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REVIEW

The many roles of urgent catheter interventions: from myocardial infarction to acute stroke and pulmonary embolism

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ABSTRACT

Introduction: Cardiovascular diseases (CVDs) are the leading cause of cardiovascular mortality and a major contributor to disability worldwide. The prevalence of CVDs is continuously increasing, and from 1990 to 2019, it has doubled. Global cardiovascular mortality has increased from 12.1 million in 1990 to 18.6 million cases in 2019. The development of therapeutic options for these diseases is at the forefront of interest concerning the extensive socio-economic consequences. Modern endovascular transcatheter therapeutic options contribute to the reduction of cardiovascular morbidity and mortality.

Areas covered: The article concentrates on the triad of the most common causes of acute cardiovascular mortality and morbidity – myocardial infarction, ischemic stroke, and pulmonary embolism. Current evidence-based indications, specific interventional techniques, and remaining unsolved issues are reviewed and compared. A personal perspective on the possible implications for the future is provided.

Expert opinion: Primary angioplasty for ST-segment elevation myocardial infarction is a well-established therapeutic option with proven mortality benefits. We suppose that catheter-based interventions for acute stroke will spread quickly from centers of excellence to routine clinical practice. We believe that ongoing research will provide a basis for the expansion of interventional treatment of pulmonary embolism soon.

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1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of cardiovascular mortality and a major contributor to disability worldwide. CVDs cause approximately one-third of all deaths, with the dominant proportion of myocardial infarction (MI), ischemic stroke (IS), and pulmonary embolism (PE). Over three-quarters of cardiovascular mortality occurs in low- and middle-income countries [1,2]. The global prevalence of CVDs is continuously increasing, and from 1990 to 2019, has doubled, from 271 million in 1990 to 523 million cases in 2019. Global cardiovascular mortality has increased from 12.1 million in 1990 to 18.6 million cases in 2019. At the same time, the global trend for disability-adjusted life years (DALYs) has doubled, and the years lived with a disability have also doubled [2].

Considering the possibilities of modern therapy, the total rate of patients with cardiovascular diseases is increasing, and their survival time is extending. This may explain the two-fold increase in prevalence and only a 50% increase in mortality.

Mini-invasive transcatheter interventions are essential and often life-saving therapeutic options for many cardiovascular diseases. This review aims to summarize and compare the approach to urgent catheter interventions for MI, stroke, and PE.

2. Epidemiology

The overview is summarized in Table 1.

2.1. Myocardial infarction

Coronary artery disease (CAD), as a combination of acute and chronic processes, is the most common cause of death worldwide [5]. MI is the acute manifestation of CAD.

The prevalence of CAD is approximately 6.4%, and of MI is around 2.0% [6].

The incidence of MI has decreased significantly in developed countries, from 287 per 100,000 in 2000 to 208 per 100,000 in 2008 [7]. A significant decrease in the incidence of ST-elevation myocardial infarction (STEMI) occurring after 1999 was observed, but the incidence of non-ST-elevation myocardial infarction (NSTEMI) versus STEMI increased threefold between 1990 and 2006 [8]. The incidence of STEMI was 50 per 100,000 in 2008, and of NSTEMI was 132 per 100,000 in 2005 [7,9]. A significant contribution to higher NSTEMI incidence is the detection of less severe MI due to the better sensitivity of laboratory tests. Concurrently, modern pharmacotherapy probably reduces the risk of transition from NSTEMI to STEMI [8].

The 1-year mortality of patients after MI of all types is approximately 7.2%. 1-month total mortality after STEMI and NSTEMI is approx. 6.7% and 4.7%, respectively. Long-term total mortality up to 10 years after STEMI and NSTEMI is approx. 19.6% and 22.8%, respectively [10]. The mortality data are different in many other studies, and the most likely explanation is the selection bias.

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Article highlights

- Cardiovascular diseases are the most significant worldwide cause of morbidity and mortality, contributing to one-third of all deaths.
- The global prevalence of cardiovascular diseases is constantly increasing.
- Mini-invasive interventions in acutely ill patients usually increase the chance of a quick return to independent life.
- Primary percutaneous coronary intervention is a well-established method for treating acute myocardial infarction with ST-segment elevations.
- Transcatheter interventions for acute stroke are concentrated in centers of excellence, but we believe in their expansion into routine clinical practice.
- Intensive research on transcatheter therapy of pulmonary embolism with promising results is currently underway.

2.2. Ischemic stroke

Ischemic stroke is the second leading cause of cardiovascular death and the major cause of disability worldwide and accounted for approximately 116 million global DALYs in 2016 [11].

The incidence of IS is increasing worldwide. The estimated incidence was 11.6 million in 2010 and increased to 13.7 million cases in 2016 worldwide. The highest increase in the incidence of stroke is located in low- and middle-income countries but is relatively stable in high-income countries [11]. The stable incidence in high-income countries can be attributed to better primary preventive care and therapy of modifiable risk factors such as hyperlipidemia and arterial hypertension.

The 1-year mortality of patients after IS is approximately 23.6% [12] and is highly influenced by the level of medical care. Thus, the risk of age-standardized stroke-related mortality is 3.6 times higher in low-income countries than in high-income countries [13,14].

Regarding the etiology of stroke, two major causes are differentiated – ischemia, which is the cause in about 87% of strokes and hemorrhage in the rest of the cases [11]. In this article, we will only focus on the endovascular treatment of ischemic strokes.

When comparing myocardial infarction and endovascular stroke treatment, one major epidemiology difference must be pointed out – the completely different ratio of patients eligible for endovascular therapy. In STEMI patients, the vast majority of cases can be treated endovascularly. This can be observed in countries with developed primary percutaneous coronary intervention (pPCI) network where up to 92% of STEMI patients receive pPCI as a primary treatment strategy [15]. On the other hand, the estimated proportion of IS that can be treated endovascularly is only 10–15% of cases [16], and the real practice data shows that an even much smaller proportion of IS patients (around 1.9% in Europe) are receiving the endovascular treatment [17].

2.3. Pulmonary embolism

Pulmonary embolism is the third leading cause of cardiovascular death and is associated with many inherited and acquired risk factors.

The prevalence of pulmonary embolism in the global population is not reliably described. Based on a study by Meignan M. et al., a high proportion of patients with deep vein thrombosis have asymptomatic PE [18].

The incidence is estimated to be approx. 60 to 70 cases per 100 000, corresponding to 10 million cases per year worldwide [19–21]. The incidence of PE is increasing worldwide, but according to the analysis of European, Asian, and North American populations, the fatality of PE is decreasing. The incidence of PE is increasing partly due to the increased sensitivity of diagnostic methods, especially CT angiography of pulmonary arteries. On the other hand, this results in a higher rate of less severe PE detection that corresponds with lower fatality [19,21,22].

The 1-year mortality of patients after PE is approximately 23.0% [23]. The mortality is often caused by co-morbid conditions causing PE.

3. Pathophysiology

3.1. Myocardial infarction

Myocardial infarction is pathologically defined as myocardial cell necrosis caused by ischemia. The definition is based on ESC criteria [24].

The long-standing presence of atherosclerosis in coronary arteries and the sudden, unpredictable rupture of a vulnerable plaque usually precede myocardial necrosis. The formation of a thrombus and arterial occlusion follows. The human heart has a poor native collateral supply, which is usually unable to provide sufficient blood supply in acute vessel occlusion [25].

The necrosis spreads from the subendocardium, which is more vulnerable to ischemia due to the epicardial course of major coronary arteries.

One of the remaining issues in MI interventional treatment remains the topic of microvascular obstruction. This is characterized by inadequate myocardial reperfusion at the microcirculatory level, after a successful reopening of the epicardial infarct-related artery, without evidence of a persistent mechanical obstruction. No-reflow mechanisms are not fully understood – distal thrombotic microembolization, vascular reperfusion injury, adrenergic microvascular constriction, and myocardial edema may contribute. Despite all efforts,

Table 1. Epidemiology of major acute cardiovascular diseases.

	Incidence per 100,000	Prevalence	30-day mortality
Myocardial infarction	208 [7]	2.0% [6]	5.9% [10]
Ischemic stroke	156 [11]	1.1% [11]	15.0% [3]
Pulmonary embolism	70 [20]	NA	10.7% [4]

microvascular obstruction significantly adversely affects cardiovascular mortality [26,27].

Due to recent advances in genetics and molecular biology, the ability to regenerate cardiomyocytes in lower vertebrate species has been proven. Current research focuses on the possibility of inducing human regenerative abilities [28].

3.2. Ischemic stroke

Ischemic stroke is defined as neurological dysfunction caused by impaired perfusion through the blood vessels to the brain [29].

The pathophysiology of IS differs in many regards from MI, which has direct consequences in the treatment decision-making process.

The main difference is in the etiology of vessel occlusion. As the MI is dominantly caused by thrombosis on the ruptured atherosclerotic plaque, the IS is much more often caused by embolization, whether from the cardiac or carotid origin. This difference led to the development of different tools and techniques used for IS endovascular treatment, as mentioned below.

After the large brain vessel occlusion occurs, the clock begins to tick. The perfusion of the tissue after the occlusion reduces significantly, and when it drops below 22 ml/100 g/min, neurons lose their function. Thus neurological symptoms occur. When the perfusion is below 12 ml/100 g/min irreversible necrosis begins to establish [30]. The well-known concept of penumbra describes these pathophysiological facts. In the center of ischemic tissue, the necrosis starts to set and grows to the periphery while reducing the amount of the tissue potentially salvageable by recanalization. On average, every 1 minute, 1.9 million neurons disappear due to ischemia [31].

The speed of necrosis spread mostly depends on the quality of leptomeningeal and the circle of Willis collaterals [32].

All these facts have direct clinical consequences. Most of the patients who will benefit from endovascular treatment are those with small ischemic core and large salvageable penumbra. In the first six hours after symptom onset, the evaluation of established ischemia is mainly done by Alberta Stroke Program early native CT (ASPECT) score. Late presenters (6–24 hours after symptom onset) require more detailed penumbra/ischemic core evaluation by CT perfusion or diffusion-weighted imaging MRI [33,34].

The second most important consequence is that the effect of the endovascular treatment is highly time-dependent, and the relation between timely reperfusion and clinical outcomes is even more closely than in the case of MI – up to 26% decrease in the probability of a good functional outcome for every 30-minute delay of reperfusion was observed [35,36].

3.3. Pulmonary embolism

Pulmonary embolism is defined as an obstruction of pulmonary circulation, typically by a thrombus. The classical origin is in the lower limb deep venous system. The size of venous thrombus in PE patients is much larger than the arterial thrombus in MI and IS.

Significant thrombotic occlusion of the pulmonary artery leads to pulmonary hypertension, right ventricular afterload increase, and may result in acute right ventricular failure. Due to ventricular interdependency, dilated and failing right ventricle decreases the preload of the left ventricle, resulting in hypotension and a decrease in coronary perfusion pressure, thus further increasing the injury to the right ventricle. This self-perpetuating cycle leads to shock and is responsible for the acute mortality of PE [20].

The outcome of the PE patient does not depend on the extent of possible necrosis of the lung tissue but on hemodynamic instability. Pulmonary infarction occurs in less than 30% of patients with PE because of the dual blood supply to the lungs via pulmonary and bronchial vessels [37].

4. Development of interventions

4.1. Cardiac catheterization

At the turn of the millennium, there was a dramatic change in the management of patients with acute STEMI – the concept of a mechanical re-opening of occluded coronary artery emerged. The PRAGUE-1 trial demonstrated the superiority of pPCI over thrombolytic therapy in patients with acute STEMI [38]. The PRAGUE-2 trial and the DANAMI-2 trial extended this novel treatment also to patients requiring transport from the local hospital [39,40]. Considering the results of these trials, it was necessary to develop a methodology to ensure the availability of catheterization laboratories. The fundamental pillars were established: 1) volume of pPCI for STEMI > 600/year per 1,000,000 inhabitants; 2) 24/7 hours of service; 3) availability for more than 70% of patients with STEMI [41].

The first generation of stents (bare metal stents) significantly improved the safety of coronary angioplasty. The drug-eluting stents have addressed the issue of restenosis due to neointimal hyperplasia [42]. The development of bioresorbable scaffolds was an intuitively very attractive idea, and promising early results were also reported for STEMI treatment [43,44]. Due to a higher risk of scaffold thrombosis and myocardial infarction, bioresorbable scaffolds were unfortunately subsequently withdrawn from the market in 2017 [42].

Thrombaspiration in pPCI seems a very intuitive and logical option – removing the thrombus should prevent distal embolization. Despite promising initial results, the results of two large randomized trials, TASTE [45] and TOTAL [46], did not demonstrate any benefit of thrombus aspiration catheters, and TOTAL showed an increase in IS, probably related to embolization of extracted thrombotic material. Thus, thrombaspiration is routinely not recommended [47].

4.2. Stroke catheterization

In the 1980s the first reports of endovascular stroke treatment attempts consisting of catheter-guided thrombolysis injected in the proximal part of the thrombus were published [48]. Subsequently, this approach was investigated in a randomized trial PROACT which revealed a significantly higher rate of reperfusion compared to placebo but with a higher risk of symptomatic intracranial hemorrhage [49].

At the beginning of the millennium, mechanical thrombectomy devices were introduced as promising tools for large vessel occlusion reperfusion [50]. One of the first endovascular devices was the retriever – a corkscrew-shaped nitinol wire used to remove the clot from the vessel [51]. Based on the results of the MERCI Trial, which showed a higher recanalization rate comparing the historical cohort with an acceptable risk of hemorrhagic complications, the device was approved for clinical use. Still, the recanalization rate of retrievers was only 46% [52].

The most significant milestone in endovascular stroke treatment was the introduction of second-generation stent retrievers. In 2012 SWIFT Trial and TREVO 2 Trial showed superiority over the first generation of retrievers [53]. And in 2015, several randomized trials using the second generation of stent retrievers, showed clear superiority of endovascular treatment compared to the best medical treatment (BMT), including intravenous thrombolysis in terms of 90 days functional neurological outcomes [54–59].

These trials completely changed the guidelines and practice and made endovascular stroke treatment the preferred approach in eligible patients with large vessel occlusion [60].

Concurrently with stent retrievers, another technique consisting of direct aspiration of clot using large bore aspiration catheters was evolving [61]. The results of the trials COMPASS, ASTER, and ADAPT FAST confirmed the non-inferiority of thrombus aspiration compared to stent retrievers [61–63].

4.3. Pulmonary embolism catheterization

Catheter-based solutions for PE already began in the 1960s. The first device was the large bore (12 French) suction catheter developed specifically for endovascular mechanical thrombectomy in PE. Then for many decades, the pharmacologic approach to PE prevailed. Catheterization techniques gained attention in 21. century again due to persistently high mortality of intermediate and high-risk subgroups of PE.

In 2013, the ULTIMA [64] randomized trial demonstrated catheter-directed thrombolysis (CDT) facilitated by ultrasound thrombus disruption as a superior method to anticoagulant therapy with heparin alone in patients with intermediate-risk PE with the primary end-point being the reversal of right-ventricular dilatation [64]. In 2015, the single-arm, non-randomized SEATTLE II [65] and PERFECT [66] trials were published, which demonstrated the safety of using CDT (with and without ultrasound facilitation) in patients with massive and sub-massive embolism, while no hemorrhagic stroke as a complication occurred. CDT enabled approximately up to a three-quarter reduction in the dose of tissue-plasminogen activator compared to systemic thrombolysis [21]. Again, the endpoints were surrogate, based on imaging of the right ventricle and pulmonary pressure measurements, not clinical ones.

A recent small pilot study compared catheter-directed thrombolysis versus standard anticoagulation therapy again with promising results in patients with intermediate-high-risk PE. There was no life-threatening bleeding, and a significant decrease in pulmonary artery systolic pressure and a significant decrease in the right-ventricle/left-ventricle ratio at 24 hours were observed [67].

5. Catheterization techniques

The overview is summarized in Table 2.

5.1. Myocardial infarction

The pPCI is a well-established urgent procedure performed on patients receiving very efficient antithrombotic treatment. The radial access results in a lower rate of bleeding complications than the femoral artery puncture and is clearly recommended by guidelines. A drug-eluting stent implantation is routine, delayed stenting can be considered individually, but not as a routine strategy [47]. The use of drug-coated balloons seems promising for a selected population and might warrant further large randomized studies. Direct stenting with less vessel manipulation might prevent no-reflow and should be considered for „soft" thrombotic lesions. On the other hand, culprit lesion calcification is severe or moderate in over 30% of STEMI patients (and likely to become more frequent in the future). It is associated with an increased risk of death, stent thrombosis, and revascularization [78]. High-pressure predilatation with non-compliant, cutting, or scoring balloons is routinely used, but their role in the specific setting of primary PCI is not well described. Rotational atherectomy and excimer laser atherectomy facilitate stent delivery and improve procedural results.

Table 2. Overview of interventional techniques.

	Myocardial infarction	Ischemic stroke	Pulmonary embolism
Access	Radial/Femoral *(arterial)*	Femoral/Brachial/Radial *(arterial)*	Femoral/Jugular *(venous)*
Device dimensions	4–8 FR [68]	6–9 FR [69]	4–26 FR [70–72]
Iodine contrast medium volume	150 ml [73]	120 ml [74]	0–120 ml [75]
Techniques *(the most used)*	- Direct stenting - Balloon pre-dilatation followed by stenting - Drug-coated balloon dilatation	- Stent retrievers - ADAPT technique - Solumbra technique	- Suction thrombectomy - Mechanical thrombectomy - Catheter-directed thrombolysis ± ultrasound facilitation
Target time	Door-to-balloon [76] 90 minutes	Door-to-recanalization [77] 90 minutes	NA

ADAPT – The direct aspiration first pass technique; FR – French

Still, these complex adjunct procedures might increase the rate of restenosis [79,80], and rotational atherectomy is rarely used in STEMI due to the risk of no-reflow, it is contraindicated in the presence of coronary thrombus. Intracoronary lithotripsy is another recently introduced option, this technique is easy and quick to use, i.e. suitable for the acute setting of pPCI, and the success rate was 90% in a recent small study [81].

Cardiogenic shock complicating STEMI is a major cause of in-hospital mortality. Intraaortic balloon pump is not routinely recommended as it did not affect mortality at 6 years follow-up [82]. Extracorporeal membrane oxygenation and left-ventricle assist devices like Impella provide excellent hemodynamic support and are used on a case-by-case basis in centers of excellence. The topics of hemodynamic support optimal timing (before or after the opening of culprit vessel) and patient selection are currently discussed, and invasive assessment of left ventricle filling pressure might have a role.

5.2. Ischemic stroke

In the endovascular treatment of IS, three basic techniques are used – stent retrievers, the direct aspiration first pass technique (ADAPT) and the Solumbra technique.

Stent retrievers are soft self-expandable meshes that are released from the microcatheter at the side of the occlusion. A few minutes after release, when the stent retriever achieves the optimal radial force, it is pulled out together with the microcatheter. In the ideal scenario, the occlusive thrombus is extracted together with a stent retriever. Stent retrievers are today routinely used together with balloon guide catheters. These catheters temporarily stop the blood flow in the internal carotid artery during the extraction of the stent retriever and facilitate the extraction of thrombus by aspiration from the balloon guide catheters during the pull-out. Several trials proved that using balloon guide catheters achieves faster recanalization, more often first-pass effect and improved clinical outcomes compared to proximal large-bore conventional guide catheters [83,84].

ADAPT technique is based on the direct aspiration of the thrombus by a large bore catheter placed at the proximal part of the thrombus using a pump [85]. Solumbra technique combines both mentioned techniques when the stent retriever is used together with aspiration from a large bore catheter.

Some data suggests that each technique could perform better in different specific settings. Stent retrievers seem to perform better in cases when the thrombus is soft and red blood cell-rich (which is represented by hyperdense vessel sign on initial non-contrast CT or blooming/susceptibility sign on magnetic resonance imaging). On the contrary, direct aspiration seems to perform better in the case of fibrin-rich thrombus when these imaging signs are not present [86,87].

5.3. Pulmonary embolism

Endovascular treatment of PE is much less developed than MI and IS. Two different patient populations are currently targeted.

(1) Catheter-based interventions are compared with standard anticoagulation in intermediate-high risk PE patients with dilated and ischemic right ventricle but stable hemodynamics. An international multicenter randomized study HI-PEITHO of catheter-directed thrombolysis facilitated by ultrasound started enrollment [88], and another randomized academic multicenter study without ultrasound facilitation will begin soon (clinicaltrials.gov No: NCT05493163). Both studies have clinical endpoints, patient safety with low-dose local thrombolysis is of paramount importance in this hemodynamically stable patient cohort, and both studies use small caliber and soft catheters. A recently published case series with new endovascular catheter combining mechanical a pharmacological reperfusion was reported, and this technique awaits further evaluation [89].

(2) High-risk PE patients are defined by hemodynamical instability and require urgent reperfusion of the pulmonary artery tree. The standard treatment is systemic thrombolysis, and mechanical reperfusion is reported in case series of thrombolysis contraindications or failure. The need for immediate reperfusion dictates larger-sized catheters use based on thrombus aspiration by suction, thrombus fragmentation by angioplasty balloons, rheolytic thrombectomy, and thrombus entrapment in nitinol-based systems, etc. All these devices are reviewed in [90] and can be combined with local thrombolytic administration [91]. These procedures are technically more complex, require manipulation of larger devices in pulmonary arteries, and have higher procedural costs.

6. Outcomes and pitfalls

The overview of complications is summarized in Table 3.

6.1. Myocardial infarction

Percutaneous coronary intervention and its high availability in developed countries led to a gradual decrease in morbidity and mortality due to STEMI and a simultaneous reduction of its risk of arrhythmic and mechanical complications.

Microvascular obstruction remains a complex problem. In patients with STEMI treated with pPCI is a major cause of the no-reflow phenomenon, and this is strongly associated with mortality and hospitalization for heart failure within 1 year [100].

Due to the increasing density of cardiocenters with 24/7 availability of catheterization laboratories, the time delay from emergency calls to interventions is shortening. However, the variable time delay from the onset of symptoms to the emergency call remains a problem, adversely affecting patient outcomes. Better patient education about symptoms accompanying acute coronary syndromes may lead to a shortening of this delay with the potential to lower cardiovascular morbidity and mortality.

6.2. Ischemic stroke

Endovascular treatment (ET) of IS in the selected group of patients with large vessel occlusion proved to be a better option providing superior clinical outcomes compared to the

Table 3. Complications of interventions.

	Total rate	Complications – overview	Individual rate
Percutaneous coronary intervention	3.4–4.8% [18,92]	• Coronary perforation	0.19–1.5% [92]
		• Coronary dissection	1.1% [93]
		• Arrhythmias VT/VF	4.3% [94]
		• No-reflow	0.6–2.0% [95]
		• Pericardial tamponade	0.12% [96]
		• Device embolization	0.2% [95]
Ischemic stroke intervention	4.0–31.0% [97]	• Intracerebral bleeding	1.9–15.8% [97]
		• Subarachnoid bleeding	1.0–5.5% [97]
		• Distal embolization	1.0–12.5% [97]
		• Arterial perforation	0.7–4.9% [97]
		• Dissection	0.6–6.7% [97]
		• Vasospasm	3.0–23.0% [97]
		• Stent detachment	0.7–3.9% [97]
Catheter-directed intervention for pulmonary embolism	2.4–3.6% [72]	• Hemorrhagic stroke	0.4–0.6% [98]
		• Pulmonary hemorrhage	NA
		• Perforation or dissection of the pulmonary artery	NA
		• Arrhythmias	NA
		• Right-sided valvular regurgitation	NA
		• Pericardial tamponade	NA
Other complications		• Contrast-induced nephropathy	<14.0% [99]

VT – ventricular tachycardia; VF – ventricular fibrillation

best medical treatment (BMT), including the administration of intravenous thrombolysis. HERMES meta-analysis, which analyzed five randomized trials comparing ET vs. BMT, showed good functional outcomes 90 days after stroke, defined as a modified Rankin Scale (mRS) score 0–2 in 46% of patients in the interventional group compared to 26.5% in the medical group (OR 2.35 (1.85–2.98); $p < 0.0001$) [101].

The functional outcome of the individual patient after endovascular treatment of IS depends on many variables. As was already mentioned, time plays a key role. The sooner the treatment is provided, the higher the odds of a good clinical outcome [35,36].

Different occlusion anatomical localization also plays an important role in terms of probabilities of good clinical outcomes. The best results are observed in isolated middle cerebral artery occlusion, contrary to much worse results in carotid occlusions or posterior circulation strokes [102].

Even though the ET for IS is an invasive procedure, the rate of clinically relevant complications using modern devices does not differ significantly when comparing patients treated by intravenous thrombolysis. In above mentioned HERMES meta-analysis, the risk of symptomatic intracranial hemorrhage was 4.4% in ET group compared to 4.3% in the BMT group [OR 1.07 (0.62–1.83); $p = 0.81$], and also the risk of parenchymal hematoma type 2 was comparable between the groups [101].

In comparison to other endovascular procedures, the risk of peri-procedural complications in endovascular stroke treatment is one of the highest, as shown in Table 3. Yet the risk of complications is outweighed by the potential benefit of the procedure in the well-indicated group of patients.

6.3. Pulmonary embolism

The endovascular approach for PE is associated with the risk of bleeding and mechanical complications. Intracranial bleeding is the most feared complication.

The PEITHO [103] trial in 2014 demonstrated an increased incidence of bleeding in patients after systemic administration of tenecteplase versus unfractionated heparin in the intermediate-risk population. Subsequently, the PERFECT [66], ULTIMA [64], SEATTLE II [65] trials of low-dose catheter-directed thrombolysis did not find any increase in major or intracranial bleeding.

Considering the larger dimensions of the devices used for endovascular interventions in high-risk PE cohorts, there is also a higher risk of mechanical complications. Complications presented in Table 3 have all been described [104], but the incidence of these rare and often device-specific complications is not well described.

Although the results of ET in PE patients so far look promising, it is still a subject of research consolidated in large cardiovascular centers with particular interest. The results await confirmation in large studies with clinical end-points.

7. Expert opinion

Interventional cardiology is a very dynamic field with great emphasis on treating acute cardiovascular diseases, where the largest mortality benefit is expected. Acutely ill patients often benefit from the minimally invasive nature of these procedures with low procedural risk and usually rapid return to independent life. The interventional treatments of myocardial infarction, stroke, and pulmonary embolism differ in many aspects – vascular access is arterial or venous, the size of the clot and intervened vascular structures span a wide range, techniques vary, and outcome measures are different. However, there are many apparent similarities:

- blood clotting plays a major role in the pathophysiology
- all these interventions need to be provided on an urgent basis with 24/7 availability of a highly skilled team of health care professionals

- all these interventions require basic vascular catheterization skills, and many techniques are overlapping or at least similar
- clinical results are closely linked to the timely application of the catheter-based intervention, especially in myocardial infarction and stroke patients ('time is muscle,' 'time is brain')
- the cost is often high, possibly limiting the spread to low-income countries – geographic variables and health care organization dictate the availability, often resulting in better coverage in densely populated regions
- research is often fast progressing, and evidence is mainly based on high-quality outcome studies

We expect that the interventional cardiologist of the future will be educated and proficient in at least two of these vascular territories. Training should also include other non-acute interventions, for example, the rapidly expanding field of structural heart procedures. Training in imaging becomes more important – in fact, the knowledge of computed tomography provides a clear advantage for stroke and pulmonary embolism interventions. Novel software is already helping to interpret computed tomography three-dimensional datasets, and automated analysis based on artificial intelligence will likely become available soon. These new skills will need to be incorporated into training programs. We would like to discuss the topic of outcome measures briefly – mortality (both total and cardiovascular) is the current gold standard in interventional cardiology. It will undoubtedly remain an important major parameter in acute life-threatening cardiovascular diseases. However, we feel that softer parameters, like speed of recovery, quality of life, treatment cost etc., are likely to become important in the future.

In conclusion, primary PCI for STEMI is a well-established and mature therapeutic option with clearly proven mortality benefits. We believe that catheter-based interventions for acute stroke will spread quickly from centers of excellence to routine clinical practice. Finally, we hope that ongoing research will provide a basis for the expansion of interventional treatment of pulmonary embolism soon.

Abbreviations

CVDs	Cardiovascular diseases
MI	Myocardial infarction
IS	Ischemic stroke
PE	Pulmonary embolism
DALYs	Disability-adjusted life years
CAD	Coronary artery disease
STEMI	ST-segment elevation myocardial infarction
NSTEMI	Non-ST-segment elevation myocardial infarction
PPCI	Primary percutaneous coronary intervention
BMT	Best medical treatment
CDT	Catheter-directed thrombolysis
ADAPT	The direct aspiration first-pass technique
ET	Endovascular treatment

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