

Background:

71 yo female p/w Chest Pain. Pt transferred to UNC for R/O Aortic Dissection. On TEE, Pt found to have Aortic Vegetation with Moderate MR and AR. Pt diagnosed with Endocarditis and Blood Cultures taken. Antibiotics held as patient appears stable and standard of care is to repeat Blood Cultures times 3. Pt abruptly decompensates overnight and dies in the morning. First set of Blood Cultures grows *Moraxella catarrhalis*: universally fatal variant of Endocarditis.

Questions from AM Report:

- 1) In patients with Endocarditis, what is the difference in morbidity and/or mortality between waiting to give antibiotics after one or three cultures?
NO STUDIES DONE
- 2) In patients with Endocarditis and moderate regurgitation, does early surgical intervention prevent excess morbidity and/or mortality?
NO STUDIES AVAILABLE
- 3) In patients with Endocarditis and septic emboli, does Heparin do harm?

Study: Tornos P. et al. "Infective Endocarditis due to *Staphylococcus aureus*: Deleterious effect of anticoagulant therapy." Archives of Internal Medicine. 1999; 159:473-475.

Design: Cohort Study

Setting: University Hospital in Barcelona, Spain

Patients: 56 patients with left-sided endocarditis with positive blood cultures for *S. aureus* diagnosed in the departments of medicine or cardiology or diagnosed by necropsy.

Set-Up: Clinical and demographic data was collected prospectively over a course of 22 years for all patients who met clinical or echocardiographic criteria for infective endocarditis (IE).

Results: Of the 56 patients, 35 had native valve IE and 21 had prosthetic valve IE. No native valve patients were found to be on any form of anticoagulation. Of the 21 prosthetic valve patients, 19 patients were orally anticoagulated. In the native valve population, 11 patients had central nervous system events. 7 of these were ischemic strokes with only 1 hemorrhagic conversion. In the prosthetic valve population, 12 patients had CNS events. 11 of these patients either had a hemorrhagic stroke or an ischemic stroke that then converted. All 11 patients proceeded to die due to their CNS event, while none died due to CNS events in the native valve cohort.

Patients with left-sided endocarditis		
36 of 56 patients with all-types of embolic events		
Valve type	22 native (0 anticoagulated)	14 prosthetic (13 anticoag)
CNS Events	11	12
Hemorrhagic Events	1	11
Deaths	0	11

Author's Conclusions:

“It seems wise to suggest that as soon as the clinical diagnosis of IE due to S aureus is indicated, even before an ischemic stroke is diagnosed, anticoagulant therapy should be immediately stopped until the septic phase of the disease, which usually lasts a few days, is overcome...The recommendation to stop anticoagulant therapy seems to be even stronger in those patients who have developed features of ischemic stroke, in whom the risk of hemorrhagic transformation is high, and in whom such a measure might modify a poor prognosis.”

Assessment of Study:

Are the results of the study valid?

1. *Were there clearly identified comparison groups that were similar with respect to important determinants of outcome, other than the one of interest?* **NO.** The authors freely compare patients with native and prosthetic valve endocarditis. These two entities likely have different risks of embolism, especially in the presence of anticoagulation.
2. *Were the outcomes and exposures measured in the same way in the groups being compared?* **YES.** Both groups had the same data acquisition/review.
3. *Was follow-up sufficiently long and complete?* **YES.** The study mainly looks at in-hospital mortality and patients were evaluated throughout their stay.
4. *Is the temporal relationship correct?* **YES.** Patients with anticoagulation either presented with hemorrhagic stroke or showed conversion in 48 hours.
5. *Is there a dose-response gradient?* **N/A.** Though it is important to note that all patients on anticoagulation were not shown to be supra-therapeutic/overanticoagulated on heparin.

What are the results?

1. *How strong is the association between exposure and outcome?* The association appears strong, as 57.9% of anticoagulated patients (11/19) had a hemorrhagic CNS event, assuming the valves play no role.
2. *How precise is the estimate of risk?* The authors themselves do not compute a relative risk or number-needed to harm. These values are:

	% heparin	% no heparin	RR	AR	NNH
Hemorrhagic Stroke	57.9	2.7	21.4	.552	1.8

Will the results help me in caring for my patients?

1. *Are the results applicable to my practice?* **YES.** The patient population was taken from a university hospital.
2. *What is the magnitude of the risk?* Significant, as 11/12 (92%) patients who had a hemorrhagic stroke, in this study, died.
3. *Should I attempt to stop exposure?* What about the other 13 embolic events?