Comparison of Clinical Outcomes in Patients Diagnosed With Submassive Pulmonary Embolism Whom Were Treated With Systemic Alteplase, Catheter Directed Alteplase or Anticoagulation Alone

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Introduction

- Pulmonary embolism (PE) is the third leading cause of cardiovascular related death in the United States and the third most common cause of death in hospitalized patients.[1,2]
- Submassive pulmonary embolism is defined as acute pulmonary embolism without systemic hypotension (Systolic Blood Pressure >90mmHg) but with evidence of right ventricular (RV) dysfunction or myocardial necrosis (myocardial necrosis is defined as elevated troponin I >0.4 ng/mL or troponin T >0.1 ng/mL).
  - RV dysfunction can be further defined as RV dilation (RV diameter/Left Ventricular (LV) diameter >0.9) or RV systolic dysfunction on echocardiogram, RV dilation on CT, elevated BNP >90 pg/mL or ProBNP >500 pg/mL, or ECG changes like new complete or incomplete right bundle branch block (RBBB), anteroseptal ST segment elevation/depression or anteroseptal T wave inversion.[3]
- Several studies have been performed which have indicated small statistical benefit in using thrombolytics in submassive pulmonary embolism with regards to decreased development of hemodynamic instability and worsening right heart strain as well as risk for bleed.[2,4]
- Catheter directed thrombolytics are not as well studied as systemic tPA in submassive pulmonary embolism; due to this lack of evidence there is no consensus whether or not this should be the treatment of choice.
- The question providers have to ask themselves is whether the risk of morbidity from the submassive PE outweighs the risk of morbidity from thrombolytic therapy. The lack of evidence needed to answer this question can lead to uncertainty regarding the correct treatment plan and patient outcome.

Hypothesis

In patients with submassive pulmonary embolism, the in hospital clinical outcome of the patient, such as rate of clinical deterioration, development of hemodynamic instability with need for escalation of care and risk of development of major bleed, is dependent on the type of intervention provided whether it be systemic thrombolysis, catheter directed thrombolysis, or anticoagulation.

Methods

- Retrospective chart review was completed from March 2016 to March 2019.
- Inclusion crtieria: Age 18 with a diagnosis of submassive pulmonary embolism (ICD-10 code I26). Charts were reviewed to confirm a diagnosis of submassive pulmonary embolism by looking for evidence of RV strain via echocardiogram, CTA chest, elevated troponin/ProBNP or ECG changes.
- ICD-10 codes were used to determine which treatment modalities had been prescribed: systemic tPA (z92.82, CPT 37195), catheter directed tPA (procedure code 3E05317) or anticoagulation alone.

3 Treatment Groups:
1. Heparin drip
2. Heparin drip + systemic tPA
3. Heparin drip + catheter directed tPa

- Variables: demographics, hospital course, development of major or minor bleed (ICD-10 R58, 161.9, D52) and development of hemodynamic instability (ICD-10 R57.9, R57.0).
- Descriptive analysis was performed outlining the differences in demographic data and adverse effects that resulted from each treatment modality.

Results

TABLE 1: Patient Demographics

	All: N=150	Heparin drip: N=117 (78.0%)	Systemic tPA + Heparin drip: N=22 (14.7%)	Catheter Directed tPA + Heparin Drip: N=11 (7.3%)
Age: (years)	66.5 (SD 14.9)	68.7 (SD 13.5)	55.6 (SD 18.9)	64.8 (SD 10.7)
Gender:				
Male	77 (51.3%)	58 (49.6%)	14 (63.6%)	5 (45.5%)
Female	73 (48.7%)	59 (50.4%)	8 (36.4%)	6 (54.5%)
Race:				
Caucasian	136 (90.7%)	106 (90.6%)	20 (90.9%)	10 (90.9%)
African American	13 (8.7%)	11 (9.4%)	1 (4.5%)	1 (9.1%)
Asian American	1 (0.7%)	0 (0.0%)	1 (4.5%)	0 (0.0%)
Length of Stay: (days)	6.4 (SD 4.6)	6.5 (SD 4.7)	6.1 (SD 4.7)	6.8 (SD 3.7)
ICU Length of Stay: (days)	1.9 (SD 3.1)	1.6 (SD 2.8)	2.9 (SD 4.3)	3.5 (SD 2.3)

TABLE 2: Adverse Effects

	All: N=150	Heparin drip: N=117	Systemic tPA + Heparin drip: N=22	Catheter Directed tPA + Heparin drip: N=11
Adverse effect of thrombolytic	2 (1.3%)	0 (0.0%)	1 (4.5%)	1 (9.1%)
Massive Bleed	9 (6.0%)	9 (7.7%)	0 (0.0%)	0 (0.0%)
Shock	14 (9.3%)	7 (6.0%)	6 (27.3%)	1 (9.1%)
Transfusion Required	9 (6.0%)	8 (6.8%)	0 (0.0%)	1 (9.1%)
Deceased	10 (6.7%)	5 (4.3%)	4 (18.2%)	1 (9.1%)

- In comparing mean age of patients in the heparin drip only group (68.7 years, n=117) and the subgroup treated with systemic tPA in addition to heparin drip (55.6 years, n=22) there was a mean difference of 13.1 years, p value<0.0001, 95% CI [6.3, 19.3].
- When comparing ICU los in the heparin drip only group (1.9 days, n=117) and the subgroup treated with catheter directed tPA in addition to heparin drip (3.5 days, n=11) there was a mean difference of 1.6 days, p value 0.07, 95% CI [-3.6, 0.14].

Discussion

- Demographically, it was found that the population of patients that received systemic tPA was more likely to be younger than those treated with heparin drip alone. Prior research has shown that providers prefer to use systemic thrombolytics in patients who are young and healthy as there is more perceived risk in using thrombolytics in those who are elderly.[1]
- On average, the ICU los for the catheter directed tPA subgroup was 1.6 days longer than in the heparin drip alone group (p value=0.07). This does not seem to line up with the current evidence to which ICU los was reported to be closer to 1.0 day on average.[5] It is unclear why there is a discrepancy in this review with current literature, whether this was facility dependent or related to longer need for higher acuity care.
- Of the patients treated with systemic tPA, there was a higher risk of development of shock (27.3%) and death (18.2%) in comparison to the other 2 groups. In general, this makes sense with current clinical guidelines which recommend systemic thrombolytics in patients who develop shock. The question this brings up is what criteria was being used in the remaining 72.7% of patients in that group that received the systemic tPA but did not have signs of shock.
- Limitations of this study include the inherent complications with this study design. In a retrospective descriptive study, it is difficult to fully understand why certain clinical decisions were made as information is not obtained in real time and reasoning is not always well documented. With tPA being a controversial treatment for submassive PE it made finding large numbers of patients difficult and therefore the number of patients in each of those subgroups was especially small.

Conclusion

This study revealed some similarities and discrepancies with current literature. This includes the expected higher rate of shock and younger age in those treated with systemic tPA, but there was also an unexpected longer ICU los in the catheter directed tPA group. This should be further explored as it could answer the uncertainty providers have concerning treatment plans and predicted patient outcomes in patients with a diagnosis of submassive pulmonary embolism.

References

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