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ORIGINAL ARTICLE

Catheter-Directed Therapy for the Management of Intermediate-High-Risk and High-Risk Pulmonary Embolism: Experience from a Single-Centre in Portugal

André Alexandre,[1,2] Bárbara Gonçalves,[2] Bruno Brochado,[1,2] David Sá-Couto,[1,2] Mariana Santos,[1,2] Diana Ribeiro,[1,2] Raquel Baggen-Santos,[1,2] André Luz,[1,2] João Silveira,[1,2] Severo Torres[1,2]

Centro Hospitalar Universitário do Porto,[1] Porto – Portugal
University of Porto,[2] Porto – Portugal

Abstract

Background: Acute pulmonary embolism (PE) is a significant cause of morbimortality. Epidemiological data in Portugal are limited, potentially leading to underdiagnosis. Catheter-directed therapy (CDT) is a promising alternative treatment, particularly for high-risk patients.

Objectives: To evaluate the impact of CDT on intermediate-high-risk and high-risk acute PE.

Methods: This is a retrospective single-centre study conducted from 2019 to 2023 in Portugal. Data included patient demographics, clinical presentation, procedural characteristics, and outcomes. Comparisons before and after the procedure were carried out, using two-sided paired Student´s T-test or McNemar´s test. *P-value* < 0.05 was considered statistically significant.

Results: Among the 21 patients included in this study, the mean age was 62.5 (±16.8) years and 57% (n = 12) were female. Bilateral PE was predominant (n=18, 86%), with fifteen patients (75%) classified as high-risk PE and five (25%) as intermediate-high-risk PE. Overweight (n = 12, 57%), hypertension (n = 9, 45%), dyslipidaemia (n = 8, 40%), immobility (n = 4, 20%), and active cancer (n=3, 14%) were prevalent comorbidities. The median Charlson Comorbidity Index score was 3.5 (IQR 1.2–4.0). Two-thirds (n = 10, 67%) of the patients with high-risk PE exhibited contraindications to systemic fibrinolysis, while one-third (n = 5, 33%) had previously undergone failed thrombolysis. CDT improved hemodynamic parameters, significantly reducing the right ventricular (RV) dysfunction after the procedure (72.2% vs 23.5%, p=0.008). There was a low incidence of bleeding complications, with only one patient (5%) experiencing life-threatening haemorrhage. Despite these improvements, in-hospital mortality remained high (n = 5, 24%). No deaths occurred within three months post-discharge.

Conclusions: Despite being in its early stages, CDT showed encouraging results in improving hemodynamic and clinical parameters in intermediate-high-risk and high-risk acute PE patients. Larger trials are warranted to further evaluate its efficacy and establish its role in treatment protocols.

Keywords: Pulmonary Embolism; Thrombectomy; Thrombolytic Therapy.

Introduction

Acute pulmonary embolism (PE) is a major global health problem, ranking as the third leading cause of cardiovascular death, after myocardial infarction and stroke, with a mortality rate exceeding 15% within three months of diagnosis.[1,2] It is also the leading preventable cause of death among hospitalised patients.[1] In Portugal, updated data reveals an incidence of 58 cases per population of 100,000 individuals, which is higher than previously reported.[1,3,4]

Classifying the severity of PE and assessing the risk of early mortality is crucial for optimal management.[5] High-risk PE, occurring in approximately 5% of all

Mailing Address: André Alexandre
Centro Hospitalar Universitário do Porto. Largo do Prof. Abel Salazar, 4099-001. Postal code: 4099-001. Porto – Portugal
E-mail: andrealexandre_1@msn.com
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Central Illustration: Catheter-Directed Therapy for the Management of Intermediate-High-Risk and High-Risk Pulmonary Embolism: Experience from a Single-Centre in Portugal

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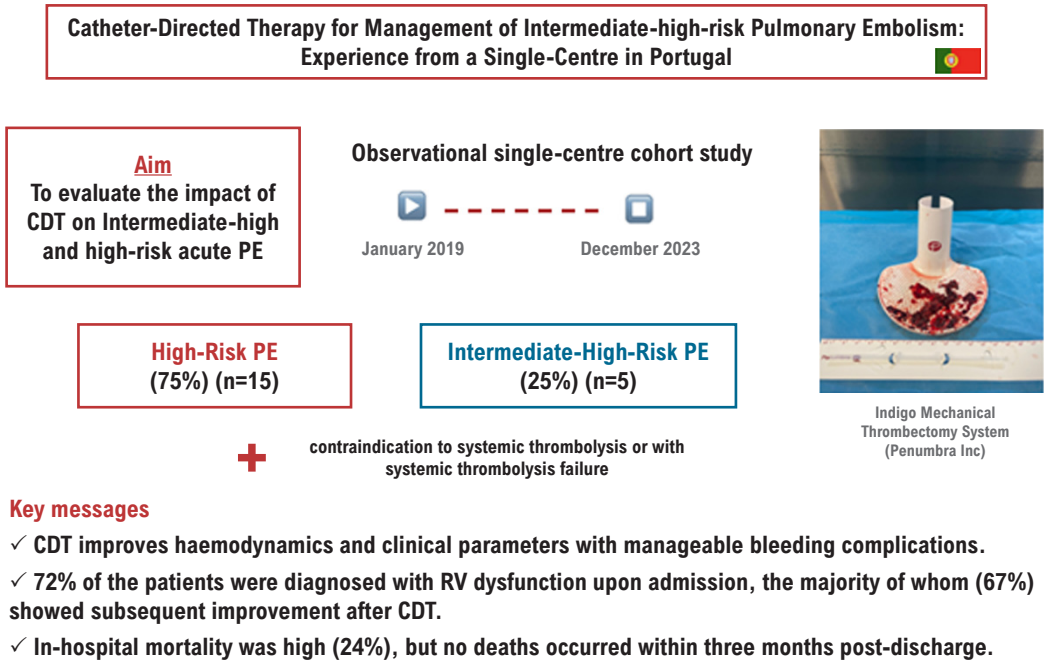

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CDT: catheter-directed therapy; PE: pulmonary embolism; RV: right ventricle/cular.

hospitalised PE patients, is associated with a very high short-term mortality rate, ranging from 18% to 64%.[6] The presence of right ventricular (RV) dysfunction and haemodynamic instability due to acute pressure overload are robust predictors of poor prognosis in those cases.[2,6]

Most PE patients respond well to anticoagulation, but those at high-risk or intermediate-high-risk may require more advanced interventions, such as systemic thrombolysis or surgical embolectomy, which carry significant risks.[1] Recently, there has been growing interest in catheter-directed therapy (CDT), namely catheter-directed thrombolysis and pulmonary aspiration thrombectomy, due to its potential for rapid reperfusion of pulmonary arteries and improved outcomes.[7-10] However, the role of CDT in PE treatment is not yet well-defined, and current recommendations are largely based on expert consensus and non-randomized studies.[1,5]

This retrospective single-centre study aims to evaluate the impact of CDT on intermediate-high-risk and high-risk acute PE at a tertiary centre in Portugal, with the goal of providing insights that could guide future clinical practice.

Methods

Study Design and Population

This is an observational single-centre cohort study of intermediate-high-risk and high-risk acute PE patients that were submitted to CDT with Indigo® Mechanical Thrombectomy System (Penumbra, Alameda, California) from January 2019 to December 2023 at a tertiary hospital in Portugal.

Patients were referred to CDT if they were 18 years or older and experienced acute PE with symptom duration equal to or less than 14 days. Prognostic stratification as intermediate-high-risk or high-risk was performed according to the 2019 European Society of Cardiology/ European Respiratory Society (ESC/ERS) Guidelines for the diagnosis and management of acute PE.[5]

According to the hospital protocol and following ESC/ ERS recommendations,[5] patients were eligible for CDT if they met one of the following criteria: high-risk PE with an absolute or relative contraindication to systemic thrombolysis; high-risk PE with systemic thrombolysis

failure (rescue reperfusion therapy); or intermediate-high-risk PE with at least one early sign of haemodynamic decompensation.

Data Collection

Information regarding patient demographics, medical history, symptoms, and physical examination was collected using the institution´s electronic database. Blood analysis results, 12-lead electrocardiogram (ECG), transthoracic echocardiogram (TTE), computed tomography pulmonary angiogram (CTPA), anticoagulation therapy, pulmonary angiographic findings, procedural characteristics, and invasive measures were also collected, as were data on in-hospital and three-month outcomes. Prognostic stratification scores from both the original and simplified Pulmonary Embolism Severity Index (PESI) were calculated, and the Charlson Comorbidity Index score was determined for each patient.

Outcomes

In-Hospital Outcomes: Efficacy and Safety

Clinical success, representing the effectiveness outcome, was defined as survival upon discharge from the hospital and achieving one of the following endpoints at 48 hours after the procedure: 1) stabilization of haemodynamic parameters, including the resolution of haemodynamic shock with no need for vasopressor support; 2) improvement of the shock index to a target ratio of <1.0 (the shock index is defined as the ratio of heart rate to systolic blood pressure, with values greater than 0.9 indicating potential haemodynamic instability);[11] 3) increase in the PaO2/FiO2 ratio, reaching values above 200; and 4) improvement in pulmonary hypertension, right-sided heart strain, or both.

The primary safety outcome, referred to as the major adverse event rate, was a combination of severe adverse events, occurring within the initial 48 hours, which included death, cardiorespiratory arrest, arrhythmias requiring specific treatment, pulmonary vascular or cardiac injury, stroke, or life-threatening bleeding. The secondary safety outcome, known as the non-serious adverse event rate, encompassed instances of moderate or mild bleeding. Bleeding events were classified by the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) bleeding criteria.[2,12]

Short-Term Outcomes: Three-Month Follow-Up

Short-term outcomes were assessed three months post-hospital discharge, focusing on symptomatic recurrence of PE, unplanned admissions due to right heart failure and all-cause mortality. Chronic thromboembolic pulmonary hypertension (CTEPH) was diagnosed following the criteria outlined in the 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension.[13]

Statistical Analyses

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software, version 29.0 (IBM Corp., Armonk, NY, USA). Categorical variables were reported by numbers and proportions (%). Continuous variables were presented as means and standard deviations (SD) for normally distributed variables, and medians and interquartile ranges for non-normally distributed variables. The Shapiro-Wilk test was used to test the normality of distribution. Clinical, laboratorial, echocardiographic and haemodynamic characteristics before and after the procedure were compared using the two-sided paired Student´s T-test for continuous variables and McNemar´s test for categorical variables. A two-sided $p\text{-}value < 0.05$ was considered to indicate statistical significance.

Ethical Approval

The study's protocol complies with the Declaration of Helsinki, and was approved by the institution's Ethics Committee, logged under protocol number 2023-232(195-DEFI/184-CE).

Results

Baseline Demographics

The present study included 21 patients with a mean age of 62.5 ± 16.8 years, the majority of whom were female (57%). Overweight (defined as body mass index greater than 25 kg/m^2) was the most frequent comorbidity (57%). Among the contributing factors to PE were hypertension (45%), dyslipidaemia (40%), immobility within 30 days of PE diagnosis (20%) and active cancer (14%). Detailed baseline demographic characteristics are provided in Table 1.

Table 1 - Baseline demographic characteristics

	Overall (n = 21)
Demographic characteristics	
Age, mean ± SD, years	62.48 ± 16.79
Female, n (%)	12 (57.1)
Medical history	
Overweight, n (%)	12 (57.1)
Arterial hypertension, n (%)	9 (45.0)
Smoking, n (%)	5 (26.3)
Dyslipidaemia, n (%)	8 (40.0)
Diabetes mellitus, n (%)	2 (10.0)
Active cancer, n (%)	3 (14.3)
Immobilization (within previous month), n (%)	4 (20.0)
Auto-immune disease, n (%)	2 (10.0)
Major surgery or trauma (within previous month), n (%)	4 (20.0)
Oestrogen use, n (%)	3 (15.0)
Coronary artery disease, n (%)	1 (5.0)
Prior myocardial infarction (within previous 3 months), n (%)	0 (0.0)
Congestive heart failure, n (%)	1 (5.0)
History of venous thromboembolism, n (%)	3 (15.0)
Charlson Comorbidity Index, median (IQR)	3.5 (1.2 – 4.0)

Baseline demographic characteristics of the study population.
IQR: interquartile range; SD: standard deviation.

Clinical Presentation and PE Characteristics

Bilateral PE was the predominant finding in most patients (86%). The cohort presented both intermediate-high-risk (25%) and high-risk (75%) acute PE cases. In the subgroup of patients with high-risk PE, two-thirds had an absolute contraindication for systemic thrombolysis, while the remaining one-third had previously undergone failed systemic thrombolysis. The great majority of patients (79%) were categorized in class III or higher of the original PESI score, indicating a moderate, high or very-high 30-day mortality risk. Additionally, 63% of patients had a simplified PESI score ≥ 1, corresponding to a 30-day mortality risk of 11%.

Dyspnoea was the primary symptom observed in the majority of individuals (61%). Initial TTE findings indicated RV dysfunction in 72% of the patients. Additional details on clinical symptoms, laboratory findings and PE characteristics can be found in Table 2.

Angiographic and Procedural Data

The right femoral vein was the most commonly used access site (90.5%). Bilateral pulmonary intervention was performed in 43% of the patients. In situ thrombolytic therapy, involving the bolus injection of alteplase via catheter, was administrated in a subset of patients (38%). The decision to employ thrombolytic therapy was made based on the responsible clinician´s judgment, considering the perceived significant presence of a blood clot rather than the clinical deterioration of the patient. For more detailed procedural characteristics, refer to Table 3.

Table 2 - Clinical and PE characteristics

	Overall (n = 21)
Clinical symptoms and signs at presentation	
Dyspnoea, n (%)	11 (61.1)
Presyncope/Syncope, n (%)	6 (33.3)
Chest pain, n (%)	6 (33.3)
Heart rate, mean ± SD, bpm	100.6 ± 19.8
Tachycardia ≥ 110 bpm, n (%)	8 (42.1)
Shock index > 1, n (%)	4 (25.0)
Systolic arterial pressure, mean ± SD, mmHg	114.7 ± 30.9
Diastolic arterial pressure, mean ± SD, mmHg	68.6 ± 20.8
Mean arterial pressure, mean ± SD, mmHg	83.4 ± 23.5
Respiratory rate ≥ 20 breaths/min, n (%)	6 (37.5)
Peripheral oxygen saturation, mean ± SD, %	89.5 ± 7.7
PaO2/FiO2, mean ± SD	231.4 ± 88.4
RV dysfunction, n (%)	13 (72.2)
RV strain on ECG, n (%)	6 (46.2)
sPAP, mean ± SD, mmHg	45.4 ± 17.7
TAPSE, mean ± SD, mm	18.7 ± 3.3
Lactate level, mean ± SD, mmol/L	3.7 ± 4.3
Creatinine, mean ± SD, mg/dL	1.3 ± 0.8
Cardiac T troponin level, median (IQR), ng/L	147 (60 – 279)
NT pro-BNP level, median (IQR), pg/mL	2906 (717 – 7934)
PE localisation	
Bilateral PE, n (%)	18 (85.7%)
Isolated right-sided PE, n (%)	2 (9.5%)
Isolated left-sided PE, n (%)	1 (4.8%)
PE risk stratification	
Original PESI score ≥ III, n (%)	15 (78.9)
Simplified PESI score ≥ 1, n (%)	12 (63.2)
Intermediate-high-risk, n (%)	5 (25.0)
High-risk with contraindication for lysis, n (%)	10 (50.0)
History of haemorrhagic stroke or stroke of unknown origin, n (%)	6 (28.6)
Major trauma, surgery or head injury, n (%)	3 (14.3)
Risk of aortic aneurysm rupture, n (%)	1 (4.8)
High-risk with failed systemic lysis, n (%)	5 (25.0)

Clinical and PE characteristics of the study population. Normal reference range: Lactate level ≤ 1.2 mmol/L; Cardiac T troponin level ≤ 14 ng/L; NT pro-BNP level ≤ 125 pg/mL.
IQR: interquartile range; PE: pulmonary embolism; PESI: pulmonary embolism severity index; RV: right ventricle/cular; SD: standard deviation; sPAP: systolic pulmonary artery pressure; TAPSE: tricuspid annular plane systolic excursion.

Table 3 - Angiographic and procedural characteristics

	Overall (n = 21)
Access site	
Right femoral vein, n (%)	19 (90.5)
Left femoral vein, n (%)	2 (9.5)
Local of intervention	
Bilateral, n (%)	9 (42.9)
Unilateral right, n (%)	6 (28.6)
Unilateral left, n (%)	6 (28.6)
PAP	
sPAP, mean ± SD, mmHg	51.5 ± 19.3
Angiographic and infusion characteristics	
Fluoroscopy time, mean ± SD, min	39.5
Contrast volume, mean ± SD, mL	207.5 ± 107.4
Thrombolytic infusion catheter, n (%)	8 (38.1)
Total t-PA dose, mean ± SD, mg	4.5 ± 6.8
Access closure	
Manual compression, n (%)	17 (94.4)
Perclose proglide system (Abbot Vascular®), n (%)	1 (5.6)

Angiographic and procedural characteristics of the study population.
SD: standard deviation; sPAP: systolic pulmonary artery pressure; PAP: pulmonary artery pressure.

In-Hospital and Short-Term Outcomes

In-Hospital Outcomes: Efficacy and Safety

In-hospital efficacy outcomes and haemodynamics' evolution after CDT are summarized in Table 4. A statistically significant improvement was observed in mean pulmonary artery pressure (PAP) and in RV dysfunction. The mean PAP decreased from 30.8 ± 12.4 mmHg at baseline to 24.6 ± 8.0 mmHg upon procedure completion, representing a mean difference of 6.2 ± 5.0 mmHg (p = 0.049). Following the procedure, there was also a significant reduction in RV dysfunction (72.2% vs 23.5%, p=0.008).

In-hospital safety outcomes are depicted in Table 5. The in-hospital mortality rate was 24% (n = 5), with the majority of these patients (n = 3, 60%) dying within 48 hours of admission.

Short-Term Outcomes: Three-Month Follow-Up

Short-term events after hospital discharge are shown in Table 5. A three-month follow-up was completed in 87% (n = 13) of the patients surviving hospital discharge, with two patients being lost to follow-up.

During follow-up, three patients (20%) were diagnosed with CTEPH. Notably, no deaths occurred within three months post-discharge (Table 5). There were also no reported symptomatic recurrence of PE, no chronic thromboembolic disease (CTED) without pulmonary hypertension nor any unplanned admissions due to right heart failure during the three-month follow-up period.

Discussion

The main findings of this study were as follows: (1) patients with high-risk PE accounted for 75% of all individuals undergoing CDT; (2) two-thirds of the patients with high-risk PE undergoing CDT showed an absolute

Table 4 - In-hospital efficacy outcomes and haemodynamic evolution after CDT

	Pre-Procedure	Post-Procedure	Absolute difference (mean)	p-value
PAP				
mPAP, mean ± SD, mmHg	30.8 ± 12.4	26.0 ± 7.9	6.2 ± 5.0	0.049
PaO_2/FiO_2, mean ± SD	231.4 ± 88.4	189.9 ± 82.4	40.9 ± 113.4	0.144
Shock index, mean ± SD	0.94 ± 0.19	0.76 ± 0.13	0.17 ± 0.22	0.015
Haemodynamic decompensation at 48 hours, n (%)	-	8 (40.0)	-	-
RV dysfunction, n (%)	13 (72.2)	4 (23.5)	-	0.008

Evolution of haemodynamics and other in-hospital efficacy outcomes after CDT. Significant associations (p-value < 0.05) are in bold.
CDT: catheter-directed therapy; mPAP: mean pulmonary artery pressure; RV: right ventricle/cular; SD: standard deviation; PAP: pulmonary artery pressure.

contraindication to systemic fibrinolysis; (3) 72% of the patients who were diagnosed with RV dysfunction upon admission, the majority of whom showed subsequent improvement after CDT; (4) in-hospital mortality was high (24%); (5) no deaths occurred within three months post-discharge (see Central Illustration).

Our cohort's mean age of 62.5 years and the predominance of females (57%) are consistent with the demographics reported in other studies on acute PE management.[2,4,14] Cardiovascular comorbidities, particularly overweight (57%), hypertension (45%), and dyslipidaemia (40%), were prevalent in our population, mirroring patterns seen in broader PE studies.[2,4,14] The frequent presence of these comorbidities underscores the importance of addressing cardiovascular risk factors in PE patients, as they significantly impact prognosis and treatment outcomes.

Acute PE can appear in a spectrum of presentations, ranging from asymptomatic to life-threatening scenarios.[2,4,14] Despite the varied clinical manifestations, dyspnoea remains the predominant symptom, as supported by studies such as PIOPED II.[15] Similarly, our study found dyspnoea to be the primary symptom in the majority of cases (61%), followed by chest pain (33%) and presyncope/syncope (33%). Additionally, tachycardia (heart rate > 100/minute), tachypnoea (respiratory rate ≥ 20 breaths/min) and hypoxemia were the most frequent signs related to acute PE observed in our study.

Stratifying acute PE is important to determine the optimal approach and requires assessing specific laboratory findings, such as levels of high-sensitivity cardiac T troponin and NT-proBNP.[5] These markers are associated with RV dysfunction, which is the most common complication and one of the most reliable predictors of poor prognosis in individuals with acute PE.[6] The high-risk nature of our cohort is reflected in the fact that 75% of the patients presented high-risk PE, with 79% classified as PESI score class III or higher. This stratification aligns with guidelines recommending aggressive treatment in high-risk patients, where RV dysfunction plays a crucial role in determining prognosis.[5,6] In our study, 72% of the patients had RV dysfunction upon admission, supporting the assumption that RV dysfunction is the most common complication of acute PE and contributing to the high in-hospital mortality. Furthermore, the ECG findings consistent with RV overload were present in only 46% of our cohort, compared to 72% of the TTE results, confirming the greater accuracy of TTE in diagnosing RV dysfunction, when compared to ECG.

Although thrombolysis is the recommended strategy for managing high-risk PE patients, several registries, such as RIETE and ICOPER, have reported low rates (20-30%) of systemic fibrinolysis use in real-world practice, further supporting the need for alternative therapies like CDT.[2,4,5,16,17] By contrast, concerns regarding the risk of life-threatening haemorrhage have reduced enthusiasm for full-dose systemic fibrinolysis and encouraged the development of alternative treatments with a lower risk of bleeding.[8,18-20]

Table 5 - In-hospital safety outcomes and short-term outcomes at 3 months of follow-up

In-hospital safety outcomes	Overall (n = 21)
Major adverse events within 48 hours, a composite of, n (%)	10 (47.6)
Death, n (%)	3 (14.3)
Arrhythmias requiring specific treatment, n (%)	3 (14.3)
Cardiorespiratory arrest, n (%)	2 (9.5)
Pulmonary vascular injury, n (%)	2 (9.5)
Cardiac injury, n (%)	1 (4.8)
Stroke, n (%)	1 (4.8)
Severe or life-threatening bleeding, n (%)	1 (4.8)
Non-serious adverse events, a composite of, n (%)	8 (38.1)
Anaemia that required transfusion, but without haemodynamic compromise, n (%)	7 (33.3)
Minor bleeding, n (%)	1 (4.8)
In-hospital death, n (%)	5 (23.8)
Obstructive shock, n (%)	3 (14.3)
Cardiorespiratory arrest during procedure, n (%)	1 (4.8)
Stroke, n (%)	1 (4.8)
Short-term outcomes at 3 months of follow-up	**Overall (n=15)**
All-cause mortality, n (%)	0 (0.0)
Symptomatic recurrence of PE, n (%)	0 (0.0)
Unplanned right heart failure admission, n (%)	0 (0.0)
CTED without pulmonary hypertension, n (%)	0 (0.0)
CTEPH, n (%)	3 (20.0)

In-hospital safety outcomes after CDT and short-term outcomes at 3 months of follow-up after hospital discharge. The short-term outcomes at the 3 months of follow-up included only those patients who survived hospitalisation (n = 15).
CDT: catheter-directed therapy; CTED: chronic thromboembolic disease; CTEPH: chronic thromboembolic pulmonary hypertension; PE: pulmonary embolism.

In our study, patients with high-risk PE accounted for 75% of all patients undergoing CDT, and two-thirds of the patients with high-risk PE undergoing CDT had an absolute contraindication to systemic fibrinolysis. The remaining one-third of patients with high-risk PE were submitted to CDT after failed systemic thrombolysis. This finding resonates with the growing body of evidence suggesting that CDT is a viable alternative in high-risk patients where systemic thrombolysis is not feasible.[8,21,22]

In our study population, 25% of the patients with intermediate-high-risk PE underwent CDT. Although the best approach for managing patients in the intermediate-high-risk PE group is still unclear, a combination of clinical variables, biomarkers and imaging studies may help identify those who would benefit most from close monitoring.[23,24] Currently, there are numerous treatment options available, including various thrombolysis dosages, catheter-directed therapies, surgical interventions and peripherally inserted devices to enhance cardiac output.[23,24] It is crucial to develop an improved method to identify which patients in the intermediate-high-risk category would benefit from such treatments.[23,24] Indeed, while aggressive treatment can be beneficial for patients at a significant risk

of decompensation, it may well pose unnecessary risks for those not facing immediate decompensation.

In our study, a significant decrease was observed in mean PAP and RV dysfunction post-CDT, which aligns with findings from such studies as ULTIMA and SEATTLE II, which reported improved haemodynamics following CDT.[21,25-27] Furthermore, all those studies showed a low incidence of major bleeding events and no fatal intracranial haemorrhage, suggesting that CDT could be extended to patients with high-risk PE who are also at an elevated risk of bleeding, such as the elderly and those with active malignancies.[2,4,6,9,21,25-27]

Nevertheless, the high incidence (48%) of major adverse events within 48 hours, including our 24% in-hospital mortality rate, underscores the severity of our patients' conditions. This mortality rate is comparable to other studies, such as those by Calé et al. and Secemsky et al., which reported in-hospital mortality rates ranging from 17% to 30%.[2,14,22] It is crucial to acknowledge that we cannot categorically attribute these events to the CDT procedure itself. The observed complications highlight the need for careful patient selection and monitoring during and after CDT.

Our study's three-month follow-up revealed no deaths or symptomatic PE recurrences, which is a positive outcome when compared to previous studies that reported significant early mortality and morbidity.[14] This suggests that patients who survive the critical in-hospital phase may have favourable outcomes with appropriate post-discharge care. The absence of recurrent PE and unplanned RV failure admissions further emphasizes the potential of CDT to provide durable benefits in high-risk PE patients.

Given the critical nature of the patients in our study and the complexity of their management, our findings support the broader adoption of CDT, particularly in settings where systemic thrombolysis is contraindicated or has failed. The establishment of multidisciplinary expert pulmonary embolism response teams (PERTs) and adherence to institutional and regional guidelines will be essential to optimize outcomes in this challenging patient population.[6]

Strengths and Limitations

This study has certain limitations that should be considered. First, the sample size is limited to a single centre, which may restrict the generalisation of the findings to the national level. Second, the small sample size may have reduced the accuracy of the results. Third, the retrospective study design resulted in some missing data, exacerbated by the fact that several cases were referred from other hospitals.

Despite these limitations, this study provides valuable insights into clinical practice and management strategies for patients with intermediate-high-risk and high-risk acute PE.

Conclusions

Acute PE continues to be a significant cause of morbidity and mortality. Although percutaneous interventions are still in their early stages, our study found that CDT improves haemodynamic and clinical parameters with manageable bleeding complications in intermediate-high-risk and high-risk patients. Larger trials are needed to further evaluate CDT's efficacy and to identify patients who would benefit most.

Author Contributions

Conception and design of the research, analysis and interpretation of the data and writing of the manuscript: Alexandre A, Gonçalves B, Brochado B; acquisition of data: Alexandre A, Gonçalves B, Brochado B, Sá-Couto D, Santos M, Ribeiro D, Baggen-Santos R, Luz A, Silveira J, Torres S; statistical analysis: Alexandre A, Gonçalves B; critical revision of the manuscript for intellectual content: Sá-Couto D, Santos M, Ribeiro D, Baggen-Santos R, Luz A, Silveira J, Torres S. Alexandre A and Gonçalves B are co-first authors and equally contributed to the study.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of the ULS de Santo Antonio and ICBAS under the protocol number 2023-232(195-DEFI/184-CE).

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