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Clinical Cardiology [ALERT]

Critical analysis of the latest clinical research in cardiovascular medicine

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ABSTRACT & COMMENTARY

Does Anticoagulant Therapy Affect Outcomes in Left Ventricular Mural Thrombus Patients?

By Michael H. Crawford, MD, Editor

SYNOPSIS: Left ventricular thrombus is an uncommon finding but one associated with a high incidence of all-cause mortality and major adverse cardiac and embolic events. Total regression of left ventricular thrombus on anticoagulant therapy reduced mortality.

SOURCE: Lattuca B, Bouziri N, Kerneis M, et al. Antithrombotic therapy for patients with left ventricular mural thrombus. *J Am Coll Cardiol* 2020;75:1676-1685.

Left ventricular thrombus (LVT) can be observed in up to one-quarter of patients with ST-elevation myocardial infarction (STEMI) and one-third of patients with dilated cardiomyopathy using optimal imaging techniques. Although guidelines recommend anticoagulation therapy for LVT, there are few data about the optimal course and type of therapy and its efficacy.

In a large Paris hospital, Lattuca et al conducted a retrospective, observational study of echocardiograms that were performed between 2011 and 2017. On each echocardiogram, two independent experts reported LVT. In discordant cases, another imaging modality, such as contrast echo, computed tomography, or magnetic resonance imaging, was performed. Patients with thrombi in other chambers were excluded. Clinical information, including anticoagulant therapy, was obtained by chart review. The study population consisted of 159 patients (mean age 58 years, 18% women, 79% ischemic etiology, and mean LV ejection fraction 32%). Anticoagulation therapy was administered to 99% of the patients: vitamin K antagonists (VKA) in 48%, direct oral anticoagulants (DOAC) in 23%, low molecular weight heparin in 23%, and unfractionated heparin in 5% for a median duration of 508 days.

Total LVT regression was achieved in 62% at a median time of 103 days. Total LVT regression after multivariate adjustment was associated with smaller

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thrombi (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.45-0.96; *P* = 0.03) and non-ischemic etiology (HR, 2.74; 95% CI, 1.43-5.26; *P* = 0.002). Major adverse cardiac events (MACE) and embolic events occurred in 37% and 22%, respectively. All-cause mortality was 19%, and major bleeding occurred in 30%.

Total LVT regression was associated with fewer deaths (HR, 0.48; 95% CI, 0.23-0.98; *P* = 0.39), whereas persistent LVT was associated with major bleeding (HR, 0.34; 95% CI, 0.14-0.82; *P* = 0.011). MACE occurred more commonly in patients with an LV ejection fraction (EF) ≤ 35% (HR, 0.46; 95% CI, 0.23-0.93; *P* = 0.029) and who were on anticoagulant therapy for less than three months (HR, 0.42; 95% CI, 0.20-0.88; *P* = 0.021). There were fewer embolic events in patients treated with anticoagulant therapy for longer than three months (HR, 0.46; 95% CI, 0.18-1.14; *P* = 0.09). The type of anticoagulant used was not associated with outcomes.

The authors concluded LVT was associated with a high risk of MACE, and LVT regression reduced this risk regardless of the anticoagulation regimen.

■ COMMENTARY

In my experience, the incidence of LVT decreased markedly after the widespread use of reperfusion therapy for acute STEMI. Lattuca et al needed to peruse 90,000 echocardiograms to find 174 potential cases of isolated LVT. Among these, 14 were eliminated because LVT was not confirmed on other imaging modalities, and one was excluded by review with the second reader. This left 159 patients for this study. This investigation did not permit an assessment of prevalence by diagnosis. Most patients had ischemic heart disease, and 35% had experienced a STEMI. Considering the mean EF of 32%, most had a reduced EF. Almost all the thrombi detected were apical, but only 15% had an aneurysm. Interestingly, 35% of the thrombi were mobile.

LVT are a well-known complication of left-sided heart diseases, and were described as far back as 1847 in autopsy studies.[1] Although relatively uncommon today, LVT are associated with an adverse prognosis. In this study, 40% of subjects experienced a cardiovascular event and 20% died over a median follow-up of 1.7 years. These are higher event rates than those seen after a STEMI in general.

Despite its uncommon nature, a LVT is an important finding whose optimal treatment is largely unknown. All major guidelines recommend an echocardiogram in post-MI and cardiomyopathy patients. If a LVT is found, prescribe anticoagulation with a vitamin K antagonist for three to six months. Based on small, observational studies, practitioners often use DOACs.

The Lattuca et al study shows LVT regression, which occurred in two-thirds of their patients, was associated with lower mortality and fewer MACE if treatment was continued for longer than three months. This was at the cost of major bleeding in more than 10% of patients. The efficacy of DOACs was equivalent to vitamin K antagonists, but this study was not powered to answer this question.

The major limitations of the Lattuca et al study were that it was retrospective, observational, and conducted from a single center. Also, contrast echo was not used routinely. I have found contrast echo increases sensitivity for detecting LVT; it should be performed in all post-MI patients and others with low EFs. If a LVT is discovered, my practice is to treat with warfarin (if there are no contraindications) for three months, then re-image. If the LVT is gone, I usually stop anticoagulation; if not, I continue treatment for another three months, and repeat as necessary. A few patients end up on indefinite anticoagulation. Outstanding issues are the role of antiplatelet agents and the comparative efficacy of DOAC, but it is hard to imagine someone conducting a randomized, controlled study of LVT patients. ■

REFERENCE

1. Virchow R. Ueber die akute Entzündung der Arterien. *Archiv f pathol Anat* 1 1847:272-378.

ABSTRACT & COMMENTARY

Warfarin vs. DOAC for Left Ventricular Thrombi

By Michael H. Crawford, MD, Editor

SYNOPSIS: A large, multicenter, observational study of the relative efficacy of warfarin vs. direct oral anticoagulants (DOACs) for left ventricular thrombi has shown that DOAC use is associated with a higher risk of embolic events than warfarin. Investigators advised caution with off-label use of DOACs.

SOURCE: Robinson AA, Trankle CR, Eubanks G, et al. Off-label use of direct oral anticoagulants compared with warfarin for left ventricular thrombi. *JAMA Cardiol* 2020; Apr 22. doi: 10.1001/jamacardio.2020.0652. [Epub ahead of print].

A high degree of patient acceptance has driven off-label use of direct oral anticoagulants (DOACs) for the treatment of left ventricular thrombi (LVT), despite a paucity of supportive data.

In three tertiary care, academic medical centers in Virginia and North Carolina, Robinson et al organized the Retrospective Evaluation of DOACs and Vascular Endpoints of Left Ventricular Thrombi (RED VELVT) observational study. From 2013 to 2019, patients with echocardiographically diagnosed LVT were identified and followed for a median of 351 days (range, 51-866 days). The resulting population consisted of 514 patients (74% men, mean age 58 years), of whom 300 were treated with warfarin and 185 with a direct oral anticoagulant (DOAC). These groups included a mixed group of 64 patients who switched treatment such that there were 236 patients exclusively treated with warfarin and 121 with a DOAC. Most switches were from warfarin to DOAC. Ninety-three patients received no oral anticoagulants, including 43 who received no anticoagulant, oral or parenteral.

There were 54 embolic events: 36 strokes and 18 systemic emboli. After a multivariate analysis, anticoagulant type was significantly associated with embolic events (hazard ratio [HR] for DOAC vs. warfarin, 2.64; 95% confidence interval [CI], 1.28-5.43; $P = 0.01$), as was a history of prior emboli (HR, 2.07; 95% CI, 1.17-3.66; $P = 0.01$). Interestingly, neither thrombus size nor mobility were associated with embolic events. Censoring the follow-up data at three, six, and 12 months did not alter the results. The authors concluded that for the treatment of LVT, DOAC use was associated with a higher risk of embolic events than warfarin, even after adjusting for other clinical factors.

■ COMMENTARY

This was an important study. In three large, academic medical centers over a six-year period, 44% of patients with LVT were treated with DOACs. At the time, these were perhaps reasonable clinical decisions. Patients do not like warfarin, and DOACs have been highly efficacious for preventing embolic events in patients with atrial fibrillation and deep venous thrombosis. Surely, LVT must be a similar blood stasis-related condition. Also, there were several small, observational studies that suggested DOACs were efficacious for LVT. However, those were single-center investigations, with small patient cohorts, shorter follow-up periods, and few embolic events. The Robinson et al study was multicenter, with more than 500 patients and 54 embolic events. Also, patients with LVT actually were contacted; the authors did not rely on chart review alone.

Why these remarkably different results? There are several possible explanations. First, DOACs may be good at preventing thrombus formation, such as atrial fibrillation, but they may not be as efficacious for resolving thrombi. Second, LVT probably involves more than just stasis. There are certainly endothelial injury factors, too, especially in acute myocardial infarction. Third, the authors of prior studies only considered visible thrombus resolution on imaging. Robinson et al focused on clinically reported embolic events. Finally, it is possible that weaknesses in the Robinson et al study biased the study in favor of warfarin.

Regarding weaknesses, this was a retrospective, observational study, which could mean there were unmeasured confounders that biased the results. To the investigators' credit, they conducted extensive sensitivity analyses, and none changed the results.

Still, there was no central review of the echoes. Other imaging results (if any other imaging occurred), were not considered. Transthoracic echo has limited sensitivity for thrombi. Thrombus escape from the LV could not be ascertained. Another reason Robinson et al focused on clinical events is that one-third of their patients did not undergo a follow-up echo. In addition, there was no information on the dosing of DOACs or adherence to this therapy. Almost all the DOACs used were factor Xa inhibitors. Finally, there

was no analysis of bleeding events or other safety information.

Despite these potential limitations, this study was carefully performed. It is the largest to address this issue to date. Also, given the low incidence of LVT, it is doubtful a randomized, controlled trial will be conducted. For now, the off-label use of DOACs for LVT should be undertaken with caution until more data are acquired. Perhaps LVT should be added to the list of conditions for which DOACs are not useful, along with mechanical prosthetic valves. ■

ABSTRACT & COMMENTARY

Benefits of Exercise in Established Atrial Fibrillation

By Michael H. Crawford, MD, Editor

SYNOPSIS: A large, long-term, prospective, Norwegian population study of patients with established atrial fibrillation revealed physical activity at or above recommended levels reduces all-cause and cardiovascular mortality vs. atrial fibrillation patients who are inactive.

SOURCE: Garnvik LE, Malmo V, Janszky I, et al. Physical activity, cardiorespiratory fitness, and cardiovascular outcomes in individuals with atrial fibrillation: The HUNT study. *Eur Heart J* 2020;41:1467-1475.

Persistent atrial fibrillation (AF) is associated with higher rates of morbidity and mortality. When AF accompanies almost every other disease, the prognosis is much worse. Physical activity (PA) is known to reduce the incidence of AF, but little is known about its value in established AF.

Garnvik et al evaluated data from the third wave of the Nord-Trøndelag Health Study (HUNT 3) from the northern region of Norway. Their goal was to assess the effect of PA and cardiorespiratory fitness (CRF) on all-cause mortality as well as cardiovascular (CV) mortality and morbidity in patients with documented AF and those free of AF. Clinical data were obtained from hospital and physician office records using standard criteria. Information on PA was obtained using a validated questionnaire, with details about frequency, intensity, and duration of exercise. Patients were classified as inactive, below recommended exercise levels, or at/above recommended exercise levels. CRF was estimated using a validated non-exercise method based on sex, age, waist circumference, resting heart rate, and PA. Patients in HUNT 3 were enrolled between 2006 and 2008 and followed until death, their first CV event, or 2015. Data analysis was adjusted for multiple clinical variables that could influence the results.

From 50,802 participants in HUNT 3, 1,117 with AF not related to an acute stressful event and with complete data were included. Approximately two-thirds of the study population were men (average age about 70 years; about 60% had persistent or permanent AF). AF patients meeting recommended PA levels recorded a significantly lower all-cause mortality rate than inactive patients (hazard ratio [HR], 0.55; 95% confidence interval [CI], 0.81-0.95), as did those with highest CRF levels vs. the lowest quartile (HR, 0.64; 95% CI, 0.47-0.89). CV mortality also was significantly lower in patients in the meeting or exceeding recommendations vs. inactive patients (HR, 0.54; 95% CI, 0.34-0.86) and those in the highest vs. lowest CRF quartile (HR, 0.61; 95% CI, 0.38-0.98).

CV morbidity and stroke rates were lower in patients at or above the recommended PA level and in those with higher CRF. CV mortality also was lowest with patients on moderate-intensity exercise vs. inactive patients (HR, 0.50) and vigorous activity vs. inactivity (HR, 0.70). AF patients who met recommended PA experienced similar rates of all-cause mortality, CV mortality, and stroke as inactive, non-AF patients. Sensitivity analyses showed the benefits of PA were not significant in obese patients (body mass index > 30 mg/kg^2). Men benefitted more from higher CRF than women. The authors concluded that higher PA and CRF reduced the long-term risk of all-cause and CV mortality in patients with AF.

■ COMMENTARY

The health benefits of PA and enhanced CRF has been shown in healthy populations and certain disease states (e.g., post-myocardial infarction). Also, recent studies have shown PA and CRF can prevent AF, but there are few data about their effects on established AF. Nevertheless, this is important because the symptoms of AF, medications used, and comorbidities often discourage patients from exercising. That is why this study is of interest. Norway would seem to be ideal for a study like the one Garnvik et al conducted. One might expect

the prevalence of AF to be high since the genetic component of AF is most common in those of Northern European descent. Additionally, Norway's national health system mandates the reporting of patient outcomes. Finally, Norwegians seem to enjoy participating in such studies because > 50% of the entire population of Nord-Trøndelag County participated in the HUNT 3 investigation. Other strengths of the Garnvik et al study included the prospective design and the long-term follow-up of about eight years. Finally, the diagnosis of AF was well validated.

There were several limitations, most importantly the association between PA/CRF and lower all-cause and CV mortality rates does not confirm causality, nor does it elucidate the mechanism of any potential benefits observed. AF may just be a marker for cardiovascular disease. Also, it is unclear whether the PA reported was occurring before or after the AF diagnosis. PA may just be a continuation of a patient's routine. Thus, prescribing exercise to a sedentary patient may not be effective. Other limitations included the fact that PA was self-reported and CRF was estimated rather than measured. The formula to estimate CRF includes resting heart rate, which could be problematic in AF. The authors did not report any data on medications or the progression of AF over time. The low rate in women, about one-third of the study population, is concerning as this would not be expected.

Despite these limitations, the results of this study support a role for regular PA and improved CRF in AF patients to help prevent the reported higher incidence of morbidity and mortality. Those AF patients who engaged in the most strenuous PA/CRF recorded event-free survival curves that approximated the inactive members of the non-AF general population. ■

ABSTRACT & COMMENTARY

Thin Evidence Supporting the Obesity Paradox in STEMI

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco; Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

Dr. Zimmet reports no financial relationships relevant to this field of study.

SYNOPSIS: This largest-to-date analysis of six randomized studies of ST-elevation myocardial infarction revealed no association between body mass index and infarct size, one-year mortality, or heart failure hospitalization.

SOURCE: Shahim B, Redfors B, Chen S, et al. BMI, infarct size, and clinical outcomes following primary PCI: Patient-level analysis from 6 randomized trials. *JACC Cardiovasc Interv* 2020;13:965-972.

The "obesity paradox" refers to the observation that although obesity contributes to many risk factors that make cardiovascular disease more likely, obese people may fare better than their normal weight counterparts in acute exacerbations of disease, such as acute myocardial infarction (MI). In ST-elevation MI (STEMI) in particular, the evidence in this area has been mixed. Yet a host of data have been built up supporting the putative obesity advantage. Some, but not all, prior studies have revealed smaller infarct sizes among overweight patients. Experimental models have demonstrated the ability of hormones produced by adipose tissue to reduce infarct size in mice.

To examine this question, Shahim et al combined patient-level data from six contemporary randomized trials of patients receiving primary percutaneous coronary intervention (PCI) for STEMI. The authors of each trial measured infarct size at a median of four days after an event, with five using cardiovascular magnetic resonance (MR) and one using 99mTc-sestamibi SPECT/CT. All collected data on body mass index (BMI), and each reported clinical endpoints that were adjudicated by independent clinical events committees.

Among the six trials, data were available for 2,238 patients with STEMI undergoing primary PCI. Analyses were performed using BMI as a continuous variable and with patients stratified according to the World Health Organization (WHO) definitions of normal weight, overweight, and obese. Among the patients analyzed for the study, 658 were classified as normal weight, 1,008 were overweight, and 586 were obese. Regarding baseline characteristics, overweight

and obese patients were more likely than normal weight patients to have diabetes, hypertension, and hyperlipidemia, but were less likely to smoke. No significant differences were seen among the BMI groups when it came to presentation of the acute MI itself.

Regardless of whether BMI was treated as a continuous variable or a categorical one, Shahim et al found no association between BMI and infarct size, microvascular obstruction, or ejection fraction (EF). During a median follow-up of 350 days, there was no unadjusted or adjusted association between BMI and the rates of death or heart failure hospitalization. Similarly, when stratified by WHO classification, these outcomes were similar among normal, overweight, and obese individuals. The authors concluded that among patients undergoing primary PCI for STEMI, there was no protective effect of increased BMI on infarct size, microvascular obstruction, EF, or one-year rates of death and heart failure hospitalization.

■ COMMENTARY

In several ways, this study was specific, dealing only with STEMI patients undergoing primary PCI and weighted toward anterior infarct and larger infarcts. Unfortunately, there was no insight regarding procedural complications, which elsewhere have been observed less often in overweight patients. By design, patients with poor early outcomes who did not make it to imaging evaluation were excluded from the analysis.

The authors acknowledged BMI is a highly imperfect measure of obesity, and that other measures, such as waist circumference and fat mass index, may be relatively advantageous. Regardless, this was by far the largest study to date of the relationships between obesity (as measured by BMI) and infarct size and hard clinical outcomes after STEMI. Most of the 2,238 subjects were evaluated by cardiac MR, which is likely the best modality for this evaluation. Three prior reports that used cardiac MR for infarct size included 89, 193, and 426 patients. Overall, Shahim et al conducted an excellent study. Their work represents the best effort to date to provide a definitive conclusion on this issue. For now, the best available evidence suggests overweight and obese patients have no advantage in terms of outcomes in STEMI — but no detriment, either. In this regard, the obesity paradox remains a point for discussion. ■

ABSTRACT & COMMENTARY

MUCH Ado About WUCH

By Michael H. Crawford, MD, Editor

SYNOPSIS: In a long-term, fixed-drug therapy of hypertension study, masked uncontrolled and white coat uncontrolled hypertension exhibited poor reproducibility over four years. This calls into question studies showing higher rates of adverse outcomes with one baseline blood pressure assessment used to categorize patients.

SOURCE: Mancia G, Facchetti R, Cuspidi C, et al. Limited reproducibility of MUCH and WUCH: Evidence from the ELSA study. *Eur Heart J* 2020;41:1565-1571.

Recent outcome studies of hypertension management have focused on masked uncontrolled hypertension (MUCH), where only office blood pressure (BP) is controlled (not home BP), and white coat uncontrolled hypertension (WUCH), where only home BP is controlled. In some studies, both have shown an increase in cardiovascular outcomes. The authors of these studies almost always only measured ambulatory BP once. Thus, the long-term reproducibility of MUCH and WUCH is unclear.

Accordingly, Mancia et al interrogated the European Lacidipine Study on Atherosclerosis (ELSA), a comparison of the effect of a calcium channel blocker to a beta-blocker on carotid intima-media thickness (CIMT) over an average of four years. The authors examined the annual assessments of office and ambulatory BP measurements for the stability of MUCH and WUCH. Only patients with at least two annual measurements were included, resulting in 1,664 subjects studied. At baseline, the prevalence of patients with white coat hypertension was 13%. After one year of treatment, the prevalence of MUCH was 18%, WUCH 21%, and controlled hypertension 45%. These relative prevalences remained constant throughout the four-year study, but there were large shifts of patients from one category to another. Only 34-41% of MUCH patients maintained this classification one or more years later, while 38-45% of WUCH patients maintained this classification. Controlled hypertension (office and ambulatory) was more consistent (46-57% persistence), as was uncontrolled hypertension (61-68%). The most common category shift for MUCH patients was to uncontrolled hypertension. Few patients among

918 with complete datasets with MUCH or WUCH maintained these classifications throughout (5% and 6%, respectively). These properties did not vary with the type of randomized treatment. The authors concluded that both MUCH and WUCH exhibit poor reproducibility over time on a constant drug regimen. This calls into question the prognostic value of these classifications if measured only once.

■ COMMENTARY

The original definition of masked and white coat hypertension came from observations in untreated patients. Outcome studies demonstrated that white coat hypertension was associated with persistent hypertension later in life. However, long-term outcomes are unclear, as is whether white coat hypertension needs to be treated pharmacologically. Masked hypertension has been associated with a higher risk of sustained hypertension, diabetes, and organ damage, which is almost as high as sustained hypertension. Masked hypertension is common. The incidence in the Hypertension Optimal Treatment (HOT) study was 25%; in the Spanish hypertension registry, it was 30%. Mancia et al recorded a rate of 18%. Also, masked hypertension has been reported in up to 16% of presumably healthy individuals, especially young people with borderline office blood pressures. However, the effect of pharmacologic treatment of isolated masked hypertension is unclear. The Mancia et al study takes these concepts into a pharmacologic hypertension treatment trial, which concerned the comparative effects of two classes of drugs on atherosclerosis measured by CIMT. The patients were put on fixed doses of lacidipine or atenolol for four years without regard for blood pressure control after the initial titration phase to a diastolic BP < 95 mmHg. This created an opportunity to study the reproducibility of MUCH and WUCH independent of drug therapy. Mancia et al demonstrated poor reproducibility of both, which was independent of the drug therapy. Patients with completely controlled or completely uncontrolled hypertension demonstrated significantly better reproducibility. Other shorter studies with measurements in two-month intervals have shown better reproducibility of these four subgroups. Hypertension is a long game, so clinicians need long-term reproducibility to assess outcomes. In MUCH patients, the most common category change was to completely uncontrolled. Considering the poor outcomes reported in other studies, it would seem that MUCH should be treated. It is less clear what to do with WUCH.

One of the strengths of the Mancia et al study was the use of standardized office and high-quality ambulatory BP measurements rather than home BP. However, other studies have shown the variability in ambulatory BP measurements is high. Weaknesses of this study included the lack of data on drug adherence and annual measurements of BP rather than more frequent assessments. Also, the authors reported no outcome data, probably because there were few events in ELSA. Pending future research, it seems patients who report high home BPs (but who record normal office BP) would be ideal candidates for ambulatory BP studies during therapy. ■

CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. **A retrospective observational study of left ventricular thrombus showed that complete regression on anticoagulant therapy is more likely in:**
   a. non-ischemic etiology.
   b. lack of an aneurysm.
   c. mobile thrombi.
   d. large thrombi.

2. **A large, multicenter, observational study of warfarin vs. direct oral anticoagulants (DOACs) for the treatment of left ventricular thrombi showed a higher incidence of embolic events with:**
   a. large thrombi.
   b. mobile thrombi.
   c. DOAC use.
   d. ischemic etiology.

3. **The obesity paradox in ST-elevation myocardial infarction patients refers to:**
   a. more capillary flow to the infarcted area.
   b. a lower incidence of MI.
   c. more atherogenic comorbidities.
   d. reduced infarct size.

4. **In serial studies that were conducted over four years, the reproducibility of white coat and masked uncontrolled hypertension was:**
   a. equivalent to completely uncontrolled hypertension.
   b. equivalent to completely controlled hypertension.
   c. better in men than women.
   d. poor.

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss the most current information related to cardiac illness and the treatment of cardiac disease;
- explain the advantages and disadvantages, as well as possible complications, of interventions to treat cardiac illness;
- discuss the advantages, disadvantages, and cost-effectiveness of new and traditional diagnostic tests in the treatment of cardiac illness; and
- discuss current data regarding outpatient care of cardiac patients.