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Treatment of high- and intermediate-high-risk pulmonary embolism by the Pulmonary Embolism Response Team: Focus on catheter-directed therapies

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Abstract

Background: *Multidisciplinary Pulmonary Embolism Response Teams (PERTs) were established to individualize the treatment of high-risk (HR) and intermediate-high-risk (IHR) pulmonary embolism (PE) patients, which pose a challenge in clinical practice.*

Methods: *We retrospectively collected the data of all HR and IHR acute PE patients consulted by PERT CELZAT between September 2017 and October 2022. The patient population was divided into four different treatment methods: anticoagulation alone (AC), systemic thrombolysis (ST), surgical embolectomy (SE), and catheter-directed therapies (CDTx). Baseline clinical characteristics, risk stratification, PE severity parameters, and treatment outcomes were compared between the four groups.*

Results: *Of the 110 patients with HR and IHR PE, 67 (61%) patients were treated with AC only, 11 (10%) with ST, 15 (14%) underwent SE, and 17 (15%) were treated with CTDx. The most common treatment option in the HR group was reperfusion therapy, used in 20/24 (83%) cases, including ST in 7 (29%) patients, SE in 5 (21%) patients, and CTDx in 8 (33%) patients. In contrast, IHR patients were treated with AC alone in 63/86 (73%) cases. The in-hospital mortality rate was 9/24 (37.5%) in the HR group and 4/86 (4.7%) in the IHR group.*

Conclusions: *The number of advanced procedures aimed at reperfusion was substantially higher in the HR group than in the IHR PE group. Despite the common use of advanced reperfusion techniques in the HR group, patient mortality remained high. There is a need further to optimize the treatment of patients with HR PE to improve outcomes.* (Cardiol J 2024; 31, 2: 215–225)

Keywords: catheter-directed therapies, high-risk pulmonary embolism, intermediate-high-risk pulmonary embolism, pulmonary embolism, Pulmonary Embolism Response Team

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Introduction

Pulmonary embolism (PE) remains the third most frequent acute cardiovascular disease, with an estimated prevalence of 100–200 cases per 100,000 people in the United States [1–3]. Obstruction of pulmonary arteries causes variable clinical manifestations, ranging from mild symptoms to cardiac arrest and death. The presence of hemodynamic instability along with the Pulmonary Embolism Severity Index (PESI) or simplified PESI (sPESI) score, troponin elevation, and evidence of right ventricle (RV) dysfunction allows us to stratify patients into high (HR), intermediate-high (IHR), intermediate-low, and low risk of early (30-day) mortality [3].

Between 1993 and 2012, in-hospital mortality due to PE declined from 7.1% to 3.2%, despite a higher number of PE-related hospitalizations during the preceding two decades [4]. Similarly, mortality in high-risk PE has decreased significantly, but the availability of advanced treatment methods remains suboptimal [5]. As well as diagnostics improvements, PE therapeutic options have expanded, especially for HR and IHR patients. Currently, in addition to standard anticoagulant therapy, treatment methods include systemic thrombolysis (ST), surgical embolectomy (SE), catheter-directed thrombectomy (CDT), catheter--directed thrombolysis (CDL), and extracorporeal membrane oxygenation (ECMO) [6]. Whereas most low-risk and intermediate-low-risk PE patients can be effectively treated with anticoagulants alone, patients with HR and IHR PE remain a therapeutic challenge, requiring more advanced treatment in addition to anticoagulation [7, 8]. This, in turn, results in an increased risk of treatment-related adverse events such as bleeding, and it requires individual risk-to-benefit consideration [9, 10].

Consequently, Pulmonary Embolism Response Teams (PERTs) were established for multidisciplinary collaboration between various specialists to facilitate the choice of optimal therapy for patients with PE [11]. PERT activity focuses particularly on HR and IHR PE; the guidelines do not cover specific issues related to patients in these subgroups, and thus the individualized approach is crucial [3, 12]. The first studies evaluating the effectiveness of PERT interventions showed improved survival rates and reduced bleeding events during the acute phase of PE treatment [13, 14]. However, a meta-analysis of 9 controlled studies showed no difference in the survival rate between the pre-PERT and PERT eras, despite the increased use of advanced treatment options [15]. These discrepancies could be explained by the fact that individual PERTs differ significantly with respect to the characteristics of the patients they consult, applied treatment strategies, and achieved results, because qualification for the specific intervention depends on local experience and available treatment modalities [15, 16]. Considering the gap in evidence in the European Society of Cardiology (ESC) guidelines regarding HR and IHR PE patients and the differences in expertise between local PERTs, a detailed assessment of PERT activities and outcomes is crucial.

To understand the factors associated with treatment outcomes and to optimize future treatment decisions, we analyzed the characteristics and treatment modalities of HR and IHR PE patients within our local PERT, the Center for the Management of Pulmonary Embolism (CELZAT), which was established in Warsaw in 2017 [17]. Considering recent technological developments in the field of catheter-directed therapies (CDTx), we provided a detailed analysis of the CDTx techniques applied within our PERT.

Methods

We retrospectively collected the data of all HR and IHR acute PE patients consulted by PERT CELZAT between September 2017 and October 2022. The diagnosis of PE was confirmed in all patients by computed tomography pulmonary angiogram (CTPA). IHR PE was defined as RV dysfunction detected by transthoracic echocardiography or CTPA and elevated troponin-T levels. HR PE was defined as hemodynamic instability or the need for cardiopulmonary resuscitation, according to the current ESC Guidelines on Acute Pulmonary Embolism [3, 17].

The HR and IHR patient population was divided into four different therapeutic subgroups: AC alone, ST, SE, and CDTx. AC alone was defined as the administration of unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), vitamin K antagonists, or direct oral anticoagulants without additional PE-specific therapies. ST referred to the intravenous administration of recombinant tissue plasminogen activator (rtPA). SE was defined as the surgical removal of the pulmonary thrombi following the incision of pulmonary arteries under extracorporeal circulation, with aorta clamping and administration of cardioplegia [18]. CDTx included CDT, CDL, or a combination of both. For CDL, a Fountain 5 F infusion catheter (Merit Medical Systems, Inc., South Jordan, UT, USA) was used, consisting of a 10-cm infusion segment inserted in

the pulmonary arteries to deliver the thrombolytic drug through gradient side holes on the catheter. For CDT, 3 thrombectomy systems were applied: Indigo CAT8 XTORQ (Penumbra Inc., Alameda, CA, USA), Indigo CAT12 XTORQ (Penumbra Inc., Alameda, CA, USA), and Cleaner XT™ (Argon Medical Devices, Plano, TX, USA). Indigo CAT8 is an aspiration thrombectomy-based system that implements automatic suction through an 8 F catheter and uses a retractable separator that moves back and forth, facilitating thrombus fragmentation [19]. Indigo CAT12 has an improved algorithm that controls automatic valves, reducing blood loss and optimizing clot removal [20]. Cleaner XT™ is a 6 F rotational thrombectomy system, utilizing a sinuous-shaped radio-opaque wire that rotates at approximately 4000 rounds per minute, facilitating gentle mechanical declotting [21]. Details of the CDTx methods applied by our PERT have previously been described [22].

Baseline clinical characteristics, risk stratification, and PE severity parameters were compared between the four treatment groups. Information about clinical and treatment data was obtained from medical records. Obesity was defined as a body mass index of 30.0 kg/m^2 or higher. As a comorbidity on admission, stroke was defined as both hemorrhagic and ischemic. A recent hospitalization, surgery, or trauma was defined as an episode that occurred within 1 month before the onset of PE. In-hospital outcomes included frequency of (i) mortality, (ii) stroke, (iii) recurrent PE/deep vein thrombosis, and (iv) bleeding complications as defined by the International Society on Thrombosis and Hemostasis (ISTH).

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics, version 27.0 (IBM, Sheffield, UK). Categorical variables were presented as numbers and percentages. Continuous variables are presented as mean and standard deviation or median with interquartile range. The chi-square test for categorized variables and one-way ANOVA or the Kruskal–Wallis test for continuous variables were used to determine differences between groups, depending on the distribution. A p-value below 0.05 was considered significant.

Results

Patient risk groups

Figure 1 shows the flow chart of subsequent patients consulted by PERT CELZAT and included in the analysis. Among 244 patients consulted by PERT since its establishment in September 2017, 134 (55%) patients have been diagnosed with low- and intermediate-low-risk PE and 110 (45%) patients with HR or IHR PE. Of the 110 patients included in the analysis, 24 (22%) patients met the criteria of HR PE and 86 (78%) patients presented with IHR PE. The therapeutic strategies in the HR and IHR groups, including the number of patients undergoing each treatment, are listed in Figure 1. Overall, 67 (61%) patients were treated with AC only, 11 (10%) were treated with ST, 15 (14%) patients underwent SE, and in 17 (15%) cases CTDx was performed.

Proportion of treatment methods according to the patient risk group

The proportion of treatment methods in PE risk subgroups is shown in Figure 1. Therapeutic modalities applied following CELZAT activation in the HR and IHR groups are presented in Figure 2. In the HR group, 20 out of 24 (83%) patients received reperfusion therapy, including ST in 7 (29%) patients, SE in 5 (21%) patients, and CTDx in 8 (33%) patients. The reperfusion method was abandoned in 4 (17%) patients due to a critical clinical condition caused by comorbidities. In the IHR group, 63 out of 86 (73%) patients were treated with AC alone and 23 (27%) patients received reperfusion therapy, including ST in 4 (5%) patients, SE in 10 (12%) patients, and CTDx in 9 (11%) patients. The indications for ST in IHR patients included clinical deterioration during AC with UFH or LMWH. The indication for SE was the presence of a thrombus in transit or acute PE on top of the chronic thromboembolism, corresponding to chronic thromboembolic pulmonary hypertension. If chronic thromboembolic pulmonary hypertension was confirmed, a pulmonary endarterectomy was performed in addition to SE.

Patient clinical characteristics

Table 1 presents a comparison of baseline characteristics of patients with HR and IHR PE, divided into four groups according to the primary treatment method: AC alone (67 patients, 61%), ST (11 patients, 10%), SE (15 patients, 14%), and CDTx (17 patients, 15%). There were no significant differences between the treatment groups regarding sex, symptoms presented on admission and most of the comorbidities, and other venous thromboembolism risk factors, depending on the treatment strategy.

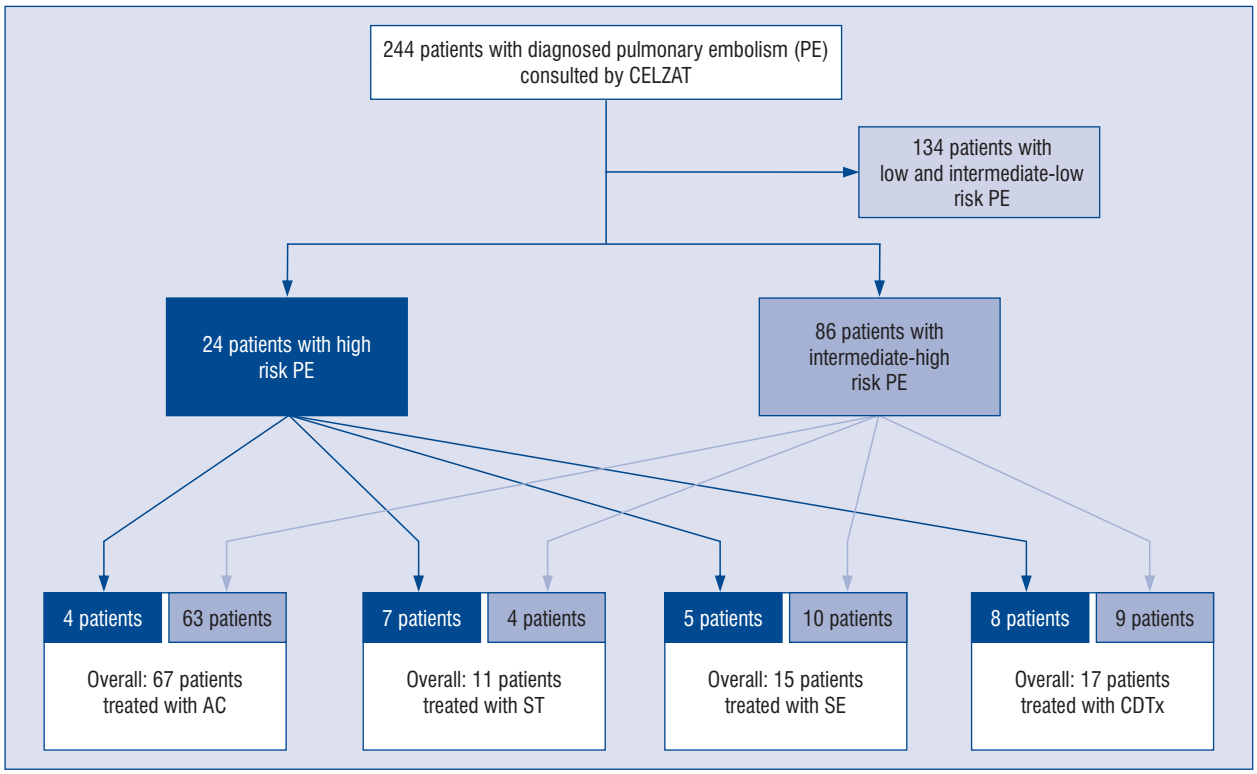

Figure 1. Flow chart of patients treated by Pulmonary Embolism Response Teams Center for the Management of Pulmonary Embolism (CELZAT); AC — anticoagulation alone; CDTx — catheter-directed therapies; PE — pulmonary embolism; SE — surgical embolectomy; ST — systemic thrombolysis.

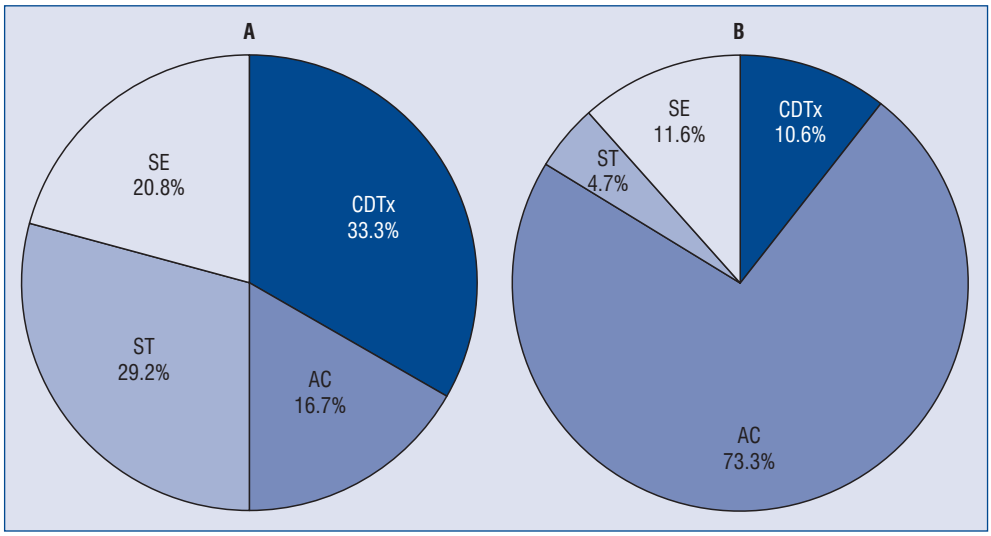

Figure 2. Therapeutic modalities applied following Pulmonary Embolism Response Team activation in high-risk (**A**) and intermediate-high-risk (**B**) pulmonary embolism subgroups, respectively; AC — anticoagulation alone; CDTx — catheter-directed therapies; SE — surgical embolectomy; ST — systemic thrombolysis.

Outcomes

The in-hospital outcome events according to mortality risk group and treatment method are shown in Table 2. The rate of in-hospital mortality was 11.8% (13/110), including 37.5% in the HR group (9/24) and 4.7% in the IHR group (4/86).

There were 4 (3.6%) minor bleeding events and 5 (4.5%) major bleeding events that required

Table 1. Baseline characteristics of patients treated with anticoagulation alone, systemic thrombolysis, surgical embolectomy, and catheter-directed therapies.

	Overall	Anticoagulation alone	Systemic thrombolysis	Surgical embolectomy	Catheter-directed therapies	P
Total (n)	110	67	11	15	17	
High risk (%)	24	4 (16.7)	7 (29.2)	5 (20.8)	8 (33.3)	
Intermediate-high risk (%)	86	63 (73.2)	4 (4.7)	10 (11.6)	9 (10.5)	
Baseline characteristics						
Age [years]	60.4 ± 16.3	63.5 ± 14.5	60.5 ± 16.5	50.2 ± 16.9	59.2 ± 13.5	**0.03**
Sex, male	59 (53.6%)	40 (59.7%)	4 (36.4%)	6 (40.0%)	9 (52.9%)	0.33
Symptoms on admission						
Dyspnea	89 (80.9%)	50 (74.6%)	8 (72.7%)	14 (93.3%)	17 (100%)	0.05
Chest pain	40 (36.4%)	25 (37.3%)	7 (63.6%)	3 (20.0%)	5 (29.4%)	0.13
Syncope	27 (24.5%)	17 (25.4%)	3 (27.3%)	2 (13.3%)	5 (29.4%)	0.73
Cough	13 (11.8%)	10 (14.9%)	2 (18.2%)	1 (6.7%)	0 (0%)	0.30
Pneumonia	11 (10.0%)	6 (9.0%)	1 (9.1%)	4 (26.7%)	0 (0%)	0.09
DVT	69 (62.7%)	43 (64.2%)	7 (63.6%)	12 (80.0%)	7 (41.2%)	0.15
Comorbidities						
Malignancy	28 (25.5%)	14 (20.9%)	1 (9.1%)	2 (13.3%)	5 (29.4%)	0.53
Coronary artery disease	14 (12.7%)	8 (11.9%)	0 (0%)	2 (13.3%)	2 (11.8%)	0.68
Chronic heart failure	9 (8.2%)	6 (9.0%)	1 (9.1%)	2 (13.3%)	0 (0.0%)	0.56
Atrial fibrillation	6 (5.5%)	5 (7.5%)	0 (0%)	0 (0%)	1 (5.9%)	0.56
Arterial hypertension	57 (51.8%)	35 (52.2%)	4 (36.4%)	7 (46.7%)	11 (64.7%)	0.5
COPD	5 (4.5%)	4 (6.0%)	0 (0%)	0 (0%)	1 (5.9%)	0.66
Diabetes mellitus	24 (21.8%)	12 (17.9%)	3 (27.3%)	4 (26.7%)	5 (29.4%)	0.67
Obesity	34 (30.9%)	17 (25.4%)	5 (45.5%)	6 (40.0%)	6 (35.3%)	0.43
Chronic kidney disease	9 (8.2%)	4 (6.0%)	1 (9.1%)	1 (6.7%)	3 (17.6%)	0.47
Stroke	10 (9.1%)	3 (4.5%)	0 (0%)	3 (20.0%)	4 (23.5%)	**0.02**
Depression	5 (4.5%)	3 (4.5%)	1 (9.1%)	1 (6.7%)	0 (0.0%)	0.69
Known thrombophilia	4 (3.6%)	2 (3.0%)	1 (9.1%)	0 (0%)	1 (5.9%)	0.61
Other VTE risk factors						
Smoking	25 (22.7%)	19 (28.4%)	1 (9.1%)	2 (13.3%)	3 (17.6%)	0.34
Indwelling catheter	4 (3.6%)	2 (3.0%)	0 (0%)	0 (0%)	2 (11.8%)	0.23
Hormonal therapy	7 (6.4%)	2 (3.0%)	1 (9.1%)	3 (20.0%)	1 (5.9%)	0.11
Recent hospitalization	28 (25.5%)	20 (29.9%)	1 (9.1%)	2 (13.3%)	5 (29.4%)	0.32
Recent surgery	11 (10.0%)	7 (10.4%)	1 (9.1%)	0 (0%)	3 (17.6%)	0.42
Recent trauma	8 (7.3%)	6 (9.0%)	0 (0%)	0 (0%)	2 (11.8%)	0.42
Prior PE	5 (4.5%)	2 (3.0%)	0 (0%)	1 (6.7%)	2 (11.8%)	0.38
Prior DVT	19 (17.3%)	14 (20.9%)	2 (18.2%)	2 (13.3%)	1 (5.9%)	0.51
PESI class						
I–II	37 (33.6%)	26 (38.8%)	3 (27.3%)	6 (40.0%)	2 (11.8%)	
III	30 (27.3%)	23 (34.3%)	3 (27.3%)	2 (13.3%)	2 (11.8%)	**0.005**
IV	18 (16.4%)	7 (10.4%)	0 (0%)	5 (33.3%)	6 (35.3%)	
V	25 (22.7%)	11 (16.4%)	5 (45.5%)	2 (13.3%)	7 (41.2%)	
Score	99 (75–123)	92 (72–107)	87 (66–109)	104 (75–119)	123 (112–174)	**0.006**
sPESI						
Score	1.55 ± 1.18	1.25 ± 1.06	2.00 ± 1.34	1.60 ± 1.18	2.41 ± 1.06	**0.001**
Clinical severity						
Intubation	13 (11.8%)	4 (6.0%)	3 (27.3%)	1 (6.7%)	5 (29.4%)	**0.02**
ICU admission	93 (84.5%)	51 (76.1%)	10 (90.9%)	15 (100%)	17 (100%)	**0.02**
Intracardiac thrombi	8 (7.3%)	2 (3.0%)	0 (0%)	6 (40.0%)	0 (0%)	**< 0.001**

Data are shown as number (percentage) or mean ± standard deviation or median (interquartile range). COPD — chronic obstructive pulmonary disease; DVT — deep vein thrombosis; ICU — intensive care unit; PE — pulmonary embolism; PESI — Pulmonary Embolism Severity Index; sPESI — simplified Pulmonary Embolism Severity Index; VTE — venous thromboembolism

Table 2. In-hospital mortality and outcome events according to risk categories and treatment methods.

	Overall	Anticoagulation alone	Systemic thrombolysis	Surgical embolectomy	Catheter-directed therapies
In-hospital mortality	**13 (11.8%)**	**6 (9.0%)**	**2 (18.2%)**	**0 (0%)**	**5 (29.4%)**
High risk	9 (37.5%)	4 (100%)	1 (14.3%)	0 (0%)	4 (50%)
Intermediate-high risk	4 (4.7%)	2 (3.2%)	1 (25.0%)	0 (0%)	1 (11.1%)
Major bleeding	**5 (4.5%)**	**2 (3.0%)**	**1 (9.1%)**	**1 (6.7%)**	**1 (5.9%)**
High risk	3 (12.0%)	1 (25.0%)	1 (14.3%)	1 (20.0%)	0 (0%)
Intermediate-high risk	2 (2.3%)	1 (1.6%)	0 (0%)	0 (0%)	1 (11.1%)
Minor bleeding	**4 (3.6%)**	**1 (1.6%)**	**3 (27.3%)**	**0 (0%)**	**0 (0%)**
High risk	2 (8.2%)	0 (0%)	2 (28.6%)	0 (0%)	0 (0%)
Intermediate-high risk	2 (2.3%)	1 (1.6%)	1 (25.0%)	0 (0%)	0 (0%)

blood transfusion and/or modification of AC therapy. There were 2 (1.8%) strokes in HR patients treated with thrombolysis. There was one fatal recurrence of PE in the IHR patient treated with systemic full-dose thrombolysis.

Catheter-directed therapies

Information about the indication for CTDx, the exact choice of treatment method, the sPESI and PESI score, the dose of rtPA, and treatment outcome are shown in Table 3. In the CDTx group, 8 (47%) patients met the criteria of HR PE, and 9 (53%) patients were evaluated as IHR PE. N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) concentrations decreased following transcatheter intervention in 90% of patients whose measurements were performed before and after the procedure. The concentrations of NT-proBNP on admission and at discharge are shown in Table 4.

In the CDL group, all patients received rtPA, with dosing varying between individuals. Three patients received 1 mg/h rtPA infusions for 10–24 h. In 1 case, a bolus of 20 mg rtPA was administered via infusion catheter at the initiation of treatment, followed by a continuous infusion of 1 mg/h for 20 h (the total dose was 40 mg of rtPA).

Complications in the CDL group occurred only in 1 patient and were related to a massive thigh hematoma, which was treated conservatively with a subsequent reduction of the anticoagulant dose. For this reason, an inferior vena cava filter was implanted on the 4th day after the CDL procedure. No other procedure-related thrombotic or bleeding events occurred in the CDTx group.

In 4 cases, an inferior vena cava filter was implanted, and the main indication was the inability to administer full-dose anticoagulant treatment.

Of the 4 in-hospital deaths in the HR group, 2 occurred in patients in whom the procedure was performed during or after cardiopulmonary resuscitation. One in-hospital death in the IHR group was observed in a patient who developed acute abdomen the day after the procedure. An autopsy was not conducted, so the exact cause of death remains unknown.

Discussion

In this manuscript, we present our experience regarding the treatment of patients with HR and IHR PE by local PERT. The main findings of our analysis are that (i) PERT consultations were more frequent in IHR PE patients, compared to HR PE (35.8% vs. 10%); (ii) the majority of patients with HR received at least one form of reperfusion therapy (ST, SE, or CDTx), while most IHR PE patients were treated with AC alone; (iii) the mortality rate in HR PE patients remains high; and (iv) CDTx was performed at a similar rate in HR and IHR patients (47% vs. 53%) and led to significant clinical improvement with a low adverse event rate.

A few studies have already demonstrated improved survival in the PERT era compared to the pre-PERT era [13, 23]. However, some studies revealed that despite a significant increase in the use of advanced treatments, the improvement in mortality rates is of borderline significance [14, 24]. This might be associated with a lack of standardized algorithms to select patients for advanced PE therapies and variable operator experience due to the imperfect effectiveness of CDTx, especially in patients with HR PE or comorbidities like malignancy. For example, our recent analysis of cancer-associated thrombosis demonstrated that oncological patients have similar in-hospital

Table 3. Clinical information about patients undergoing catheter-directed therapies.

No.	Sex, age [years]	PE risk	Indication for CDTx	sPESI score	PESI score	Treatment	Cumulative rtPA dose	Outcome at discharge
1	M, 72	High	History of ischemic stroke in the last 6 months	3	232	CDT	N/A	In-hospital death
2	F, 76	Intermediate-high	No improvement after 24-h anticoagulation treatment	2	116	CDT	N/A	In-hospital death
3	F, 54	Intermediate-high	History of ischemic stroke in the last 6 months	2	114	CDT + IVCf	N/A	III NYHA FC
4	F, 56	High	History of ischemic stroke in the last 6 months	2	126	CDT	N/A	III NYHA FC
5	M, 63	Intermediate-high	High risk of cancer-related bleeding	2	123	CDT	N/A	I NYHA FC
6	M, 49	Intermediate-high	No improvement after 24-h anticoagulation treatment	1	79	CDL + IVCf	40 mg	I NYHA FC
7	F, 47	Intermediate-high	No improvement after 24-h anticoagulation treatment	2	87	CDL	24 mg	I NYHA FC
8	M, 45	Intermediate-high	No improvement after 24-h anticoagulation treatment	2	95	CDL	10 mg	I NYHA FC
9	F, 65	High	Recent major orthopedic surgery	3	195	CDT + CDL + IVCf	20 mg	II NYHA FC
10	F, 51	High	Severe general condition due to metastatic cancer	4	131	CDT + CDL	20 mg	In-hospital death
11	M, 44	High	Intervention during CPR	2	124	CDT + ST	140 mg	In-hospital death
12	F, 53	Intermediate-high	History of hemorrhagic stroke	3	123	CDT + SE	N/A	III NYHA FC
13	M, 65	High	Infection after ICD implantation, respiratory failure	5	175	CDT	N/A	II NYHA FC
14	M, 36	High	Intervention after cardiac arrest and CPR	3	196	CDT + ST	2 × 50 mg	In-hospital death
15	M, 74	High	Recent pelvic fracture, treated surgically	3	174	CDT	N/A	II NYHA FC
16	M, 62	Intermediate-high	Recurrence of PE during anticoagulation therapy	1	112	CDT + IVCf	N/A	II NYHA FC
17	F, 84	Intermediate-high	No improvement after 24-h anticoagulation treatment	1	84	CDL	10 mg	II NYHA FC

CDT — catheter-directed thrombectomy; CDL — catheter-directed thrombolysis; CPR — cardiopulmonary resuscitation; F — female; ICD — implantable cardioverter-defibrillator; IVCf — inferior vena cava filter; M — male; N/A — not applicable; NYHA FC — New York Heart Association Functional Classification; PE — pulmonary embolism; PESI — Pulmonary Embolism Severity Index; sPESI — simplified PESI; SE — surgical embolectomy; ST — systemic thrombolysis; rtPA — recombinant tissue plasminogen activator

Table 4. N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) measurements before and after catheter directed therapies.

Case no.	Risk group	Treatment	NT-proBNP [pg/mL]		
			At admission	At discharge	Difference
1	High	CDT	24120	Death	N/A
2	Intermediate-high	CDT	12523	Death	N/A
3	Intermediate-high	CDT + IVCf	476	1515	+1039
4	High	CDT	N/D	1229	N/A
5	Intermediate-high	CDT	1974	483	–1491
6	Intermediate-high	CDL + IVCf	4029	499	–3530
7	Intermediate-high	CDL	3072	66	–3006
8	Intermediate-high	CDL	1463	126	–1337
9	High	CDT + CDL + IVCf	682	191	–491
10	High	CDT + CDL	19857	Death	N/A
11	High	CDT + ST	N/D	Death	N/A
12	Intermediate-high	CDT + SE	3767	1577	–2190
13	High	CDT	5220	4937	–283
14	High	CDT + ST	991	Death	N/A
15	High	CDT	2130	N/D	N/A
16	Intermediate-high	CDT + IVCf	891	350	–541
17	Intermediate-high	CDL	14956	404	–14552

CDT — catheter-directed thrombectomy; CDL — catheter-directed thrombolysis; IVCf — inferior vena cava filter; N/A — not applicable; N/D — no data; SE — surgical embolectomy; ST — systemic thrombolysis

survival rates to non-oncological patients but worse long-term outcomes because of their underlying neoplastic disease [25]. Hence, our analysis is crucial to understand the factors associated with treatment outcomes and optimize future treatment decisions of PERT.

Considering the unsatisfactory outcomes, especially in HR PE patients, multiple technologies are being developed to improve CDL and CDT. However, the clinical efficacy of CDTx has been demonstrated only in single-arm trials with surrogate endpoints, warranting caution when interpreting the results. In a previously published meta-analysis of 11 studies including 65,589 patients, 30-day mortality was 2-fold lower in the CDTx group than in the ST group (7.3 vs. 13.6%; odds ratio [OR]: 0.51, 95% confidence interval [CI]: 0.38–0.69, $p < 0.001$). The rates of adverse events such as myocardial injury, cardiac arrest, stroke, and major bleeding complications were lower in the CDTx group compared to the ST group ($p < 0.001$ for all) [26]. In the present publication, patients treated with CDTx accounted for 7% of all PERT consultations (17/240), with 8 out of 17 (47%) patients in the HR group. Among patients treated with CDTx, the overall mortality was 29% (5/17), with substantially lower mortality in IHR patients compared to those with HR PE (11% vs. 50%, respectively). A meta-analysis of 1168 patients showed that 30-day mortality in IHR PE patients treated with CDL was 0% (95% CI: 0–0.5%). In turn, a much higher 30-day mortality rate (8.0%, 95% CI: 3.2–14.0%) was observed in HR PE patients treated with CDL, confirming the survival rate discrepancies between these two groups observed in our analysis [27]. The high mortality rate in HR PE patients in our study might be because patients qualified for CDTx were often so-called "no-other--option" patients and at much higher mortality risk, as assessed by the PESI score, compared to patients qualified for ST. Such a high mortality rate indicates that HR patients with contraindications for ST are an especially vulnerable subgroup who require immediate evaluation and therapy optimization to maximize their chances of survival.

Regarding CDL efficacy, all patients in our study were treated successfully and discharged from the hospital with New York Heart Association class improvement. Importantly, they all had IHR PE, and in 90% of them a decrease in NT-proBNP levels was noted after the intervention. Concerning the safety of the CDTx procedures, only 1 patient

developed a complication after CDL — a thigh hematoma treated conservatively, considered a major adverse event with a hemoglobin drop from 11.7 to 7.9 g/dL. In other studies, minor bleeding events, including hematomas, occurred in 9% to 27% of cases [28, 29]. In a meta-analysis, the major bleeding rate of CDL for HR and IHR PE patients was 4.6%, most of which required transfusion [30]. In turn, no adverse events occurred in 13 patients treated with CDT, similarly to our study. As for the Indigo aspiration system, the EXTRACT-PE Trial showed that only 1.7% of patients experienced major complications [31]. As well as clinical trials, a MAUDE database report presented real-world data regarding the device's safety [32]. Out of 2118 reports gathered during the study period, only 67 (3.2%) were related to the Indigo aspiration system, and the most common failures were lightning unit malfunction and rotating hemostasis valve malfunction. Three (4.5%) patients died during the observation. Considering the types of thrombectomy and the amount of equipment offered by different companies, a comparison of different CDT devices is needed to find the best efficacy by using many modalities synergistically and tailoring the device to the needs of each patient.

Recently, a clinical consensus statement regarding CDTx has been published by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function, which is a practical guide for CDTx and is complementary to the current guidelines [33]. Also, the Polish PERT Initiative has published an expert opinion on the use of CDTx in high-risk PE patients [34]. The introduction of PERTs, along with the publication of the ESC consensus statement, is an ideal moment to implement new devices, develop standardized protocols for CDL and CDT, and establish directions for future research [35–37].

Limitations of the study

A major limitation of our study is the small number of patients receiving interventional treatment within the PERT. In addition, this is a single PERT experience. Furthermore, data regarding baseline characteristics, procedural data, and outcomes were extracted from medical records. In some cases, data were missing due to an emergency clinical situation (e.g., a procedure performed during cardiopulmonary resuscitation) or in-hospital mortality.

Conclusions

PERT-CELZAT consultations resulted in primary reperfusion therapy in 83% of HR PE patients with an observed high mortality rate (37.5%), and in 26.7% of IHR PE patients with 4.7% mortality. CDTx was used in 15.5% of cases (17/110), and the results are still suboptimal, especially in the HR PE group, likely due to the initially severe condition of patients who qualified for CDTx. The therapy of patients with PE requires an individual approach due to the specificity of the disease, as well as concomitant risk factors or complications, which make the decision regarding the choice of treatment difficult and require interdisciplinary discussion, preferably within an expert group such as a PERT. Because there are no clear data from randomized controlled trials regarding the possible advantage of any transcatheter treatment, a PERT should have experience with various therapeutic methods, adjusting the choice of therapy to the patient's unique clinical situation. Due to the constant development of CDTx technologies, the PERT armamentarium will undoubtedly expand, which may translate into better treatment results. There is an urgent need to (i) establish more detailed selection criteria that might improve clinical outcomes in HR and IHR PE patients, especially those who qualified for CDTx, and (ii) compare currently available treatment methods to improve outcomes further.

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