Catheter Directed Thrombolysis As a Modality of Management For Pulmonary Embolism: Risk Stratifying with Pulmonary Embolism Severity Index

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INTRODUCTION AND JUSTIFICATION

- Pulmonary Embolism (PE) affects more than 900,000 Americans annually with an estimated 60,000 – 100,000 deaths per year and an estimated one-month mortality rate of 10%-30%[1].
- According to the American Heart Association (AHA), risk stratification of PE's is categorized as either massive (MPE), submassive (SPE), or non-massive based on various hemodynamic and clinical factors.
- The Emergency Department (ED) is often utilized for management and subsequent prevention of further adverse outcomes of PE, but diagnostic and therapeutic challenges arise due to variability in presentation and response to treatment.
- The Pulmonary Embolism Severity Index (PESI) is a composite metric that can also be used to determine prognosis of PE in the ED as a 30-day outcome, informing treatment options through a 5-point scale.
- AHA supports Catheter-Directed Thrombolysis (CDT) or Systemic Thrombolysis (ST) involving alteplase administration for management of an MPE, which has been shown to raise the risk of adverse outcomes post intervention with no standard of care recommended for SPE.
- These outcomes and uncertainties make it imperative to determine the benefits and adverse outcomes associated with either treatment for both MPE and SPE while also seeing if existing tools can be used as a clinical decision tool for ED physicians.
- The objective of this study is to analyze CDT or ST/no treatment for outcomes and investigate PESI profiles for each treatment among for MPE and SPE patients. This analysis can inform ED management and cardiovascular interventions for a spectrum of healthcare professionals.

METHODS

- In this retrospective study, data was obtained via 2 methods
- Inclusion criteria: Patient > 18 years of age presenting with an MPE or SPE and received treatment based on their group
- Both prisoners and pregnant patients were excluded from this study
- EMR data was reviewed twice by different teams across all metrics collected including demographics, vital signs, medical history, serum biomarkers (e.g. troponin and NT-proBNP) and echocardiography.
- PESI was spit into low risk (tiers 1,2) and high-risk (tiers 3,4,5,).

First data set was gathered from prospectively from patients presenting with either a MPE or an SPE who were treated with CDT (**defined as cases**): N = 432

Second data set was collected retrospectively from patients presenting with MPE or SPE who were treated with a systemic thrombolytic or anti-coagulant only (**defined as controls**): N = 611

A propensity score match method was used for standardization that included race, age, BMI, Gender, PESI Risk, diagnosis of a Massive vs. Submassive PE
N = 336

Cases: N = 168

Controls: N = 168

Low risk PESI: N = 96 & High Risk PESI: N = 240

- Comparators were defined and logistics regressions + Chi-Squared analysis were done between metrics and comparators using SPSS.

Table 1: Defining Outcomes and Analyzing Against Variables To Determine Subpopulations with Adverse or Positive Outcomes With Each Treatment Modality

Outcome	Category of Variables Hypothesized to be Correlated with All Outcome Between Both Treatments
Negative Outcomes	• Demographic Hospital Index • **Pulmonary Embolism Severity Index (PESI)** • Inpatient Procedures and Medication • Biomarkers (e.g. Troponin and Brain Natriuretic Peptide) • History of PE or DVT • Anticoagulant use • Presence of Hypertension • Length of Stay • History of Aspirin use
Bleeding Complications	
Mortality	
Right Ventricular Dilation	
Positive Outcome	
Decrease in RV Hypokinesis between baseline and post CDT echo (Attribute of RV Dysfunction)	

RESULTS

Table 2: Value of Variables Post Propensity Score Match Between the Cases and Control Groups

Variable Name	Value Among Both Groups: N = 336 (%)	Cases: N = 168 (%)	Controls N = 168 (%)	*p (2-tailed)*
Race				
African American	224 (66.7)	107 (63.7)	117 (69.6)	0.247
White/Other	112 (33.3)	61 (36.3)	51 (30.4)	
Age		60.8		0.631
BMI		33.94		0.540
Gender				
Male	163 (48.5)	79 (47.0)	84 (50.0)	0.585
Female	173 (51.5)	89 (53.0)	84 (50.0)	
PESI				
Low Risk (1-2)	96 (28.6)	46 (27.4)	50 (29.4)	0.629
High Risk (3-5)	240 (71.4)	122 (72.6)	118 (70.2)	
PE Status				
Massive	208 (61.9)	102 (60.7)	106 (63.1)	0.653
Submassive	128 (38.1)	66 (39.3)	62 (36.9)	

Table 3: Analysis of Comparators Against Each Treatment Modality

Variable	Total: N = 336 (%)	Cases: N = 168 (%)	Controls: N = 168 (%)	*p (2-tailed)*
Bleeding Complications				
Present	40 (11.9)	13 (18.5)	9 (5.4)	*0.0003*
Not Present	296 (88.1)	137 (81.6)	159 (94.6)	
Mortality				
Yes	20 (6.0)	9 (5.4)	11 (6.5)	0.645
No	316 (94.0)	159 (94.6)	157 (93.5)	
Right Ventricular Dilation				
Yes	130 (38.7)	46 (35.4) at admission to 46 (35.4) post-procedure	10 (7.7) at admission to 28 (21.5) post-procedure	*0.0131*
No	230 (61.3)			
Decrease in RV Hypokinesis Between Baseline and Post- CDT				
Yes	93 (27.7)	43 (46.2) at admission to 34 (36.6) post-procedure	5 (5.4) at admission to 11 (11.8) post-procedure	*0.0133*
No	243 (72.3)			

RESULTS CONT.

Table 4: Investigation of PESI Against Comparators

Comparators	PESI Category	*Cases (%)*	*Control (%)*	*P (2-tailed)*
Mortality	Low Risk (N=96)	2 (2.1)	0 (0.0)	*0.170*
	High Risk (N=240)	9 (3.8)	9 (3.8)	*0.941*
Bleeding Complications	Low Risk (N=96)	10 (10.4)	0 (0.0)	*0.001*
	High Risk (N=240)	21 (8.8)	9 (3.8)	*0.015*
Length of Stay (Days)	Low Risk (N=96)	5.5 (5.7)	3.8 (4.0)	*0.013*
	High Risk (N=240)	9.4 (3.9)	6.9 (2.9)	*0.005*

Table 5: Multiple Logistic Regression Analysis Between Comparators and Hypothesized Correlates Associated with Positive or Adverse Outcomes in CDT Patients (N = 186)

Comparator	Hypothesized Correlate (In Both MPE and SPE) from patients who underwent CDT	*p (2-tailed)*
Mortality	Elevated Brain Natriuretic Peptide (BNP)	*0.015*
	History of Deep Vein Thrombosis (DVT)	*0.043*
	History of Aspirin Use	*0.012*
Bleeding Complications	Length of Hospitalizations	*0.015*
Decrease in RV Hypokinesis Between Baseline and Post-CDT Echo	**No correlates were significant or close to being significant**	

CONCLUSIONS

- This study does not show conclusively whether CDT or ST/no were more effective than the other but, does show a significant increase in bleeding complications among those who underwent CDT.
- Regardless of PESI score, it could be seen that CDT intervention was associated with a greater incidence in complications as well as a longer length of hospital stay.
- Further studies need to be done to stratify and identify those patients who would truly benefit from CDT both among the MPE and SPE groups.

LIMITATIONS

- While the integrity of the propensity matching was determined to be viable, it can be strengthened by controlling for more variables.

FUTURE DIRECTIONS

- Define further comparators to strengthen comparison as well as produce a nuanced analysis on hypothesized outcomes to determine further characteristics that can influence adverse or positive outcomes among SPE and MPE patients.
- Use this analysis to develop a novel decision-making algorithm for ED physicians to efficiently administer treatment for better prognosis while also saving crucial time.

[1] Beckman, M. G., W. C. Hooper, S. E. Critchley, and T. L. Ortel. "Venous Thromboembolism: A Public Health Concern." [In eng]. Am J Prev Med 38, no. 4 Suppl (Apr 2010): S495-501.

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