Anticoagulation After Anterior Myocardial Infarction

*Primum non Nocere, or First Do No Harm*

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Left ventricular (LV) mural thrombus is a common complication of anterior myocardial infarctions (MIs). Although this incidence has significantly decreased with reperfusion therapies, contemporary studies still note LV thrombus in 3% to 15% of anterior MIs treated with percutaneous coronary revascularization (1,2). Furthermore, pooled analyses suggest a more than 5-fold increased risk for systemic embolism with LV thrombus after anterior MI, and anticoagulation therapy is associated with a significant decrease in this embolic risk (3). As such, the 2013 American College of Cardiology Foundation/American Heart Association ST-segment elevation myocardial infarction (STEMI) guidelines recommend anticoagulation for patients with acute MI and asymptomatic LV mural thrombus (Class IIa, Level of Evidence [LOE]: C) (4). Given the increased risk of bleeding with anticoagulation and dual antiplatelet therapy, these guidelines suggest lower international normalized ratio goals (2.0 to 2.5) in this clinical setting (Class IIb, LOE: C).

Anticoagulation after anterior MI with risk factors for mural thrombus formation is much more controversial, as the risk of clinically-significant thromboembolism in contemporary practice is not well understood. Currently, the 2013 American College of Cardiology Foundation/American Heart Association STEMI guidelines state that anticoagulation therapy may be considered for patients with STEMI and anterior apical akinesis or dyskinesis (Class IIb, LOE: C) (4). However, this recommendation is based largely on older studies, and it is unknown if the benefits of anticoagulation outweigh the known bleeding risks in current practice. Triple therapy (aspirin, clopidogrel, and warfarin) after percutaneous coronary intervention (PCI) is associated with a 2- to 5-fold greater risk of major bleeding compared with dual antiplatelet therapy (1,5,6).

There are good reasons to consider anticoagulation after anterior MI. Larger infarctions, anterior locations, and lower ejection fractions are associated with higher rates of mural thrombus formation (2,7,8). In addition, a meta-analysis of 307 patients from 4 studies conducted prior to the use of thrombolytics suggests that anticoagulation decreases the incidence of LV thrombus formation by 68% (3). Furthermore, the risk of ischemic stroke is highest following acute MI, with an incidence of about 1.5% to 3.6% (3,9). This risk is greatest in the first month and is also more common in patients with anterior infarctions and lower ejection fractions (9–11). Importantly, anticoagulation has been shown to reduce the incidence of stroke and mortality after acute MI in randomized studies from the pre-thrombolytic era (12,13).

However, not all studies find a link among anterior MI, LV thrombus, and embolic events. In the thrombolytic era, the low molecular weight heparin dalteparin reduced LV thrombus formation by 37% in 517 randomized patients after anterior acute MI. However, this therapy had no impact on early thromboembolic events (14). Similar findings were echoed in a larger observational study of 2,949 patients, in which anticoagulation failed to reduce the incidence of stroke after anterior MI (10).

The study by Le May et al. (15) published in this issue of JACC: Cardiovascular Interventions builds on these prior observations and reports the outcomes of anticoagulation in 460 STEMI patients with apical

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dysfunction after PCI. This study is important, as it is
the largest study from the PCI era to evaluate anti-
coagulation in this population, and the authors should
be congratulated for investigating a controversial topic
for which the best practice is unknown. In this study,
patients requiring anticoagulation for LV thrombus,
atrial fibrillation, valvular heart disease, or venous
thromboembolism were excluded. The authors found
that anticoagulation was actually associated with an
increased incidence of stroke (3.1% vs. 0.3%, p = 0.02),
major bleeding (8.5% vs. 1.8%, p < 0.0001), mortality
(5.4% vs. 1.5%, p = 0.04), length of stay, and read-
missions. Furthermore, after propensity matching,
anticoagulation was still associated with a 4-fold
greater incidence of net adverse cardiac events. In
multivariable analysis, the odds of net adverse cardiac
events remained higher in patients treated with anti-
cogulation. These findings certainly question the
routine use of triple therapy in this population.

There are limitations to the current analysis. The
study was not randomized, and it is possible that the
outcomes of the study were related to differences
between groups, even after propensity matching. In
addition, the current analysis may not represent
current practice, as several recent studies suggest
that aspirin can often be omitted when anticoa-
gulation is warranted after PCI. In the 573-patient
randomized WOEST (What is the Optimal antiplatElet
and anticoagulant therapy in patients with oral anti-
cogulation and coronary StenTing) trial, omission
of aspirin decreased major bleeding complications
(44.4% vs. 19.4%, p < 0.0001) without any increase in
ischemic events (16). These findings were echoed in a
larger real-world registry of 12,165 patients undergo-
ning PCI requiring anticoagulation (17). Whether the
omission of aspirin would have influenced the results
of the current trial is unknown.

In conclusion, the current study by Le May et al.
(15) warns against the routine use of anticoagulation
in patients with anterior MI with apical dysfunction
without evidence of mural thrombus. Given the
bleeding risks, triple therapy should probably be
avoided in these patients. Whether the combination
of clopidogrel and warfarin without aspirin is more
effective than dual antiplatelet therapy in these pa-
tients is unknown, and randomized studies should
be considered to investigate this strategy. Until such
a trial is conducted, if anticoagulation is used after
anterior MI, clinicians should probably consider
omitting aspirin, adding proton pump inhibitors,
targeting lower international normalized ratio ranges,
shortening the anticoagulation course (3 months),
and using radial access. Furthermore, it should be
noted that the safety of the novel anticoagulant and
antiplatelet therapies in this setting has not been
tested. Ultimately, better risk assessment tools are
needed to guide therapeutic decisions balancing the
risk of LV thrombus formation and thromboembo-
lim with the risk of bleeding.

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