

Utility of Hypercoagulable Work-up in Predicting Post-Operative Complications in Total Artificial Heart (TAH) Implant Patients at Cedars-Sinai Medical Center

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Aim

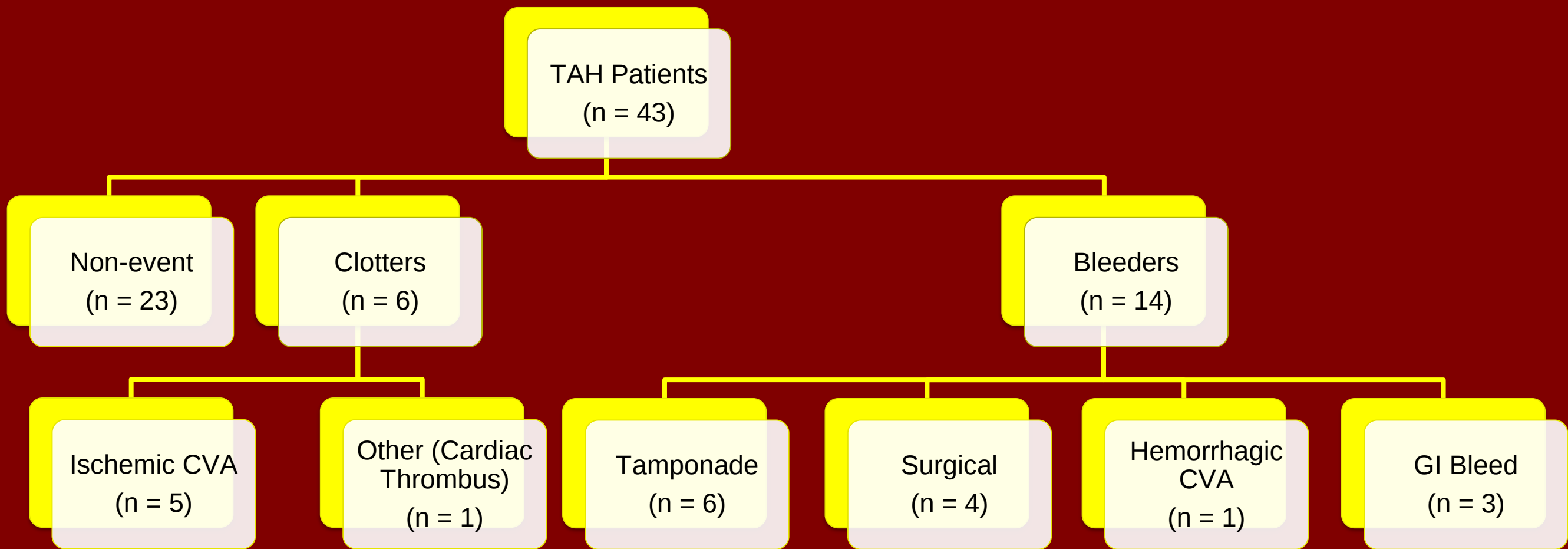
- The purpose of this study was to assess the predictability of the hemostasis baseline pre-operative workup and thromboelastography-platelet mapping (TEG-PM) parameters with the development of hematological adverse events within 30 days, after TAH implantation.

Background

- Circulatory support devices such as TAH have increasingly become a common treatment for end stage heart failure patients as a bridge to transplant or destination therapy (investigational).
- Hematologic complications such as thrombotic and bleeding events remain clinical challenges in managing patients requiring these devices.
- Despite antithrombotic prophylactic therapy for the prevention of post implant thromboembolic stroke, the thrombotic causes of adverse events and death remain virtually unknown.
- A comprehensive pre-operative hemostasis workup has been implemented, including TEG-PM pre-operatively and TEG-PM post-operatively to guide therapy and to assess hemostasis.

Methods

- This study evaluated patients implanted with TAH (n=55) from 01/2012 to 06/2017.
- Inclusion Criteria:** TAH patients with baseline, postoperative TEG-PM tracings and pre-operative laboratory work up (43 patients).
- Exclusion Criteria:** Patients with limited or no TEG/thrombophilia (10 patients) or were unable to consent (2 patients) were excluded.
- Additionally, inherited and acquired risk factors associated with hematologic complications such as INTERMAC profile, pump time during device implantation, blood pressure, INR, aPTT, presence of active infection, and history of diabetes were recorded.



Results

TEG-PM Tracings and Parameters

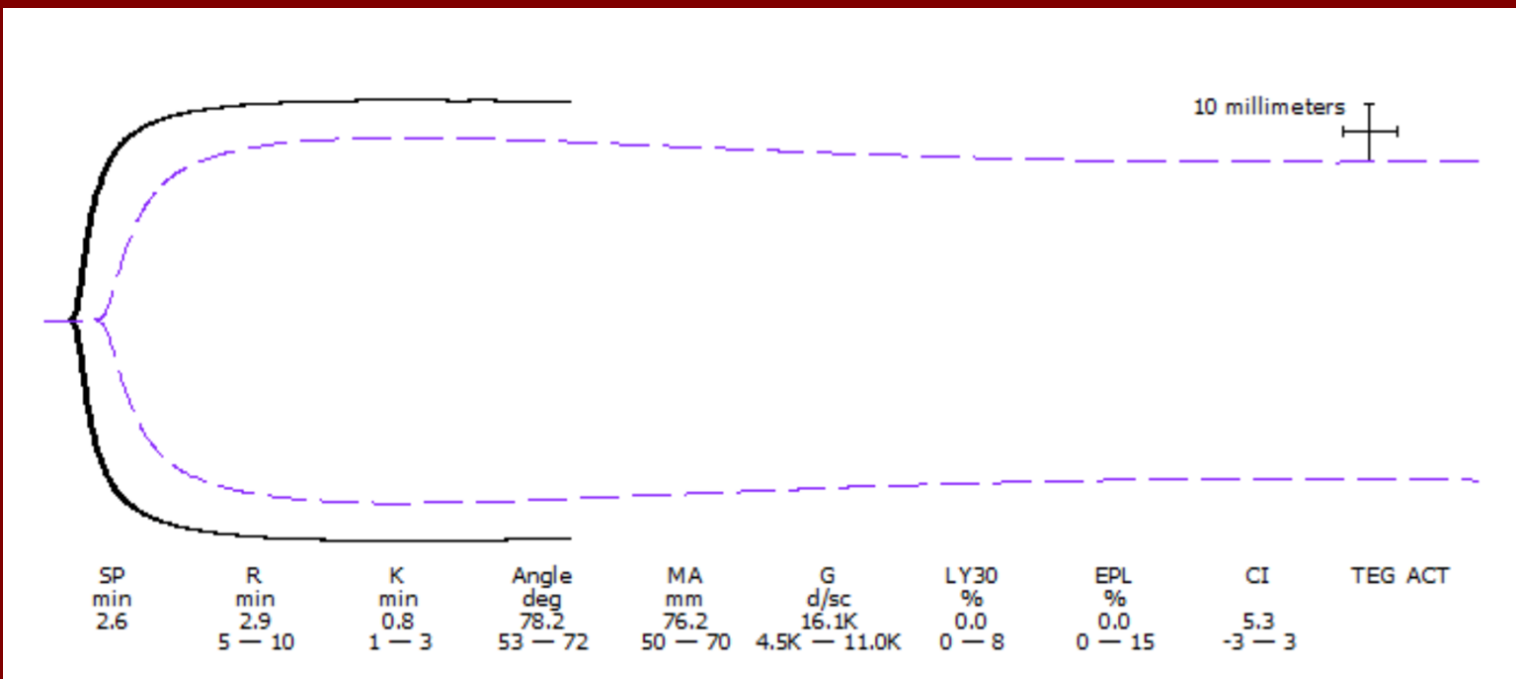


Figure 1. Thrombin Generated TEG-PM Tracings and Parameters:

TEG-PM coagulation index (CI) appeared to be the single most statistically significant parameter that can be used to designate a patient as normocoagulable. Patients with TAH devices recommend to be maintained at CI $\leq$ 1.2

Table 1. Thrombophilia Risk Factors

Thrombophilia Work-up	Non-event Group	Clotters	Bleeders	Association with Event (Y/N)
Lupus Anticoagulant (patients)	Pos*: 11/23 (48%) Neg: 6/23 (28%) N/A: 6	Pos: 2/6 (33%) Neg: 4/6 (67%)	Pos: 3/14 (21%) Neg: 8/14 (57%) N/A: 3	N Overall 16/42 (37%) pos
Antiphospholipid Antibodies (patients)	Pos: 5 (22%)	Pos: 4 (67%)	Pos: 4 (29%)	N
Other (patients)	FVL [†] pos: 1	Low ATIII: 1	FVL [†] pos: 1	N

•Data represented as median (range).

*Positive

[†]Factor V Leiden mutation

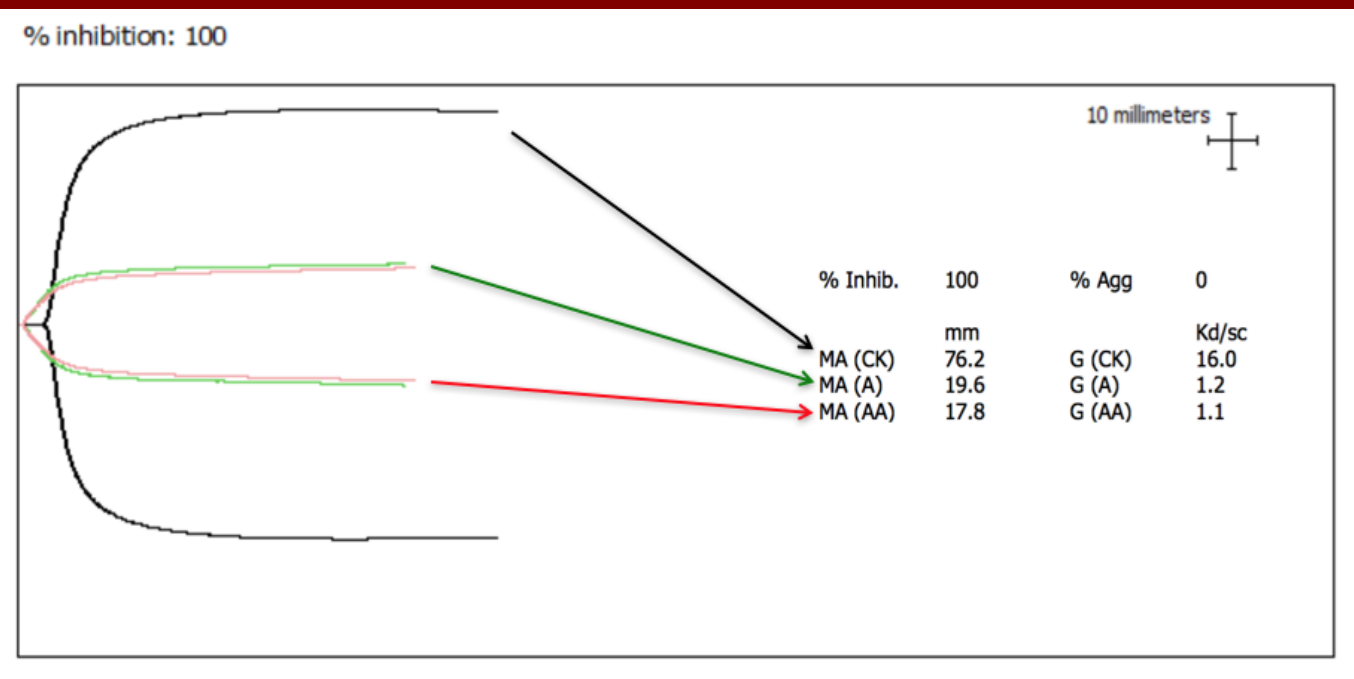


Figure 2. TEG® PM Tracing and Parameters:

MA-CK, baseline tracing; MA-A, activator tracing (fibrin clot only); MA-AA, residual activity of platelets inhibited by aspirin

Results (Continued)

Table 2. General Risk Factors

Risk Factors	Non-Event	Clotters	Bleeders	Association w/ event (Y/N)
Prior Short-Term Device	3.1 days (1-6 days) = 7/23 patients (30.4%)	3 days (1-5 days) = 3/6 patients (50%)	4 days (3-5 days) = 2/14 patients (14%)	N
Pump Time (minutes)	188 (109-243)	187.5 (156-322)	178 (106-257)	N
INTERMAC Profile (patients)	I: 8 II: 7 III: 2 IV: 2 N/A: 4	I: 3 II: 0 III: 1 IV: 2 N/A: 0	I: 2 II: 7 III: 0 IV: 2 N/A: 0	N
BMI	25.7 (19.3-40.2)	26.7 (22.8-31.7)	26 (19.2-38.7)	N
Blood Pressure	N/A	Not elevated Median: 113/64	N/A	N
Hx DM (patients)	6/23 (26%)	2/6 (33%)	4/14 (29%)	N
INR at event time	N/A	1.3 (1.2-1.8)	1.4 (1.1-2.1)	Y = Clotters N = Bleeders
LDH (patients)	N/A	Elevated: 3 Not available: 3	N/A	
Active Infection (patients)	8/23 (35%) *Within 30 days	4/6 (67%) *Around time of implantation	5/14 (36%) *Around time of implantation	Y—High rate of post-operative infection overall (40%)
HIT	16/23 negative 7 not tested	6/6 negative	11/14 negative 3 not tested	N
#Days on device	186 (6-831)	27 (10-66)	88 (12-511)	N
PTT	N/A	N/A	36 (25-95)	

Table 3. TEG-PM Parameters

	Baseline TEG Parameters			Post-Device Implantation		
	Non-event (n=23)	Clotters (n=6)	Bleeders (n=14)	Non-event (n=23)	Clotters (n=6)	Bleeders (n=14)
MA	66.6±8.2	64.1±8.3	64.8±7.9	73.1±13.8	72.8±4.9	69.1±5.2
MAAA	47.2±23.2	60.7±11.5	55.3±21.4	50.9±16.7	43.2±13.3	47.6±12.7
MAADP	41.3±18.8	54.7±10.4	59.0±22.0	47.6±17.8	47.4±9.3	46.6±17.1
CI	0.6±2.8	2.3±3.0	0.8±2.9	1.9±3.2	2.3±1.0	0.9±1.3
INR				1.4±0.6	1.3±0.2	

- See Figure 1 for TEG description and parameters.
- TEG within 3 days of the thrombotic event vs non-event within 10 days were compared.
- Not statistically but clinically significant baseline CI in the clotters group was higher (hypercoagulable) compared to non-events (P = 0.19).
- Not statistically but clinically significant event CI in the clotters group was higher compared to non-events (P = 0.22).
- R non-events were higher compared to the R clotters group.

Discussion

- Hematologic events occurred on average 5.5 days after implantation for thrombotic events and 7.5 days after for bleeding events, indicating a necessity for early adequate anticoagulation therapy.
- Comprehensive pre-operative hemostasis workup did not reveal inherited thrombophilia risk factors associated with adverse events.
- Of all hypercoagulable work-up, lupus anticoagulant (LA) appears to be the most important factor, as it can interfere anticoagulation management.
- Infection may contribute to the incidence of clotting and bleeding events.
- Baseline TEG (CI) can identify patients who would be at risk for post-device implantation events.

Summary

- This study supports a targeted, rather than comprehensive, pre-operative screening work-up, that would also include baseline TEG analysis and lupus anticoagulant.
- The serial TEG-PM (CI) can identify patients with suboptimal anticoagulation early in therapy as it appears to play the most important role during this critical period.
- Results of this study will be considered for quality assurance of the current hypercoagulable work-up protocol, as well as for optimizing appropriate anticoagulation strategies in the immediate post-operative period for MCS patients and minimizing healthcare costs by reducing ordering of unnecessary laboratory work-up.

References

- Volod O, Lam L, Lin G, et al. Role of Thromboelastography During Platelet Mapping (TEG PM) and International Normalized Ratio (INR) in Defining "Normocoagulability" Anticoagulation for Mechanical Circulatory Support (MCS) Devices: A Pilot Retrospective Study. ASAIO J 2016; 2016 Sep 20.