It is often said that pulmonary hypertension due to thromboembolic disease is an uncommon condition. However, its incidence is probably much higher than is generally appreciated, although precise figures are unavailable. The incidence is probably higher because most cases of pulmonary embolism are asymptomatic and go undetected, and also most cases of pulmonary hypertension also go undetected until right heart failure causes more extensive investigation.

In 1975 it was estimated that there were 630,000 symptomatic episodes of acute massive pulmonary embolism in the United States each year, and though most cases of pulmonary embolism are asymptomatic, and though the United States population has increased by a third since that time, even this figure would make pulmonary embolism three times as common as cerebrovascular accidents and half as common as acute myocardial infarction.

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The finding of pulmonary emboli at autopsy is surprisingly common, and autopsy studies have also shown that the diagnosis of acute pulmonary embolism was unsuspected in 70–80% of those in whom it was the principal cause of death. Evidence of acute pulmonary emboli is seen in 5–30% of autopsies, and evidence of massive thrombosis of major pulmonary arteries is seen in about 1%. There is thus ample evidence that acute pulmonary embolism is common and often unsuspected, and sometimes gives rise to the chronic residua that lead to pulmonary hypertension.

Systematic studies of the physiological events in patients after massive pulmonary embolism have not been performed. Most survivors of acute embolic events usually resolve their emboli by lytic mechanisms without sequelae, but some do not. In a certain number of cases, the thrombus becomes organized, with a thickened, fibrous and occlusive remnant within the vessel lumen. This produces obstruction of pulmonary artery flow, and subsequent pulmonary hypertension. Secondary mechanisms also sometimes play a role: areas of the pulmonary vascular bed that are unaffected by occlusive thrombus develop secondary pulmonary hypertensive changes that are often not reversible. Whether this is a result of an “Eisenmenger-like” change, when open vessels are exposed to the increased pressure and flow that results from shunting from occluded or narrowed vessels, or whether changes occur in previously normal vessels as a result of secretion of factors such as endothelin, is as yet uncertain. However, the changes that occur are not operable, and may be permanent, and this has caused us increasingly to advocate early intervention when possible (now that the risk of the operation is so low), to avoid these changes.

The diagnosis of thromboembolic pulmonary hypertension in the living is difficult. Patients may often be asymptomatic until the advanced stages of the disease, when right heart failure makes the diagnosis more obvious. Most cannot give a history of deep venous thrombosis, or thromboembolic events. A majority of patients, once diagnosed correctly, describe having had the diagnosis delayed for several months or even years, and have seen several physicians before pulmonary hypertension was suspected.

The initial steps in the diagnosis hinge upon a suspicion of pulmonary hypertension. The clinical signs may be cryptic, with signs of right heart failure not emerging until the later stages of the disease. Indeed, many patients
have normal pulmonary artery pressures and clinical examination at rest, but experience severe pulmonary hypertension on exercise.

Adjunctive testing may not be helpful. The chest X-ray may be normal, though later signs of right heart enlargement, enlargement (or rarely calcification) of the pulmonary arteries, and perhaps paucity of vascularization of the lung fields should be sought. Echocardiography will demonstrate right atrial enlargement, septal hypertrophy, and tricuspid regurgitation. The calculation of the degree of pulmonary hypertension is made by measurement of the reverse gradient across the tricuspid valve.

Once the diagnosis of pulmonary hypertension is made, differentiation from other causes of pulmonary hypertension is aided by a perfusion lung scan. In most cases this will show patchy defects that coincide with the areas of pulmonary artery occlusion. Patients with primary pulmonary hypertension, on the other hand, tend to exhibit a mottled or “moth-eaten” appearance on lung scan. The lung scan, though helpful in indicating a probable diagnosis, can severely under-estimate the degree of vascular occlusion.

The definitive test is the pulmonary arteriogram, and it could be argued that this should be applied in every patient with pulmonary hypertension. The defining feature of chronic emboli on arteriogram is lack of perfusion to the periphery in areas fed by major segments of the pulmonary arteries. Isolated filling defects may also be seen in larger arteries. Characteristically, major thrombi recanalize and organize, and the resulting webs and bands can often be seen on angiogram. Long-standing occlusions may lead to post-stenotic dilatation and pouches.

It is often perceived that the performance of an arteriogram in the presence of pulmonary hypertension is dangerous, but this perception must be based on anecdotal experience. Several thousand such arteriograms have now been done at our center with no mortality, and no serious morbidity. An adequate amount of contrast should be power-injected, and good quality cut films obtained. Angiograms made with a small amount of contrast, or by digital subtraction, are generally not helpful, and certainly are not in equivocal cases. CT scans will not adequately demonstrate the segmental defects that are often a major part of this disease, and so, if the diagnosis is equivocal, we currently always advocate an angiogram.

The pulmonary hypertension that results after chronic occlusion of the vessels by thrombus is caused by a mechanical occlusion of the pulmonary arteries by fibrous thickening and, as expected, neither anticoagulants nor vasodilators are effective in treating the condition. The benefit of medical therapy is restricted to the treatment of right heart failure with diuretics and anticoagulation to prevent further embolization and the risk of further local thrombus. Survival with continued medical therapy is poor, and is proportional to the degree of hypertension. Patients with mean pulmonary artery pressures over 30 mmHg have a 30% 5-year survival rate; those with pressures over 50 mm a 10% survival at 5 years.

Once the diagnosis of pulmonary hypertension is established, together with the fact that this is the result of pulmonary emboli, selection for surgery is made on the basis of the degree of incapacity and the degree of pulmonary hypertension. As mentioned previously, our increasing awareness of the changes that can arise in the pulmonary vascular bed in areas unaffected by pulmonary emboli has resulted in a tendency to earlier operation. Patients over 45 undergo coronary angiography.

The options for surgical treatment are either transplantation or pulmonary endarterectomy. Transplantation, though still applied for this condition, is inappropriate. The results with transplantation must be analyzed to include the risk of death on the waiting list, the peri-operative risk, the expense and risk of immunosuppressive agents, and the possibility of infection or rejection for the remainder of the patient’s life. In good hands the one-year survival rate with transplantation for pulmonary hypertension is 80%, and there is a progressive decrement in survival each year thereafter.

Pulmonary endarterectomy is a surgical therapy that can be scheduled at the patient’s convenience, and is permanently curative. A handful of patients have required a second pulmonary endarterectomy (≤ 1%) – but in almost every case an avoidable reason was identified–incomplete primary operation, or failure to maintain postoperative anticoagulation and inferior vena caval filtration.

Though historically described as a pulmonary thromboendarterectomy, a better term for the operation that is performed is pulmonary artery endarterectomy or pulmonary endarterectomy (PEA). This is because thrombus is found in a minority of cases, and the operation hinges upon successful endarterectomy of the intimal, and part of the medial, layers of the pulmonary artery, to remove the fibrous component of the disease.

The condition, with rare exceptions, is bilateral, since embolic or thrombotic conditions usually affect both sides. In addition, for the patient to be symptomatic and
pulmonary hypertensive, both sides must be compromised. The surgical approach, to be curative, must therefore also be bilateral. A median sternotomy is therefore performed, in order to reach both sides. The use of cardiopulmonary bypass is essential, both to allow cardiorespiratory stability during occlusion of one pulmonary artery during endarterectomy, and because the use of circulatory arrest is fundamental to the operation.

After substantial occlusion of pulmonary arteries, the pulmonary parenchyma is kept viable by bronchial arterial flow, and a typical patient will exhibit greater bronchial flow than is normally encountered. Though there have been occasional reports of the operation being performed without circulatory arrest, the pulmonary vasculature cannot be completely cleared without this because bronchial flow obscures the operative field. Cardiopulmonary bypass allows a bilateral approach, cooling with hypothermic arrest and complete visibility of the distal pulmonary vasculature.

The essentials of the operation, therefore, include a median sternotomy, cardiopulmonary bypass, and the cooling of the body to 20 C, followed by circulatory arrest. The endarterectomy plane is found within the right pulmonary artery, and followed out to segmental and sub-segmental branches. It is very important to stay within the correct plane; a layer that is too superficial will not be effective, and a deep layer that causes perforation of the vessel is usually fatal. Usually the entire endarterectomy on one side can be performed within one 20-minute arrest period, after which the patient is re-perfused while the pulmonary arteriotomy is repaired. The procedure is then repeated on the left side. Because of the cooling and re-warming phases, cardiopulmonary bypass times are in the order of four to five hours.

Probably less than 5,000 of these operations have been done. The largest experience comes from the University of California Medical Center (UCSD), where the number of operations has now exceeded 2,400.

Risk analysis shows that post-operative pulmonary vascular resistance is the primary determinant for mortality. Although a high pre-operative pulmonary vascular resistance [PVR] (> 1,000 ) has been described as a major risk factor, in fact it is the post-operative PVR that is the determining factor: a post-operative PVR < 500 carries an operative risk of < 1%. If this value is > 500 the risk is 10%. Thus an important assessment of pre-operative risk is to match the assessed PVR with the degree of angiographic obstruction, though, even with discordance of this measurement, the patient may still be improved enough to enjoy normal life. It also emphasizes that the key to the operation is to remove all occluding material—survival depends on achieving a low PVR post-operatively.

The care of the patient post-operatively is similar to that for patients undergoing more routine heart surgery, with the exception that an early, aggressive diuresis is instituted, and the hematocrit is maintained above 30. A significant complication that may occur in these patients is the “reperfusion response”. In its true form this is a reperfusion edema that occurs in a small minority of patients. However, the term is applied to the radiological appearance in any patient who demonstrates an increasing radiological opacity on chest X-ray after operation, and in many cases the appearance may be due to other factors—such as infection. In any event, approximately 10% of patients exhibit this re-perfusion edema to a significant extent in the first few days, often limited to the areas that have been endarterectomized, and supportive treatment must be maintained until its resolution. This may require prolonged ventilation.

In the majority of patients the postoperative course is uneventful, and the median hospitalization is 9 days. A reduction in pulmonary pressures and resistance to normal levels and the corresponding improvement in pulmonary blood flow are generally both immediate and sustained. Echocardiography shows that right ventricular geometry rapidly reverts to normal, with the elimination of tricuspid regurgitation. More than 90 percent of operative survivors attain NYHA function class I or II status at two-year follow-up. The operative mortality in our last 500 patients is in the range of 3%.

Pulmonary endarterectomy is thus a curative operation for chronic, thromboembolic, pulmonary hypertension. This is a disease that is a commonly overlooked cause of shortness of breath and physical incapacity. Though the operation is technically demanding and requires experience, its application for the manifestation of thromboembolic pulmonary hypertension should be encouraged. The prognosis for affected patients without intervention is poor. Transplantation for the condition is not appropriate, and medical therapy is ineffective.

Many other centers have now started programs in the surgical treatment of thromboembolic disease, including some excellent centers in Japan. It is gratifying to see the wider application of this operation, which will save many lives and enrich the lives of many patients suffering from pulmonary hypertension.