

CLINICAL INVESTIGATION

Outcomes of catheter-directed interventions in high-risk pulmonary embolism—a retrospective analysis

Freyr Einarsson¹ | Charlotte Sandström² | Kristina Svennerholm¹ | Jonatan Oras¹  | Christian Rylander¹ 

¹Department of Anaesthesiology and Intensive Care Medicine, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden

²Department of Radiology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden

Correspondence

Christian Rylander, MD, Associate Professor, Department of Anaesthesia and Intensive Care, Sahlgrenska University Hospital, 413 45 Gothenburg, Sweden.

Email: christian.rylander@vgregion.se

Background: First-line treatment of high-risk pulmonary embolism with persistent hypotension and/or signs of shock is intravenous thrombolysis. However, if thrombolysis is contraindicated due to risk of serious bleeding, or if it yields insufficient effect, surgical thrombectomy or catheter-directed intervention (CDI) plus anticoagulation is recommended. The aim of this study was to assess the outcomes of the CDI modality introduced in a tertiary referral centre in 2013.

Methods: Retrospective comparison between patients treated with CDI plus anticoagulation ($n = 22$) and patients treated with anticoagulation only ($n = 23$) as used before the CDI technique was available. The main outcomes of interest were 90-day survival and reduction of right to left ventricle diameter (RV/LV) ratio, using the Fischer's exact test and a mixed model, respectively, for statistical analysis.

Results: Ninety-day survival was 59% after CDI and 61% after anticoagulation only; $P = .903$. The rate of RV/LV ratio reduction was 0.4 units higher per 24 hours in the CDI group (median 2.1 pre-treatment), than in the anticoagulation only group (median 1.3 pre-treatment); $P = .007$.

Conclusion: In patients with high-risk pulmonary embolism, 90-day survival was similar after treatment with CDI plus anticoagulation compared to anticoagulation only. The mean reduction in RV/LV ratio was larger in the CDI group. Our results support the use of CDI in selected patients, respecting the limitations and potential side effects of each technical device used.

1 | INTRODUCTION

According to current international guidelines, high-risk pulmonary embolism (PE) is defined by obstructive shock with signs of hypoperfusion, persistent hypotension with systolic blood pressure (SBP) below 90 mmHg or a drop in SBP of more than 40 mmHg lasting longer than 15 minutes.¹ Patients with suspected high-risk PE should be given a loading-dose of heparin and then be treated with systemic intravenous (IV) thrombolysis when the diagnosis is established.¹

However, if IV thrombolysis is contraindicated due to risk of serious bleeding, or if it yields insufficient effect, surgical thrombectomy or catheter-directed intervention (CDI) is recommended.^{1,2}

Different CDI techniques can be used alone or in combinations: mechanical fragmentation, aspiration thrombectomy, catheter-delivered local thrombolysis, and rheolytical thrombectomy with aspiration of fragments.³ For the complex clinical therapeutic decision in acute high-risk PE cases, specialized pulmonary embolism response teams (PERT) have been advocated, particularly in multidisciplinary

*These authors contributed equally to the work.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Acta Anaesthesiologica Scandinavica* published by John Wiley & Sons Ltd on behalf of Acta Anaesthesiologica Scandinavica Foundation

settings.^{4,5} In our institution, CDI was introduced in 2013 as a treatment option for patient with high-risk PE and contraindications to, or insufficient effect from, IV thrombolysis after individual evaluation by a specialized pulmonary embolism response team (PERT).⁶ The aim of this study was to evaluate the outcomes from CDI plus anticoagulation and to compare them to anticoagulation alone which was the precedent alternative in these patients.

2 | METHODS

The study was approved by the Swedish Ethical Review Authority (Dnr 2019-00827) including a waiver of informed consent due to its retrospective nature. Data were handled and stored according to the European General Data Protection Regulation (GDPR). The manuscript was prepared according to the STROBE guidelines for observational studies.⁷

2.1 | Design

Retrospective study of patients with high-risk PE treated by CDI followed by anticoagulation between July 2013 and December 2018. A historic cohort of patient treated for high-risk PE with anticoagulation only (AC group) between January 2006 and June 2013 was used for comparison. Data were retrieved from medical records and quality registries.

2.2 | Patients

Eligible patients were identified by the local code for pulmonary angiography in the database of the radiology department or by the ICD-10 codes I26.0 or I26.9 and the local code for pharmacological thrombolysis in the database of the intensive care unit (ICU). Inclusion criteria were 1) adult patient >18 years old with a diagnosis of PE established by computed tomography pulmonary angiography (CTPA) or an assumed PE diagnosis based on RV dilatation on echocardiography and a history compatible with acute PE; 2) SBP below 90 mm Hg; 3) absolute contraindication to, or insufficient effect from, IV thrombolysis. The absolute contraindications were defined by the existing standard operation procedure (SOP) for IV thrombolysis which did not change over the study period: 1) trauma or surgery involving the central nervous system within the last two months; 2) ischemic or hemorrhagic stroke with intracerebral hemorrhage within the last three months; 3) surgery, major trauma, biopsies or puncture in anatomical regions with non-compressible blood vessel within the last ten days; 4) spinal or epidural puncture within the last 48 hours; 5) active bleeding or high risk of bleeding due to coagulation disturbances; 6) ongoing anticoagulation therapy. Exclusion criteria were 1) acute surgical thrombectomy or extracorporeal circulatory assist initiated before the assigned treatment; 2) no active treatment initiated.

Editorial Comment

This retrospective cohort presents initial outcomes after initiating catheter-directed interventions for pulmonary embolism, with comparison to a historical cohort that fulfilled criteria but received anticoagulation only. Mortality of both groups was high and similar, but right ventricular strain indicators appear to decrease earlier with invasive intervention. This approach is demonstrated to be feasible as a treatment modality in selected patients.

2.3 | Clot burden

The clot burden was assessed by interpreting CT scans according to the pulmonary angiographic Miller score proposed by Miller⁸ and adapted for CT scans by Bankier.⁹ With this system, the clot burden score is assigned a number between 0 and 16 where 0 corresponds to the absence of emboli and 16 corresponds thrombus in all segmental arteries or saddle embolism.

2.4 | Right heart dilatation

The diameters of the right and left heart ventricles (RV and LV) were defined as the maximal distance between the ventricular endocardium and the interventricular septum perpendicular to the long axis in axial views according to standards on CTPA^{10,11} or echocardiography images.¹² Dilatation of the right ventricle was defined as RV/LV ratio >0.9.¹⁰ For pre-treatment values, RV/LV ratios from the routine CTPA images were used. For post-treatment values, we used measurements from echocardiography images performed by an intensive care specialist certified in echocardiography¹³ and blinded to the treatment, clinical signs, and outcomes of the patient.

2.5 | Catheter directed interventions

Vascular access was established via the right femoral vein with ultrasound guidance using an 8-12F sheath introducer to the right atrium and a coaxial 6-7F sheath introducer to the pulmonary artery. Initial mechanical fragmentation was achieved either with a pigtail catheter (different manufacturers), a 5x20 - 10x40 mm non-compliant-balloon catheter (Admiral® Xtreme, Medtronic, Minneapolis, MN, USA) or a 6F rotating device (Rotarex®, Straub Medical AG, Wangs, Switzerland). Rheolytic fragmentation was achieved using a 6F hydrodynamic catheter (AngioJet Ultra PE®, Boston Scientific, Marlborough, MA, USA).¹⁴ In the United States, this device, which was originally designed for thrombectomy in peripheral and coronary vessels, carries a "black box warning" required by the Food and Drug Administration (FDA) due to serious complications when applied in PE.¹⁵ To minimize the risk of bradycardia,¹⁶ hypothetically caused by the release of adenosine from

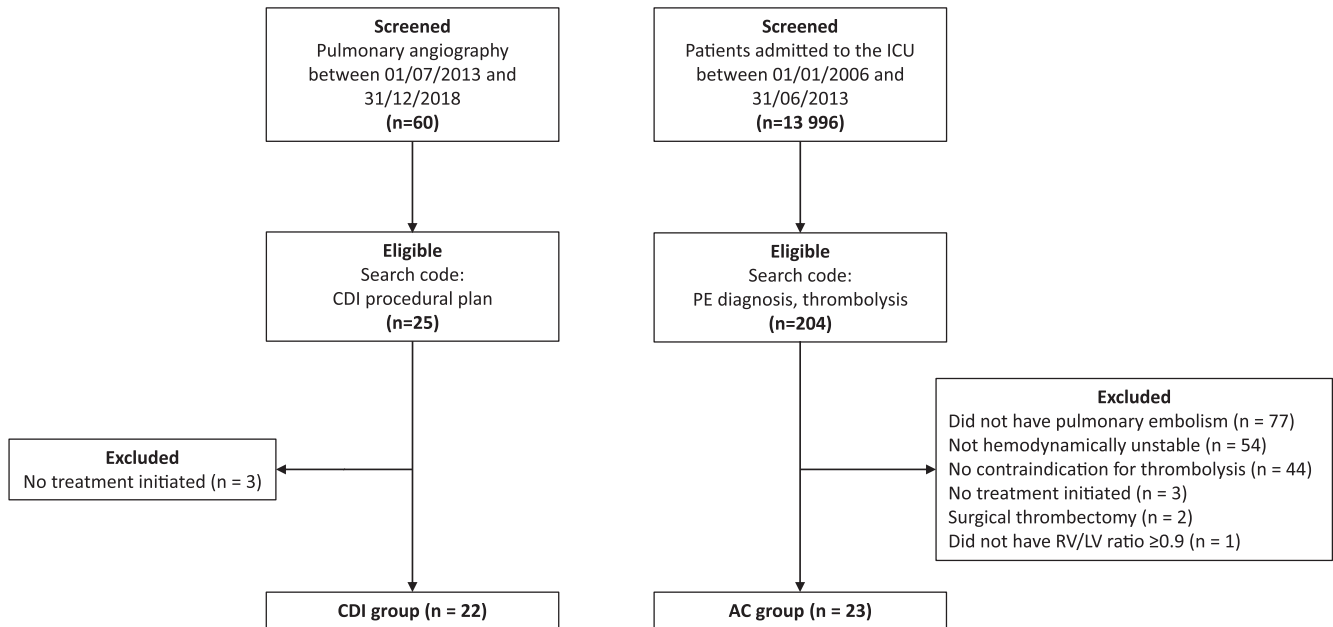


FIGURE 1 Flowchart of patient inclusion and exclusion in the study

disrupted platelets,¹⁷ our standard operation procedure (SOP) dictates that rheolytic fragmentation must be undertaken in short bursts of maximum 10 seconds while the cardiac rhythm is observed and normal frequency is secured. Optional small doses (5-20 mg) of Alteplase were applied at the end of the procedures to exert best possible effect in fragmented or perforated thrombi.^{18,19} Technical success was defined as reaching a desired position for fragmentation. Procedural success was defined as technical success in the absence of major procedural complications.²⁰ Clinical success was defined as an overall amelioration of heart rate, oxygen saturation, and systemic blood pressure plus a dose reduction of any vasopressor infusion.

2.6 | Anticoagulation

All patients were administered an initial bolus dose of IV heparin 100 IU/kg in the emergency department. After ICU admission, patients in the AC group were started on an IV infusion of heparin 30 E/ml targeting an Activated Partial Thromboplastin Time (APTT) value of 70-100 seconds. Patients in the CDI group were started on an equivalent infusion in the ICU after completion of the CDI procedure.

2.7 | Outcomes

The main predefined outcomes of interest were survival to 90 days and reduction of RV/LV ratio. We also assessed maximum changes in serum creatinine and the length of stay (LOS) in the ICU and in the hospital for patients surviving the first 24 hours after initiation of the treatment.

2.8 | Statistical Methods

Descriptive statistics were used for group characteristics and outcomes. Comparisons between groups were performed using the Fischer's exact test for categorical variables and the Mann-Whitney U-test for continuous variables. A linear mixed model, with adjustment for timing of pre- and post-treatment imaging, was used to compare the rate of RV/LV ratio reduction between groups. P-values ≤ 0.05 were considered significant. All analyses were performed using SPSS (v24.0, IBM Statistics, IBM Corp, Armonk, NY, USA).

3 | RESULTS

Out 229 patients eligible during the entire screening period, 22 patients were submitted to CDI plus anticoagulation and 23 patients received anticoagulation only (Figure 1). There was no CDI treatment performed during the period from which the AC cohort was recruited. No patient was lost to follow-up. All the patients had acute high-risk PE classified as IV or V according to the Pulmonary Embolism Severity Index.¹ Baseline characteristics did not differ between the groups (Table 1). Vital parameters before the respective treatment did not differ between the groups except for the RV/LV ratio which was higher in the CDI group (Table 2). The median (IQR) clot burden assessed by the Modified Miller Score was 16 (16, 16) in the CDI group vs 12 (5, 16) in the AC group; $P = .016$.

In the CDI group, all patients had the PE diagnosis established by CTPA. Three eligible patients were excluded because the scheduled treatment by CDI was never initiated; two of them improved hemodynamically prior to the intervention, which was consequently inhibited, and one patient succumbed due to circulatory shock

TABLE 1 Baseline characteristics

Category	Variable	CDI (n = 22)	AC (n = 23)	p-value
Demographic	Age, years	70 (63 - 77)	68 (61 - 76)	.737
	Women	11 (50)	14 (61)	.554
Medical history	Hypertension	11 (50)	10 (43)	.768
	Coronary artery disease	3 (14)	3 (13)	>.999
	Atrial fibrillation	3 (14)	3 (13)	>.999
	Heart failure	0 (0)	1 (4)	>.999
	Risk factor for CVD	11 (50)	10 (43)	.768
	COPD	0 (0)	3 (13)	.233
	DVT	1 (5)	2 (9)	>.999
	PE	3 (14)	2 (9)	.665
	Stroke	5 (23)	2 (9)	.242
	Liver disease	0 (0)	1 (4)	>.999
	Renal disease	0 (0)	0 (0)	>.999
	Rheumatic disease	0 (0)	2 (9)	.489
	Psychiatric disease	0 (0)	2 (9)	.489
	Malignancy	5 (23)	10 (43)	.208
Other	12 (55)	6 (26)	.071	
Contraindication to thrombolysis	Recent trauma	2 (9)	1 (4)	.608
	Recent surgery	7 (32)	11 (48)	.365
	Recent ischemic stroke	2 (9)	1 (4)	.608
	Recent hemorrhagic stroke	3 (14)	0 (0)	.109
	Active bleeding	2 (9)	1 (4)	.608
	Risk of local bleeding ^a	4 (18)	8 (35)	.491
	Ongoing anticoagulation	0 (0)	1 (4)	>.999
	Failed first thrombolysis	2 (9)		

Abbreviations: CDI, Catheter Directed Intervention plus anticoagulation; AC, Anticoagulation only; CVD, Cerebrovascular Disease; COPD, Chronic Obstructive Pulmonary Disease; DVT, Deep Vein Thrombosis; PE, Pulmonary Embolism.

Data except age presented as number (%).

Age presented as median (interquartile range).

p-values refer to Fischer's exact test for categorical variables and to the Mann-Whitney U-test for continuous variables.

^aie from the GI tract, advanced cancer, etcetera.

before the start of the intervention. Two patients were subjected to surgical thrombectomy due to recurrent PE shortly after CDI; one of them died after 10 days and the other one was still alive after one year. Different CDI techniques were applied at the discretion of the interventionist (Table 3). Individual procedures and clot burden are detailed in the appendix (Table S1). One patient reacted to rheolytic fragmentation with an episode of asystole and another patient displayed repeated bouts of hypotension due to failing right heart performance. However, both conditions resolved spontaneously. Due to progressing circulatory shock, one patient was given rescue IV thrombolysis during the intervention, despite identified contraindications. However, no bleeding complications occurred. No patient received rescue thrombolysis after the completed CDI. The

procedure was classified as clinically successful in all except three patients who succumbed to circulatory shock unrelated to the intervention and in two patients who died due to irreversible shock in the ICU within a few hours after the intervention.

In the AC group, the PE diagnosis was based on CTPA in 18 patients and on echocardiographic RV dilatation combined with clinical presentation and history in five patients. Three eligible patients were excluded because active treatment with anticoagulation was never initiated; they were considered to suffer from conditions other than small pulmonary emboli that had been diagnosed but deemed clinically insignificant. Three patients received rescue thrombolysis due to progressive circulatory shock despite identified contraindications, but no bleeding complications occurred.

TABLE 2 Physiological parameters before the start of active treatment

	CDI (n = 22)	AC (n = 23)	P value
RV/LV ratio	2.1 (1.6 - 2.7)	1.3 (1.1 - 1.6)	<.001
Systolic Blood Pressure (min), mm Hg	90 (70 - 95)	85 (70 - 105)	.936
Systolic Blood Pressure (mean), mm Hg	110 (103 - 130)	108 (97 - 123)	.725
Heart rate (mean), beats per minute	108 (95 - 115)	100 (87 - 114)	.127
Lactate (max), mmol/l	3.2 (1.5 - 6.2)	3.5 (2 - 6.2)	.428
pH (min)	7.39 (7.24 - 7.44)	7.34 (7.28 - 7.4)	.459
Respiratory frequency (max), bpm	26 (24 - 34)	23 (20 - 32)	.293

Abbreviations: CDI, Catheter Directed Intervention plus anticoagulation; AC, Anticoagulation only. Data presented as median (interquartile range).

RV/LV ratio, Right Ventricular to Left Ventricular diameter ratio.

Min and mean blood pressures are the respective minimal and mean individual values.

P-values refer to the Mann-Whitney U-test.

TABLE 3 Catheter directed interventions in 22 patients. Several patients were submitted to multiple techniques

	Patients (n)
Mechanical thrombectomy	
Pigtail/balloon catheter	12
Balloon catheter	2
Rotating device	2
Rheolytic fragmentation	20
Aspiration thrombectomy	3
Catheter directed thrombolysis	9

Ninety-day survival was 59% after CDI and 61% after anticoagulation only ($P = .903$). Among the nine non-survivors in the CDI group, causes of death were PE in eight and cerebral infarction with herniation in one patient. Among the nine non-survivors in the AC group, causes of death were PE in six, lung cancer in one, thyroid cancer in one, and an unknown cause in one patient who died at 75 days after intervention in a different hospital. The median (interquartile range) RV/LV ratios before treatment were 2.1 (1.2-3.5) in the CDI group compared to 1.3 (0.8-2.2) in the AC group; $P < .001$ but the RV/LV ratio before treatment did not differ between 90-days survivors and non-survivors; 1.60 (0.8-3.5) vs 1.45 (1.0-3.2); $P = .706$. The median (interquartile range) RV/LV ratios after treatment did not differ between the groups; CDI (n = 17) 1.3 (0.6-2.7) vs AC (n = 13) 1.0 (0.4-1.5); $P = .053$. The reduction rate of RV/LV ratio per 24 hours was 0.4 units higher in the CDI group than in the AC group (Figure 2); $P = .007$. In a multivariable model, adjusting for RV/LV ratios, treatment with CDI was not associated with 90-days mortality (OR [95%CI] 0.54 [0.12-2.52]; $P = .436$).

Serum creatinine values available from a limited number of medical records (CDI n = 16; AC n = 15) increased more after CDI

treatment than after the initiation of anticoagulation only, 24.5 (-9.0-68.0) $\mu\text{mol/l}$ vs -2.0 (-20.0-68.0) $\mu\text{mol/l}$; $P = .031$. However, these changes were temporary without any oliguric renal failure. There was no difference in median (interquartile range) ICU LOS; CDI 56 (9-372) h vs AC 30 (8-692) h; $P = .114$, or hospital LOS; CDI 11 (1-35) days vs AC 20 (1-100) days; $P = .248$.

4 | DISCUSSION

The main finding of this study was that 90-day survival in patients with acute high-risk PE and contraindications to, or insufficient effect from, IV thrombolysis did not differ between two cohorts, treated with CDI followed by anticoagulation or with anticoagulation only. This parallels results from another single centre study in which, however, the crude survival was substantially higher.²¹ In contrast with the present study, the choice of treatment was made by the attending physician and not by PERT consensus in about half of the cases and most of the patients had intermediate-risk PE. Indeed, numerous CDI studies of intermediate-risk PE and some of high-risk PE report higher survival rates.²² Still, numbers similar to the present result have been reported for subgroups of patients in shock^{20,23} and the low survival in our cohort may reflect that we included severely compromised patients for whom active treatment was tried as a last resort. This was also seen in the AC group, where a few patients received rescue thrombolysis as judged by the attending physician. On the other hand, 6-month mortality reported in two of eight CDI studies of hemodynamically unstable patients in a systematic review was 47.3% (Bajaj 2016). We chose a shorter interval to follow-up due to an increasing risk of death from non-cardiovascular causes with time, but our mortality approximating 40% after three months, may indicate recruitment of similarly complex patients.

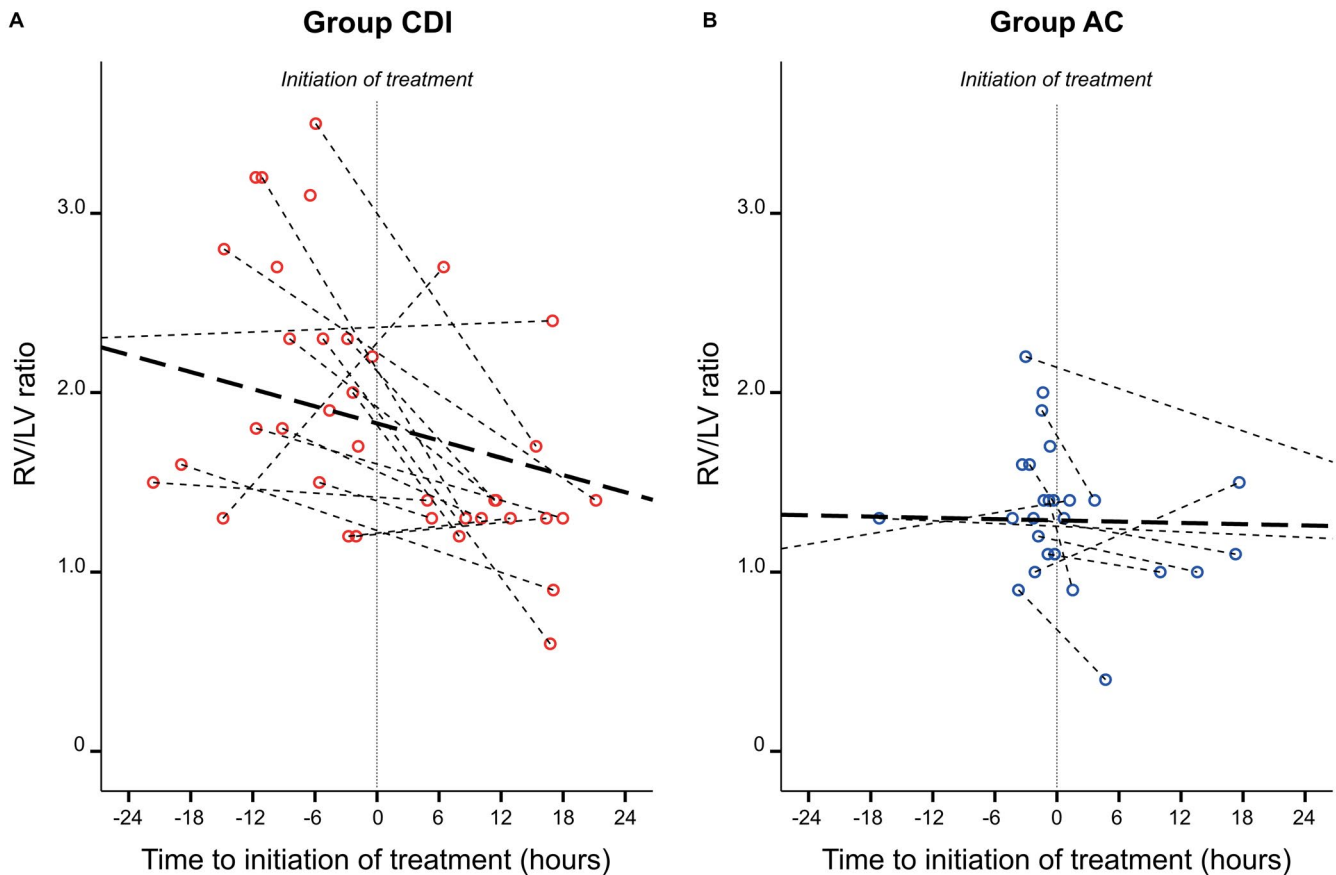


FIGURE 2 CDI, Catheter Directed Intervention plus anticoagulation; AC, Anticoagulation only; RV/LV ratio, Right Ventricular to Left Ventricular diameter ratio; The X-axis depicts hours from start of treatment indicated by the vertical line. In the AC group, two points of follow-up fell outside the first 24 hours post-treatment; The black dashed lines represent average change [Colour figure can be viewed at wileyonlinelibrary.com]

Furthermore, the CDI group showed a larger mean reduction in RV/LV ratio over time in the acute phase, although their RV distension was substantially higher before the treatment. It is apparent that the difference in baseline RV/LV ratio could explain the difference in RV/LV reduction rate but our finding from everyday practice corroborates results from other case series describing the effects of different CDI techniques.^{15,22} High RV/LV ratios have been associated with increased mortality rates,²⁴⁻²⁷ but in our material the survival rate did not differ between the groups. One explanation for this could be that RV/LV ratio is a poor predictor of mortality when circulatory decompensation has already occurred. Alternatively, if the high RV/LV ratio indicated that the patients in the CDI group were sicker and at greater risk of dying, their treatment may have been more effective, lowering the mortality to a level similar to the AC group. However, this remains speculative and our case series does not allow conclusions about effectiveness. Although faster hemodynamic restitution hypothetically could result in shorter ICU and hospital stays, we found no such difference between the groups.

Catheter directed intervention has been reported to improve RV function in intermediate-risk PE²⁸ and it is often considered for patients with intermediate-risk PE who are considered to benefit from thrombolysis, but who have a high risk for hemorrhagic

complications.²⁹ Notwithstanding that reports on CDI describe heterogeneous patient groups and techniques, the use of CDI as the primary treatment for patients with PE has increased,^{30,31} especially in patients with intermediate-risk PE.²² From a short-term perspective, CDI is more resource demanding than IV thrombolysis or anticoagulation only, yet it has been suggested that the net result is in favour of CDI³² due to faster reversal or even prevention of hemodynamic decompensation. While there are recent experimental studies based on a PE model³³⁻³⁶ and an ongoing clinical trial of Low Dose Catheter Directed Thrombolysis for Acute Pulmonary Embolism (BETULA; ClinicalTrials.gov Identifier: NCT03854266), clinical outcomes of CDI techniques have not been reported from the Scandinavian countries.

The CDI procedure in our institution includes various techniques depending on individual conditions for access to and distribution of emboli in the pulmonary circulation. Rheolytic fragmentation, using the AngioJet® system with a catheter approved for use in the pulmonary vessels, was applied in all but two patients, in whom the Rotarex® system was used. In view of earlier reports of serious side effects from rheolytic thrombolysis,¹⁶ and recommendations both for³⁷ and against³⁸ its use, the results from this study should be of general interest. With application of our SOP which highly restricts

the duration of rheolytic fragmentation runs, severe side effects occurred in only 2 of 20 patients. Indeed, similar experience has recently been reported by others.³⁹ Finally, the CDI procedures also appeared safe as to renal function as the increase in serum creatinine that we observed was temporary without any oliguria.

4.1 | Limitations

The retrospective design with comparison between two small cohorts differing in time and the dependence on data retrieved from medical records inevitably hampers the quality and volume of information retrieved for analysis. Another weakness inherent to the retrospective design was the lack of standardized procedures to measure the heart dimensions before and after the treatment. To compensate for this, we reanalysed CTPA and echocardiography images using robust points of measurement¹⁰ known to yield good agreement between ventricle dimensions on CTPA and echocardiography.⁴⁰ The two groups were well-matched as to demographics, physiological conditions, and PE presentation but the imbalanced RV/LV ratios together with the small number of patients may have impacted on the outcome results, especially the higher rate of RV/LV reduction in the CDI group. Furthermore, the predominance of rheolytic thrombectomy combined with mechanical fragmentation and the selection of high-risk PE patients in our CDI cohort limits the comparison to other studies.

5 | CONCLUSION

When introduced in our institution, treatment with CDI plus anticoagulation yielded similar results as the preceding therapy with anticoagulation alone in patients with high-risk PE and contraindication to, or insufficient effect from, IV thrombolysis. Our results support the use of CDI in selected patients, respecting the limitations and potential side effects of each technical device used.

ACKNOWLEDGMENTS

The authors are indebted to Lisa Hägerström, CCRN, for invaluable assistance with data retrieval for the study. This research was supported by departmental funding only and did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All authors declare that they have no conflicts of interest.

CONFLICT OF INTEREST

None.

FUNDING INFORMATION

The Sahlgrenska Academy at the University of Gothenburg.

ORCID

Jonatan Oras  <https://orcid.org/0000-0001-8890-6752>

Christian Rylander  <https://orcid.org/0000-0002-4534-7150>

REFERENCES

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J*. 2019.
2. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. *Chest*. 2016;149:315-352.
3. Noshier JL, Patel A, Jagpal S, Gribbin C, Gendel V. Endovascular treatment of pulmonary embolism: Selective review of available techniques. *World J Radiol*. 2017;9:426-437.
4. de Winter MA, Vlachojannis GJ, Ruigrok D, Nijkeuter M, Kraaijeveld AO. Rationale for catheter-based therapies in acute pulmonary embolism. *Eur Heart J Suppl*. 2019;21:116-122.
5. Myc LA, Solanki JN, Barros AJ, et al. Adoption of a dedicated multidisciplinary team is associated with improved survival in acute pulmonary embolism. *Respir Res*. 2020;21:159.
6. Svennerholm K, Lapidus L, Malm CJ, et al. Acute pulmonary embolism with hemodynamic compromise. Management and treatment. *Lakartidningen*. 2014;111:669-672.
7. Vandembroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18:805-835.
8. Miller GA, Sutton GC, Kerr IH, Gibson RV, Honey M. Comparison of streptokinase and heparin in treatment of isolated acute massive pulmonary embolism. *BMJ*. 1971;2:681-684.
9. Bankier AA, Janata K, Fleischmann D, et al. Severity assessment of acute pulmonary embolism with spiral CT: evaluation of two modified angiographic scores and comparison with clinical data. *J Thorac Imaging*. 1997;12:150-158.
10. Quiroz R, Kucher N, Schoepf UJ, et al. Right ventricular enlargement on chest computed tomography: prognostic role in acute pulmonary embolism. *Circulation*. 2004;109:2401-2404.
11. Jimenez D, Lobo JL, Monreal M, Otero R, Yusen RD. Prognostic significance of multidetector computed tomography in normotensive patients with pulmonary embolism: rationale, methodology and reproducibility for the PROTECT study. *J Thromb Thrombolysis*. 2012;34:187-192.
12. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2015;16:233-270.
13. Thomas JD, Zoghbi WA, Beller GA, et al. ACCF 2008 Training Statement on Multimodality Noninvasive Cardiovascular Imaging A Report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training Developed in Collaboration With the American Society of Echocardiography, the American Society of Nuclear Cardiology, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society for Vascular Medicine. *J Am Coll Cardiol*. 2009;53:125-146.
14. Bonvini RF, Roffi M, Bounameaux H, et al. AngioJet rheolytic thrombectomy in patients presenting with high-risk pulmonary embolism and cardiogenic shock: a feasibility pilot study. *EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*. 2013;8:1419-1427.

15. Kuo WT, Gould MK, Louie JD, Rosenberg JK, Sze DY, Hofmann LV. Catheter-directed Therapy for the Treatment of Massive Pulmonary Embolism: Systematic Review and Meta-analysis of Modern Techniques. *J Vasc Interv Radiol*. 2009;20:1431-1440.
16. Dwarka D, Schwartz SA, Smyth SH, O'Brien MJ. Bradyarrhythmias during use of the AngioJet system. *J Vasc Interv Radiol*. 2006;17:1693-1695.
17. Syed T, Tamis-Holland J, Coven D, Hong MK. Can glycopyrrolate replace temporary pacemaker and atropine in patients at high risk for symptomatic bradycardia undergoing AngioJet mechanical thrombectomy? *J Invasive Cardiol*. 2008;20:19a-21a.
18. De Gregorio MA, Guirola JA, Kuo WT, et al. Catheter-directed aspiration thrombectomy and low-dose thrombolysis for patients with acute unstable pulmonary embolism: Prospective outcomes from a PE registry. *Int J Cardiol*. 2019;287:106-110.
19. Schmitz-Rode T, Janssens U, Schild HH, Basche S, Hanrath P, Gunther RW. Fragmentation of massive pulmonary embolism using a pigtail rotation catheter. *Chest*. 1998;114:1427-1436.
20. Chechi T, Vecchio S, Spaziani G, et al. Rheolytic thrombectomy in patients with massive and submassive acute pulmonary embolism. *Catheter Cardiovasc Interv*. 2009;73:506-513.
21. Avgerinos ED, Liang NL, El-Shazly OM, et al. Improved early right ventricular function recovery but increased complications with catheter-directed interventions compared with anticoagulation alone for submassive pulmonary embolism. *J Vasc Surg Venous Lymphat Disord*. 2016;4:268-275.
22. Avgerinos ED, Saadeddin Z, Abou Ali AN, et al. A meta-analysis of outcomes of catheter-directed thrombolysis for high- and intermediate-risk pulmonary embolism. *J Vasc Surg Venous Lymphat Disord*. 2018;6:530-540.
23. Pieraccini M, Guerrini S, Laiolo E, et al. Acute Massive and Submassive Pulmonary Embolism: Preliminary Validation of Aspiration Mechanical Thrombectomy in Patients with Contraindications to Thrombolysis. *Cardiovasc Intervent Radiol*. 2018;41:1840-1848.
24. Becattini C, Agnelli G, Germini F, Vedovati MC. Computed tomography to assess risk of death in acute pulmonary embolism: a meta-analysis. *Eur Respir J*. 2014;43:1678-1690.
25. Bazeed MF, Saad A, Sultan A, Ghanem MA, Khalil DM. Prediction of pulmonary embolism outcome and severity by computed tomography. *Acta radiol*. 2010;51:271-276.
26. Ghaye B, Ghuysen A, Willems V, et al. Severe pulmonary embolism: pulmonary artery clot load scores and cardiovascular parameters as predictors of mortality. *Radiology*. 2006;239:884-891.
27. Meinel FG, Nance JW, Schoepf UJ, et al. Predictive Value of Computed Tomography in Acute Pulmonary Embolism: Systematic Review and Meta-analysis. *The American Journal of Medicine*. 2015;128(747-59):e2.
28. Kucher N, Boekstegers P, Müller Oliver J, et al. Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism. *Circulation*. 2014;129:479-486.
29. Avgerinos ED, Chaer RA. Catheter-directed interventions for acute pulmonary embolism. *J Vasc Surg*. 2015;61:559-565.
30. Zarghouni M, Charles HW, Maldonado TS, Deipolyi AR. Catheter-directed interventions for pulmonary embolism. *Cardiovasc Diagn Ther*. 2016;6:651-661.
31. Avgerinos ED, Abou Ali AN, Liang NL, et al. Predictors of failure and complications of catheter-directed interventions for pulmonary embolism. *J Vasc Surg*. 2017;5:303-310.
32. Tu T, Toma C, Tapson VF, et al. A Prospective, Single-Arm, Multicenter Trial of Catheter-Directed Mechanical Thrombectomy for Intermediate-Risk Acute Pulmonary Embolism. *The FLARE Study*. 2019;12:859-869.
33. Kramer A, Mortensen CS, Schultz JG, Lyhne MD, Andersen A, Nielsen-Kudsk JE. Inhaled nitric oxide has pulmonary vasodilator efficacy both in the immediate and prolonged phase of acute pulmonary embolism. *Eur Heart J Acute Cardiovasc Care*. 2020. 2048872620918713.
34. Lyhne MD, Schultz JG, Kramer A, Mortensen CS, Nielsen-Kudsk JE, Andersen A. Right ventricular adaptation in the critical phase after acute intermediate-risk pulmonary embolism. *Eur Heart J Acute Cardiovasc Care*. 2020. 2048872620925253.
35. Schultz J, Andersen A, Gade IL, Ringgaard S, Kjaergaard B, Nielsen-Kudsk JE. A porcine in-vivo model of acute pulmonary embolism. *Pulm Circ*. 2018;8:2045893217738217.
36. Schultz J, Andersen A, Lyhne MD, et al. Terlipressin Increases Systemic and Lowers Pulmonary Arterial Pressure in Experimental Acute Pulmonary Embolism. *Crit Care Med*. 2020;48:e308-e315.
37. Margheri M, Vittori G, Vecchio S, et al. Early and Long-Term Clinical Results of AngioJet Rheolytic Thrombectomy in Patients With Acute Pulmonary Embolism. *Am J Cardiol*. 2008;101:252-258.
38. Kuo WT, Sista AK, Faintuch S, et al. Society of Interventional Radiology Position Statement on Catheter-Directed Therapy for Acute Pulmonary Embolism. *J Vasc Interv Radiol*. 2018;29:293-297.
39. Das S, Das N, Serota H, Vissa S. A retrospective review of patients with massive and submassive pulmonary embolism treated with AngioJet rheolytic thrombectomy with decreased complications due to changes in thrombolytic use and procedural modifications. *Vascular*. 2018;26:163-168.
40. Ende-Verhaar YM, Kroft LJM, Mos ICM, Huisman MV, Klok FA. Accuracy and reproducibility of CT right-to-left ventricular diameter measurement in patients with acute pulmonary embolism. *PLoS One*. 2017;12:e0188862-e188962.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Einarsson F, Sandström C, Svennerholm K, Oras J, Rylander C. Outcomes of catheter-directed interventions in high-risk pulmonary embolism—a retrospective analysis. *Acta Anaesthesiol Scand*. 2021;65:499–506. <https://doi.org/10.1111/aas.13753>