# Comparison of the Usefulness of Enoxaparin Versus Warfarin for Prevention of Left Ventricular Mural Thrombus After Anterior Wall Acute Myocardial Infarction

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**Left ventricular (LV) thrombus is one of the most common complications in patients with anterior acute myocardial infarction (AMI) and LV dysfunction. Although anticoagulation is frequently prescribed, data regarding the appropriate drug, duration, risks, and effect on echocardiographic indices of thrombus are lacking. Moreover, given the difficulty in obtaining adequate anticoagulation with warfarin, it is possible that short-term treatment with a more predictable agent would be effective. We randomized 60 patients at high risk of developing LV mural thrombus (anterior acute myocardial infarction with Q waves and ejection fraction ≤40%) to receive either enoxaparin 1 mg/kg (maximum 100 mg) subcutaneously every 12 hours for 30 days or traditional anticoagulation (intravenous heparin followed by oral warfarin for 3 months). Clinical evaluations and transthoracic echocardiograms were obtained at baseline, in-hospital, and at 3.5 months. There were no differences between the groups regarding baseline demographics, acute echocardiographic findings, and in-hospital outcomes. The length of hospital stay tended to be shorter for the enoxaparin group (4.6 vs 5.6; p = 0.066) and the corresponding hospital costs ($25,837 vs $34,666; p = 0.18). At 3 months, bleeding and thromboembolic events were rare and similar between enoxaparin and warfarin groups. Although more patients had probable mural thrombus in the enoxaparin group compared with warfarin at 3.5 months (15% vs 4%; p = 0.35), this was not significantly different. In conclusion, the use of enoxaparin tends to shorten hospitalization and lower cost of care. However, at 3.5 months, there appears to be numerically higher (but statistically insignificant) rates of LV thrombus in the enoxaparin group.**  **(Am J Cardiol 2015;115:1200−1203)**

We organized a pilot trial that randomized patients with anterior acute myocardial infarction (AMI) to a simple abbreviated anticoagulant regimen (enoxaparin for 1 month) versus traditional anticoagulation (unfractionated heparin followed warfarin for 3 months).

## Methods

Sixty patients with large anterior AMI (anterior Q-wave AMI and ejection fraction [EF] ≤40%) were enrolled within the first 7 days of AMI. Anterior AMI was defined as pathological Q waves (>0.04 seconds wide and >2 mm deep) in at least 3 contiguous anterior precordial ($V_1$ to $V_6$) leads that were presumed to be new and creatine kinase peak >5 times the upper limit of normal with positive MB band.

Patients were excluded if they had any of the following: medical conditions that would prohibit discharge within 48 hours, cardiogenic shock, angina at rest unresponsive to medical therapy, sustained ventricular arrhythmias, surgical procedures anticipated in the next few months that would require discontinuation of anticoagulation, baseline hemoglobin ≤9 g for women or ≤10 g for men, platelet count <100,000, creatinine >2.0 mg/dl, international normalized ratio (INR) >1.3, stroke within past 6 months or a previous documented intracranial or subarachnoid hemorrhage, active bleeding, major surgery within past 2 weeks, acute pericarditis, women of childbearing potential, expected survival <6 months, cardiac surgery during the index admission, allergy to aspirin, heparin, warfarin, or pork products, history of recurrent thromboembolic disease, Protein C, S, or antithrombin III deficiency, known bleeding disorder, current use of warfarin, or need for chronic anticoagulation (atrial fibrillation and prosthetic valve). The protocol was approved by the institutional review boards of all sites, and informed consent was obtained from all patients. Patients were randomized (1:1) by telephone once screening was completed.

Patients randomized to enoxaparin received 1 mg/kg (maximum 100 mg) subcutaneously every 12 hours for 1 month. Unfractionated heparin was discontinued before enoxaparin use. In patients randomized to warfarin, heparin was continued until a therapeutic INR was reached (2.0 to 3.0). Oral warfarin was prescribed for 3 months, and INR was monitored every 2 to 4 weeks to maintain a therapeutic level (INR 2.0 to 3.0). All patients received clopidogrel for

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See page 1203 for disclosure information.

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Table 1
Baseline characteristics

| Variable | | Enoxaparin (N=30) | Warfarin (N=30) | Pvalue |
|---|---|---|---|---|
| Age (Years) | | 57±10 | 58±11 | 0.59 |
| Women | | 2 (7%) | 5 (17%) | 0.42 |
| Height (cm) | | 174±8 | 177±10 | 0.17 |
| Weight (kg) | | 89±24 | 94±15 | 0.089 |
| African-American | | 1 (3%) | 3 (10%) | 0.58 |
| Asian | | 2 (7%) | 0 | |
| European-American | | 25 (83%) | 26 (87%) | |
| Hispanic | | 1 (3%) | 1 (3%) | |
| Other | | 1 (3%) | 0 | |
| Hypertension | | 22 (73%) | 15 (52%) | 0.086 |
| Diabetes mellitus | | 6 (20%) | 8 (27%) | 0.54 |
| Peripheral vascular disease | | 0/29 (0%) | 1/29 (4%) | 1.00 |
| Prior myocardial infarction | | 1 (4%) | 6 (20%) | 0.10 |
| Prior percutaneous transluminal coronary angioplasty | | 0/30 | 1/29 (4%) | 0.49 |
| Prior coronary bypass | | 1 (3%) | 0 | 1.00 |
| Current smoker | | 16 (53%) | 16 (53%) | 1.00 |
| Malignancy | | 3 (10%) | 3 (10%) | 1.00 |
| Chronic obstructive Pulmonary disease | | 1 (3%) | 1 (3%) | 1.00 |
| Killip class: | 1 | 27 (90%) | 25 (83%) | 0.59 |
| | 2 | 2 (7%) | 3 (10%) | |
| | 3 | 0 | 2 (7%) | |
| | 4 | 1 (3%) | 0 | |
| Heart rate (lowest) | | 64±10 (61%) | 63±15 (63%) | 0.84 |
| Heart rate (Highest) | | 97±19 (92%) | 96±16 (96%) | 0.89 |
| SBP (lowest) (mmHg) | | 92±18 (94%) | 95±28 (92%) | 0.69 |
| SBP (Highest) (mmHg) | | 146±25 (148%) | 138±21 (139%) | 0.24 |
| Creatinine (mg/dl) | | 1.08±0.25 (1%) | 1.05±0.24 (1%) | 0.55 |
| Reperfusion: - Any | | 29 (97%) | 29 (97%) | 1.00 |
| Lytics | | 8 (27%) | 10 (35%) | 0.40 |
| Percutaneous coronary intervention (with stent) | | 22 (73%) | 24 (83%) | 0.38 |
| Chest pain onset to reperfusion (hours) | | 11.4±15 | 8.9±7.0 | 0.93 |
| Peak creatine phosphokinase (U/L) | | 3517±1919 (3355%) | 3219±1790 (3051%) | 0.50 |

Table 2
Invasive angiographic data

| Variable | Enoxaparin (N=30) | Warfarin (N=30) | Pvalue |
|---|---|---|---|
| Ejection fraction % | 36±6 | 34±10 | 0.34 |
| No. of coronary arteries narrowed: | | | |
| 1 | 13 (43%) | 15 (50%) | 0.098 |
| 2 | 13 (43%) | 6 (20%) | |
| 3 | 4 (13%) | 9 (30%) | |
| Infarct related coronary artery: | | | |
| Left anterior descending: | 28 (93%) | 30 (100%) | |
| Left main: | 1 (3%) | 0 | |
| Saphenous vein graph: | 1 (3%) | 0 | 0.49 |
| Final TIMI-3 flow | (N=29) | (N=30) | 1.00 |
| | 26 (90%) | 27 (90%) | |

Table 3
Clinical outcomes

| | Variable | Enoxaparin (N=30) | Warfarin (N=30) | Pvalue |
|---|---|---|---|---|
| **1 Month** | Died | 0 | 1 (3%) | 1.00 |
| | Any bleed requiring treatment | 1 (3%) | 1 (4%) | 1.00 |
| | Revascularization | 3 (10%) | 1 (4%) | 0.61 |
| | Reinfarction | 1 (3%) | 0 | 1.00 |
| | Stroke or systemic embolization | 0 | 0 | *** |
| **3 Months** | Died | 0 | 1 (4%) | 1.00 |
| | Any bleed requiring treatment | 1 (4%) | 2 (7%) | 1.00 |
| | Revascularization | 6 (21%) | 1 (3%) | 0.052 |
| | Reinfarction | 3 (11%) | 0 | 0.11 |
| | Stroke or systemic embolization | 0 | 0 | *** |

at least 1 month after percutaneous coronary intervention for a bare metal stent, throughout the study duration for drug-eluting stents, and aspirin was continued indefinitely.

Complete blood count was checked for enoxaparin-treated patients at days 14 and 30 and INR as per local protocol (at least monthly) in the warfarin group. Patients were contacted at 1 and 3 months to reconfirm compliance with the study drug and assess bleeding complications and clinical evidence of embolization. Transthoracic echocardiograms were performed at baseline after consent and repeated at 3.5 months after randomization.

All echos were read by the echocardiographic core laboratory by a single reader (PM) blinded to treatment arms. Detection of thrombus at baseline was not a requirement for protocol participation. Thrombi were defined as distinct areas