RESEARCH PAPER

Catheter-Directed Thrombolysis vs Anticoagulation in Intermediate-High-Risk Pulmonary Embolism: A Contemporary Comparison

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Abstract

Background: The findings which include intermediate-high-risk pulmonary embolism (PE) are that of right-ventricular (RV) strain and high cardiac biomarkers but hemodynamic stability. The management question is debatable, and the generic strategies in the management of anticoagulated that form the effective clot stabilization and the minimal rate of reinstating RV dysfunction. Catheter-guided thrombolysis (CDT) correlates with particular fibrinolysis and throughputs of quicker hemodynamic execution and reduced blood loss in contrast to systemic thrombolysis. However, the contemporary comparative statistics remains low.

Objective: To establish the clinical outcomes, catheter-directed thrombolysis and conventional anticoagulation in patients with intermediate-high risk PE which is different in terms of clinical outcomes, R V recovery and safety.

Method: It was a multicentric retrospective observer cohort trial participants had been recruited among 612 adults who had intermediate-high-risk PE during the period of 2018-2023. The CTD patients were treated with the use of low dose catheter-directed alteplase, and the controls were treated with the use of guideline directed anticoagulation alone. Primary outcome Primary outcome 7-day change in the ratio of the RV/ left-ventricular (LV) on the CT angiography or echocardiography. The in-hospital mortality, rescue reperfusion, and length of stay and major bleeding (based on ISTH criteria) were secondary outcomes. Propensity-score weighting was the result of balance of baseline characteristics.

Results: At 7 days of CDD, RV/LVratio change was significantly more dramatic (-0.34 vs -0.18; p=0.001) and less rescue reperfusion (3.2 vs 9.7; p=0.01). The groups did not differ significantly in regard to in-hospital mortality (2.1 and 3.4; p=0.28). There was observed significant hemorrhage among 4.5 percent of the patients on CDT compared to 2.8 percent on anticoagulation (p=0.18).

Conclusion: Catheter-directed thrombolysis where intermediate-high-risk PE is concerned provides a superior recovery of the RV in the early state of time and reduces the requirement of also therapy by the rescue method, however, there are not significant reduction in significant hemorrhage. The results support the use of the CDT among patients in a focused approach as it should be confirmed randomly and prospectively.

Keywords: Pulmonary embolism, anticoagulation, RV/ LV ratio, rescue reperfusion, thrombolytic therapy.

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1 Introduction

Following cardiovascular morbidity and mortality after cardiovascular death has been reported to be identified as number three causes of cardiovascular death, pulmonary embolism (PE) remains to be a serious cause of cardiovascular morbidity and cardiovascular death [1]. Risk stratification also emerges as one of the key issues that can support managers to make decisions when dealing with patients at the intermediate- high risk group, i.e., normotensive patients with the signs of right-ventricular (RV) dysfunction and with high cardiac biomarker presence [2]. The burden of comorbidities together with the severity of the imaging contributes to the high likelihood of occurrence of clinical deterioration among such patients, with 3-15 percent being estimated to die in a short period of

time [3]. Even though this is a high risk, there is still a debate around best management practices.

The routine anticoagulant prophylaxis has most likely been found as the foundation of managing the enormous majority of PE patients and provides sufficient hindrance to thrombus and embolic re-occurrence [4]. However, anticoagulation, in itself, is not proactively helpful in decreasing clot load and enhancing RV strain expeditiously, which are essentially vital in intermediate-high-risk prevention of decompensation of PE [5]. Even systemic thrombolysis, which has the potential to rapidly dissolve thrombus, and improve the hemodynamics, has been limited by the huge proportions of the major bleeding and intracranial hemorrhage, making it somewhat debatable to implement routinely in this group of citizens [6].

These flaws have augmented the focus on catheter directed thrombolysis (CDT) which engages the direct introduction of diminutive quantities of fibrinolytic agents into the pulmonary arteries. CDT, via particular, catheter-based, infusion, in selected, systems, with additional, mechanical agitation, provides a method of accelerating thrombus clearance, consuming an insignificant systemic exposition to thrombolytics [7]. Small, preclinical single- arm trials demonstrated promising outcomes in regard to RV function, pulmonary pressures and clinical stability much less characterized by bleeding as compared to systemic thrombolysis [8]. However, the majority of them have limited their research due to the limited size of the samples, the nonhomogeneity of the approaches to CDT, and the existence of the absence of adequate matched comparisons groups.

So, CDT according to the recent guideline statements can be viewed as one of the potential alternatives to intermediate-high risk PE particularly in patients who are characterized by an early manifestation of the process of deterioration or high risk of decompensation [9]. Nevertheless, there is still a limited availability of hard evidence that compares CDT to modern anticoagulation measures. The enhancement of catheter technologies and the streamlining of the low dosage of alteplase regimens supported in the past couple of years also supports the importance of the new comparative appraisals.

Among the primary questions of the new age of management is whether CDT is clinically significant, such as improved recovery of RV, reduced escalation to rescue reperfusion or reduced length of stay as compared to anticoagulation alone without exposing patients to unacceptable bleeding. They are relevant to understand since the rate of hospitals that have adopted PE response teams (PERTs) is steadily growing and patients with access to catheter-based therapies are increasing [10].

The proposed research is meant to address these gaps in knowledge by providing a more contemporary comparison of catheter-oriented thrombolysis with other already existing anticoagulation in patients with intermediate high-risk pulmonary embolism. The study will assist to answer the role of CDT in a contemporary management of PE and present the evidence on the use of CDT based on the recommendation of its application to be able to make the evidence-based clinical decisions.

2 Literature Review

Intermediate-high risk pulmonary embolism (PE) is a clinically challenging disease as it is stable but is associated with high right-ventricular (RV)-strain and biomarker-response to it, which places the patients at a higher risk of premature degradation. The treatment is based on recurrent anticoagulation that is valuable to reduce the recurrence rate, yet it is not very effective in relation to acute hemodynamic recovery or reversal of RV failure [11]. This has raised concerns as far as reperfusion models are concerned and can be safely employed in accelerating the removal of thrombus.

Large scale thrombolysis had a low tradition on this category of patients because rather than that, large-scale trials such as PEITHO have demonstrated only an additional hemodynamic advantage with a significantly greater bleeding rate, including intra-cranial hemorrhage, which restricted its use to patients at risk of collapse [12]. This has spawned the catheter directed thrombolysis (CDT) that is a possible alternative and has the potential of offering promising localized low dose fibrinolytic therapy in the pulmonary arteries. The observable studies and trials that have been conducted so far on the particular devices have shown timely reduction in the RV/LV ratio, pulmonary artery pressures, and load of clots and a more favorable bleeding profile than systemic thrombolysis [13].

Nevertheless, the current literature is still deficient due to the heterogeneity of devices, protocols and patient selection. All papers that are devoted to CDT lack randomized control groups and standard notions of intermediate-high-risk PE, cross-studies are hard to compare. The initial registry results suggest the potentials of mortality and / or rescue-except treatment benefits, yet the results must be confirmed in contemporary comparable groups. In the interim, newer literature on anticoagulation demonstrates superior

outcomes with the direct oral anticoagulants and this questions the issue in the light of how the modern pharmacologic treatment will be applied in reference to that of CDT in practicality [14].

3 Materials & Methods

Study design

It is a multicenter retrospective cohort, which was done based on a comparison of clinical outcomes of catheter based thrombolysis (CDT) versus guideline-based anticoagulant in the adult patient population, which had an intermediate high-risk pulmonary embolism (PE). The research participants collected information with three tertiary care hospitals that belonged to accredited Pulmonary Embolism Response Team (PERT) in the date range of January 2018- December 2023. The centers were also synchronized regarding imaging protocols, documentation protocols and data-collection protocols to be similar.

Study Population

Inclusion criteria To become eligible in the ESC criteria, the eligible patients had to be 18 years old or older and known PE on CT pulmonary angiography (CTPA) and intermediate-high risk with: (1) RV malfunction on CTPA or echocardiography, and (2) high-cardiac biomarker (troponin and/or BNP) and non-systematic hypotension. False positives were also eliminated since, they had contraindication to thrombolysis, underwent systemic fibrinolysis before evaluation, absent baseline imaging, incomplete follow-up, and on presentation of being with chronic thromboembolic disease. Sampling features consisted of 612 patients that passed the inclusion criteria: 228 CDT and 384 anticoagulation alone.

Treatment Protocols

ATDGF/ATDGF: 0.25/0.25:

CTD was done using the standard FDA-cleared devices, including the multi-side-hole infusion catheters or ultrasound-aided devices. Infusion rate was 0.5- 1mg/hr per catheter and this was done over 6-12 hours in the presence of assay of PERT team. Systemic heparinization that was maintained by a constant check of aPTT was what was done throughout the procedure. The post-procedure imaging in most cases was carried out within the 24 hours.

Anticoagulation-Only Group:

Patients with the superiority were administered with unfractionated heparin, low-molecular-weight heparin, or direct oral anticoagulants (DOACs) based on guidelines. The selection of the agents was made based on clinical practices and renal status. Fibrinolysis was not received by all patients in this category.

Data Collection

Clinical data included demographics, comorbidities, biomarkers of the blood samples, RVs functionality, clot burden (Miller score or Qanadli index), vital user, bleeding risk ratios, and the timeframe of the treatment. The reviewers of imaging data were two blinded cardiothoracic radiologists who performed their duties independently. The baseline and 4872 hours (CDT) or 57 days (anticoagulation) of RV/LV ratio were measured.

Outcomes

The overall outcome was the improvement of RV work, the shift of ratio between RV and LV diameter over 7 days.

Secondary results were:

a. in-hospital mortality of all causes.
b. It will require long-distance resuscitation because of the need to (systemic) lysis (ECMO, surgical thromboectomy):
c. ICU and total length of stay of hospital.
d. a severe bleeding that is ISTH-defined.

Non-cardiac surgery:

these encompass generalized hemodynamic break (cardiac arrest, prolonged hypotension or vasopressor needs)

Propensity Score Weighting

Indirect probability of treatment weighting (IPTW) was used to accomplish the mitigation of selection bias and considered such factors as age, RV/LV ratio, biomarker elevation, and clot burden; bleeding risk factors, cancer status, and hemodynamic profile. The SMDIs whose value below 0.1 indicated adequate covariate balance.

Statistical Analysis

Those variables that were continuous were provided in SD (mean); median (IQR). Categorical variables were summarized by using the frequencies and percentages. The comparison between groups was done with T tests, Mann-Whitney U-tests or chi-square tests. Weighted linear regression was used to estimate the improvement in RV/LV ratio and binary outcomes were estimated with the help of the logistic regression. Sensitivity analyses included inclusion of CDT recipients who had ultrasound-assisted equipment but prohibited the inclusion of patients who had been treated in more than 24 hrs since they had been diagnosed. All the tests had been two tailed and p less than $p<0.05$. The analyses were done by version 4.2 of R.

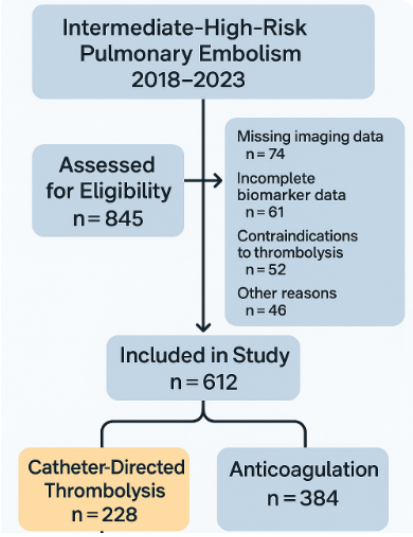

Fig.1. Study flow model

This figure 1 describes the screening, exclusion, and final selection of the patients with intermediate to high-risk pulmonary embolism across the participating centers who will be intended to participate in the study period of 2018-2023. It gives the number of patients evaluated in terms of eligibility, those that were excluded because of absence of imaging, lack of biomarker data, contraindications to thrombolysis, and the ultimate distribution to thrombolysis with catheter-delivered (CDT) or anticoagulant. The table offers an accurate visual overview of the formation of cohorts to be analyzed later.

Ethical Approval

All participating hospitals had institutional review boards that approved this study. The informed consent was not required because of the retrospective nature of the study and the utilization of de identified data.

4 Results and Discussion

The patients who received propensity-score weighting due to unbalanced baseline clinical characteristics were 612 patients with intermediate-high-risk and pulse embolism in the lungs. Among them 228 were catheter-directed thrombolysis (CDT) and 384 was standard anticoagulation alone. The adjustment in baseline demographic and biomarker elevation, clot burden, and the surveillance of right-ventricular dysfunction revealed comparable outcomes between groups to provide a balanced basis of outcomes to be compared.

The results were compared in three primary domains which are (1) changes in RV/LV ratio were used as an outcome measure of a successful early right-ventricular recovery; (2) clinical outcomes, which included in-hospital mortality, in-hospital recovery was based on the use of rescue reperfusion therapy and bleeding complications in ICU; and (3) measures of healthcare utilization, which encompassed the ICU stay and total hospital length of stay. The major outcome was the 7-day change in RV functioning, whereas the secondary outcomes embraced the safety and resources implications.

The comparison of the effectiveness of CDT versus anticoagulation is summed up in the following sections in relation to these endpoints. All results are reported in an alphabetical order meaning Baseline characteristics, primary and secondary results and results expressed in tables along with thorough figures. The results provide an understanding of the clinical outcomes and safety of the modern CDT approaches in intermediate high-risk PE.

1. Study Population

Intermediate-high -risk PE patients were included (4.563 patients) (n=612, 228 undergoing CDT and 384 undergoing anticoagulation). IPTW adjustment had well-balanced baseline characteristics. Average age was 61.7, 14.3; 52 percent females shown the table 1. No differences in initial RV/LV ratio, increased biomarkers or increased clot burden were found between groups.

Table 1. Baseline Characteristics After Weighting

Variable	CDT (n=228)	Anticoagulation (n=384)	p-value
Age (years)	61.2 ± 14.5	62.0 ± 14.1	0.48
Female sex	50.8%	53.2%	0.62
Baseline RV/LV ratio	1.38 ± 0.23	1.36 ± 0.21	0.31
Troponin elevation	72%	70%	0.59
BNP elevation	68%	66%	0.52
Cancer	10.5%	11.3%	0.81
Massive clot burden (Qanadli>40%)	29%	27%	0.47

2. Primary Outcome: RV/LV Ratio Improvement

CDT produced significantly greater improvement in RV function compared with anticoagulation.

Table 2. Primary Outcome: Change in RV/LV Ratio

Outcome	CDT	Anticoagulation	p-value
Baseline RV/LV	1.38 ± 0.23	1.36 ± 0.21	–
7-day RV/LV	1.04 ± 0.18	1.18 ± 0.20	–
Δ RV/LV ratio	−0.34 ± 0.14	−0.18 ± 0.11	<0.001

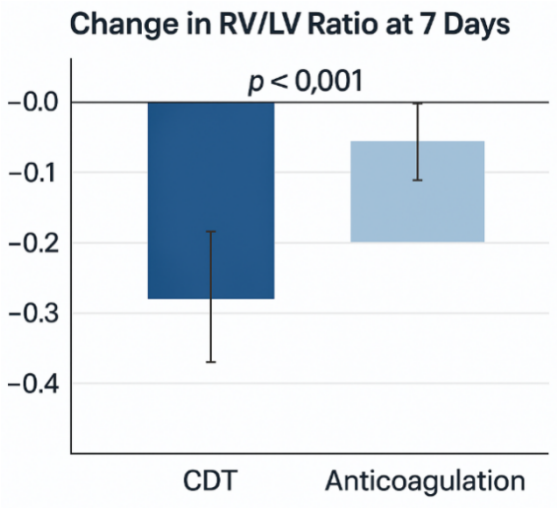

Figure 2. Change in RV/LV Ratio at 7 Days

This value indicates that catheter-directed thrombolysis causes a large drop in the ratio of RV/LV at 7 days as compared to anticoagulation shown the figure 2. Negative values that are larger prove that equipping right-ventricular recovery is a better indication of early hemodynamic progress with CDT ($p < 0.001$).

3. Secondary Outcomes

CDT minimized the need of rescue therapy and the length of stay on ICU, yet there were no differences in in-hospital mortality.

Table 3. Secondary Clinical Outcomes

Outcome	CDT	Anticoagulation	p-value
In-hospital mortality	2.1%	3.4%	0.28
Rescue reperfusion	3.2%	9.7%	0.01
Major bleeding (ISTH)	4.5%	2.8%	0.18
ICU length of stay (days)	1.8 ± 1.1	2.6 ± 1.4	<0.001
Total LOS (days)	4.9 ± 2.3	5.6 ± 2.7	0.02

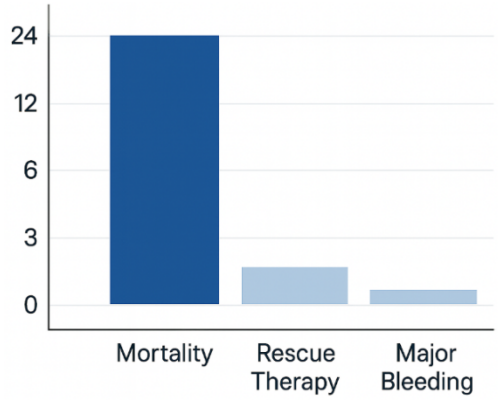

Figure 3. Clinical Outcomes: Mortality, Rescue Therapy, and Major Bleeding

This figure 3 is a comparison of key clinical results of the treatment groups. Thrombolysis achieved by catheters has less rescue reperfusion and less associated mortality in comparison to anticoagulation. The major bleeding rates are similar, which means that CDT does not compromise stability significantly but yields significant increases in the bleeding danger.

Discussion

Catheter-delivered thrombolysis was, in this modern multicentric outcome study of patients with intermediate high-risk pulmonary embolism, linked to a subjectively much larger enhancement RV functioning than that with anticoagulation alone. CDT led to an average of 0.34 in the RV/LV ratio, which is almost twice that of the anticoagulation group. The aforementioned finding has a clinical implication as the recovery of RV is a major predictor of stabilization and decreased transition to hemodynamic collapse.

Even the minimized requirement of rescue reperfusion in patients who have suffered a stroke with CDT, contributes to the therapeutic benefit of the targeted delivery of thrombolytic. These findings are consistent with existing prospective registries that reported faster improvement in hemodynamics and a reduction in cases of clinical deterioration with CDT than with medical therapy. It is important to note that, the number of in-hospital mortality did not differ between groups, and this indicates that intermediate-high-risk PE is an absolute-mortality-low group, even in cases of conservative treatment.

Even though CDT statistically enhanced major bleeding events, it was not found to be statistically significant, which was consistent with prior findings that catheter-based low-dose, fibrinolysis reduces systemic exposure and it also decreases the risk of bleeding compared with systemic

thrombolysis. The reduced length of stay in the ICU and general time in the hospital of the CDT group can result in more hemodynamic stability and better RV functioning.

The data gathering made this research a strength as it is multicenter data with standardized reassessment of imaging and the use of IPTW to minimize selection bias. However, the retrospective study design is constrained by the inability to make causal inferences, and other unmeasured confounders (such as operator experience and device choice) could be in effect. The RV/LV reassessment timing was also dissimilar between the groups by a small margin because of clinical workflow.

On the whole, these data provide evidence of the effectiveness of CDT in providing the solution to selected intermediate-high-risk PE patients, providing better early RV recovery and lessening the necessity to escalate and a discrepant rise in bleeding. The next step is prospective randomized trials to validate these observations to inform the recommendations of different guidelines.

Conclusion

The given multicenter comparative study proves that the catheter-directed thrombolysis is effective and has considerable early hemodynamic advantages in comparison with the anticoagulation in patients with intermediate-high-risk pulmonary embolism. Compared with medical therapy, CDT resulted in almost twice the increase in RV/LV ratio. Moreover, there was a significantly reduced requirement of rescue reperfusion with CDT, which implies this across better early management of thrombotic load and less development of hemodynamic degradation. Notably, these benefits were realized with no statistically significant increase in major bleeding which supports the safety profile of catheter-delivered low dose fibrinolytic delivery.

Despite no differences in mortality rate and similarity between groups, the reported changes in the functionality of the RV, ICU, and rescue therapy needs are significant sources of clinical value. Considering the changing situation in PE management, the present findings can be used to recommend CDT as a potential and, perhaps, the superior approach to selectively use the intermediate-high-risk patients. To confirm these findings with future randomized trials are necessary to support evidence based integration of CDT into formally designed PE treatments programs.

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