Cardiovascular Revascularization Medicine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Prophylactic warfarin post anterior ST-elevation myocardial infarction: A systematic review and meta-analysis☆,☆☆

Nathaniel Moulson [a], Stephen A. LaHaye [a], Olivier F. Bertrand [b], Jimmy MacHaalany [a,*]

[a] Kingston General Hospital, Division of Cardiology, Kingston, Ontario, Canada
[b] Institut Universitaire de Cardiologie et de Pneumologie de Québec, Division of Cardiology, Quebec City, Quebec, Canada

ARTICLE INFO

Article history:
Received 31 March 2017
Received in revised form 1 May 2017
Accepted 3 May 2017
Available online xxxx

Keywords:
Triple therapy
Warfarin
LV thrombus
ST elevation myocardial infarction

ABSTRACT

Objectives: To determine the role of warfarin (WF) prophylaxis in the prevention of left ventricular thrombus (LVT) formation and subsequent embolic complications following an anterior ST elevation myocardial infarction (STEMI) complicated by reduced left ventricular ejection fraction (LVEF) and wall motion abnormalities.
Background: The role of oral anticoagulation prophylaxis, in addition to dual antiplatelet therapy (DAPT), in the current era of percutaneous coronary intervention has not been well studied, despite being a class IIb recommendation in the AHA/ACC STEMI guidelines.
Methods: The Cochrane search strategy was used to search PubMed, Embase and the Cochrane library for relevant results. Four studies, two retrospective, one prospective registry, and a randomized feasibility control trial met criteria for inclusion. Data was pooled using a random effects model and reported as odds ratios (OR) with their 95% confidence intervals (CI). Primary outcomes of interest were rate of stroke, major bleeding and mortality.
Results: Pooled analysis included 526 patients in the No WF group and 347 patients in the WF group. No statistical difference in rate of stroke (OR: 2.72 [95% CI: 0.47–15.88; $p = 0.21$]) or mortality (OR: 1.50 [95% CI 0.29–7.71; $p = 0.63$]) was observed. Major bleeding was significantly higher in the WF group (OR: 2.56 [95% CI: 1.34–4.89; $p = 0.004$]).
Conclusions: The routine use of DAPT and WF for prophylaxis against LVT formation following an anterior STEMI with associated decrease in LVEF and wall motion abnormalities, appears to result in no mortality benefit or reduction in stroke rates, but may increase the frequency of major bleeding.

1. Introduction

The development of a left ventricular thrombus (LVT) is a well described complication of anterior ST-elevation myocardial infarctions (STEMI) associated with significant wall motion abnormality and reduced ejection fraction [1]. In the current era of primary percutaneous coronary intervention (PCI), the incidence of LVT in anterior STEMI has significantly declined, from 40% before the era of reperfusion therapy, to as low as 4% [2,3]. A recent retrospective analysis confirmed that a reduced left ventricular ejection fraction (LVEF), and anterior STEMI are both risk factors for development of an LVT [2]. Development of an LVT is also associated with approximately a 5-fold increase (odds ratio (OR) 5.45) in the risk of systemic embolization, which includes stroke [4,5]. Nonetheless, these data cannot apply to our current practice as they were based on figures obtained prior to the current era of primary PCI and the routine use of dual-antiplatelet therapy (DAPT).

The American Heart Association currently gives a class IIa recommendation for the treatment of an LVT complicating a STEMI with a vitamin K antagonist (VKA) [6]. Prophylaxis with a VKA, such as warfarin (WF) is also recommended for patients with anterior apical akinesis or dyskinesis following a STEMI (class IIb) [6]. Both of these recommendations are based on limited evidence.

Recent studies have attempted to address the role of WF prophylaxis in addition to the current standard of care, DAPT, to prevent LVT formation in anterior STEMI associated with reduced LVEF and wall motion abnormalities [7–10]. These studies are limited in size, with the larger two studies being retrospective in nature, and the only randomized trial being a 20-patient randomized feasibility trial. Therefore the aim of this meta-analysis was to combine these results to compare the use of WF and no WF for prevention of LVT in the era of PCI and concurrent DAPT.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
☆☆ Disclosures: There is no conflict of interest to disclose.
* Corresponding author at: Kingston General Hospital, 76 Stuart Street, Kingston, Ontario, Canada, K7L 2V7. Tel.: +1 613 548 6666.
E-mail address: jmach@magma.ca (J. MacHaalany).

http://dx.doi.org/10.1016/j.carrev.2017.05.002
1553-8389/

2. Methods

A literature search was performed with the use of the PubMed database, EMBASE and Cochrane Library. Results were individually reviewed by two independent reviewers (N.M. and J.M.) for relevance. Discrepancies between datasets were resolved by consensus. Exclusion criteria for studies were: 1) studies reporting only in abstract format or conference presentation or without access to full data or manuscript; 2) non-English articles; 3) studies reporting no direct comparison of WF versus No WF; 4) studies with no possibility of separating individual outcomes; and 5) studies that did not use DAPT.

Relevant data was extracted and entered in Review Manager software ([Revman] version 5.3 (Nordic Cochrane Centre, Copenhagen, Denmark)). Key words used were: "warfarin," "anterior wall myocardial infarction," "anterior STEMI," "anterior ST elevation myocardial infarction," "anterior ST segment elevation myocardial infarction," "anterior ST elevation MI," "anterior myocardial infarction," "ST segment elevation myocardial infarction," and "anterior."

Data was pooled using a random effects model, and reported as OR with their 95% confidence intervals (CI). Heterogeneity was based on the I^2 statistic test with I^2 value of <25% considered low heterogeneity, 25% to 50% moderate, and a value of >50% substantial heterogeneity. Funnel plots were constructed and inspected visually for evidence of publication bias. The weight of each trial on the overall results of meta-analysis outcome was calculated as a percentage of the number of patients in that given trial over the total number included in each outcome analysis.

Primary outcome measures of interest in all four studies included stroke, death and major bleeding. Definitions of major bleeding varied but were grouped under the outcome of major bleeding episodes for analysis. Two of the four studies did not categorize stroke into hemorrhagic versus ischemic and therefore these outcomes were grouped for analysis. All outcome measures in the studies were obtained between three and six-months post-discharge from the primary hospital admission.

3. Results

One hundred and forty-five results were reviewed, with four studies included in the final analysis (Fig. 1). Two studies were retrospective, one was a prospective registry and one was a randomized control feasibility trial. All were unicentric studies (Table 1). One of the four studies did not have atrial fibrillation or other indications for WF as an exclusion criteria (Table 1).

Pooled analysis resulted in a total of 873 patients, with 347 in the WF group and 526 in the No WF group being analyzed. Baseline characteristics of the pooled population are shown in Table 2. Average age of the two groups was similar and relatively young (WF: 60.9 years old vs. No WF 61.8 years old). Male sex predominated in both groups (WF: 77% vs. No WF: 72%). Baseline co-morbidities including hypertension, diabetes, smoking history, dyslipidemia, previous myocardial infarction and stroke were all similar between the two groups. 97% of patients in both groups received DAPT therapy. 93% of patients in the WF group and 94% of patients in the No WF group underwent PCI. High rates of optimal medical therapy were achieved in both groups, with only beta-blockers (83%) in the WF group not having a rate over 90%. Total duration of triple therapy with WF was between 3 and 6 months.

All four studies performed pre-discharge echocardiograms, and three performed follow-up examinations (Table 3). LVEF in the WF group was slightly lower with an average of 36% compared to 40% in the No WF group. Follow-up echocardiographic studies revealed average LVEFs of 41% in the WF group and 46% in the No WF group.

A complete data set of baseline characteristics (Table 2), including cardiovascular medications and follow-up echocardiograms (Table 3), was available in 67% (584/873) of the pooled patient population. Given the limited population size, patients with incomplete data sets were included in the analysis.

No statistical difference between the two groups was found relating to the rate of stroke (OR: 2.72 [95% CI: 0.47–15.88; $p = 0.27$]) or mortality (OR: 1.50 [95% CI 0.29–7.71; $p = 0.63$]) (Fig. 2A & B). Heterogeneity

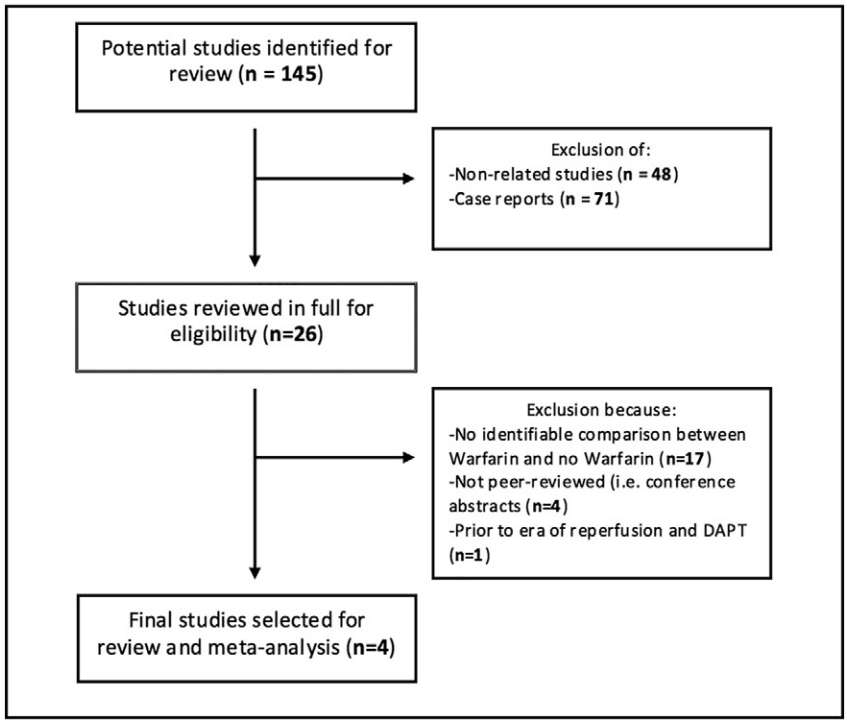

Fig. 1. Flowchart depicting study selection for meta-analysis.

Please cite this article as: Moulson N, et al, Prophylactic warfarin post anterior ST-elevation myocardial infarction: A systematic review and meta-analysis, Cardiovasc Revasc Med (2017), http://dx.doi.org/10.1016/j.carrev.2017.05.002