



Surgical treatment for chronic thromboembolic pulmonary hypertension: an historical perspective

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Chronic thrombotic occlusion of the pulmonary arteries that results in pulmonary hypertension is now recognized as being relatively common, and surgical treatment of the condition is being increasingly applied throughout the world. However, the condition was not described until 90 years ago, and just 60 years ago less than 200 cases of the syndrome had been reported. At that time the condition was thought to be inoperable. Surgery for the acute phase of pulmonary embolism was attempted beginning 100 years ago, with minimal success until cardiopulmonary bypass was developed and could be used to stabilize the patient during induction of anesthesia and the surgical removal of the embolus. Pulmonary endarterectomy was suggested as a possible surgical approach to the chronic condition in 1956, and the first planned pulmonary endarterectomy was performed in 1957. Over the next thirty years several operations were attempted in Europe and the United States. By 1989 it is likely that fewer than 250 cases of pulmonary endarterectomy had been attempted, with a mortality rate of greater than 20%. Some cases of pulmonary endarterectomy had been carried out successfully at the University of California, San Diego (UCSD), beginning in 1970. The technique of the operation was refined, and in 2003 the results of 1,500 of these operations performed at UCSD were described, with a mortality rate of less than 5%. The good results obtained in San Diego encouraged other groups internationally to start their own programs and the operation is now well established, with good results. The following discourse traces the development of surgery, first for acute pulmonary embolism, and also, growing out of that experience, an operation for chronic pulmonary embolism.

Keywords: History; pulmonary endarterectomy; pulmonary hypertension



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Introduction

The operation of pulmonary endarterectomy has evolved relatively recently but is now established as an effective way of restoring pulmonary blood flow after chronic pulmonary arterial occlusion.

First, recognition of the disease as a distinct entity was required. It was just sixty years ago that the syndrome was still regarded as reportable. Then, the early experience with acute pulmonary embolectomy helped establish some basic principles for the operation in its chronic phase.

This report traces the establishment of the disease and its recognition, and the development of the operative techniques to the current status.

Historical perspective

René-Théophile-Hyacinthe Laennec, a French physician who invented the stethoscope, was the first to describe the entity of pulmonary embolism in 1819 (1). He also linked the condition to deep venous thrombosis. Laennec later

died of tuberculosis at the age of forty-five.

Subsequently, the German physician Rudolf Virchow [1821–1902] in 1846 identified three broad categories of factors thought to contribute to thrombosis: hypercoagulability, stasis or turbulence, and endothelial injury or dysfunction (2). These factors were later called Virchow's triad.

Jean Cruveilhier was born in Limoges, France. In 1825 he succeeded Pierre Augustin Bécclard [1785–1825] as professor of anatomy. He performed extensive research involving the vascular system, being remembered for his studies of phlebitis, of which he believed to “dominate all of pathology”.

The German surgeon Friedrich Trendelenburg [1844–1924] was the first to describe an operative approach for acute pulmonary embolectomy in 1908 (3). This procedure was carried out on a patient who was dying, unconscious and without a pulse, and moribund to the point that no anesthesia was required to conduct the operation. Through a vertical incision to the left of the sternum and a horizontal extension over the second rib, he opened the pericardium and passed a rubber tape around the aorta and pulmonary artery. After compressing the tape, he incised the pulmonary artery, removed the clot, closed the pulmonary arteriotomy with a clamp, and removed compression from the vessels, all within 45 seconds. He then repaired the pulmonary arteriotomy. The patient survived the operation but died of heart failure fifteen hours later. A second patient described also had immediate survival but died of hemorrhage from the internal mammary artery thirty-seven hours after operation (4).

On 18 March 1924, Kirschner performed the first successful pulmonary artery embolectomy—Trendelenburg's operation. Complete functional recovery was reported (4) and Steenberg reported the first survivor of the “Trendelenburg operation” in the United States in 1958 (5). By that time there had been twelve reports of successful embolectomy in the European literature.

Denton Cooley in 1961 (6) and Sharp in 1962 (7) described the use of cardiopulmonary bypass to stabilize the patient during pulmonary embolectomy, with a substantial improvement in survival.

Although acute pulmonary embolism, and its origin from the legs or pelvis, had been well recognized by the 1920s, chronic occlusion of the pulmonary arteries was first described by Lungdahl in 1928 (8). He wrote of two women, one aged thirty-eight and one fifty-one, who had suffered chronic symptoms of shortness of breath, cyanosis,

and palpitations. Eventually both died of right heart failure and at autopsy chronic pulmonary arterial obstruction was found with marked dilatation of the proximal main pulmonary artery, and right ventricular hypertrophy.

Lungdahl also noted increased vascularity of the bronchial circulation and the fact that the lungs were free of infarction. It had been noted by Trendelenburg that almost uniquely, the lungs do not infarct after occlusive embolism, because of its dual blood supply: from the pulmonary artery and the bronchial arteries. Lungdahl pointed out that it was likely that the obstruction was due to pulmonary emboli. The concept at the time was that *cor pulmonale* was caused by primary thrombosis of the pulmonary artery, not pulmonary embolism.

Means and Mallory reviewed the cases of chronic thrombotic occlusion of the pulmonary arteries in 1931 but found only six cases in the literature (9), and a review in 1934 (10) found only twenty-four case reports. Hollister and Cull reviewed the literature for chronic pulmonary emboli and could find only 100 cases reported prior to 1941 (11). Notably one group of fourteen cases was derived from a single study of 706 autopsies (12). The other series of fourteen cases was derived from admissions to Northwestern University Hospital, a single 335-bed teaching hospital, over a ten-year period (13). It was clear from these two studies that thrombotic pulmonary occlusion was not being recognized as a cause of pulmonary hypertension. Hollister and Cull found a comparable number of cases reported from 1941 to 1955, and in 1956 stated “*it is probable that no more than 200 cases of the syndrome have been reported in the medical literature to date*” (11).

Thus prior to 1956, just sixty-five years ago, the entity of chronic thrombosis within the pulmonary arteries was still considered a reportable rarity. Even then there remained uncertainty as to whether this entity represented spontaneous thrombosis “*in situ*” (the etiology favored at the time) or embolization.

Houk *et al.* in a review in 1963 (14) found approximately 250 reported cases of chronic thromboembolic obstruction of the major pulmonary arteries. In only six of these was the diagnosis established before death, and in three surgical treatment was attempted. The prevalent opinion at the time was that chronic thrombotic occlusion was not amenable to surgical correction (11,15–17).

Surgery for the condition was first described in 1950, in a patient who underwent a left thoracotomy by the Chief of Surgery at Johns Hopkins Hospital, Dr. Alfred Blalock, in January 1948 (15).

The left pulmonary artery was found to be small, with proximal occlusion, though aspiration with a needle distally produced red blood. The artery was cut and divided and found to contain organized thrombi. No attempt was made to remove the obstruction, and the situation was thought to be inoperable. The patient was discharged from hospital without improvement.

In 1951 Boucher performed a pneumonectomy in a patient suspected of a pulmonary aneurysm. The pathology showed chronic thrombotic obstruction of the pulmonary arteries (18).

Endarterectomy was suggested as a possible surgical approach to this condition in 1956 (11), and the first planned pulmonary endarterectomy was performed in 1957 by Hurwitt and colleagues on a patient operated upon with inflow occlusion and systemic hypothermia (19). A transverse sternotomy was used. When inflow occlusion was carried out by temporarily occluding the inferior and superior vena cavae, the patient arrested and could not be resuscitated, although inflow occlusion was only used for two and a half minutes.

Philip Allison was the second Nuffield Professor of Surgery in Oxford, and was responsible for the development of the heart-lung machine in England. He also pioneered the use of heart valve homografts and pig xenograft valves, starting in 1957. Allison performed a right lower lobectomy in a fifty-nine-year-old man who was subsequently found to have chronic thrombotic occlusion of the lobe (20).

Using a right thoracotomy, he encountered dense adhesions, which were bloody, and subsequent experience has shown that these adhesions are common after chronic occlusion of the pulmonary arteries. The patient recovered but was admitted to hospital again three months later with left-sided chest pain and heart failure. He died, and at autopsy massive thromboembolic obstruction of the left main pulmonary artery was found, most of it chronic. In March 1958 Allison performed the first successful embolectomy for recurrent emboli—again with the technique of inflow occlusion (20).

The patient was cooled to 29 °C in a water-bath, and then the chest was opened through a trans-sternal approach. An embolectomy (not a true endarterectomy) was performed using suction and forceps. However, *“a mass of tough thrombus was removed from the right pulmonary artery. After this, suction was effective in drawing out many lengths of softer ‘tailed’ thrombus, the tails representing branches of the artery”*. The patient survived and was improved. This was probably the first successful thromboendarterectomy.

In July 1961 Snyder operated upon a seventy-one-year-old man initially suspected of having a tumor, at the San Diego Naval Hospital (21).

A right thoracotomy was made, through the fifth intercostal space. There were upper lobe adhesions. No tumor was found, but a thickened pulmonary artery encountered. No pulsations were palpable below the right upper lobe pulmonary artery, and a longitudinal incision was made in the pulmonary artery. A thrombotic mass was removed with endarterectomy spoons. An angiogram performed in August 1961 showed a patent pulmonary artery. Snyder concluded *“The findings in the present case unequivocally demonstrate that the pulmonary artery, after occlusion for a considerable number of years, continues to maintain a relatively normal relationship to the pulmonary veins at the capillary level, that the pulmonary alveolar membrane is not irreparably damaged by prolonged pulmonary artery occlusion, and that functional return of the affected lung may be expected after pulmonary endarterectomy”*. This reinforced Trendelenburg’s hypothesis that the lungs were protected by its dual blood supply.

In 1963 Houk and colleagues described a case operated upon through a bilateral anterior thoracotomy approach, in November 1961 (14). Though it was not used, cardiopulmonary bypass was available, and they referenced the success with cardiopulmonary bypass in acute embolectomy and suggested that perhaps cardiopulmonary bypass should be used electively for operation on chronic thrombotic occlusion. Ken Moser, a co-author, was a pulmonologist who later came to San Diego, where he was instrumental in the initiation of the program at the University of California (UCSD). Charles Hufnagel, the surgeon, invented the first artificial heart valve in the early 1950s. The progress of this patient was updated in reports in 1965 (22) and he was asymptomatic more than three years after the surgery.

A further successful case, of a forty-two-year-old man, was now also presented (23). The operation had been carried out through a median sternotomy incision on May 18, 1962. Cardiopulmonary bypass was on standby. A true thromboendarterectomy was again performed here, and a large thrombotic mass was freed by blunt dissection medially and sharp dissection distally. The patient was discharged on June 9th. Moser reemphasized that the same technical advances that had rendered emergency pulmonary embolectomy and open-heart surgery possible had now made pulmonary thromboendarterectomy feasible in selected patients with massive thromboembolic pulmonary

artery occlusion. He stated that *“our present consensus is that bypass should be available on a standby basis in all cases and is required if extensive bilateral obstruction is to be corrected. Perhaps bypass should be used in all cases to permit more detailed exploration of the pulmonary arterial tree, but the problems associated with bypass must be balanced against the advantages of its use in each case”*. In the early 1960's the status of cardiopulmonary bypass, of course, was far from what it is today. To Moser's knowledge the May 1962 patient, operated on at Georgetown University by Dr. Charles Hufnagel, was the first with this disorder in whom the diagnosis was made before operation and successful correction achieved.

Moser pointed out that the successful cases demonstrated that extensive well-organized thrombi, having obstructed major pulmonary vessels from months to years, could be removed successfully. Furthermore, the reclaimed lung areas were shown to be able to safely accept the sudden return of blood flow and to resume adequate respiratory function. He pointed out that there were three major reasons for considering thromboendarterectomy: hemodynamic, alveolo-respiratory, and prophylactic. The hemodynamic goal is to prevent or ameliorate right ventricular compromise due to pulmonary hypertension. The alveolo-respiratory objective is to improve respiratory function by removing a large ventilated but un-perfused physiologic dead space. The prophylactic goal is to prevent retrograde extension of the obstruction which might result in further cardiorespiratory deterioration or death.

In addition to the above two successful cases, Moser described two in whom surgical correction could not be achieved and the patients died in the post-operative period. The first of them was operated upon in April 1964. Hypotension developed during induction of anesthesia and was accentuated by temporary occlusion of the right main pulmonary artery. The procedure was abandoned. Hypotension persisted however, and the patient died two hours later. The other case was the same described in more detail by Jones *et al.* in 1965 (24).

This was a thirty-seven-year-old man with a previously fractured right arm and a separate injury to the right leg, who also had varicose veins. The operation was carried out on 1st April 1964. The chest was entered through a bilateral anterior thoracotomy with cardiopulmonary bypass standby, though bypass was not used. Dense vascular adhesions were found diffusely between the lungs, chest wall and pericardium throughout both hemi-thoraces. The right lung was freed by sharp dissection and the right main

pulmonary artery isolated. An incision was made in the right pulmonary artery and extended into the branches of the upper lobe. *“These vessels were entirely patent proximally; however, at the segmental and sub-segmental level they were relatively bloodless and were occluded by fibrous webs of material having a peculiar moth-eaten appearance. There was no identifiable lumen”*. Similar changes were found in the lower lobe, and it was concluded that *“there was no proximal block amenable to endarterectomy, and the more distal lesions were inoperable”*. Seven and a half liters of blood were required to replace that lost during dissection of the vascular adhesions on the right. The patient became hypotensive and died twenty-four hours later. Jones concluded *“it is patently clear that we were dealing with a patient with inoperable chronic obstructive disease of the pulmonary arteries”*.

Of course, subsequently it became clear that the condition could be operated upon, and the webs and the “moth-eaten appearance” represented bands and partial resolution of thrombus which resulted in fibrotic tissue. This would later be recognized as pathognomonic of chronic pulmonary emboli.

Dr. Scannell probably performed the first operation using cardiopulmonary bypass, in 1964 at the Massachusetts General Hospital (25). The patient was a thirty-nine-year-old physician with dyspnea and chest pain. At cardiac catheterization, his pulmonary artery pressures were found to be 100/30 with a mean of fifty-five. A bilateral anterior thoracotomy was performed. The patient arrested upon opening the chest, and he was placed on cardiopulmonary bypass. Though this was a case of chronic thrombotic occlusion, an embolectomy was performed with forceps and by squeezing the lung. Post-operatively the patient developed severe pulmonary edema with a *“high degree of residual pulmonary hypertension”* and died two hours after operation. Autopsy showed residual clot and fibrous bands, adherent to the intima, which *“couldn't merely be picked off”*.

Frater *et al.* in 1965 discussed the case of a twenty-three-year-old farm worker operated upon on September 4, 1963 (26). This patient presented with a pulmonary artery aneurysm originally thought to be mycotic. Subsequent angiography demonstrated pulmonary artery occlusion. A left anterolateral thoracotomy was made, with cardiopulmonary bypass standby, though again bypass was not used. The pulmonary artery pressures were unchanged postoperatively, and the patient was not benefited.

Nash and colleagues, in 1968, described a case (27) where a large thrombus was removed under cardiopulmonary bypass from the left pulmonary artery. Nash performed his

operation in June 1966. A left thoracotomy was performed at the level of the fourth rib. Using cardiopulmonary bypass, he developed a line of cleavage between the thrombus and the left pulmonary artery wall, and the entire thrombus was removed. This again was a true endarterectomy with a typical cast specimen. The patient recovered fully and went back to normal activity. A subsequent arteriogram was performed and showed a patent left main pulmonary artery.

By the end of the 1960's then, a true appreciation of this disorder was appearing. It had become clear that a formal endarterectomy needed to be done to remove all parts of the chronic thrombotic mass, and that for this to be done completely, it required bypass. A lateral thoracotomy was often associated with massive vascular adhesions and excessive blood loss.

Dr. Moser had moved from Georgetown to San Diego, and 1973 Drs. Moser and Nina Braunwald (the surgeon) presented the first case that was operated upon at the University of California, San Diego (UCSD) (28). This patient was a sixty-seven-year-old man who underwent surgery on July 14, 1970. Through a right lateral thoracotomy a pulmonary thromboendarterectomy was performed using cardiopulmonary bypass. The thrombus was removed with forceps and embolectomy spoons. In addition, gallstone forceps and also a balloon catheter was passed into both lungs and good back-bleeding obtained. The patient was discharged from hospital and returned to full activity.

Moser and Braunwald observed that the patient had a "two compartment pulmonary vascular bed". The first "compartment", the open pulmonary arteries, probably had advanced changes of pulmonary hypertension because of the increased pressure and flow to which they had been subjected. The closed vascular bed (the second "compartment") had never been subjected to high pressures and therefore retained its normal structure. In this patient the thromboembolism was known to have been established for ten years or more, and this was the first documentation of the ability to remove such material and to achieve long-term patency at operation. The pulmonary vascular resistance (PVR) fell from 1,208 to 640.

David Sabiston, who had trained under Blalock, and now was at Duke University, in 1977 (29) presented six new patients and published a very helpful summary paper. He found a total of twelve patients previously reported in the literature in whom pulmonary embolectomy was performed, which together with his patients of six brought the total to eighteen. In his six patients, five improved postoperatively.

In three of the patients' bypass was used, and in two a median sternotomy was performed.

Christian Cabrol, a French cardiac surgeon best known for performing Europe's first heart transplant at Pitié-Salpêtrière Hospital in 1968, reported on a series of sixteen patients operated upon in Paris in 1978 (30). In the first two operations, the main pulmonary artery was approached through a median sternotomy, using cardiopulmonary bypass. The other patients were operated upon with a lateral thoracotomy. In his series of sixteen patients there were six deaths, and ten were alive six months to ten years after operation. Three patients had an excellent result, six patients had good results and one of the ten survivors was only moderately improved.

In 1980, Daily (31) described a further four patients undergoing operation at UCSD, with three survivors. The four patients in his series underwent pulmonary thromboendarterectomy between February 1, 1975, and May 4, 1978, at UCSD. All procedures were performed through median sternotomy. The phrenic nerves were identified and retracted anteriorly. On the right side a pulmonary arteriotomy was performed in the right upper lobe and in the pulmonary artery distal to right upper lobe branch. The superior pulmonary vein was retracted inferiorly to improve exposure of the right upper lobe and intermediate pulmonary arteries. On the left a single arteriotomy was used. Circulatory arrest was used in three patients. Daily at this time reviewed the English literature and found a total of thirty-six patients that had been treated operatively. Median sternotomy had been used only five times.

Vincent Dor and colleagues reported on a further twelve patients in 1981 (32), and Joe Utley and Ken Moser updated the UCSD series in 1982 (33). Utley and Moser discussed a further ten patients who were operated on between July 1977 and June 1981 at UCSD. Five patients had complete obstruction of a pulmonary artery. Again, a median sternotomy was performed, and the heart-lung machine was used to cool the patients' temperature to 16 °C or less. The endarterectomy was performed with circulatory arrest. The importance of not dividing the azygos vein or mobilizing it because of its significance as a collateral venous channel in patients with inferior vena caval interruption was emphasized.

Only one of the ten patients died, and all survivors showed improvement in hemodynamic function. Utley pointed out the importance of fiber-optic headlights for improved vision, long dissecting instruments, and fine-

tipped long suction instruments. No neurological deficits were encountered from the circulatory arrest, though one patient had transient bilateral phrenic nerve dysfunction. Dr. Utley, in his closing statements, emphasized that *“the technique of circulatory arrest is absolutely essential for this distal thromboendarterectomy because the bronchial circulation is increased so greatly in these patients that one really cannot see distally in pulmonary circulation to locate the segmental vessels unless the circulation is totally arrested”*.

In 1984, Randolph Chitwood from Duke University reviewed the world's literature to date (34) and found a total of 85 cases managed surgically, with a mortality rate of 22%. By 1989 there had been occasional other case reports of the surgical treatment of chronic pulmonary thromboembolism (35-37), but it is likely that at that time less than 250 cases of pulmonary endarterectomy had been attempted in the world, with a mortality rate more than 20%.

Over the next decade most of the subsequent surgical experience in pulmonary thromboendarterectomy was reported from the UCSD medical center (38). One thousand five hundred cases were done in the twelve years between 1990 and 2002.

In this landmark paper (38) basic surgical principles were established. A median sternotomy must be used, hypothermic circulatory arrest must be established, and both sides (left and right pulmonary vasculature) must be addressed. Specialized surgical instruments had been developed and a classification system for the disease was established. It was emphasized that there was no degree of right ventricular failure that would rule out operation, and that regardless of the PVR all patients should be operated upon. The mortality rate in these 1,500 cases was less than 5%.

After the publishing of this paper and the results that could be achieved, widespread application of the operation was carried out internationally.

Conclusions

Adapting from the early experience, 5,000 cases have now been done at UCSD, the leading program for pulmonary thromboendarterectomy. The results obtained at this institution encouraged other centers to begin programs. There is now an international registry for the procedure, which is presently being done in many countries throughout the world. The entity remains under-diagnosed, but its increasing recognition has now saved thousands of lives and

returned many patients suffering from shortness of breath and right heart failure to normal lives.

From a reportable entity just sixty years ago, the condition of pulmonary hypertension due to chronic thromboembolic pulmonary hypertension is now widely recognized, and, building on the success at UCSD in the recognition and treatment of this disease with pulmonary endarterectomy, centers around the world have initiated successful programs in the recognition and cure of this condition.

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Footnote

Conflicts of Interest: Both authors have no conflicts of interest to declare.

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