Title

A Multicenter Randomized Placebo-Controlled Trial of Intravenous Thyroxine for Heart-Eligible Brain Dead Organ Donors

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APPENDIX A: Study Forms

Document Date: 01 December 2020

A Multi-OPO Randomized Control Trial of T4 vs Placebo **Screening Worksheet #1**

To be filled out on EVERY Brain-dead donor

OPO: _____

Donor UNOS #: _____

Date: ____ / ____ / 20____ (mm/dd/yyyy)

Inclusion Criteria: (Must have *ALL 4* inclusion criteria)

1. _____ Declared dead by neurologic criteria
2. _____ Authorization for organ donation and research
3. _____ Donor age 14-55 years inclusive, and weight ≥ 45 kg (100 lbs.)
4. _____ Must be on 1 or more of the following vasopressors and/or inotropes at the start of the study:
    a. _____ norepinephrine
    b. _____ epinephrine
    c. _____ neosynephrine
    d. _____ dopamine
    e. _____ dobutamine
    f. _____ milrinone

Exclusion Criteria: (Must *NOT* have any exclusion criteria)

1. _____ Brain-death declared >24 hours ago
2. _____ CAD or MI (by hx, EKG, or previous cardiac cath) that would exclude transplantation
3. _____ Significant valvular heart disease (by hx or echo) that would exclude transplantation
4. _____ Previous sternotomy or cardiac surgery
5. _____ Donor is in a VA hospital
6. _____ Received IV or po T4/T3 in the last month (including home medication)
7. _____ Known HIV+ serology
8. _____ Other reason:_____

*****If the donor has all 4 inclusion criteria and no exclusion criteria, he/she is eligible for the study and should be randomized to either T4 or NS, and the infusion should be started as soon as possible.*****

☐ **ELIGIBLE** (go to worksheet) ☐ **NOT ELIGIBLE – STOP!**

All worksheets are to be submitted to the OPO research coordinator

Revised 10/22/2020

Worksheet #2

Multi-OPO Randomized Control Trial of T4 vs Placebo Data Collection Worksheet

UNOS number: _____ (revised 11/5/2020)

OPO: _____

1. Admission to the hospital: Date: ____ / ____ / 20____; Time: ____:____ (all times in 24:00)
2. Brain Death: Date: ____ /____ / 20____; Time: ____:____

Go to Sharepoint, **Multi-OPO T4 RCT randomization sheet** to identify the next randomization.

3. Randomized to: ☐ **T4** ☐ **NS**

Draw ***free T4, TSH prior to starting T4 / NS infusion.

4a. Baseline results before starting T4 or saline: Weight _____ kg

4b. Vent settings: f _____ Vt _____ cc FiO2 _____ PEEP _____ PaO2 _____

Labs: (most recent before starting protocol) [enter 999 if data not available]

c. Highest Troponin I (before starting protocol) _____ ng/ml
d. ALT _____
e. AST _____
f. Bilirubin _____
g. Creatinine _____ BUN _____
h. Amylase _____
i. INR _____
j. Calcium (total) _____ *or* k. Calcium (ionized) _____

5. T4 or NS started: Date: ____ /____ / 20____; Time: ____:____

   (needs to be started within 24 hours of brain-death declaration)

6. T4 rate: 30mcg/hr [500 mcg/ 500 cc NS at 30 cc/hr = 30 mcg/hr]
   a. Was T4 started at 30 mcg/hr Yes ____ No ____
   b. If No, what was the reason: _____

7. NS rate 30 cc/hr [should be equal to the normal T4 dose, i.e. 30 cc/hr] *The donor may be on additional IV fluids as needed, but needs to have a separate IV of NS @ 30 cc/hr to match the fluid intake with the T4 protocol.*
    a. Was NS started at 30 cc/hr? Yes ____ No ____
    b. If No, what was the reason: _____

*** *Please fill out the Multi-OPO RCT T4 Vasopressor Flow Sheet #3.* ***

__The only allowed doses of T4 are 30 mcg/hr, 20 mcg/hr, 10 mcg/hr__. Decrease the dose by 10 mcg/hr, if a lower dose is needed.

8. Was the T4 dose <u>decreased</u> before 12 hours? Yes ____ No ____
   If Yes, what was the reason? (check all that apply)
    a. ____Tachycardia (HR increased more than 20 bpm over baseline and is > 120 bpm)
    b. ____Hypertension (Systolic BP increased >30 mmHg and is >180 mmHg)
    c. ____Arrhythmia: ____ a fib/flutter; _____ SVT; _____ V tach; _____ PVCs(>6/min)
    d. ____Other: _____

9. Was the T4 dose <u>stopped</u> before 12 hours? Yes ____ No ____
   If Yes, what was the reason? (check all that apply)
    a. ____Tachycardia (HR increased more than 20 bpm over baseline and is > 120 bpm)
    b. ____Hypertension (Systolic BP increased >30 mmHg and is >180 mmHg)
    c. ____Arrhythmia: ____ a fib/flutter; _____ SVT; _____ V tach; _____ PVCs(>6/min)
    d. ____Other: _____

10. Time first echo ***ordered*** after T4/NS started:
    Date: ____ /____ / 20____; Time: ____:____

11. Ejection Fraction from first echo: _____%

12. If the donor was on T4 and completed the 12-hour protocol, was the T4 stopped within 60 minutes after the 12-hour study period? If the T4 stopped before 12 hours, answer N/A and go to #15.

    _____ Yes [skip to #15] _____ No [go to #13] _____N/A [skip to #15]

If the donor was in the NS group, skip to question #14.

13. What was the reason the T4 was continued beyond the study period?
    a. Still on vasopressors _____
    b. Still on inotropes _____
    c. Physician's preference _____
    d. Other _____
    e. Dose of T4 _____ mcg/hr
    f. Time T4 stopped: Date: ____ /____ / 20____; Time: ____:____

    Go to Question #15.

14. If the donor was randomized to NS, did the donor receive T4 after enrollment in the study ("open-label")?
    ____ Yes ____ No

    If yes, what was the reason?
    a. Still on vasopressors _____
    b. Still on inotropes _____
    c. Physician's preference _____
    d. Other _____
    e. Dose of open-label T4 _____ mcg/hr
    f. Time open-label T4 started: Date: ____ /____ / 20____; Time: ____:____
    g. Time open-label T4 stopped: Date: ____ /____ / 20____; Time: ____:____

15. If more than 1 echo was performed, fill in the data below: [enter 999 in EF if not done]
    a. 2nd echo: EF _____% Date: ____ /____ / 20____; Time: ____:____
    b. 3rd echo: EF _____% Date: ____ /____ / 20____; Time: ____:____
    c. 4th echo: EF _____ % Date: ____ /____ / 20____; Time: ____:____

Draw *free T4* before going to the OR or at end of donor management on all donors in the study (T4 and control group)

16. Baseline Serum free T4 _____ ng/dl TSH _____ mIU/L

17. Serum free T4 level _____ ng/dl prior to OR**.**

18. Was heart transplanted ? Yes_____ No _____

If heart *not* transplanted, what was the reason? (check all that apply)

a. ____Decreased EF, poor function,
b. ____CAD: 1 vessel ____ 2 vessel ____ 3 vessel ____
c. ____LVH
d. ____Size
e. ____Medical history *(smoking, diabetes, HTN, etc)*
f. ____Positive serologies
g. ____Increased risk
h. ____Match list exhausted
i. ____Recipient issues
j. ____Intra-op decline
k. ____Surgical injury
l. ____Valvular disease
m. ____Other _____

ADVERSE EVENTS: Please identify **any new** adverse events that occurred in the donor, **regardless if they received T4 or NS**, after the start of the study:

19. **Did the donor experience any of the following adverse events?** Yes ____ No ____
If YES, please check all that occurred:

a.____ Severe hypertension (BP >200 mm Hg)

b.____ Tachycardia (HR> 150; including sinus tach, SVT, PSVT)

c.____ Fever (>102 degree)

d.____ A fib or a flutter

e.____ Ventricular ectopy (>6 VPCs/min, bigeminy, trigeminy)

f.____ V tach (spontaneously resolved)

g.____ V tach (requiring cardioversion)

h.____ V fib (requiring defibrillation)

i.____ cardiac arrest*

j.____ cardiac death prior to the OR*

k.____ new skin rash

l.____ other: _____

19 m**. Was the adverse event related to the T4 infusion?**

____ YES ____ NO ____ UNCERTAIN

19 n**. Please describe the adverse event:** _____

_____

*These events need to be reported to the DSMB.

20. Name of person filling out worksheet: _____

Date: _____

For the Research Coordinator: After the case is completed, please upload the SRTR data to the Excel Spread sheet.

T4 Vasopressor Flow Sheet #3

UNOS #: _____ OPO: _____ Date Enrolled: _____ [*randomized to* T4: ___ *or* NS: ___]

					BLOOD PRESSURE		VASOPRESSOR AND INOTROPE DOSES (ENTER ZERO IF NOT ON THE DRUG)						
INTERVAL	Time (Military) (HR:min)	T4 Dose (mcg/ hr)	Saline Dose (cc/hr)	Heart Rate	☐ Invasive ☐ Non-Invasive		Levophed* (mcg/min)	Epi* (mcg/kg/ min)	Neo* (mcg/min)	Dopamine (mcg/kg/ min)	Dobutrex* (mcg/kg/ min)	Milrinone (mcg/kg/ min)	Vaso* (U/hr)
					Sys	Dias							
BASELINE *Before* first dose of T4/NS	:												
2 HOURS	:												
4 HOURS	:												
6 HOURS	:												
8 HOURS	:												
10 HOURS	:												
12 HOURS	:												
END OF DONOR MGMT[1]													
12-hour intake: _____ ml					Date Vasopressor Ended		___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	
12-hour output:_____ ml					Time Vasopressor Ended		:	:	:	:	:	:	
12-hour NET I/O:_____ ml							*Norepinephrine	*Epinephrine	*Neosynephrine		*Dobutamine		*Vasopressin

Date/Time T4 stopped *(Use Military Time):* _____/_____/_____ at _____:_____

Notes/Comments: _____

Name of coordinator filling out worksheet: _____

[1] End of Donor Management is defined as when the donor was sent to the OR or was extubated in the ICU if no organs are procured.