things that confound this situation. Study methodology from all literature is perspective observational, single center study, small sample size, loss follow up and diversity of time on admission ¹²⁻¹⁴.

DVT Prophylaxis in TBI Patients Tropical Climate

A literature discuss the use of DVT prophylaxis in TBI in tropical climate. The incidence rate is 0% and survival rate 100%. Low incidence rate of DVT caused by small sample size, loss of followup and ethnic protective factor of Asia races. A literature, single center and small sample size can't accurately described actual incidence rate of DVT ¹².

Without DVT Prophylaxis in TBI Patients Tropical Climate

Two literatures reported TBI cases in TBI in tropical climate without given prophylaxis. The incidence rate ranged from 5.3% - 6.8% with mean 6.25%. The incidence rate is 6% from pooled analysis for incidence rate with homogenous sample. The incidence rate higher than incidence rate in the group with prophylaxis but lower than DVT in major trauma and cold climate. It can caused by post acute or rehabilitation phase admision which has passed from peak of hipercoagulation state. In areas with tropical climate get more UV rays from the sun every year, UV ray increase vitamin D synthesis, upregulation of thrombomodulin and downregulation tissue factor. It can reduce risk of obtained DVT. The protective effect of Asian races, majority of the study population, are known to have a lower propensity to develop DVT. High antithrombin, low protein C, and low protein S in Asian races are protective factors against DVT ^{13,14}.

LIMITATION

The limitations of this research are no RCT studies design from literatures obtained, high risk of bias and small sample size.

V. CONCLUSION

The incidence of DVT in TBI in tropical climate is low on average 5% (0-6.8%). There was no difference in the outcome of DVT in TBI in tropical climate which given and without DVT prophylaxis. Asian races ethnic protective factor and UV ray exposure contributed to the low of incidence rate. Prevention of DVT is still recommended for the use of prophylaxis, mechanical compression and early mobilization in cases of TBI to prevent the occurrence of DVT.

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