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Full Length Article

The effect of activated clotting time values for patients undergoing percutaneous coronary intervention: A systematic review and meta-analysis

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ABSTRACT

Our aim was to illustrate the effect of higher activated clotting time (ACT) values versus lower ACT values on thrombotic or hemorrhagic events in coronary atherosclerotic heart disease (CHD) patients undergoing percutaneous coronary intervention (PCI). PubMed, Embase, Web of Science, and Cochrane Library were searched. Observational studies assessing ACT related major adverse cardiac event (MACE) and major bleeding were included. Studies were allocated into three groups. Group 1 included studies with low percentage of participants prescribed with glycoprotein IIb/IIIa inhibitors ([GPI] ≤30%), Group 2 with high percentage of participants prescribed with GPI (>30%), and Group 3 with routine direct thrombin inhibitors (DTI) prescription. The cutoff is designed as 300 s (290–310 s) for Group 1, and 250 s (240–260 s) for Group 2. With regard to MACE and major bleeding in Group 1, there was no significant difference between higher ACT values and lower ACT values (risk ratio [RR] for MACE, 1.16, 95% confidence interval [CI], 0.65–2.05, $p = 0.62$, $I^2 = 94\%$, RR for major bleeding, 0.96, 95% CI, 0.66–1.40, $p = 0.83$, $I^2 = 0\%$). Likewise, no significant difference was found in Group 2 between higher ACT values and lower ACT values (RR for MACE, 1.15, 95% CI, 0.97–1.35, $p = 0.10$, $I^2 = 0\%$, RR for major bleeding, 0.85, 95% CI, 0.45–1.60, $p = 0.61$, $I^2 = 83\%$). In conclusion, ACT may not have a substantial effect on thrombotic or hemorrhagic complications. Under current clinical practice, target ACT may be higher than what is necessary to prevent thrombotic events. We may achieve a relative low ACT level to preserve efficacy and enhance safety.

1. Introduction

Among the high-developed countries, the United States has witnessed declines in CHD-related mortality since 1986 [1–3]. Obviously, the decline in mortality is ascribed both to improved techniques and to potent therapies [4].

Peri-procedural anticoagulation is necessary to protect patients from thrombus forming on the wire, balloon, and catheter [5]. Since unfractionated heparin (UFH) is familiar to most cardiologists, can be titrated with ACT, and is inexpensive, it is still normally used during PCI. According to data from the National Cardiovascular Data Registry [6], UFH is widely used in this recommendation (about 60% of patients with non-ST elevation myocardial infarction [NSTEMI] undergoing PCI received UFH). UFH is an anticoagulant agent which has a variable pharmacokinetic and pharmacodynamics profile and a narrow therapeutic window [7], so guidelines [8] from the United States suggest ACT to guide UFH dosing.

Optimizing the balance between thrombotic and hemorrhagic complications is a major challenge of anticoagulation during PCI. Retrospective analyses showed a positive association between ACT and thrombotic [9,10] or hemorrhagic [11] complications. However, these studies might not properly reflect current circumstances when dual antiplatelet therapy (DAPT) and coronary artery stenting are widely used.

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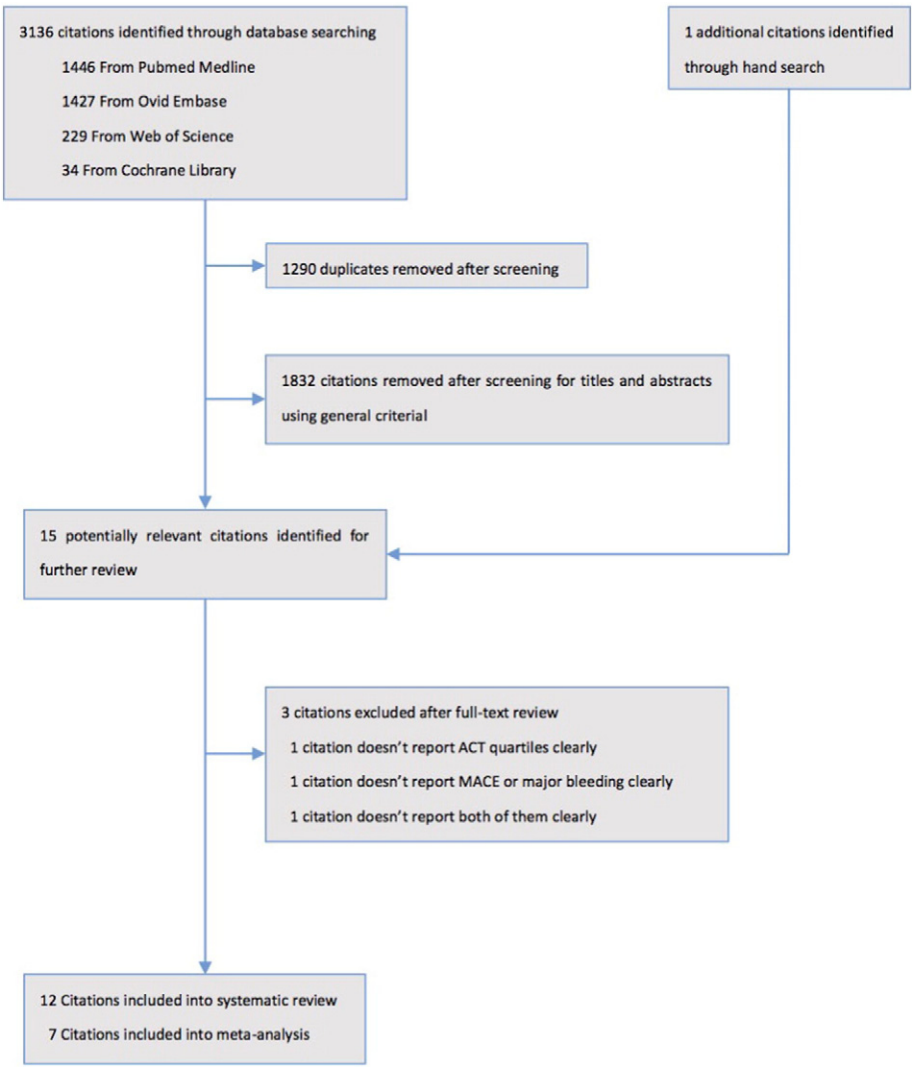

Fig. 1. Study selection sample flow diagram.

And these studies may have some confounding that we may not notice. On the contrary, more recent analyses have found no association between ACT and thrombotic [12,13] or hemorrhagic [14] complications. At which point UFH is adequate or ACT values are optimal remains debatable, and literature in this topic lacks a pooled evidence. The aim of this study is to determine the relationship between ACT values and thrombotic or hemorrhagic complications for patients undergoing PCI.

2. Method

We performed a systematic review to evaluate the current evidence and to collect and synthesize available data. A search strategy was developed by a librarian of Sichuan University West China School of Medicine. We searched PubMed Medline (1946 to 1 April 2016), Embase (1947 to 2016 Week 12), Web of Science, and Cochrane Library for

Table 1
Study characteristics.

Source	Design	Region	Number	Population	Follow-up	Quality[a]
Chew et al. [10]	Observational	USA	6146	All patients	7 days	6
Ashby et al. [22]	Observational	USA	793	All patients[b]	In hospital	6
Pinto et al. [24]	Observational	USA	378	NSTE-ACS	Bleeding, In hospital	6
Tolleson et al. [11]	Observational	USA	1991	All patients	MACE, 30 days	7
Brener et al. [12]	Observational	USA	9974	All patients	MACE, in hospital	6
Cheneau et al. [26]	Observational	USA	495	All patients[b]	In hospital	6
Cruz-Gonzalez et al. [25]	Observational	USA	120	All patients	In hospital	6
Montalescot et al. [23]	Observational	France	3528	All patients	Bleeding, in hospital; MACE, 30 days	6
Bertrand et al. [14]	Observational	Canada	1234	All patients[b]	30 days	7
Bangalore et al. [21]	Observational	USA	6542	All patients	Bleeding, in hospital; MACE, 12 months	8
Rozenman et al. [13]	Observational	Israel	1624	STEMI	30 days	7
Ducrocq et al. [17]	Observational	France	1882	NSTE-ACS	Bleeding, in hospital	6

NSTE-ACS indicates non ST elevation acute coronary syndrome; STEMI, ST elevation myocardial infarction; ACS, acute coronary syndrome; MACE, major cardiac adverse events.
[a] Newcastle-Ottawa quality assessment scale for observational studies.
[b] Patients included except for STEMI.