

Effect of Left Ventricular Systolic Dysfunction on Response to Warfarin

Background:

- Patients on chronic warfarin therapy are often also found to have co-morbid conditions such as heart failure.
- Correlation has been shown between risk of over anticoagulation and presence of heart failure due to lower warfarin dose requirement in heart failure.
- No studies have evaluated warfarin response in patients with left-ventricular systolic dysfunction (LVEF <40%).

Objective:

- To assess the effect of LVSD on warfarin dose requirement, anticoagulation control, and risk of over-anticoagulation and major hemorrhage.

Methods:

- Prospective cohort
- Duration was 2 years or shorter if therapy did not last 2 years
- Inclusion criteria: patients initiating warfarin therapy at a clinic approved by IRBs at UAB and Emory. Exclusion criteria not mentioned.
- 1,497 patients enrolled, 143 excluded from analysis due to missing LVEF data
- Dose calculated as average warfarin dose needed to maintain INR 2-3
- Outcome measures: warfarin dose (mg/day), percent time in target range 2-3, risk of over-anticoagulation, and risk of hemorrhagic complications

Results:

- 1,354 patients completed study (1,140 in nonLVSD and 214 in LVSD group)
- Patients with LVSD had lower dose requirement than those without (4.9mg/day vs. 5.9mg/day), and an 11% lower daily dose requirement after adjusting for variants known to affect warfarin dose. PTTR was similar among those with LVSD and those without (51% vs. 53%) and remained unchanged after accounting for variants. Patients with LVSD were not at increased risk of over-anticoagulation, even after adjusting for variants (INR >4; HR 1.01, 95% CI 0.82-1.25; p=0.91). The incidence of hemorrhage was similar between those with LVSD and those without (9.3/100p-yrs vs. 8.4/100p-yrs; IRR = 1.10; 95% CI 0.72-1.64; p=0.63).
- Authors: patients with LVSD require lower doses of warfarin

Strengths:

- The authors acknowledged their lack of hepatic function data and inability to conclude that cardio-hepatic syndrome is a possible mechanism for the lower warfarin dose requirement.
- No dropouts

Limitations:

- Linear interpolation method to assess PTTR – not an accurate measure

- PTTR values were 51% and 53% - poor INR control
- No criteria established for major bleeding events
- Antiplatelet therapy excluded from list of significant predictors of warfarin dose
- No power
- 11% lower daily dose not clinically meaningful
- No hepatic function data
- Vitamin K intake self-reported and averaged

Conclusion:

- An 11% reduction in daily dose is insignificant, as a normal dose change is 10-20% of the total weekly dose.
- Due to the issues with data handling, the absence of hepatic function data, and the minimally significant 11% difference in warfarin dose that was found in the study, these results have little clinical value.
- Further study needs to be done with more accurate data handling methods and hepatic function screening.

Reference:

Ather S, Shendre A, Beasley TM, Brown T, Hill CE, Prabhu SD, et al. Effect of Left Ventricular Systolic Dysfunction on Response to Warfarin. *Am J Cardiol.* 2016;118:232-236.