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ARTYKUŁ SPECJALNY / *STATE-OF-THE-ART REVIEW*

Contemporary methods for the treatment of pulmonary embolism — is it prime-time for percutaneous interventions?

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INTRODUCTION

Methods of percutaneous interventional therapy have revolutionised contemporary cardiac treatment, mainly with regard to interventions in coronary arteries and treatment of structural heart diseases but also in pulmonary circulation diseases. Acute pulmonary embolism (aPE), because of its frequent occurrence and high risk of death, is a serious epidemiological problem [1]. Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease; however, it carries a high risk of development of severe right ventricle (RV) failure [2]. In both situations, the main reason for haemodynamic disorders is mechanical occlusion of pulmonary arteries with clots. It therefore seems logical that mechanical unblocking of pulmonary vessels and prevention of recurrent embolism with interventional cardiology or radiology techniques should be considered as potentially improving outcomes. In this article, current possibilities for interventional treatment of aPE and CTEPH as well as the opportunities and limitations related to the application of venous filters have been discussed. Due to the fact that new therapeutic possibilities have become available, a multidisciplinary team of physicians should decide on selection of a particular technique, and this is connected with the increasing popularity of Pulmonary Embolism Response Teams (PERT) and CTEPH-teams, who are responsible for optimisation of therapeutic procedures in aPE and CTEPH, respectively [3]. Recently, a multidisciplinary PERT has been established in the Central Clinical Hospital of the Medical University of Warsaw.

THE PLACE OF INTERVENTIONAL TECHNIQUES IN THE TREATMENT ALGORITHM OF ACUTE PULMONARY EMBOLISM

According to current recommendations, the choice of treatment method in aPE is based on the foreseen probability of early death. This probability is assessed on a clinical basis at the stage of a justified suspicion of PE. The presence of shock or significant hypotension identifies patients with a high risk of death, which can be expected within the coming minutes or hours if the reason for haemodynamic instability is aPE. Such a situation, therefore, requires an immediate differential diagnosis and, if PE is confirmed, application of primary reperfusion therapy. In contrast to acute coronary syndromes, in the case of high-risk aPE, thrombolytic therapy is the preferred method of primary reperfusion. Until recently, surgical embolectomy was suggested in the European Society of Cardiology (ESC) Guidelines as an alternative to thrombolytic treatment in the case of overly high risk of serious bleeding or ineffectiveness of thrombolysis [4]. However, aPE can occur anywhere, often in places where emergency availability of cardiac surgery is limited. Consequently, in such situations most contra-indications to thrombolysis in life-threatening, high-risk aPE become relative. In real world settings the registries — including the Polish ZATPOL registry — show a significant percentage of patients suffering from high-risk aPE, who were not treated with thrombolysis or cardiac surgery but remained on intravenous anticoagulation alone.

Shock caused by sudden mechanical occlusion of a significant part of the pulmonary vascular bed with potentially removable clots undoubtedly justifies higher risk treatment, even if it only allows for partial recovery of pulmonary flow, and at the same time a systemic flow, thereby saving a patient's life. A less explicit situation exists for patients in whom a high risk of death during the course of aPE is assigned on the basis of hypotension, the definition of which includes an element that is difficult to assess objectively: a drop in systolic blood pressure (SBP) by at least 40 mm Hg compared to usually stated values. Regardless of the definition of hypotension, it is not certain whether choosing only one parameter — SBP — does not leave other patients perhaps also seriously compromised without sufficiently intense therapy. Many papers have shown an increased risk of death in patients without shock or hypotension, but with a significant RV overload, visible on imaging examinations, particularly when they are accompanied by biochemical signs of myocardial injury [5, 6]. This group of patients were selected in the recent ESC Guidelines as a subgroup named as intermediate-high risk PE [4]. In the multicentre PEITHO trial, it was shown that such patients can avoid haemodynamic deterioration if they receive primary reperfusion with an intravenous bolus dose of tenecteplase [7]; unfortunately this was related to a significant increase in the frequency of bleedings, particularly intracranial, compared to a group receiving placebo. Ultimately, both groups did not differ in terms of short-term or long-term mortality, nor frequency of development of CTEPH [8]. The ESC Guidelines recommend, as well as intravenous anticoagulation, to only monitor those patients with intermediate-high risk PE, and a possible rescue reperfusion in the case of a secondary haemodynamic collapse [4].

So, does this mean that primary reperfusion in aPE will only be applied in shock or acute hypotension? Currently, this is not explained thoroughly because the PEITHO trial also seems to show potential benefits of fibrinolytic treatment in an intermediate-high risk group. Before extending indications for thrombolytic treatment of aPE, the criteria defining an intermediate increased-risk group, for example, with the use of so-called Bova criteria, should be tightened [9]. A criterion of moderate hypotension (SBP between 90 and 100 mm Hg) and tachycardia (heart rate ≥ 110/min) should be included in the symptoms of RV overload, together with a method for restricting the risk of bleeding during primary reperfusion, by searching for a safer technique based on reduction of the thrombolytic dosage [10] or its administration in connection with application of ultrasound energy, mechanical fragmentation, homogenisation, or suction. In the case of an increased risk of bleeding, enumerated percutaneous interventional techniques can be applied without a thrombolytic treatment.

According to the ESC Guidelines, in the presence of contra-indications to applying a full dosage of systemic thrombolysis or when this therapy is ineffective, as an alternative for surgical pulmonary embolectomy, percutaneous treatment should be applied with the use of a catheter (class of recommendation IIa/level of evidence C) [4]. The current guidelines of the American College of Chest Physicians (ACCP) [11] in patients with aPE associated with hypotension and who have a high bleeding risk, failed systemic thrombolysis, or shock that is likely to cause death before systemic thrombolysis can take effect, suggest catheter-assisted thrombus removal if appropriate expertise and resources are available. This recommendation refers to mechanical interventions with or without catheter-directed thrombolysis. If no mechanical intervention is to be performed, ACCP suggests systemic thrombolytic therapy using a peripheral vein.

METHODS OF INTERVENTIONAL TREATMENT OF ACUTE PULMONARY EMBOLISM

Trans-catheter methods of percutaneous treatment of aPE make use of a variety of different mechanisms based on the mechanical defragmentation of clotting material in connection with or without direct administration to a pulmonary artery of a thrombolytic drug. Currently, we have a limited amount of data from prospective randomised trials regarding the effectiveness and safety of trans-catheter therapy in patients diagnosed with aPE. The first prospective randomised clinical trial comparing the effectiveness of anticoagulant treatment with unfractionated heparin with an ultrasound-assisted catheter-directed thrombolysis (USAT), causing accelerated disaggregation of fibrin, was Ultrasound-Accelerated Thrombolysis in Pulmonary Embolism (ULTIMA) with a total number of 59 patients with aPE and echocardiographic signs of RV overload, defined as the ratio of dimensions of the RV to the left ventricle (LV) > 1.0 [12]. In a group of patients treated with USAT using a modified tissue plasminogen activator (t-PA) dose (10–20 mg in a 15-h infusion), a significant drop of systolic pressure in the pulmonary artery from 52.0 mm Hg to 39.7 mm Hg and an improvement of the cardiac index from 2.5 L/min/m^2 to 3.9 L/min/m^2 was observed. The results of ULTIMA were confirmed in the SEATTLE II trial, in which a prospective assessment of USAT with EkoSonic Endovascular device was made for improvement of haemodynamic parameters and the RV/LV size index [13]. One hundred and fifty patients with massive or sub-massive aPE (according to the American standards), with RV overload, defined as the ratio of RV/LV size above 0.9 when assessed with computed tomography, were included into the study. Each of the patients participating in the SEATTLE II trial received a total dose of 24 mg t-PA. In the case of one-sided location of clots, the thrombolytic infusion lasted 24 h (dose 1 mg/h), whereas in the case of two-sided aPE, the treatment regime consisted of a 12-h infusion (dose 2 mg/h) through each of the catheters located in the left and right pulmonary artery. After 48 h of observation, a significant improvement of the RV/LV index, approximately 25%, was observed, and additionally a 30% drop in the systolic pulmonary arterial pressure was achieved. One patient from the group of 150 under observation in the SEATTLE II trial suffered complications in the form of a haematoma at the injection site with accompanying hypotension that met the criteria of a major bleeding according to the GUSTO classification. It needs to be underlined at this point that, in contrast to the results of the trial devoted to systemic thrombolysis, none of the patients from the SEATTLE II trial suffered bleeding complications within the central nervous system, and the frequency of occurrence of moderate bleeding events according to the GUSTO classification did not exceed 10%. Hence, the genuine clinical benefit achieved with the use of USAT has a relatively high level of safety, making it a more profitable form of therapy compared to systemic thrombolysis. An undeniable limitation, however, is the high cost of ultrasound catheters as well as the lack of definitive evidence that ultrasounds improve treatment results when compared to thrombolytic infusion through a catheter located in a pulmonary artery. One might also be concerned that, in the case of a wider application of intervention methods, especially when used by less experienced operators, outcomes will probably be worse than those achieved in reference centres conducting clinical trials.

The results of the collective meta-analysis of 35 observational trials and registries of interventional procedures aggregating the data regarding 594 patients with high-risk PE show a relatively high effectiveness of invasive forms of treatment (86.5%), defined as stabilisation of haemodynamic parameters, recovery from hypoxaemia, and early survival during hospitalisation. A majority of the patients (69%) were treated with an embolic material defragmentation procedure utilising a pigtail catheter, and the proportion of patients who received a thrombolytic therapy was 66% [14]. Clinical benefit was achieved in particular by patients treated with a local catheter-assisted thrombolysis, in whom the result of the therapy was better than in the group treated only with a mechanical thrombectomy. The percentage of patients who suffered from complications during the therapy, such as haematoma at the injection site, transient bradycardia, acute renal failure or haemoptysis, was 7.9%. The frequency of occurrence of major bleeding complications, including bleedings to the central nervous system (seen in one person from the group of 594 patients) or haematomas at the injection site requiring administration of blood transfusion was 2.4%. What is interesting is that 76% of the patients who suffered from major complications were treated with the use of an AngioJet device, which is mainly related to an adverse effect from bradykinin released from degradation of platelets during the procedure.

BALLOON PULMONARY ANGIOPLASTY IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

The frequency of occurrence of CTEPH in patients after aPE is still the subject of some controversy; however, it appears that it does not exceed 1% [15]. In October 2017, according to a survey conducted by the Working Group on Pulmonary Circulation of the Polish Society of Cardiology, the number of patients with CTEPH remaining under the care of PH centres in Poland amounted to 367. Additionally, the international CTEPH registry shows that about 25% of patients with confirmed CTEPH did not have an explicit clinical episode of aPE previously [16]. This manifests into too low a level of recognisability of CTEPH in Poland, which is also observed in other countries [17].

The essence of CTEPH is a lack of or incomplete recanalisation of clots in pulmonary arteries causing the presence of fibrous endovascular structures mainly consisting of connective tissue and not resembling 'fresh' clots observed during aPE. According to the current definition, CTEPH can be recognised when, after a minimum three-month period of effective anticoagulant treatment, the value of mean pulmonary arterial pressure is greater or equal to 25 mm Hg and imaging examinations of pulmonary arteries show deficits of perfusion or fulfilment defects typical for CTEPH [18]. Right heart catheterisation and pulmonary angiography are basic diagnostic examinations in confirmation of CTEPH and qualifying a patient for surgical treatment (Fig. 1) [19]. A primary method for treating CTEPH is surgical pulmonary endarterectomy (PEA). However, 36% of patients cannot be treated surgically because of the distal location of clots or co-morbid conditions increasing significantly the perioperative risk [16]. Until recently, the prognosis for patients who were not qualified for PEA was very poor — the probability of a three-year survival was 67–70% [20, 21]; however, the situation for this group of patients was improved by the introduction of balloon pulmonary angioplasty (BPA) into clinical practice. BPA includes the performance of percutaneous angioplasty within branches of the pulmonary artery of a size between 2 mm and 8 mm. After BPA, no restenosis is observed, therefore, implanting vascular stents is not necessary. Usually, in order to achieve a haemodynamic effect, several procedural sessions should be performed because of the threat of post-reperfusion oedema resulting from acute overload by the recovered blood flow of the pulmonary parenchyma that was not earlier perfused. The first report regarding interventional treatment of CTEPH was published in 2001 [22]. Because of the high frequency (61%) of reperfusion oedema aggravating respiratory insufficiency and subsequently requiring mechanical ventilation (17%), interest in this method of treatment for subsequent years was minimal and it was not until the experiences of the Japanese centres became known that a real explosion of interest in BPA occurred [23–25]. In the following years, the positive impact of BPA on pulmonary haemodynamics [26], echocardiographic parameters of RV overload [27], and biomarker levels [28] was confirmed. Along with the number of performed procedures, safety measures are also improving. In Poland, the first BPA procedure in CTEPH was performed in 2013 [29], and in the same year, Andreassen et al. [30] described the first European series of 20 patients treated with BPA. The technique used by Andreassen et al. [30] consisted of attempts to bring back patency of the closed vessels and achieve an optimal angiographic result incorporating quite an aggressive procedural technique with the use of vascular guidewires of high stiffness. However, a technique suggested by Okayama group [31] and other Japanese centres [26] involving performance of dilations in lesions with easier morphology (rings and webs) and the use of undersized balloon catheters of maximum diameter 2.0–2.5 mm at the time of first procedure when pressure in the pulmonary artery is still high seems to have an impact on reduction of perioperative complications (Fig. 2) [32]. Supplementing initial dilations optimises the effect with catheters of a size being 100% up to 110% of vessel diameter in situations when mean pulmonary arterial pressure drops below 35 mm Hg, as well as attempting to recanalise lesions of the type of subtotal or total occlusion.

The most common reason for damaging a vessel during BPA is perforation with a vascular guidewire. Less frequent complications include damage to a vessel caused by a balloon of too large a diameter or dissection of a wall by a guiding catheter. A further risk, which is related to the occurrence of bleeding to pulmonary parenchyma, results more from intensification of respiratory failure caused by exclusion of part of a lung from work, rather than from blood loss [33]. The majority of complications can be managed through inflation of a balloon catheter proximally to the injury site, blocking blood inflow [34], while the ultimate option is intravascular embolisation or implanting a covered stent [35].

The technique of BPA procedure is not explicitly specified; a morphological assessment with the use of intravascular ultrasound or optical coherent tomography allows for a more precise selection of balloon size to suit vessel diameter — particularly at the final stage of optimisation of treatment or procedures performed in larger vessels. Application of a pressure wire aims at haemodynamic assessment of the significance of lesions as well as being one of the techniques for reducing the risk of reperfusion oedema. Arbitrarily, the value of the pressure ratio through the lesion below 0.8 (without application of adenosine) is assumed as identifying a significant stenosis. Performing dilation with a balloon catheter with a gradually increased diameter, maintaining a mean pressure value distally from a lesion below 35 mm Hg, is to protect against reperfusion oedema [36]. So far, the advantage of procedures performed with the use of additional intravascular devices over traditional angiography-controlled procedures has not been directly compared. The use of intravascular devices

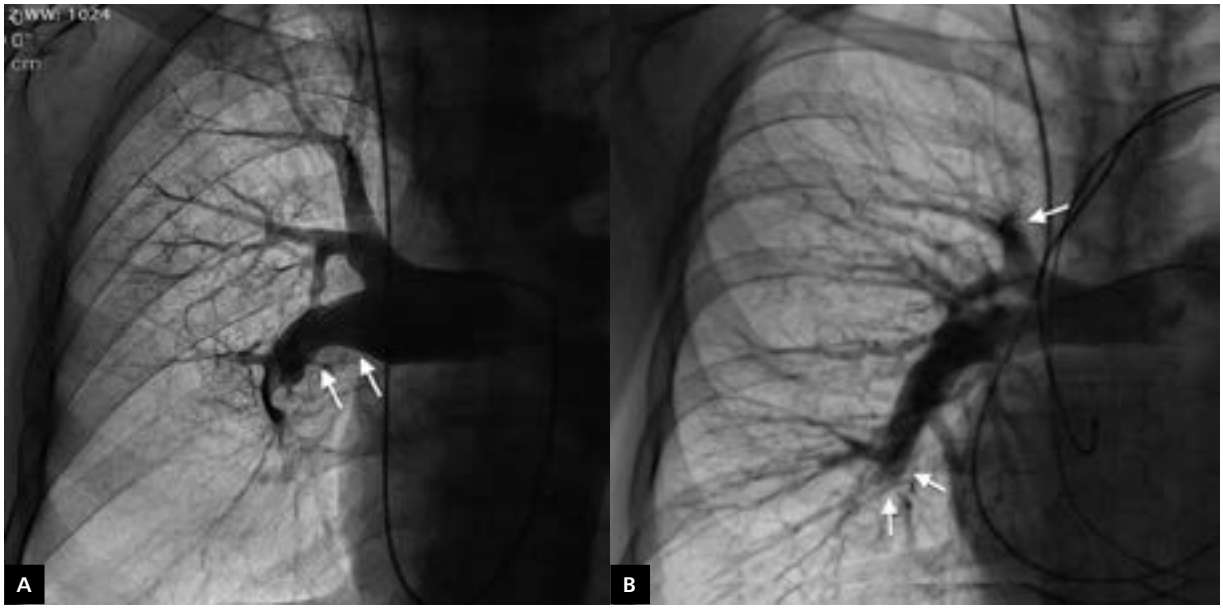

Figure 1. Pulmonary angiography of two patients with chronic thromboembolic pulmonary hypertension; **A.** Post-embolic lesions located at the level of the main trunk or right pulmonary artery — proximal disease (arrows); **B.** Thrombi originating from pacemaker leads located at the segmental and sub-segmental level — distal disease (arrows)

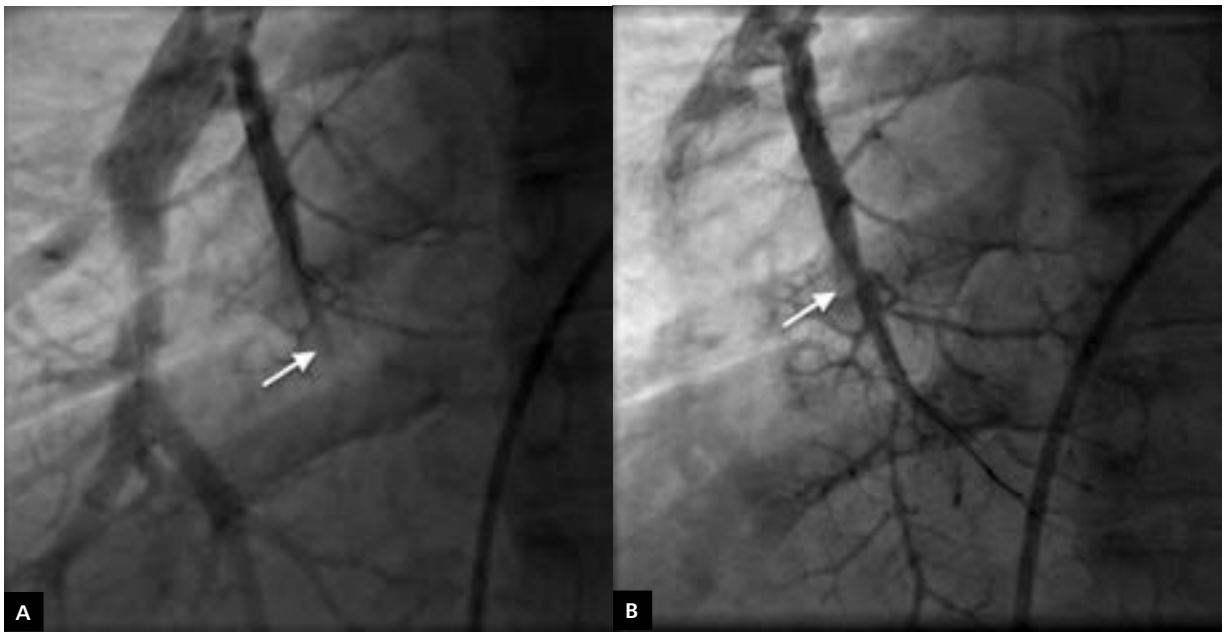

Figure 2. Balloon pulmonary angioplasty of segmental branch (A7) of right lower lobe artery; **A.** Chronic total occlusion of A7 segmental branch (arrow); **B.** Flow restored after dilatation with 2.5-mm balloon. Arrow indicates residual lesion left for final therapy during next procedure because of significantly elevated pulmonary artery pressure (mPAP 48 mm Hg)

increases the dose of radiation as well as increasing the use of a contrast media and the costs of the procedure, resulting in most experienced BPA centres' intravascular imaging and pressure wire not currently being routinely applied [31].

A therapeutic aim suggested by the leading Japanese centres is normalisation of the pressure in the pulmonary artery, defined as mean pulmonary artery pressure (mPAP) < 20 mm Hg [37]. Achieving such a therapeutic goal certainly requires the skill to reach vessels of all the segments of the lungs and performance of a greater number of angioplasties. Preparing a "road map" of such a procedure on the basis of a three-dimensional reconstruction of computed

tomography examinations seems to be very useful (Fig. 3). However, even procedures not leading to normalisation of pressure in the pulmonary artery but rather, characterised by reduction of pulmonary vascular resistance comprising about 50%, in a significant way improves patients' quality of life [38] and provides for survival at the level of 94% over a two-year observation — comparable with PEA procedures [32]. The impact of the choice of procedural technique and treatment goals for long-term follow-up requires further studies.

Balloon pulmonary angioplasty also seems to be a valuable therapeutic option when pulmonary hypertension persists after a PEA procedure. BPA procedures can be performed as elective in the long-run after PEA [39, 40], in the form of a one-time hybrid [41] procedure, but also as a rescue procedure in the event that no possibility exists to disconnect haemodynamic support in the early post-operative period [42]; however, the latter is related to the highest mortality. Supplementing invasive methods of CTEPH treatment — PEA and BPA — is pharmacotherapy with the use of drugs for pulmonary arterial hypertension [43]. Such a procedure does not affect the part of the pulmonary vascular bed that is permanently closed by clotting material, but instead maximally dilates and protects vessels free from clots against secondary damage. An issue that remains open is answering the question as to whether application of a pharmacological treatment should precede performance of BPA procedures. Currently, the majority of patients subjected to BPA are administered targeted pulmonary arterial hypertension therapy [44]. In a recent meta-analysis comparing, in an indirect manner, both methods showed that BPA has a greater impact on reduction of pulmonary arterial pressure and pulmonary vascular resistance, but the studies regarding BPA are of lower quality [45]. The ongoing trail, abbreviated to Riociguat Versus Balloon Pulmonary Angioplasty in Non-Operable Chronic Thrombo-Embolic Pulmonary Hypertension (RACE, NCT02634203) in a direct manner compares the effectiveness and safety of BPA and pharmacological treatment with riociguat — its initial results are expected in 2018. The current ESC/ERS Guidelines give BPA the class of recommendation IIb and level of evidence C in order to treat patients disqualified from surgical procedures or with persistent pulmonary hypertension after PEA [18]. Taking into account the numerous scientific evidence that has been shown since the publication of the Guidelines in 2015, one should expect that the recommendation class for BPA will, in the next edition of guidelines, be higher.

CONTROVERSIES RELATED TO APPLICATION OF VENOUS FILTERS

Implantation of a filter in an inferior vena cava, usually below the level of renal veins (Fig. 4), protects a patient against embolism with material coming from veins of the lower extremities and the pelvis, which constitutes the source of PE in most cases. A filter does not lead to resolution of clots in veins of lower extremities or the pulmonary artery in any way. The current ESC Guidelines recommend application of venous filters in patients with aPE in situations where no possibility exists to administer anticoagulant therapy because of absolute contraindications, a necessity to discontinue anticoagulation in the case of complications or a recurrence of PE despite adequate anticoagulation [4]. The classification of recommendation for implantation of a filter in the above indications is class IIB/level of evidence B and the reason for a relatively low grade of recommendations is the results of PREPIC-1 and PREPIC-2 studies. In the PREPIC-1 study, 400 patients with proximal venous thrombosis with or without aPE were randomised for implantation of a filter with continuation of anticoagulant therapy or to a group of anticoagulant therapy without a filter. In an acute period of disease (up to the 12th day), implantation of a filter reduces the risk of PE from 4.8% to 1.1% (OR 0.22; 95% CI 0.05–0.90) without impacting on reduction of mortality [46]. In an eight-year observation, symptomatic PE occurred in 6.2% of the patients with an implanted filter and 15.1% of the patients without a filter ($p = 0.008$). Venous thrombosis occurred in 35.7% and 27.5% of the patients, respectively ($p = 0.042$). No differences in mortality between either of the groups of patients were observed [47]. A total of 399 patients with aPE and accompanying venous thrombosis were subject to the PREPIC-2 study with application of randomisation in an analogous way as in the PREPIC-1 study. After three and six months, no significant differences in mortality and frequency of occurrence of symptomatic PE were found [48]. The PREPIC study differs in the type of filter used — in the PREPIC-1 study, permanent filters were applied and they could not be removed. This was related to higher incidence of deep vein thrombosis of the lower extremities in a remote period of time after implantation. Even in the case of application of anticoagulant therapy, frequency of occurrence of clots within a filter is 30%, of which the majority are asymptomatic [49]. Clinical interpretation of such findings is unclear because it is difficult to state whether a clot was formed locally because of thrombosis in the structures of a filter or if the clot in pulmonary circulation was caught by a filter. Regardless of which interpretation is true, sedimentation of clots within the filter is responsible for increased incidence of venous stasis and venous thrombosis within lower extremities in a remote period after implantation. In the PREPIC-2 study, retrievable filters were used, which can remain in the vessel as a permanent filter but can also be endovascularly removed in a situation when contraindications for anticoagulant therapy cease (Fig. 5). Currently, such filters are standard in an everyday clinical practice. In the PREPIC-2 study, 153 out of 164 (93%) implanted filters which qualified to be removed were removed. The data from the real world show that the procedure of implantation of a filter is overused, particularly in primary prevention of venous thromboembolism in trauma patients. Furthermore, the

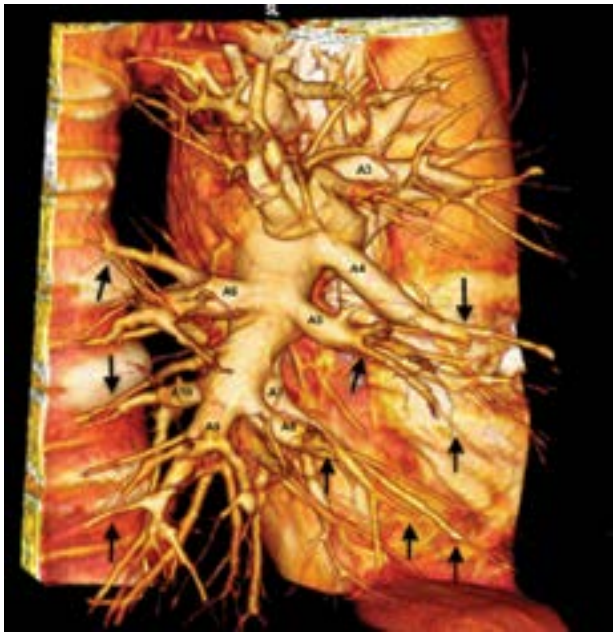

Figure 3. Three-dimensional volume rendering of contrast--enhanced computed tomography of the chest — anatomy of right pulmonary artery. Arrows indicate post-embolic lesions located at the sub-segmental level — patient underwent effective balloon pulmonary angioplasty

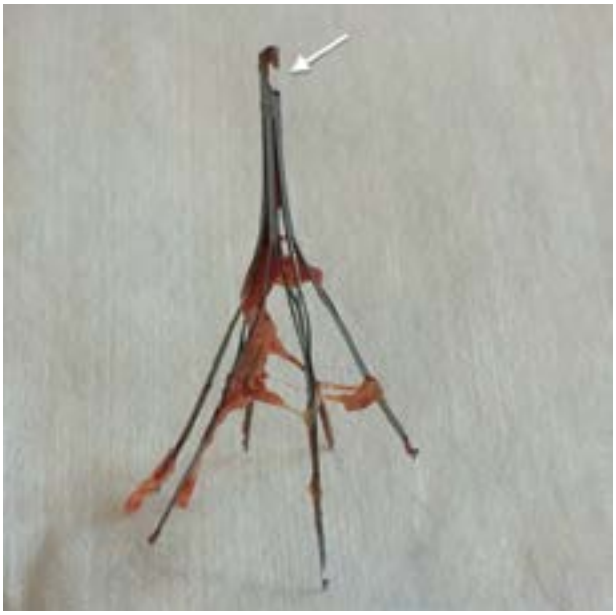

Figure 5. Filter removed after successful orthopaedic treatment of 33-year-old male with complicated pelvis fracture and acute pulmonary embolism occurred just before the bone surgery. The remnants of thrombi captured by filter are visible at the filter's struts. Arrow indicates hook at the top of the filter designed for percutaneous removal with vascular snare

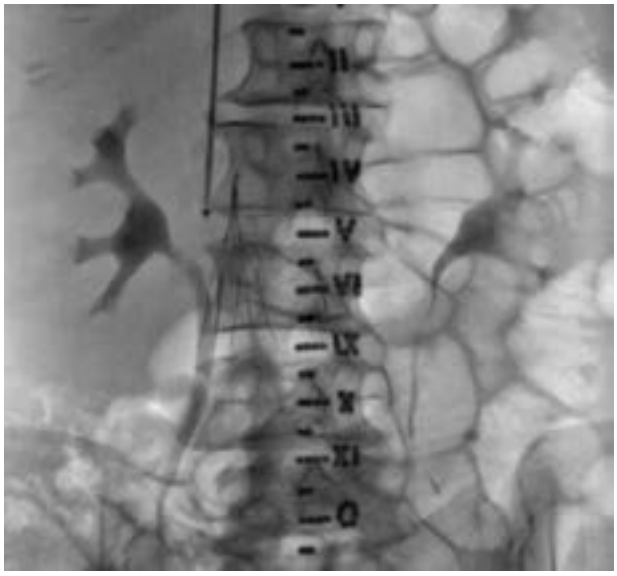

Figure 4. Venous filter (Option Elite, Argon Medical) implanted in inferior vena cava in 52-year-old cancer patient with recurrent pulmonary embolism despite adequate anticoagulation. Filter implanted from jugular approach, correctly expanded, and positioned below level of renal veins

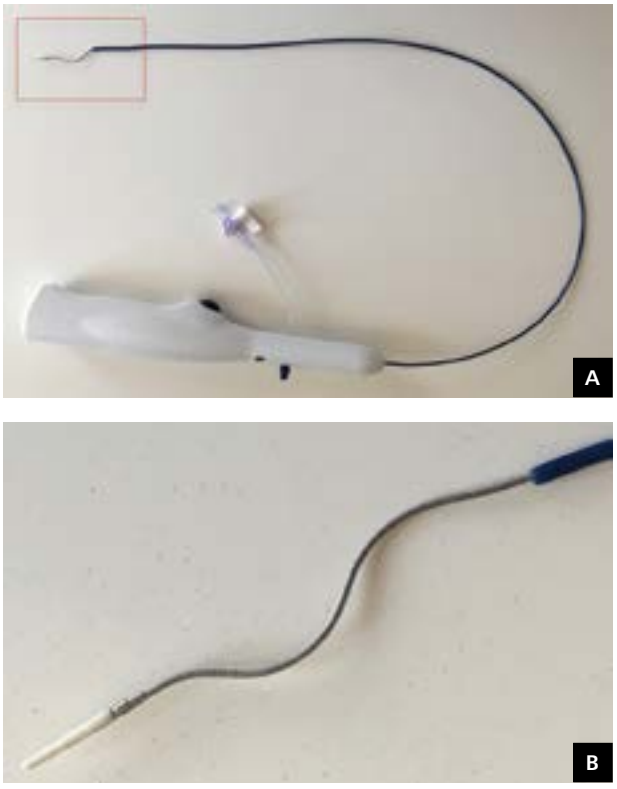

Figure 6. **A**. Cleaner XT — the 6 F rotational thrombectomy system (Argon Medical). Red rectangle (**B**, zoom) shows moveable wire element for mechanical de-clotting

percentage of removed filters is significantly lower than was observed in the PREPIC-2 study and usually does not exceed 40% [50]. Implantation of filters for patients with aPE, who

must be subject to an urgent operation — for example, for oncologic or orthopaedic indications — require special considerations in order to provide anti-embolic protection in the perioperative period when anticoagulants must be stopped. In such situations, a decision needs to be taken individually, retrievable filters should be applied, and the device removed immediately when contraindications to continue anticoagulation therapy cease to exist.

OPERATION SCHEME OF THE CENTRE FOR MANAGEMENT OF PULMONARY EMBOLISM

This year in the Central Clinical Hospital of the Medical University of Warsaw, the Centre for Management of Pulmonary Embolism (CELZAT) was established. The Centre will be responsible for coordination of treatment of patients with aPE with haemodynamic instability, hospitalised in a multi-profile academic hospital. A key element for the operation of CELZAT is an initial clinical assessment and risk stratification of aPE patient made by an attending physician. A subsequent step is to activate a tele-medical module for consultation after prior diagnosis of aPE of a high or intermediate-high risk of death. In the composition of an interdisciplinary team of physicians, apart from an attending physician, there are also specialists in interventional cardiology, interventional and clinical radiology, cardiac intensive care, anaesthesiology, and cardiac surgery. Depending on the clinical condition of a patient and co-morbid diseases, council can be expanded with persons having other specialisations — for example: a neurologist, a haematologist, a respiratory physician, a general surgeon, or a vascular surgeon. An analysis of particular cases takes place with the use of the web based platform for tele-consultations, which enables analysis of clinical data and results of additional examinations in real time. During tele-consultations, decisions are taken, e.g. regarding the possibility to optimise pharmacological treatment and indications for mechanical ventilation or extracorporeal membrane oxygenation. At this stage, indications for invasive diagnostics with pulmonary angiography and a possible catheter-assisted treatment with the use of a Cleaner device (Argon Medical) (Fig. 6) or AngioJet (Boston Scientific) are considered.

In cases where aPE with shock or significant haemodynamic disorders is confirmed, patients with contraindications for thrombolytic treatment or after ineffective thrombolytic treatment are qualified for cardiac surgery. In the case of high perioperative risk or no possibility to perform an urgent surgery, techniques of interventional treatment are preferred (Fig. 7).

SUMMARY

Looking ahead at interventional techniques for treating PE it seems that BPA in CTEPH will be of greatest significance. One can expect that in subsequent years the group of patients with CTEPH referred to PEA will be limited to patients with a low or moderate operation risk and thrombi located in proximal pulmonary arteries that have a volume large enough so that their removal is only possible during surgical procedure. The remaining patients will be treated more and more with BPA supplemented with modern pharmacotherapy.

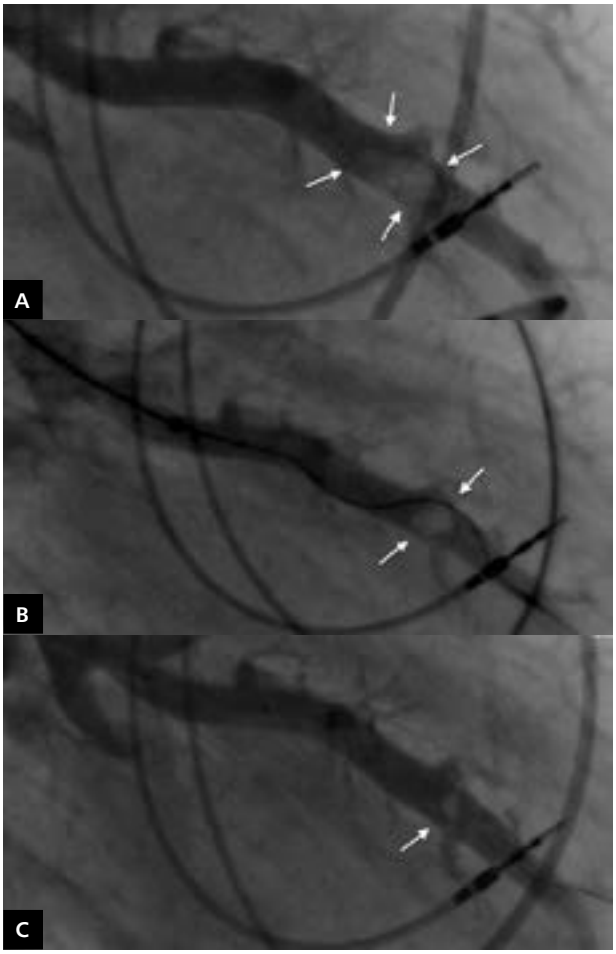

Figure 7. Percutaneous pulmonary embolectomy in acute pulmonary embolism with Cleaner XT device. Floating thrombus (arrows) in segmental artery of middle lobe (**A**), working element passed through thrombus (arrows) (**B**), and residual lesion after successful intervention (arrow) (**C**)

The large volume of clots in pulmonary arteries, which leads to aPE with haemodynamic disorders will probably remain the prime limitation of development of interventional techniques in the treatment of aPE. Because of the relatively small percentage of patients with aPE, who cannot be effectively treated pharmacologically, clinical trials assessing new interventional techniques in a reliable way will face additional difficulties. In the context of no reliable data allowing for comparison of effectiveness of particular methods for treating aPE, interdisciplinary PERTs will have greater significance because they make individual therapeutic decisions. Among these decisions, there will be indications for implantation of venous

filters, which, although they do not contribute to removing or dissolving clots, effectively protect against potentially fatal pulmonary embolism.

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