Akutní plicní embolie se středním rizikem

(nové postupy v léčbě)

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Kardiocentrum

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Akutní plicní embolie – „nevyřešené“ onemocnění?

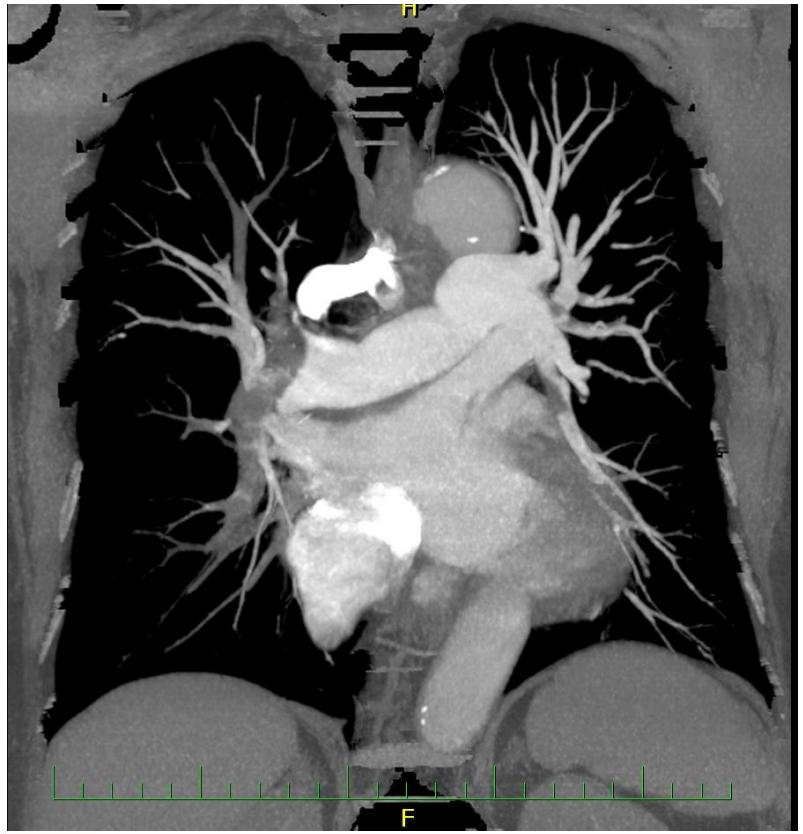

Table 9 Classification of PE based on early mortality risk

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Early mortality risk		Indicators of risk: Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III–V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	(+)	+	(+)
Interme-diate	Intermediate–high	-	+	+	+
	Intermediate–low	-	+	One (or none) positive	
Low		-	-	-	Assessment optional; if assessed, negative

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

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2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 1	Epidemiology of major acute cardiovascular diseases		
	Incidence per 100,000	Prevalence	30-day mortality
Myocardial infarction	208[5]	2.0%[4]	5.9%[88]
Ischemic stroke	156[9]	1.1%[9]	15.0%[89]
Pulmonary embolism	70[18]	NA	10.7%[90]

1. Klancik V., Kocka V., Expert Review of Cardiovascular Therapy, Vol 21, 2023

ESC Guidelines - Doporučené postupy léčby z roku 2019

Recommendations for acute-phase treatment of intermediate- or low- risk PE (1)

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Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic work-up is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.	I	A
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A

NOAC = non-vitamin K antagonist oral anticoagulant; LMWH = low molecular weight heparin; VKA = vitamin K antagonist; UFH = unfractionated heparin.

www.escardio.org/guidelines

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

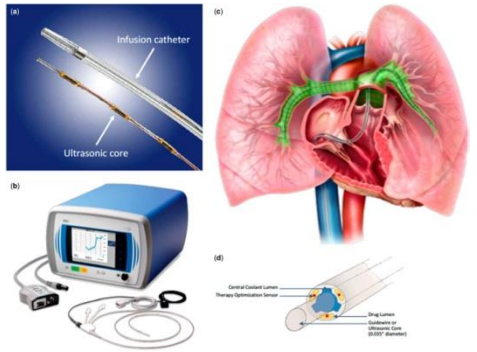
Proč se zabývat intermediate-risk pacienty?

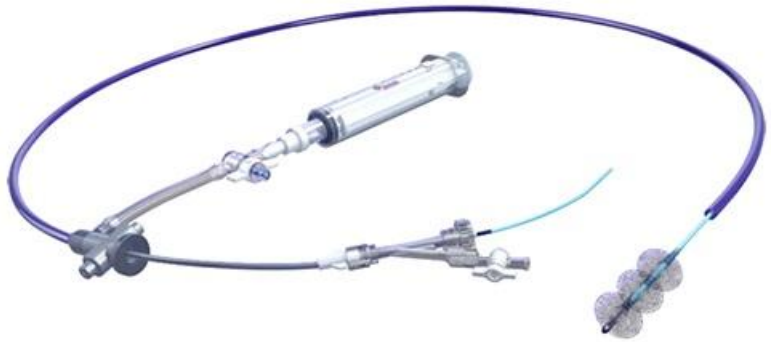
- Nejčetnější skupina pacientů s akutní plicní embolií
- Mortalita pacientů s intermediate-high risk akutní PE (cca 6.0-7.7%[2]) dostatečně nízká?
- Nové léčebné možnosti? Farmakologické x intervenční x kombinace?
- Snížení mortality bez zvýšení rizika komplikací léčby?
- Další aspekty … zkrácení hospitalizace?, incidence CTEPH?, kvalita života?, ekonomické aspekty?

2. Becattini C, Agnelli G, Lankeit M, Masotti L, Pruszczyk P, Casazza F, Vanni S, Nitti C, Kamphuisen P, Vedovati MC, De Natale MG, Konstantinides S. Acute pulmonary embolism: Mortality prediction by the 2014 European Society of Cardiology risk stratification model. *Eur Respir J.* 2016;48:780-6.

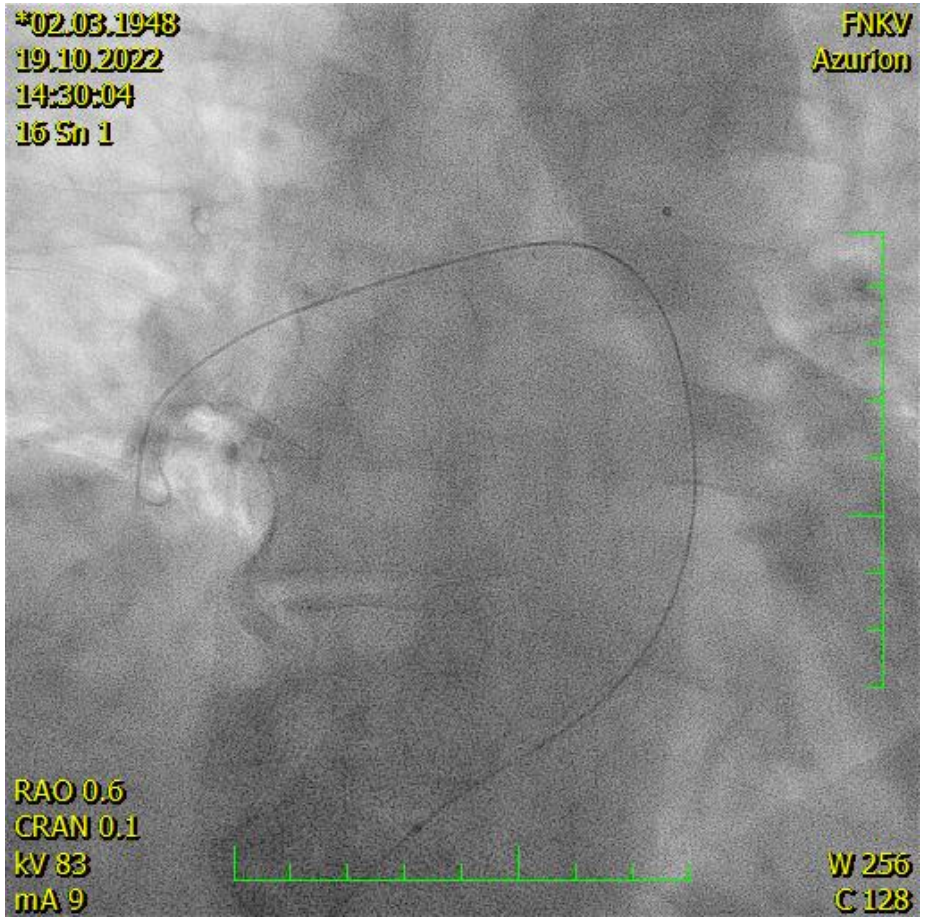
Dostupné intervenční metody léčby plicní embolie

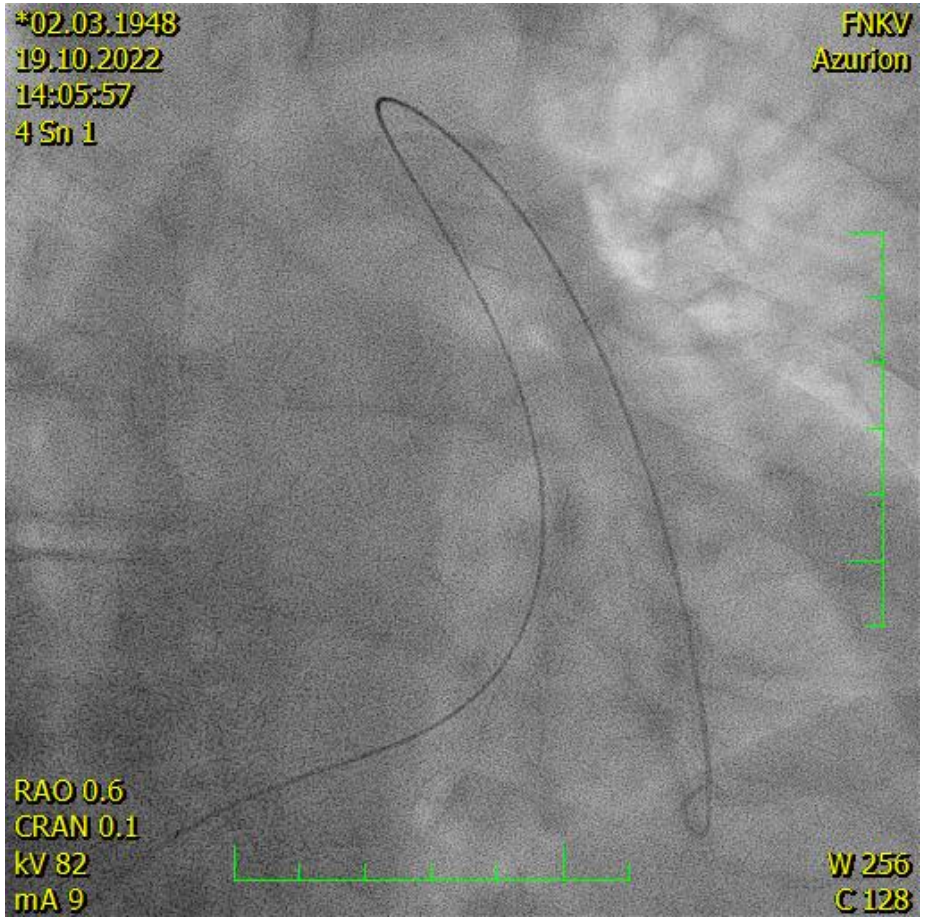
- Lokální trombolýza (prostá či UZ facilitovaná)
- Aspirační mechanická trombektomie
- **Výběr metody s ohledem na klinický stav a riziko krvácení**



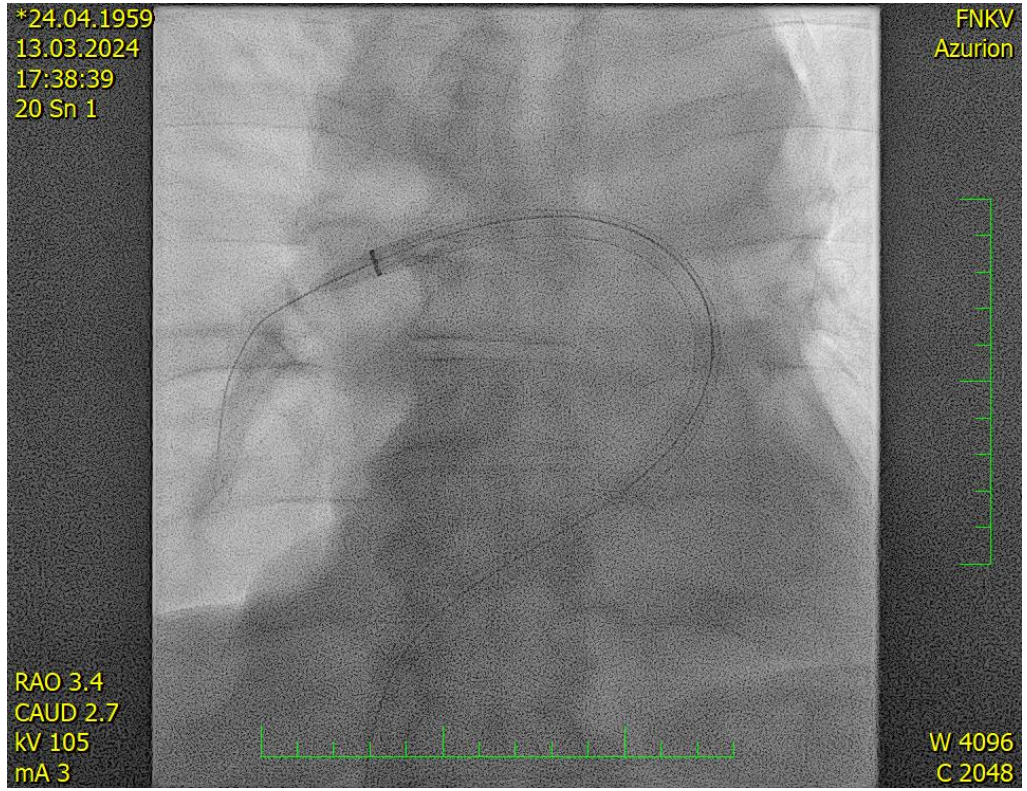


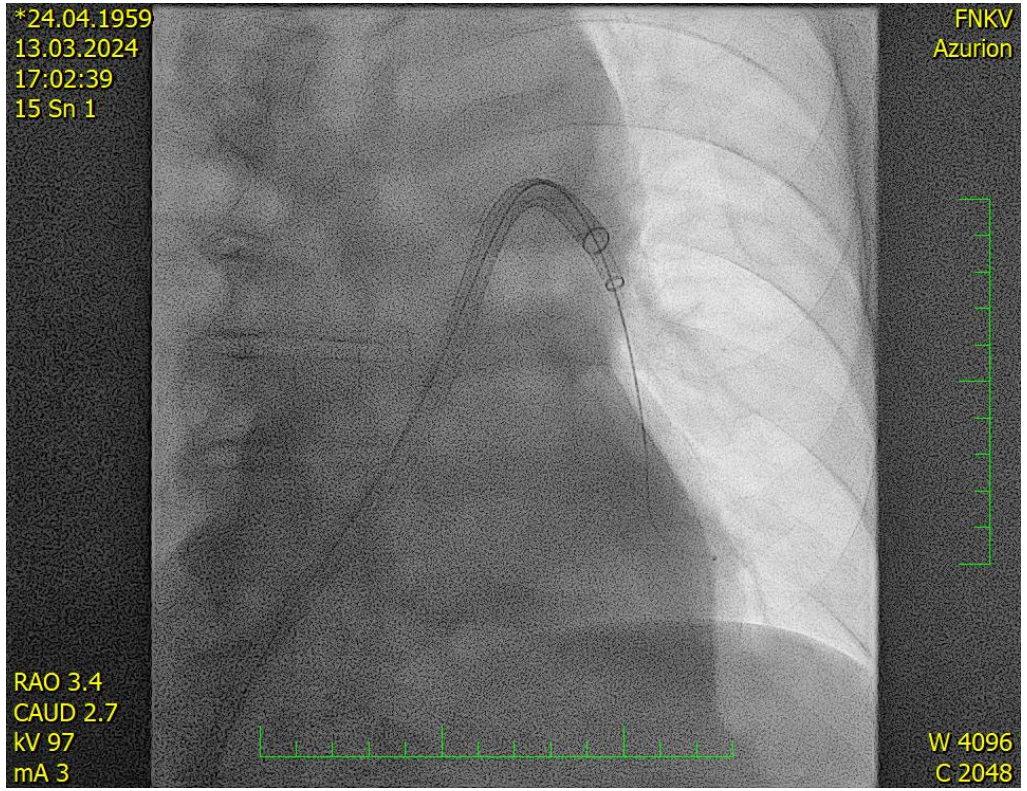
Lokální trombolýza (4-6 French)





Aspirační trombektomie – systém FlowTriever





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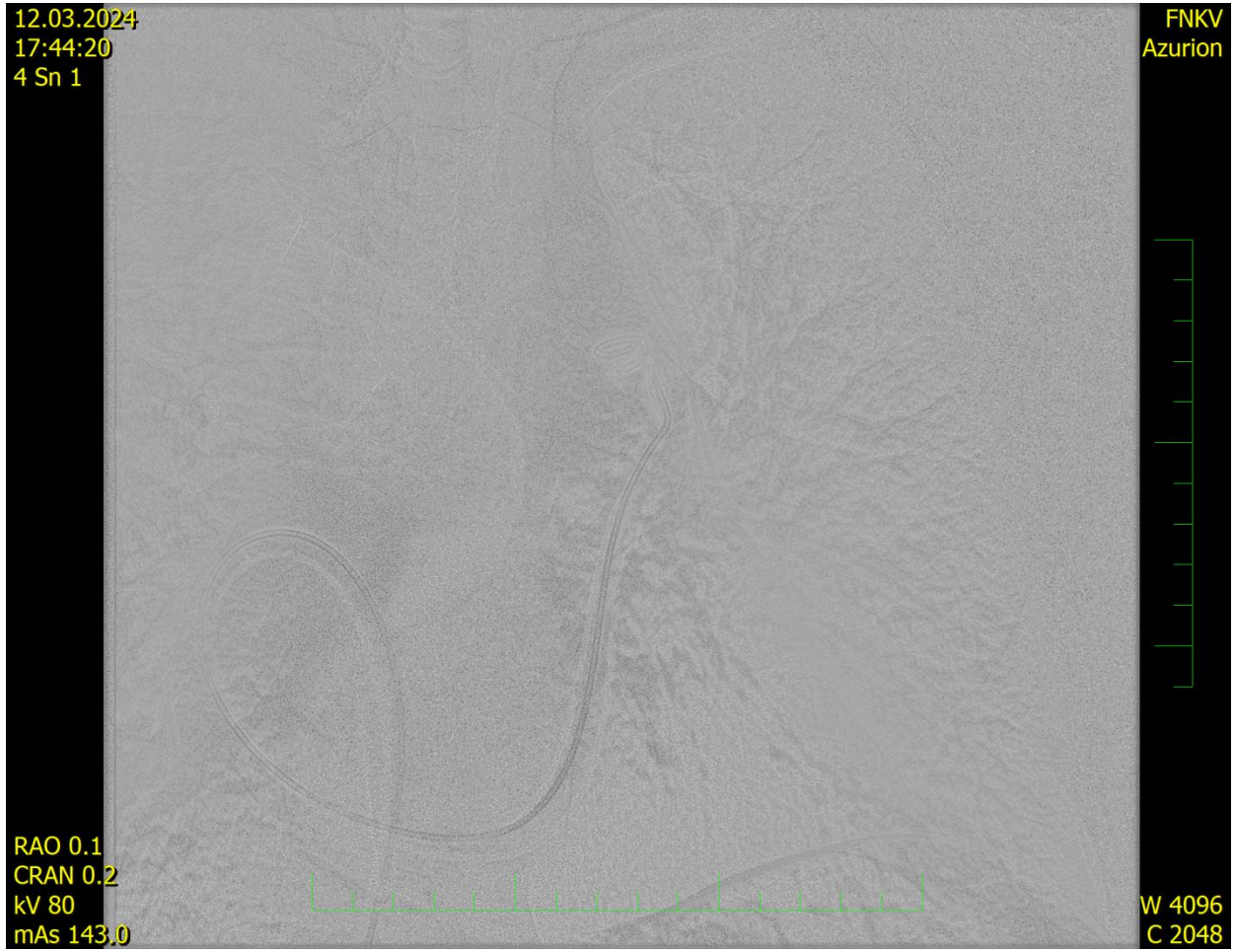
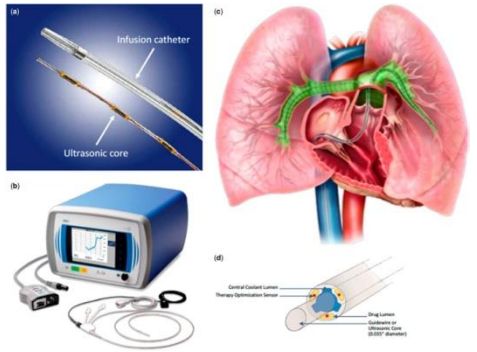
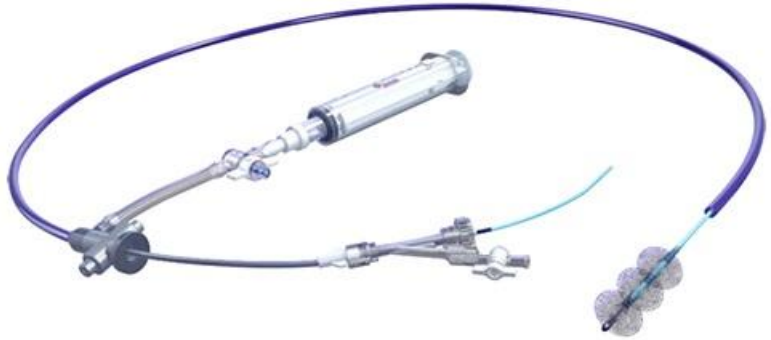


Existují dostupná data pro tyto metody? Opora v Guidelines?

- ESC Guidelines 2019
- ESC Position paper 2022 (konsensus expertů)
- Registry, malé randomizované studie, metaanalýzy
- **Blíží se výsledky randomizovaných studií s „tvrdými“ klinickými end-pointy**





Postavení katetrizační léčby dle „současných“ Guidelines

Recommendations for acute-phase treatment of high-risk PE (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	IIa	C
Norepinephrine and/or dobutamine should be considered in patients with high-risk PE.	IIa	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.	IIb	C

ECMO = extracorporeal membrane oxygenation.

Recommendations for acute-phase treatment of intermediate- or low- risk PE (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Reperfusion treatment		
Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.	I	B
As an alternative to rescue thrombolytic therapy, surgical embolectomy or percutaneous catheter- directed treatment should be considered for patients with haemodynamic deterioration on anticoagulation treatment.	IIa	C
Routine use of primary systemic thrombolysis is not recommended in patients with intermediate- or low-risk PE.	III	B

ESC Position paper 2022 – konsensus expertů

PERIPHERAL INTERVENTIONS
EXPERT CONSENSUS

Percutaneous treatment options for acute pulmonary embolism: a clinical consensus statement by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions

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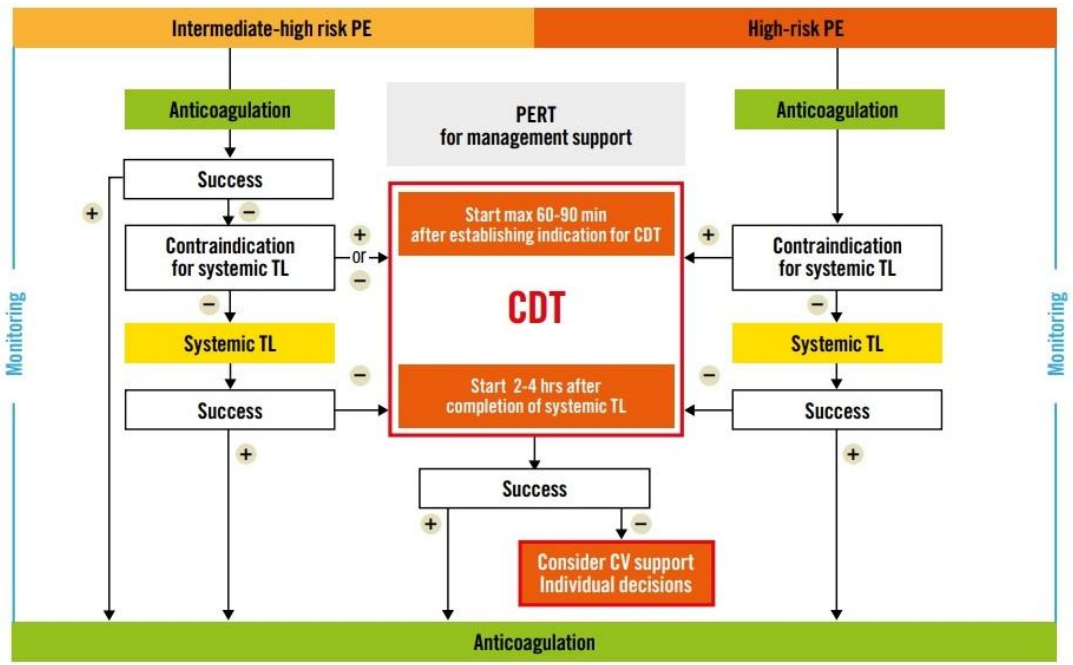
EuroIntervention 2022;18:e623-e638 published online ahead of print September 2022 ■ published online

EuroIntervention

CENTRAL **ILLUSTRATION** Proposed algorithm and timelines of catheter-directed therapies (CDT) in high-risk and intermediate-high risk pulmonary embolism (PE).



CV: cardiovascular; PERT: Pulmonary Embolism Response Team; TL: thrombolysis

Přehled publikovaných prací 2014 - 2022

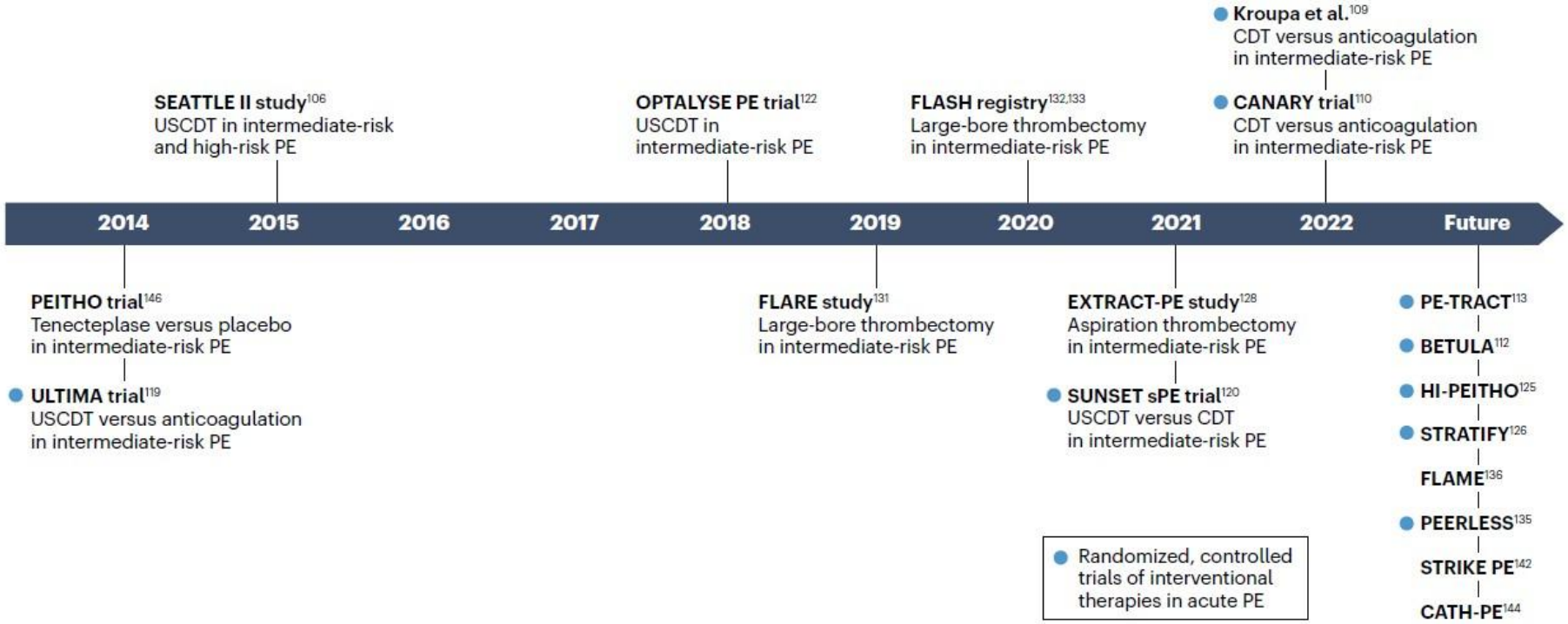


Fig. 1 | Timeline of studies of interventional therapies in PE. To date, four randomized controlled trials investigating interventional therapies in acute pulmonary embolism (PE) have been published. Five more randomized controlled trials are ongoing. Trials comparing different interventional strategies against standard-of-care and in a head-to-head comparison are particularly needed. CDT, catheter-directed thrombolysis; USCDT, ultrasound-assisted catheter-directed thrombolysis.

3. GÖTZINGER, Felix; LAUDER, Lucas; SHARP, Andrew S. P.; LANG, Irene M.; ROSENKRANZ, Stephan et al. Interventional therapies for pulmonary embolism. Online. *Nature Reviews Cardiology*. 2023, roč. 20, č. 10, s. 670-684. ISSN 1759-5002.

Randomizované studie

Table 4 | Published RCTs on catheter-directed therapies in PE

Study	Device	Number of patients	Cohort	Comparison	Efficacy outcomes	Safety outcomes
Kroupa et al.[109]	Cragg–McNamara	23	Intermediate-risk PE	CDT versus anticoagulation	Reduction in RV-to-LV ratio in 7 of 12 patients versus 2 of 11 patients (P=0.03) Decrease in systolic PAP by >30% in 11 of 12 versus 2 of 11 patients (P=0.001) Reduction in Qanadli score: no significant difference	Safety end points achieved in both groups: no intracranial or life-threatening bleeding reported
CANARY[110]	Cragg–McNamara	85	Intermediate–high-risk PE	CDT versus anticoagulation	Mean RV-to-LV ratio: 0.7 versus 0.8 (P=0.01) RV recovery in 43 of 46 patients versus 28 of 39 patients (P=0.009)	Bleeding: 8 versus 0 Death: 0 versus 3
ULTIMA[119]	EKOS	59	Intermediate-risk PE	USCTD versus anticoagulation	Reduction in RV-to-LV ratio 0.30 versus 0.03 (P<0.001)	Minor bleeding: 4 versus 0
SUNSET sPE[120]	Cragg–McNamara, Uni-Fuse or EKOS	82	Intermediate-risk PE	CDT versus USCDT	Reduction in mean RV-to-LV ratio: 0.59 versus 0.37 (P=0.01) Reduction in mean difference in thrombus score: −10 versus −9 (P=0.76)	Major bleeding: 0 versus 2

CDT, catheter-directed thrombolysis; LV, left ventricular; PAP, pulmonary artery pressure; PE, pulmonary embolism; RCT, randomized controlled trial; RV, right ventricular; USCDT, ultrasound-assisted catheter-directed thrombolysis.

3. GÖTZINGER, Felix; LAUDER, Lucas; SHARP, Andrew S. P.; LANG, Irene M.; ROSENKRANZ, Stephan et al. Interventional therapies for pulmonary embolism. Online. *Nature Reviews Cardiology*. 2023, roč. 20, č. 10, s. 670-684. ISSN 1759-5002.

PEERLESS RCT

A

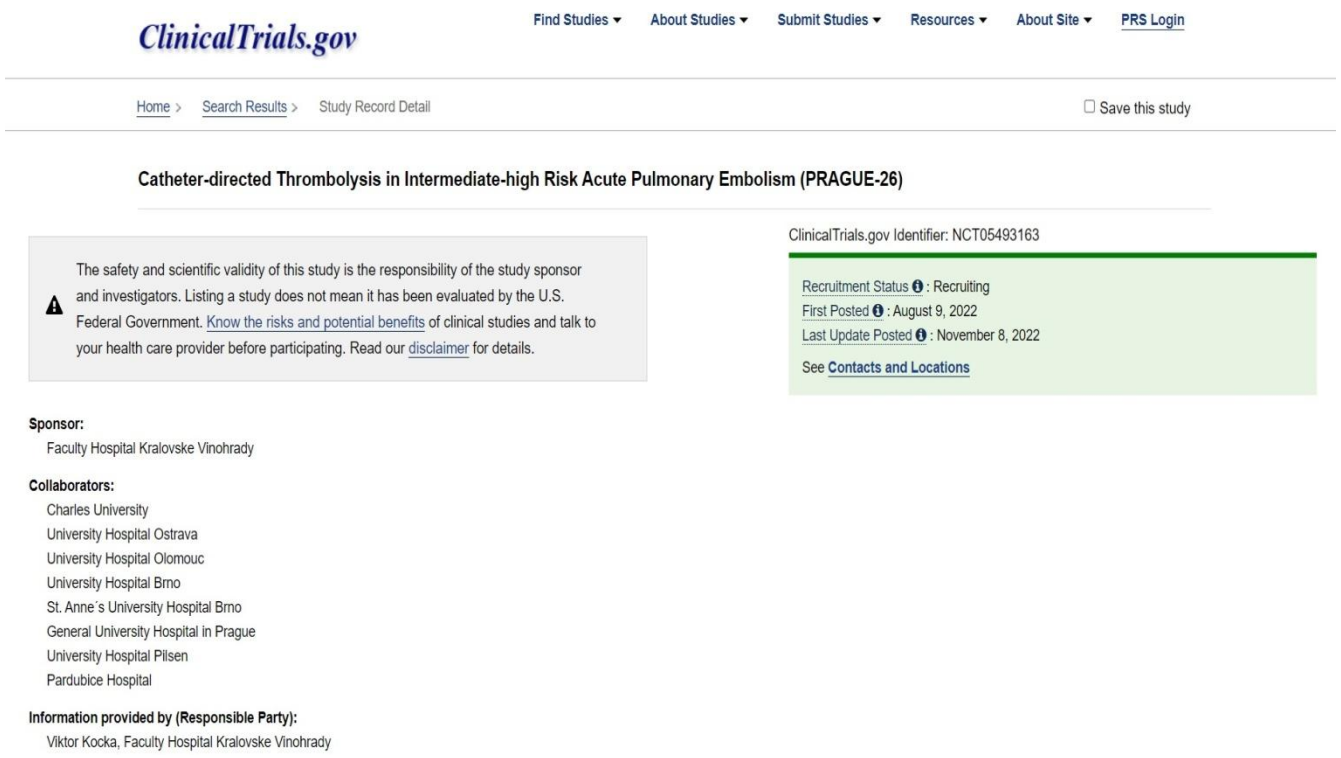
	CDT wins, n	LBMT wins, n	Win Ratio Endpoints	Win ratio [95% CI]	*P* value
Primary Endpoint: 5-component win ratio	10,509	52,693		5.01 [3.68 – 6.97]	<0.001
Secondary Endpoint: 4-component win ratio	5912	7925		1.34 [0.78 – 2.35]	0.30

B

		CDT events, n (%)	LBMT events, n (%)	Odds Ratios for Clinical Outcomes	Odds ratio [95% CI]	*P* value
1	**All-cause mortality**	1 (0.4)	0 (0.0)		2.99 [0.12 – 73.70]	1.00
2	**Intracranial hemorrhage**	1 (0.4)*	2 (0.7)		0.50 [0.04 – 5.51]	0.62
3	**Major bleeding**	19 (6.9)	19 (6.9)		0.99 [0.51 – 1.92]	1.00
4	**Clinical deterioration and/or escalation to bailout therapy**	15 (5.4)	5 (1.8)		3.09 [1.11 – 8.63]	0.04
5a	**Postprocedural ICU admission**	272 (98.6)	114 (41.6)		95.4 [34.6 – 263.6]	<0.001
5b	**If ICU admitted, stay >24 hours**	178 (65.4)	53 (46.5)		2.18 [1.40 – 3.40]	<0.001

Studie PRAGUE-26 (Česká republika)

- CDT versus standardní antikoagulace u pacientů s intermediate-high risk PE
- 558 pacientů
- 11 center v ČR
- 350 pacientů randomizováno k 3.5.2025



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Catheter-directed Thrombolysis in Intermediate-high Risk Acute Pulmonary Embolism (PRAGUE-26)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT05493163

Recruitment Status : Recruiting
First Posted : August 9, 2022
Last Update Posted : November 8, 2022

See Contacts and Locations

Sponsor:
Faculty Hospital Kralovske Vinohrady

Collaborators:
Charles University
University Hospital Ostrava
University Hospital Olomouc
University Hospital Brno
St. Anne´s University Hospital Brno
General University Hospital in Prague
University Hospital Pilsen
Pardubice Hospital

Information provided by (Responsible Party):
Viktor Kocka, Faculty Hospital Kralovske Vinohrady

Budoucnost?

Table 6. Ongoing trials. (*) Plus anticoagulation. CDT: Catheter-directed therapy; DVT: deep vein thrombosis; PE: pulmonary embolism; USAT: ultrasound-accelerated thrombolysis.

Trial	Design	Population	Sample	Intervention	Control	Primary Outcomes
PRAGUE-26	Multicenter, randomized	Intermediate–high-risk PE	558	CDT *	Anticoagulation monotherapy	Clinical composite of all-cause mortality, PE recurrence, or cardiorespiratory decompensation

Table 6. *Cont.*

Trial	Design	Population	Sample	Intervention	Control	Primary Outcomes
HI-PEITHO	Multicenter, randomized	Intermediate–high-risk PE	406	USAT *	Anticoagulation monotherapy	Composite of PE-related mortality, cardiorespiratory decompensation or collapse, or non-fatal symptomatic and objectively confirmed PE recurrence
STRATIFY	Multicenter, 1:1:1 randomized	Intermediate–high-risk PE	210	USAT or low-dose thrombolysis *	Anticoagulation monotherapy	Miller score
STORM-PE	Multicenter, randomized	Intermediate–high-risk PE	100	Aspiration embolectomy (Indigo system) *	Anticoagulation monotherapy	Reduction in RV-to-LV ratio
NCT05612854	Multicenter, randomized	Intermediate–high-risk PE	200	Indigo Aspiration System (8 Fr), CDT or pigtail mechanical fragmentation *	Anticoagulation monotherapy	MACE
PEERLESS	Multicenter, randomized	Intermediate–high-risk PE	550	Aspiration embolectomy (FlowTriever system) *	CDT *	All-cause death, intracranial hemorrhage, major bleeding, haemodynamic decompensation
PEERLESS II	Multicenter, randomized	Intermediate risk PE	1200	Aspiration embolectomy (FlowTriever system) *	Anticoagulation monotherapy	Haemodynamic decompensation, all-cause hospital readmission, bailout therapy
PE-TRACT	Multicenter, randomized	Sub-massive PE, proximal pulmonary artery thrombus, and right ventricular dilation	500	CDT or mechanical thrombectomy *	Anticoagulation monotherapy	Peak oxygen consumption, NYHA class, major bleeding
DEFIANCE	Multicenter, randomized	Symptomatic unilateral iliofemoral DVT	300	Mechanical thrombectomy (ClotTriever System) *	Anticoagulation monotherapy	Vessel patency rate
NCT06124768	Single-center, observational	Acute iliofemoral DVT	210	Mechanical Thrombectomy via ipsilateral deep calf venous access or contralateral femoral venous access	Mechanical thrombectomy via ipsilateral popliteal venous access	Vessel patency rate
NCT05286710	Single-center, randomized	Acute iliofemoral DVT	160	Mechanical Thrombectomy via distal calf venous access or contralateral femoral access	Mechanical thrombectomy via ipsilateral popliteal venous access	Incidence of post-thrombotic syndrome

4. Cavallino, C.; Franzino, M.; Abdirashid, M.; Maltese, L.; Bacci, E.; Rametta, F.; Ugo, F. Novel Challenges and Therapeutic Options for Pulmonary Embolism and Deep Vein Thrombosis. J. Pers. Med. **2024**, 14, 885.

Závěr

- **Katetrizační intervence představují další dostupnou možnost léčby**
    - Pro pacienty, u kterých standardní léčba selhala/selhává
    - Pro pacienty, u kterých není možné standardní léčbu z určitého důvodu použít (např. nepřiměřeně vysoké riziko krvácení)

    - PERT tým FNKV, PERT tým FN Brno a další vznikají!
    - Dostupnost katetrizačních intervencí v režimu 24/7
- **S narůstající evidencí se budou pravděpodobně v budoucnu rozšiřovat i indikace katetrizační léčby (léčba první volby u vybraných pacientů?)**

- **ESC Guidelines pro léčbu akutní PE velmi pravděpodobně až v roce 2027**