Early experience with pulmonary endarterectomy in Bulgaria—case series

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Background: Pulmonary arterial hypertension (PAH) is a condition that limits the quality of life and life expectancy. The predicted mortality at 1 year is estimated at 30–40% without treatment. Of the types of PAH, chronic thromboembolic pulmonary hypertension (CTEPH) is most amenable to treatment and guidelines recommend pulmonary endarterectomy (PEA) surgery for 'operable' patients (where disease is found in the proximal pulmonary vessels). Traditionally these patients were referred to a European centre with the complexities of international travel, pre- and post-operative care, and funding. We sought to establish a national PEA programme to serve the Bulgarian population and avoid some of the problems of international healthcare.

Case Description: A total of 11 patients underwent PEA in 2 cardiac centres in Bulgaria (Acibadem Hospital and Government Hospital Lozenetz Sofia). The age of patients ranged from 22 to 80. The preoperative pulmonary vascular resistance (PVR) ranged from 309 to 1,906 dynes/sec/cm^{-5}. For the surviving patients the average PVR reduction was 615 dynes/sec/cm^{-5} at 6 months, the average intensive care unit (ICU) stay 6.7 days, and hospitalisation 15.2 days. Nine out of 11 patients survived to hospital discharge and 6 months follow, all with normalised PVR and exercise tolerance.

Conclusions: We present our results of initial experience with PEA in Bulgaria with encouraging results. Our work shows that inter-European relationship for healthcare can be productive and offer safe treatment on local level.

Keywords: Case series; pulmonary arterial hypertension (PAH); pulmonary endarterectomy (PEA)

Submitted Sep 02, 2022. Accepted for publication Jan 08, 2023. Published online Mar 07, 2023.
doi: 10.21037/atm-22-4370
View this article at: https://dx.doi.org/10.21037/atm-22-4370

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Introduction

Background

Pulmonary arterial hypertension (PAH) is a condition that limits the quality of life and life expectancy. Following diagnosis in symptomatic (breathless) patients, the predicted mortality at 1 year is estimated at 30–40% without treatment (1). Depending on the aetiology, the treatment strategies vary in invasiveness and success rate. Of the types of PAH, chronic thromboembolic pulmonary hypertension (CTEPH) is most amenable to treatment and guidelines recommend pulmonary endarterectomy (PEA) surgery for 'operable' patients (where disease is found in the proximal pulmonary vessels) (2). It is a better alternative to balloon pulmonary angioplasty in terms of long-term survival. PEA involves cardiopulmonary bypass (CPB) with deep hypothermic circulatory arrest to allow endarterectomy of the main, lobar, segmental and subsegmental branches of the diseased pulmonary arteries. PEA offers excellent outcomes with hospital mortality below 4.7% and 3-year survival of 89% (3).

Rationale and knowledge gap

PEA is a highly complex surgical intervention with a multitude of potential morbidity and risks. Many of the serious complications suffered by these patients in the peri-operative period are unique to PEA and cannot be managed by conventional means. Persistent postoperative PAH is the worst prognostic indicator for perioperative mortality (2), airway haemorrhage is an infrequent but potentially fatal complication, and reperfusion lung injury can cause profound hypoxaemia. Despite these risks, the overall 5-year survival is still favourable at 76%, and 90% for those who survived to hospital discharge (4).

Organisation of PEA services is a complex process involving diagnosis of patients, identification of surgical candidates, pre-operative management, intra and immediate post-operative management, and appropriate follow up. Training a team of medical professionals with adequate expertise is challenging as the number of patients is relatively small and the risks are high. Traditionally patients identified as surgical candidates for PEA were referred to a European centre with the complexities of international travel, pre- and post-operative care, and funding.

Objective

The incidence of CTEPH is estimated at 2.3% of pulmonary embolism survivors (5). With an incidence of venous thromboembolism is 100 in 100,000 in the general population (6), it is estimated that there could be approximately 150 CTEPH sufferers at any one time in Bulgaria (population of 6,520,314 according to the national census of 2021). We sought to establish a national PEA programme to serve Bulgarian population and avoid some of the problems of international healthcare. We present the following cases in accordance with the AME Case Series reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4370/rc).

Highlight box

Key findings

- Pulmonary endarterectomy is a curative treatment for chronic thromboembolic pulmonary hypertension. However, this is an operation of high complexity with high morbidity and mortality. Therefore, training and supervision for new centers is important.

What is known and what is new?

- High volume pulmonary endarterectomy centers offer better results in terms of mortality.
- Appropriate training and on-site supervision for new international centers can offer safe surgery with adequate results.

What is the implication, and what should change now?

- Report here about implications and actions needed.

Case description

This is a prospective multicentre case series where consecutive cases were recorded and analysed. A team of physicians, surgeons, anaesthetists, and perfusionists were trained in a high-volume centre at Royal Papworth Hospital in the UK. The surgeon, perfusionist, and referring physicians visited the UK centre for training. In addition, the lead surgeon underwent formal training as a visiting fellow. The anaesthetist from Royal Papworth Hospital travelled to Bulgaria for all operations.

All patients who presented with symptoms of CTEPH and were referred for surgical treatment had their imaging and investigations discussed with the UK centre. Patients with distal disease or malignancy involving other organs were excluded from the recruitment. Both the surgery and conduct of perfusion were initially directly supervised on site by the UK centre. As experience grew the supervision was transferred to indirect. Surgery was performed using

strict adherence to Royal Papworth Hospital Protocol in tertiary centres in Sofia, Bulgaria.

The haemodynamic perioperative data and surgical outcomes, as well as 6-month follow-up data were prospectively collected. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Waiver of consent was granted by the Ethics Committee of the Lozenetz University Hospital, Sofia, Bulgaria.

A total of 11 consecutive patients undergoing PEA surgery in Sofia, Bulgaria between 2017 and 2020. Surgery was performed in 2 cardiac centres consecutively, first 3 cases were in Acibadem Hospital and the rest in Government Hospital Lozenetz Sofia. The age of patients ranged from 22 to 80. The preoperative pulmonary vascular resistance (PVR) ranged from 309 to 1,906. The results from PEA are presented and summarised in *Table 1*.

All patients had surgically resectable disease affecting main pulmonary vasculature and specimens were histologically analysed post-operatively (*Figure 1*). Although the initial plan was to avoid patients with malignancy, the clinical deterioration of two patients who had tumour in the pulmonary vessels (1 myxoma and 1 vascular sarcoma) warranted surgery in the local centre as opposed to transfer to a larger centre. The patient with myxoma was complicated by recurrent seedlings of thromboembolism and organisation. The other patient had vascular sarcoma which was complicated by thromboembolism and organisation of the thrombus. The rest of the patients had organised thromboembolic disease only.

Most of the patients have an uneventful postoperative course. One patient suffered immediate re-perfusion injury and needed support with central veno-arterial extracorporeal membrane oxygenation (C-VA ECMO) for 36 hours. This was subsequently converted to veno-venous extracorporeal membrane oxygenation (VV ECMO) for additional 5 days, and successfully explanted. There were 2 deaths in the immediate postoperative period: The first patient recovered well and was extubated in good cardiorespiratory status on postoperative day 1. He had developed immediate renal failure which did not require treatment, and was in negative fluid balance. However, on postoperative day 2, he developed respiratory failure. The PEA team was not informed. The intensive care unit (ICU) team attempted but failed re-intubation which resulted in cardiac arrest. The second patient had pre-operative diagnosis of a tumour invading pulmonary artery bifurcation and the main branches. He had symptoms of right ventricular and liver failure. The surgery was deemed of higher risk (7) and was expedited with a satisfactory surgical result. However, the patient developed multi-organ failure and died on post-operative day 7.

All surviving patients were followed up at 6 months and haemodynamic parameters were recorded on follow up. There was no loss to follow up. The average PVR reduction was 615 dynes/sec/cm^{-5} at 6 months, the average ICU stay 6.7 days, and hospitalisation 15.2 days.

Functional status improved in all patients, and some returned to work. Patient 3 improved initially and resumed physical exercise, including cycling. However, she was also diagnosed with vasculitis 3 years later and exercise tolerance worsened again. Repeat computer tomography pulmonary angiography (CTPA) did not show recurrence of thromboembolism.

Discussion

We present the results of initial experience with PEA in Bulgaria with encouraging results. Outcomes such as haemodynamics, length of hospital stay and residual pulmonary hypertension are comparable to reported data (8). We acknowledge that CTEPH is a rare condition and not always suitable for surgical treatment. The international experience demonstrates that large volume centres offer better results in terms of mortality and morbidity (8,9) as well as improved functional status. However, the practicalities of funding and referral of these patients to large centres are complex.

CTEPH in countries where there is no existing system for referrals and treatment can progress to extremes of pathophysiology, and render patients in a very high surgical risk category. In Bulgaria, this treatment had not been offered before. Detailed pre-operative discussion of each individual case with an experienced team is important. On site proctoring is complex in arranging time and location of surgery, but is crucial for the start of a new programme. Nevertheless, it is cost-efficient and offers options for further development of local expertise. Our work shows that inter-European relationship for healthcare can be productive and offer safe treatment at a local level.

A second observation from our limited case series was that patients in countries with limited recognition and referral network can encounter patients at extremes of pathophysiology. For some of these patients ECMO support is needed.

Table 1 Perioperative data of pulmonary endarterectomy in Bulgaria

Patient No.	Age (years)	Gender	Date	WHO class	Preoperative sildenafil	Procedure	Pulmonary pressures (systolic/diastolic/mean) (mmHg)	PVR (dynes/sec/cm^{-5})	PVR post-PEA (dynes/sec/cm^{-5}	DHCA time (mins)	ICU stay (days)	Hospital stay (days)	Survived	6 months MPAP (mmHg)	6 months PVR (dynes/sec/cm^{-5})	MPAP reduction (mmHg)	PVR reduction (dynes/sec/cm^{-5})	Complications
1	22	Male	Sep-17	IV	Y	PEA	91/39/57	790	257	20+20	3	11	Y	22	242	35	548	N/A
2	40	Male	Sep-17	III	Y	PEA	131/62/89	1,093	172	20+20+8	7	15	Y	18	218	71	875	Status epilepticus
3	67	Female	Dec-17	III	Y	PEA + CABG	100/14/53	1,333	280	20+20+20	28	39	Y	25	270	28	1063	Reperfusion injury, ECMO
4	37	Male	Jul-18	II	Y	PEA + MVR	52/22/35	618	531	20+18	3	14	Y	23	188	12	430	N/A
5	55	Female	Jul-18	III	Y	PEA	79/31/48	659	345	20+20	4	12	Y	15	169	33	490	N/A
6	80	Male	Apr-19	III	N	PEA + MVR	55/20/35	720	200	22+17	5	14	Y	18	222	17	498	N/A
7	57	Male	Apr-19	III	N	PEA	42/21/27	309	328	19+17	3-non survivor	3	N	N/A	N/A	N/A	N/A	Respiratory failure, renal failure, failure to re-intubate in ICU on day 2
8	67	Male	Apr-19	II	N	PEA	52/23/34	455	326	20+15	3	10	Y	16	190	18	265	N/A
9	38	Female	Aug-19	II	N	PEA + RV myxoma excision	63/32/40	850	180	15+10	3	8	Y	15	176	25	674	N/A
10	36	Male	Aug-19	IV	Yes	Sarcoma excision	78/33/47	1,906	211	22+20	7-non survivor	7	N	N/A	N/A	N/A	N/A	Sarcoma, reperfusion injury, multiorgan failure
11	32	Female	Feb-20	III	N	PEA	102/27/53	914	142	18+18	4	14	Y	22	222	31	692	N/A

PVR, pulmonary vascular resistance; PEA, pulmonary endarterectomy; DHCA, deep hypothermic circulatory arrest; ICU, intensive care unit; MPAP, mean pulmonary artery pressure; Y, Yes, N, No; CABG, coronary artery bypass grafting; MVR, mitral valve replacement; RV, right ventricle; ECMO, extracorporeal membrane oxygenation; N/A, not applicable.

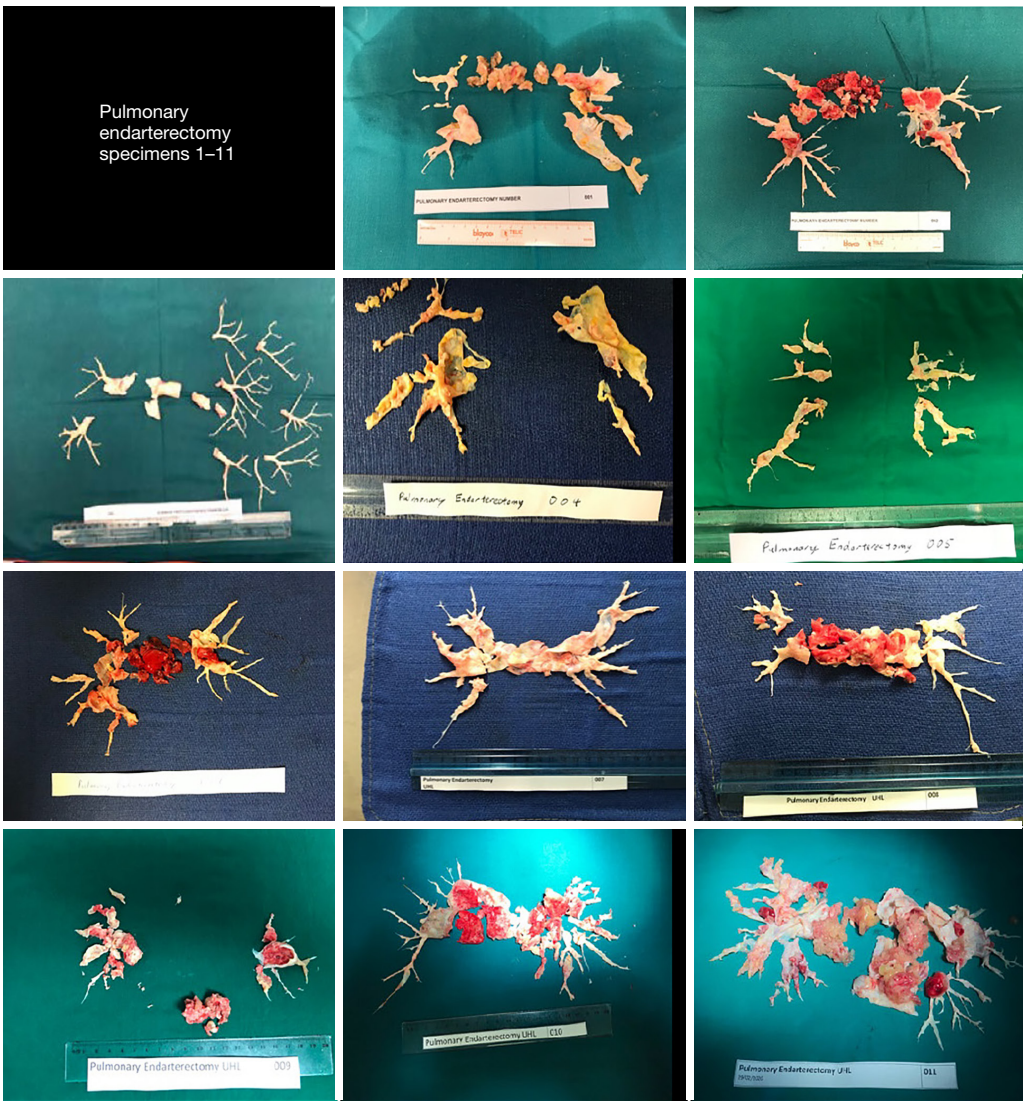

Figure 1 Pulmonary endarterectomy specimens.

Thirdly, one of non-survivors had very high PVR preoperatively and a presumed diagnosis of vascular sarcoma. He was quoted high mortality risk. The practicality of this patient being transferred to a large centre was complicated by rapidly worsening right ventricular and liver failure. Whether in the future such patients can be diagnosed early and transferred to a large centre with potentially better outcome is speculative.

Key findings

On site training and supervision for complex surgical treatment for CTEPH for new international centers can be challenging but lead to safe surgery with adequate results. This can avoid international medical transfers and offer excellent care to patients in their own country.

Strengths and limitations

The limitations of this work are many, but the main one is the small numbers. Secondly, our programme was negatively impacted by limitations of foreign travel imposed by COVID-19 restrictions in 2020. Finally, further collaboration for training of junior doctors can be

challenging with licensing rules in some countries.

Comparison with similar researches

We present 11 patients with CTEPH who underwent PEA and the average PVR reduction was 615 dynes/sec/cm^{-5} at 6 months, the average ICU stay 6.7 days, and hospitalisation 15.2 days. Nine out of 11 patients survived to hospital discharge and 6 months follow, all with normalised PVR and exercise tolerance. These results are comparable with large centres worldwide. However, our mortality was 18.18%, which is higher than the reported average.

Explanations of findings

The higher mortality in our case series is likely to be attributed to the inexperience of the team in caring for these highly complex patients at the start of a new program. Additionally, the number of cases is small.

Implications and actions needed

Further education and training of the local medical and surgical teams has already been done and will continue in the future.

Conclusions

In this case series, we have demonstrated that for complex and infrequent surgical cases, international collaboration for onsite teaching in a large volume centre followed by proctoring in another country can be a safe export of expertise with reasonable results. We are working towards improving the referral network and training with the aim to further develop the programme in Bulgaria.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the AME Case Series reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4370/rc

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4370/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4370/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Waiver of consent was granted by the Ethics Committee of the Lozenetz University Hospital, Sofia, Bulgaria.

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Cite this article as: Ignatov G, Ng CY, Tan Z, Velchev V, Kurkchieva T, Whitbread JC, Valchanov KP. Early experience with pulmonary endarterectomy in Bulgaria—case series. Ann Transl Med 2023;11(5):216. doi: 10.21037/atm-22-4370

