A CASE OF PULMONARY ENDARTERECTOMY IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION – A HAPPILY COMPLETED ODYSSEY

E. Dimitrova, D. Kyuchukov, M. Peneva, B. Kunev
National Heart Hospital – Sofia

Abstract. Chronic thromboembolic pulmonary hypertension is a rare condition that is usually a consequence of prior acute pulmonary embolism. It is caused by persistent obstruction of pulmonary arteries by organized thrombi resulting in redistribution of blood flow and secondary pulmonary microvascular remodelling. Thus, pulmonary vascular resistance and pulmonary artery pressure are increased leading to right ventricle pressure overload, development of right heart failure and death. In eligible patients pulmonary endarterectomy is the standard of care and it can result in complete normalization of haemodynamics and right ventricular morphology and function. We present the case of a patient with chronic thromboembolic pulmonary hypertension with severe right ventricular dilation and dysfunction and refractory heart failure. After successful pulmonary endarterectomy we observed almost complete normalization of hemodynamics and restoration of right ventricular dimensions and function, as well as significant clinical improvement.

Key words: chronic thromboembolic pulmonary hypertension, pulmonary (thrombo)endarterectomy, balloon pulmonary angioplasty, drug therapy

Address for correspondence: Assoc. Prof. Elena Dimitrova, PhD, National Heart Hospital, Clinic of cardiology, Konyovitsa 65 Str, Bg – Sofia 1309, e-mail: elena.sv@gmail.com

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ВЪВЕДЕНИЕ
Хроничната тромбоемболична пулмонална/белодробна хипертония (ХТБХ, СТЕРН) е рядко заболяване, което се причинява на персистираща обструкция на белодробните артерии от организирани тромби, които води до преразпределение на кръвотока и вторично ремоделране на белодробното макро- и микроаскапарно русло [1]. Теши процеси водят до увеличаване на белодробното съпротивление (БСС) и налягането в белодробната артерия (БА) с развитие на деснокамерна недостатъчност и смърт. Въпреки че точната патогенеза на заболяването не е напълно изяснена, ХТБХ се разглежда като късно следствие от преживян белодробен тромбоемболизъм (БТЕ), дължащо се на комбинация от дефектна анигиогенеза, нарушена фибринолиза и ендотелна дисфункция [2]. ХТБХ представлява единствената потенциално лечима форма на белодробна хипертония (БХ), като при подходящи пациенти „златен стандарт” е оперативното лечение – пулмонална тромбендартеректомия (ПЕА), а при неподходящи за оперативно лечение или при персистираща/рецикурентна БХ след ПЕА влизат в съображение меди каментозна терапия и интервенционално лечение (балонна пулмонална ангиопластика, БПА).

КЛИНИЧЕН СЛУЧАЙ
Представяме мъж на 63 години с преживян през 4 години масивен белодробен тромбоемболизъм, лекуван консервативно. Впоследствие са установени прогресиращи прояви на десностранна сърдечна недостатъчност (СН) на фона на хронична антикоагулантна терапия с ривароксабан 15 mg. В допълнение пациентът е с анамнеза за хронично бъбречно заболяване при хистологично диагностицирана мембранозна нефропатия II-III стадий с нефротичен синдром и проведено имуносупресивно лечение в миналото, рентген на гърдите показва левостранна нефропатия. Незадължително към анамнезата се прибавят хистологични данни от хистологичен сечение на бъбреците, при които бяха уточнени орнаментацията и съдова обструкция на д narginите венозни и артериални вени. В допълнение пациентът далеч не е използвал антикоагуланти и застойни прояви не са наблюдавани през дълъг период.

Приемането на пациентът се извършва със значително обременено тегло на ВСС с критични симптоми, включително хипотония (95/50 mmHg), дълбока цианоза, ядрено-диспноично дишане и сатурация наоколо 90%. Електрокардиограмата демонстрира синусов ритъм с ясен право- и лево-аксиален блок, артериално налягане 90/60 mmHg с изразен отечен сърдечен индекс. Венозни доплерови снимки показват частична реканализация на венозните вени, по-често до венозните вени в областта на левия бъбрец.

ВЪЗМОЖНИ СЪЩЕСТВУВАЩИ МЕХАНИЗМИ НА РАЗВИТИЕ НА ХТБХ
ХТБХ е рядко заболяване, което се причинява на персистираща обструкция на белодробните артерии от организирани тромби, които води до преразпределение на кръвотока и вторично ремоделране на белодробното макро- и микроаскапарно русло [1]. Теши процеси водят до увеличаване на белодробното съпротивление (БСС) и налягането в белодробната артерия (БА) с развитието на деснокамерна недостатъчност и смърт. Въпреки че точната патогенеза на заболяването не е напълно изяснена, ХТБХ се разглежда като късно следствие от преживян белодробен тромбоемболизъм (БТЕ), дължащо се на комбинация от дефектна анигиогенеза, нарушена фибринолиза и ендотелна дисфункция [2]. ХТБХ представлява единствената потенциално лечима форма на белодробна хипертония (БХ), като при подходящи пациенти „златен стандарт” е оперативното лечение – пулмонална тромбендартеректомия (ПЕА), а при неподходящи за оперативно лечение или при персистираща/рецикурентна БХ след ПЕА влизат в съображение медикаментозна терапия и интервенционално лечение (балонна пулмонална ангиопластика, БПА).

ИТВОЗДАНИЕ
Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare disease caused by persistent obstruction of pulmonary arteries by organized thrombi resulting in redistribution of blood flow and secondary pulmonary microvascular remodelling [1]. Thus, pulmonary vascular resistance (PVR) and pulmonary artery (PA) pressure are increased leading to right ventricle (RV) pressure overload and in the end stages development of right heart failure (HF) and death. Although the exact pathogenesis of the disease has not been fully elucidated, CTEPH is considered a late sequela of prior acute pulmonary embolism (PE) resulting from a combination of defective angiogenesis, impaired fibrinolysis and endothelial dysfunction [2]. CTEPH is the only potentially curable form of pulmonary hypertension (PH) and in eligible patients surgical treatment – pulmonary thromboendarterectomy (PEA), remains the standard of care. In patients who are not eligible for surgery or have persistent/recurrent PH after PEA drug therapy and interventional treatment (balloon pulmonary angioplasty, BPA) should be considered.

КЛИНИЧЕН СЛУЧАЙ
This is the case of a 63-year-old man with a history of medically treated massive pulmonary embolism 4 years ago on chronic anticoagulant treatment with rivaroxaban 15 mg with subsequent hospitalisations for progressive right-sided heart failure (HF). A few years before the event the patient was diagnosed with membranous nephropathy grade II-III complicated by nephrotic syndrome and administered immunosuppressive treatment. He also underwent radiation therapy for nasal tumour and had a COVID-19 interstitial pneumonia. He was admitted to the Cardiology department of National Heart Hospital due to severe cardiac decompenensation with signs of malperfusion and congestion (anasarca). Upon presentation he was mildly cyanotic, tachydyspnoic with oxygen saturation of 90% on room air, with blood pressure 90/60 mmHg, heart rate of 85/ min and generalised oedema. The ECG demonstrated sinus rhythm with right-axis deviation and right bundle branch block. The venous Doppler sonography of the lower limbs was significant for partial recanalisation of the left femoral and popliteal veins with characteristics of old phlebothrombosis. The echocardiographic exam-
tension (prevailing) and volume overload with severe systolic failure (RV basal diameter 64 mm, TAPSE/S' 6/4) and evidence of systemic pulmonary hypertension – systolic pressure in the pulmonary artery (SPAP) 100 mmHg (given RA pressure 20 mm Hg) based on massive tricuspid regurgitation jet, intact left heart, hemodynamically insignificant pericardial effusion (Figure 1) (https://10.3897/bgccardio.30.e120323.suppl.1, https://10.3897/bgccardio.30.e120323.suppl.2). In a period of two weeks the patient was treated with low-dose oxygen, two pleural drainage procedures, catecholamines infusion with dobutamine and dopamine, high-dose intravenous furosemide and empiric antibiotic therapy with ceftriaxone, as a result his condition improved, and clinical decongestion was achieved. In differential diagnostic aspect CTEPH was considered given the concomitant nephrotic syndrome as a prerequisite for hypercoagulable state. Later on, the patient was found positive for antiphospholipid syndrome (lupus anticoagulant and anticardiolipin antibodies) as well as a heterozygous for MTHFR mutation (homocysteine metabolism), which itself appeared a low-risk factor for thrombophilia. There were no features of systemic lupus erythematosus or any other more commonly observed autoimmune disease. The subsequent diagnostic algorithm consisted of CT (Figure 2) and right heart catheterization (RHC). The former confirmed the presence of bilateral lobar and right-sided segmental PE with 60% stenosis of the right pulmonary artery, total occlusion of the right middle lobar artery and its branches, bilateral occlusion of lower lobar arteries as well as the singular branch. The RHC showed precipapillary pulmonary hypertension with systolic/mean pressure in the PA 103/62 mm Hg, normal pulmonary capillary wedge pressure of 10 mm Hg, significantly elevated PVR 18.8 WU (1504 dyn·s·cm⁻⁵) and reduced cardiac index 2.1 l/min/m². Given the above evidence it was decided by the heart team that the patient was indicated for PEA as the “gold standard” approach. Two months later in an expert centre in Italy prof. Andrea Maria D’Armini and colleagues performed a successful bilateral PEA followed by an uncomplicated postoperative period – the surgical specimen is shown in Figure 3. A vena cava filter was inserted preoperatively through the right internal jugular vein considering the patient’s hypercoaguable state. The postoperative CT and RHC demonstrated remarkable results with full recanalization of the right pulmonary artery, bilateral lobar and segmental branches and remaining stenosis at the subsegmental level as well as a newly developed one in a branch of the left upper lobar artery. RHC parameters indicated almost
Случай на пулмонална ендартеректомия при хронична левостранен горнолобарен клон. Хемодинамичните показатели от ДСК отчетоха почти пълно нормализиране на хемодинамиката със средно налягане в белодробната артерия 25 mm Hg (спад 60%) и БСС 2,5 WU (200 dyn·s·cm⁻²) (спад > 85%) при повишен сърдечен индекс до 5,1 l/min/m². Ехокардиография на първия месец се установи обратно развитие на ДК обременяване с редукция в базалния размер до 46 mm, спад в систолното налягането в белодробната артерия до 50 mm Hg при подобена ДК систолна функция (TAPSE /S’ 12/8.7) (фиг. 4) (https://10.3897/bgcadio.30.e120323. suppl.3, https://10.3897/bgcadio.30.e120323. suppl.4). Клинично пациентът е със сатурация на атмосферен въздух 95%, подобрен функционален капацитет (изходен 6-минутен тест с ходене 90 метра спрямо 160 метра при изписването) и с компенсирана СН на фон на ниска доза фуроземид 20 mg. Предвид антифосфолипидния синдром подлежи на доживотна терапия с витамин K-антагонист (VKA).

Fig. 1. Echocardiography before PEA (parasternal long-axis view and apical 4 chamber view) – marked right ventricular and right atrial dilation

Fig. 2. CT-scan before PEA – presence of proximal thromboembolic obstructions, severe RV dilation and bilateral pleural effusions

complete normalization of hemodynamics – mean PA pressure 25 mmHg (60% reduction) and PVR 2.5 WU (200 dyn·s·cm⁻²) (> 85% reduction) and increased cardiac index of 5.1 l/min/m². The echo exam after the first month demonstrated reversal of the RV strain pattern with RV size reduction (46 mm), reduced SPAP 50 mmHg and enhanced RV systolic function (TAPSE /S’ 12/8.7) (Figure 4) (https://10.3897/bgcadio.30.e120323.suppl.3, https://10.3897/bgcadio.30.e120323.suppl.4). The patient’s overall status was also improved with oxygen saturation of 95% on room air, increased functional capacity (6-minute walk distance 90 m compared to 160 m after surgery) and no evidence of right-sided HF on a low dose furosemide 20 mg. Considering the antiphospholipid syndrome the patient was prescribed life-long anticoagulation with vitamin K antagonist (VKA).
В патогенезата на ХТБХ като водеща се разглежда „емболичната хипотеза“. Приема се, че след настъпил венозен tromboемболизъм по все още не напълно изяснени причини настъпва не-пълна резолюция и организация на тромба, водеща до съдова оклузия и облитерация. Именно тази фибротична трансформация на тромба, който, от една страна, предизвиква фиксирована механична обструкция на белодробни артерии, а от друга, води до увеличаване на кръвотока към незасегнатите части на белодробното съдово русло, стои в основата на еволюцията на заболяването. Заедно с колатералното кръвоснабдяване от системната циркулация, увеличените кръвоток и shear-стрес в незасегнатите участъци допринасят за микро-

**Обсъждане**

Regarding the pathogenesis of CTEPH the “embolic hypothesis” is the most widely held. It suggests that after an episode of acute venous thromboembolism there is incomplete resolution and organization of thrombus leading to vascular occlusion and obliteration due to mechanisms which have not been fully elucidated. The hallmark of CTEPH is fibrotic transformation of arterial thrombus causing fixed mechanical obstruction of pulmonary arteries and leading to overflow of the open pulmonary arterial bed. Together with collateral supply from systemic arteries, the increased blood flow and shear stress in the unaffected areas lead to microvascular remodelling causing a
васкулярно ремоделиране с прогресирано покачване на БСС. Микроваскулярното ремоделиране включва вазоспазъм, гладкомускулна пролиферация, ендотелна дисфункция и пролиферация, in-situ тромбоаза – процеси, които водят до прогресия на заболяването и са подобни на тези при белодробна артериална хипертония [4, 5].

По данни от регистри заболяваемостта и честотата на ХТБХ са съответно 2-6 случая/млн. и 26-38 случая/млн. население [3]. След преживяване симптоматичен остър БТЕ докладваната честота на ХТБХ, потвърдена с дясна сърдечна катетеризация, е 0,4-6,2% [2]. Много състояния представляват рискови фактори за ХТБХ – наличие на антикардиолипинови антитела, повишени нива на фактор VIIIa, възпалителни чревни заболявания, миелопролиферативни заболявания (есенциална тромбоцитемия, полицитемия вера), злокачествени заболявания, спленектомия, хипотиреоидизъм на високи дози хормон-заместителна терапия, перманентни вътресъдови устройства като кардиостимулятори, централни венозни пътища, вентрикуло-атриални шънтове [3]. От голямо практическо значение е въпросът за рутинното скриниране на пациентите с преживян БТЕ. Според актуалните препоръки на ESC при пациенти с доказан остър БТЕ се препоръчва проследяване след 3-6 месеца антикоагулация за оценка на наличието и тежестта на диспнея или ограничения физически капацитет. При липса на симптоми и/или рискови фактори за ХТБХ не се препоръчват допълнителни изследвания, а вторична профилактика и нова оценка при евентуална поява на симптоми. При наличие на диспнея или ограничен физически капацитет като следваща стъпка се препоръчва проведение на транстеракална ехокардиография. При установяване на БХ или повишен ехокардиографска вероятност за БХ трябва да се обмислят допълнителни образни изследвания [1].

Според новата хемодинамична дефиниция, залягала в актуализираните препоръки на European Society of Cardiology (ESC) от 2022 г., за БХ се приема наличие на средно налягане в БА над 20 mm Hg. ХТБХ принадлежи към група 4 от клиничната класификация на БХ – БХ, дължаща се на белодробна артериална обструкция. В процеса на постъпяване на диагнозата трябва да бъдат отхвърлени по-честите причини за повишаване на налягането в БА (левостранно сърдечно заболяване и полимопния, съответно група 2 и 3 БХ), белодробна артериална хипертония (група 1), както и някои по-редки заболявания, водещи до белодробна артериална обструкция, като злокачествени и незлокачествени тумори, артериит, вродени или придобити пулмонални стенози, парезити и емболизация на чужди тела [3]. Тази широка диференциална диагноза се progressive increase in PVR. Microvascular remodeling includes vasospasm, smooth muscle cell proliferation, endothelial dysfunction and proliferation, in-situ thrombosis – processes resulting in disease progression and resembling the ones involved in pulmonary arterial hypertension [4, 5].

In registries the reported incidence and prevalence of CTEPH are 2-6 cases per million and 26-38 cases per million respectively [3]. After prior symptomatic acute PE, the reported prevalence of CTEPH, confirmed by right heart catheterization, is 0,4-6,2% [2]. Medical conditions that are associated with an increased risk of CTEPH include presence of anti-cardiolipin antibodies, increased levels of factor VIIIa, inflammatory bowel disease, myeloproliferative disorders (essential thrombocythemia, polycythemia vera), cancer, splenectomy, hypothyroidism with high-dose replacement therapy, permanent intravascular devices such as pacemakers, central venous lines and ventriculo-atrial shunts [3]. The issue of routine screening of patients with prior acute PE is of great practical importance. According to the recent ESC guidelines patients with confirmed acute PE should be evaluated after 3-6 months of anticoagulation for presence and severity of dyspnoea and functional limitation. In the absence of symptoms and/or risk factors for CTEPH no further diagnostic evaluation is recommended but rather secondary prophylaxis and new evaluation in case of symptom recurrence. In patients with persisting dyspnoea and poor physical performance trans-thoracic echocardiography is recommended as the next step. In case of confirmed PH or high echocardiographic probability of PH further imaging should be considered [1].

According to the updated haemodynamic definition supported by the current ESC guidelines from 2022 PH is defined as mean pulmonary artery pressure above 20 mm Hg. CTEPH belongs to group 4 according to the clinical classification of PH – PH due to pulmonary artery obstruction. In the diagnostic process some more frequent causes for increased pulmonary artery pressure should be excluded (left heart disease or lung disease, group 2 or 3 respectively), pulmonary arterial hypertension (group 1), as well as some rare conditions leading to pulmonary artery obstruction such as malignant and non-malignant tumours, arteritis, congenital or acquired pulmonary arterial stenoses, parasites and foreign body embolism [3]. This broad differential diagnosis is re-
nal, requiring due to the substantial differences in pathogenesis and treatment of CTEPH as compared to other types of PH.

The symptoms of CTEPH are non-specific, related to progressive right ventricular dysfunction and in the early stages they are induced by exercise [3]. That is why early diagnosis remains a challenge and even in expert centres the median time from symptom onset to diagnosis is 14 months [6]. When present, the clinical symptoms of CTEPH may resemble those of acute PE or of pulmonary arterial hypertension [1]. The main symptom is progressive dyspnoea on exertion. Other symptoms include fatigue, palpitations, haemoptysis, fluid retention, syncope [3]. Rare symptoms caused by pulmonary artery dilation include exertional chest pain due to dynamic compression of the left main coronary artery, dysphonia due to compression of the left laryngeal recurrent nerve (cardiovocal or Ortner’s syndrome), shortness of breath, cough, lower inspiratory tract infections and atelectasis due to compression of bronchi. Clinical signs of CTEPH include cyanosis, accentuated pulmonary component of the second heart sound, right ventricular third heart sound, systolic murmur of tricuspid regurgitation and diastolic murmur of pulmonary regurgitation. With disease progression signs of overt RV forward and backward failure appear [3]. It is important to keep in mind that regarding symptoms of CTEPH there are two possible clinical scenarios, and a history of prior symptomatic PE is not mandatory. Patients usually present with progressive dyspnoea, fatigue and signs of right HF months or years after an acute PE. Some patients however have no documented history of PE and their clinical presentation is the same as in other types of PH, which may additionally delay the diagnosis.

To ensure accurate diagnosis in patients with CTEPH, a standardized evaluation, including various imaging, laboratory, and functional tests, is recommended. These tests are grouped in two main directions - preliminary screening and subsequent anatomical clarification with proof of operability. Routine tests such as chest X-ray and electrocardiogram may show abnormalities suggestive of the diagnosis, but generally, they have a low sensitivity and specificity. Blood gas analysis and pulmonary function tests may be normal or have some abnormalities, but they are more useful for
CT is a standalone instrument that has high sensitivity and specificity in the diagnosis process, as it enables indirect measurement of RV pressure and demonstrates the presence of PH at rest. The typical echocardiographic features of CTEPH are not specific and include the classic signs of right ventricular strain – RV hypertrophy and dilation, severe tricuspid regurgitation, and a leftward shift of the interventricular septum. A pericardial effusion may be seen, and in many instances, high right atrial pressures may reopen a previously closed foramen ovale [7]. Left ventricular contractility, as well as valvular function may also be assessed. The ventilation-perfusion lung scan is the essential screening test for CTEPH. This method has high sensitivity and specificity, and a normal lung scan excludes the diagnosis [8-10]. RHC is mandatory for establishing the diagnosis PH and must include measurement of right-sided pressures, PVR, cardiac output, and pulmonary capillary wedge pressure. Simultaneously a conventional pulmonary angiography can be performed to image the branches of the pulmonary artery. Left heart catheterization and selective coronary angiography are indicated if the patient is more than 40 years old or in the presence of risk factors to rule out concomitant coronary artery disease. These invasive evaluation tests also provide evidence of valvular heart disease and indicate whether concomitant surgery at the time of pulmonary endarterectomy will be required. In high-volume centres the rate of complications related to RHC is very low – 1,1% adverse events and 0,55% procedure-related mortality [3]. Conventional pulmonary angiography and multislice CT scan with contrast enhancement remain the “gold standard” for imaging of the pulmonary arteries and choice of treatment method. Pulmonary angiography shows CTEPH - specific changes – organized thrombi forming bands and webs, intimal thickening, fully occluded vessels as well as pruning of distal pulmonary arteries [11-12]. The typical CT-findings in CTEPH are thromboembolic masses attached to the vessel wall, bands, enlarged central pulmonary arteries, variations in the distribution and dimensions of peripheral vessels, heterogeneous lung perfusion (mosaic perfusion) as well as parenchymal scars from prior pulmonary infarctions. CT has high sensitivity and specificity.
Desobliteratio on the basis of an in vivo diagnostic assessment.
Аторностеноз (PEA) was developed by Pat O. Daily in San Diego, California and has been only slightly modified over the next years [20]. PEA is performed via a median sternotomy with the use of extracorporeal circulation in deep hypothermia and periods of circulatory arrest. A classification proposed by Jamieson according to the anatomical localization of the obstructive thromboembolic changes and their percentage distribution is presented in Table 1 [19].

Performing surgical PEA is associated with a few typical complications that can be superimposed on the complications occurring in any open-heart surgery (arrhythmias, atelectasis, wound infection, pneumonia, mediastinal bleeding, postoperative delirium, etc). One such complication is persistent PH. If the operation was performed correctly, this failure is due to type IV disease that was not sufficiently well evaluated preoperatively. This is also the most common cause of death after PEA. Correct diagnosis, followed by successful PEA, leads to an almost immediate reduction of PVR and normalization of hemodynamics along with an increase in cardiac output. A study by Iversen et al. investigated the reduction of PVR and reported a more than 80% reduction to the sixth postoperative month (from a mean of 1045 to 194 dyn.s.cm⁻⁵) [21]. The decrease of RV afterload can be confirmed by echocardiography through regression of RV hypertrophy, normalization of RV dimensions, and reduction of tricuspid regurgitation [22]. The final result of PEA can be assessed a minimum of 6-12 months after surgery. The reported survival at long-term follow-up is > 75% in the sixth

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<th>Level</th>
<th>Description</th>
<th>Percentage</th>
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<td>0</td>
<td>No evidence of thromboembolic stenosis and vascular wall lesions</td>
<td></td>
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<tr>
<td>I</td>
<td>Obstructive material in the main pulmonary arteries</td>
<td>15%</td>
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<tr>
<td>II</td>
<td>The disease starts at the lobar branches</td>
<td>55%</td>
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<tr>
<td>III</td>
<td>The disease starts at the segmental branches</td>
<td>30%</td>
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<td>IV</td>
<td>The disease starts at the subsegmental branches</td>
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Drug therapy is mandatory in all patients with CTEPH regardless of the chosen approach (surgical, interventional or conservative). All patients must receive lifelong therapeutic anticoagulation with increasing use of direct oral anticoagulants (DOAC) in clinical practice despite the lack of data from randomized trials. In patients with antiphospholipid syndrome (about 10% of CTEPH patients) anticoagulation with vitamin K antagonists (VKA) is recommended. That is why screening for antiphospholipid syndrome should be performed at CTEPH diagnosis [3]. Although PEA remains the current “gold standard” for CTEPH treatment registry data show that up to 40% of patients are inoperable due to inaccessible lesions, out-of-proportion PH and severe comorbidity [28]. In these cases, and in patients with persistent/recurrent PH after PEA specific PH therapy should be considered. It is used to manage the microvascular component which is present together with the thromboembolic obstructions. However, no data exist on the effect of treatment in patients with contraindications for surgery or those refusing PEA. Riociguat is the only drug with class I recommendation for patients with inoperable CTEPH or persistent/recurrent PH after PEA based on the results from CHEST trials [3]. Riociguat is an oral stimulator of soluble guanylate cyclase (sGC) and affects one of the main pathways in PH pathogenesis – NO-sGC-cGMP, eventually leading to increased production of cGMP, which results in vasodilation and antiproliferation. In CHEST-1 riociguat after 16 weeks of therapy increased 6-minute walk distance with 46 meters and reduced pulmonary vascular resistance by 31% versus placebo [29].
The open-label extension (CHEST-2) confirmed the long-term efficacy and safety of riociguat [30]. Treprostinil, a prostacyclin analogue, as a subcutaneous infusion has been studied in a phase 3 randomized controlled trial in patients with inoperable CTEPH or persistent/recurrent PH after PEA – significant improvement in 6-minute walk distance at week 24 was achieved in patients receiving a high dose compared to a low dose [31]. Other medical therapies approved for group 1 PH (phosphodies- terase 5 inhibitors and endothelin-receptor antagonists) have been used off-label as their efficacy in inoperable CTEPH has not been proven by randomized controlled trials and registry data [3].

Interventional treatment for CTEPH consists of balloon dilation of pulmonary artery segments. A staged procedure with a limited number of dilated segments per session is preferred. The number of sessions and the results depend on experience. BPA has become an established therapeutic option for inoperable or persistent/recurrent PH after PEA reducing significantly PVR (by 49-66%) and improving RV function and exercise capacity [32-35]. Long-term outcomes are promising but evidence is still scarce [36]. It must be kept in mind that BPA is associated with serious procedural and post-procedural complications such as vascular injury due to wire perforation, lung injury with haemoptysis and/or hypoxia, as well as complications related to vascular access and contrast administration [2, 3]. Therefore, this procedure should be performed in high-volume CTEPH centres [3].

Most patients in everyday practice require multimodal approach with PEA, BPA and medical therapy according to current guidelines for the management of CTEPH because of presence of mixed anatomical lesions in a single patient – proximal and distal lesions combined with microvascular involvement [3]. The CTEPH treatment algorithm is provided in Figure 5 [2].

Additionally, an inferior vena cava filter was inserted preoperatively in the presented case. Its aim is to prevent embolization of venous thrombi in the pulmonary arteries. In patients with CTEPH such a filter is usually inserted preoperatively or if not done earlier, may be inserted early after surgery. This routine however has not been formally studied and has been abandoned at some of the leading surgical centres [2].
Представеният клиничен случай показва основните стъпки в диагностично-терапевтичния процес при пациенти с ХТБХ, както и непосредствения резултат от проведеното успешно хирурлично лечение.


