Single-Center, Retrospective, Observational Analysis of Patients with Submassive Pulmonary Embolism (PE) Receiving Catheter-Directed Thrombolysis

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Disclosure

I have the following potential conflicts of interest to report:

[x] Consulting: Cook Medical, Endologix, Aztra-Zenica, Boston Scientific, Gore, Jansen

Pulmonary Embolism

- According to The US Surgeon General **100,000-180,000 deaths/yr ***
- 20% die during first 24 hours
- 11% die within first 3 months
- Up to 10% who survive have chronic pulmonary hypertension

*www.Ncbi.nlm.nih.gov/books/NBK44178

Jaff, MR et al. Circulation.2011;123:1788-1830

Not All PE are Created Equal

- Patients diagnosed with PE are often risk-stratified
  - Based on hemodynamic instability
    - Massive vs submassive
  - Right ventricular function
    - High-risk vs. low-risk submassive

- RV dysfunction = predictor of adverse early outcome
- ICOPER registry revealed RV hypokinesis as independent predictor of 30-day mortality

Goldhaber SZ et al. Lancet.1999;353:1386-1389

Intermediate-Risk PE

- ‘Submassive’ PE
- High-risk features without overt hemodynamic compromise
  - RV dysfunction (CTPE or echo)
    - RV dilation (RV diameter/LV diameter >0.9) echo or CT
    - RV systolic dysfunction on echo
  - Elevated cardiac biomarkers (troponin I or T)
  - “High–risk” Clinical markers:
    - Hypoxic
    - Tachycardia

Intermediate-Risk PE

- Data suggests this population has 3-15% mortality rate Kucher, N et al. Circulation.2014;129:479-486
- Optimal treatment method not well delineated
- PEITHO trial suggested full-dose systemic thrombolysis (single-bolus TNK):
  - Reduced hemodynamic decompensation
  - Increased major bleeding and stroke

Meyer, G. el al. N Engl J Med.2014;370:1402-1411

Ultrasound-assisted Thrombolysis (SEATTLE II)

- Single-arm, low dose lysis acute (massive - 31pts) and submassive PE (119)
- RV/LV ratio ≥0.9
- 24 mg TPA (1mg/hr) or 1mg/hr (bilateral)
- Primary outcome change in chest CT RV/LV ratio @ 48hr
- Primary safety = major bleeding at 72 hr

Piazza G. et al. JACC Card Interventions. 24 August 2015

Seattle II

- RV/LV diameter ratio 1.55 vs. 1.13 ($p<0.0001$)
- Mean sPA decrease 51.4 vs. 36.9 mmHg
- One GUSTO-defined severe groin bleed, HoTN
- 16 ‘moderate’ events in 15 pts (10%)
- No ICH

Intermediate-Risk PE

- Is there a role for single bolus, low-dose, catheter-directed thrombolysis (CDT) in the intermediate-risk (submassive PE) population?
  - Safe
    - Major bleeding complications
  - Effective
    - Unload the RV
  - Cost
    - Pig tail catheter verses ultrasound catheter(s) with control unit

CDT for Submassive PE at Riverside Methodist Hospital

- February 2013-April 2014, 29 normotensive patients with acute pulmonary embolism, deemed intermediate-risk (RV dysfunction or elevated cardiac biomarkers)

Brought to catheterization suite for assessment of PA pressure and administration of a single bolus of Tenecteplase (TNK) via a catheter in the pulmonary artery or RV outflow tract

Statistical Methods

- Demographics and clinical characteristics of pts described using means, SD, medians
- Ranges for continued variables
- Frequencies and percentages for categorical variables
- Change in PA pressure was evaluated using a paired t-test
- Statistical significance was set at $p<0.05$

Demographic and Clinical Characteristics	n=29
Placement of inferior vena cava (IVC) filter, n (%)	17 (58.6)
Troponin level, n (%)	
Positive	17 (58.6)
Negative	10 (34.5)
Not applicable	2 (6.9)
Pre-intervention RV dysfunction, n (%)	28 (96.6)
PA pressure prior to treatment, mean (SD)[a]	50.3 (12.3)
PA pressure after treatment, mean (SD)[b]	44.1 (11.2)
Change in PA pressure, mean (SD)[c]	-7.7 (8.2)
Thrombolytic dose, mg, n (%)	
5	2 (6.9)
10	8 (27.6)
15	7 (24.1)
20	12 (41.4)
Length of stay, median (range)	3.0 (1.0 – 23.0)
Had follow up transthoracic echocardiogram (TTE), n (%)[d]	21 (72.4)
RV function on follow up TTE[e]	
Normal	19 (90.5)
Abnormal <30 days	1 (4.8)
Abnormal ≥ 30 days	1 (4.8)
Death related to procedure[f]	0 (0.0)

CDT for Submassive PE at Riverside Methodist Hospital

- Average Age: 59.6 years
- 19 Male
- 10 Female
- Length of stay 3.0 days (median), 4.6 days (average)
- Average dose of TNK = 15 mg
  - Majority received 20 mg (~ 1/3 the systemic dose)

PA pressure change

- Pulmonary artery systolic pressure (pre-intervention)
  - 24 recorded
  - Range: 29 mm Hg to 75 mm Hg
    - Average 50.3 mm Hg
- Mean -7.7 mmHg (SD:8.2) p=0.004

Alive at Discharge

- 29/29 (100%) of patients were alive at discharge
- 1 patient died 2 weeks later unrelated to procedure (complications of leukemia)

Major Adverse Events for all Patients Treated with TNK

- No significant bleeding complications requiring transfusion
- No reported intracranial hemorrhage

Non-Procedure Related Event

- Major Adverse Events
  - One received 10 mg TNK for submassive PE, discharged on Xarelto 3 days later.
    - Returned 17 days later with acute, embolic stroke.

RV Function Assessment

- Of 29 alive at discharge:
  - 20 had one month echo (69%)
  - 5 lost to follow-up
  - 3 without repeat echo, no reported dyspnea at follow-up
  - 1 had repeat echo within 24 hours

RV Function Assessment at 30 days

- 19/20 (95%) normal reported RV function
- 1/20 ‘mildly’ reduced RV function
  - Had highest initial PA systolic pressure of true submassive group, 75 mmHg

Conclusion

- In this patient population, single-bolus low-dose CDT with TNK was observed to be safe and seemed to help mitigate against RV dysfunction at 30 days
  - Further trials are needed, including randomized clinical trials
    - Single bolus vs. ultrasound assisted
    - Route?
      - IV vs. Catheter-Assisted

Thank You

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