Surgical Treatment of Chronic Thromboembolic Pulmonary Hypertension

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Pulmonary hypertension as the result of chronic pulmonary thromboembolic disease is a serious condition with poor long-term prognosis. The condition is one of the more common cardiovascular diseases affecting Americans, yet it is severely underdiagnosed. Pulmonary thromboendarterectomy is the definitive treatment for chronic pulmonary hypertension as the result of thromboembolic disease; however. it is an uncommon procedure, primarily because of lack of recognition on the part of the clinicians. Patients affected by chronic thromboembolic pulmonary hypertension (CTEPH) may present with a variety of debilitating cardiopulmonary symptoms. However, once diagnosed, there is no curative role for medical management, and surgery remains the only option. Palliation therapy with medical management in order to delay surgery carries the risk of prolonging the disease and irreversibly damaging unaffected pulmonary vasculature.

The prognosis for patients with pulmonary hypertension is poor, and it is worse for those who do not have intracardiac shunts. Thus, patients with primary pulmonary hypertension and those with pulmonary hypertension due to pulmonary emboli fall into a higher risk category than those with Eisenmenger syndrome and encounter a higher mortality rate. In fact, once the mean pulmonary pressure in patients with thromboembolic disease reaches 50 mmHg or more, the 3-year mortality rate approaches 90%.[1]

Clinical Presentation

There are no signs or symptoms specific for chronic thromboembolism. The most common symptom associated with thromboembolic pulmonary hypertension, as with all other causes of pulmonary hypertension, is exertional dyspnea. This dyspnea is out of proportion to any abnormalities found on clinical examination. Like complaints of easy fatigability, dyspnea that initially occurs only with exertion is often attributed to anxiety or being "out of shape." Syncope, or presyncope, is another common symptom in pulmonary hypertension. Generally, it occurs in patients with more advanced disease and higher pulmonary arterial pressures.

Nonspecific chest pains or tightness occur in approximately 50% of patients with more severe pulmonary hypertension. Hemoptysis can occur in all forms of pulmonary hypertension. Peripheral edema, early satiety, and epigastric or right upper quadrant fullness or discomfort may develop as the right heart fails. Some patients with chronic pulmonary thromboembolic disease present after a small acute pulmonary embolus that may produce acute symptoms of right heart failure. A careful history brings out symptoms of dyspnea on minimal exertion, easy fatigability, diminishing activities, and episodes of anginalike pain or light-headedness. Further examination reveals the signs of pulmonary hypertension.

The physical signs of pulmonary hypertension are the same no matter what the underlying pathophysiology. Initially the jugular venous pulse is characterized by a large A-wave. As the right heart fails, the V-wave becomes predominant. The right ventricle is usually palpable near the lower left sternal border, and pulmonary valve closure may be audible in the second intercostal space. Occasional patients with advanced disease are hypoxic and slightly cyanotic. Clubbing is an uncommon finding.

The second heart sound is often narrowly split and varies normally with respiration; P2 is accentuated. A sharp systolic ejection click may be heard over the pulmonary artery. As the right heart fails, a right atrial gallop usually is present, and tricuspid insufficiency develops. Because of the large pressure gradient across the tricuspid valve in pulmonary hypertension, the murmur is high pitched and may not exhibit respiratory variation. These findings are quite different from those usually observed in tricuspid valvular disease. A murmur of pulmonic regurgitation may also be detected.

Diagnosis

To ensure diagnosis in patients with chronic pulmonary thromboembolism, a standardized evaluation is recommended for all patients who present with unexplained pulmonary hypertension. This workup includes chest radiography, which may show either apparent vessel cutoffs of the lobar or segmental pulmonary arteries or regions or oligemia suggesting vascular occlusion.

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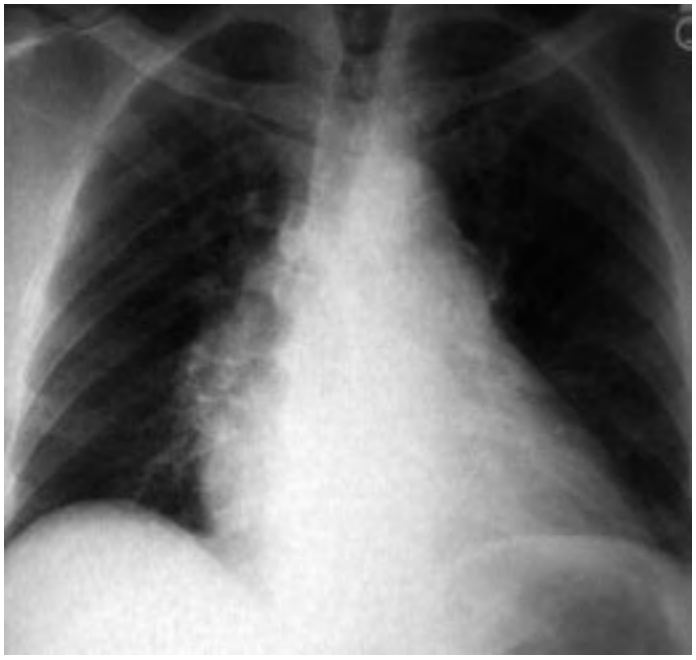

Figure 1. Chest radiograph of a patient with chronic thromboembolic pulmonary hypertension. Note the enlarged right atrium and right ventricle, and the hypoperfusion in several areas of the lung fields.

Central pulmonary arteries are enlarged, and the right ventricle may also be enlarged without enlargement of the left atrium or ventricle (**Figure 1**). However, one should keep in mind that despite these classic findings, a large number of patients might present with relatively normal findings on chest radiography, even in the setting of high degrees of pulmonary hypertension. The electrocardiogram demonstrates findings of right ventricular hypertrophy (right axis deviation, dominant R-wave in V1). Pulmonary function tests are necessary to exclude obstructive or restrictive intrinsic pulmonary parenchymal disease as the cause of pulmonary hypertension.

The ventilation-perfusion lung scan is the fundamental test for establishing the diagnosis of unresolved pulmonary thromboembolism. An entirely normal lung scan excludes the diagnosis of both acute and chronic unresolved thromboembolism. The usual lung scan pattern in most patients with pulmonary hypertension either is relatively normal or shows a diffuse nonuniform perfusion.[2-5] When subsegmental or larger perfusion defects are noted on the scan, even when matched with ventilatory defects, pulmonary angiography is appropriate to confirm or rule out thromboembolic disease.

Currently, pulmonary angiography still remains the gold standard for diagnosis of CTEPH. Organized thromboembolic lesions do not have the appearance of the intravascular filling defects seen with acute pulmonary emboli, and experience is essential for the proper interpretation of pulmonary angiograms in patients with unresolved, chronic embolic disease. Organized thrombi appear as unusual filling defects, webs, or bands, or completely thrombosed vessels that may resemble congenital absence of the vessel[5] **(Figure 2).** Organized material along a vascular wall of a recanalized vessel produces a scalloped or serrated luminal edge. Because of both vessel-wall thickening and dilatation of proximal vessels, the contrast-filled lumen may appear relatively normal in diameter. Distal vessels demonstrate the rapid tapering and pruning characteristic of pulmonary hypertension **(Figure 2).**

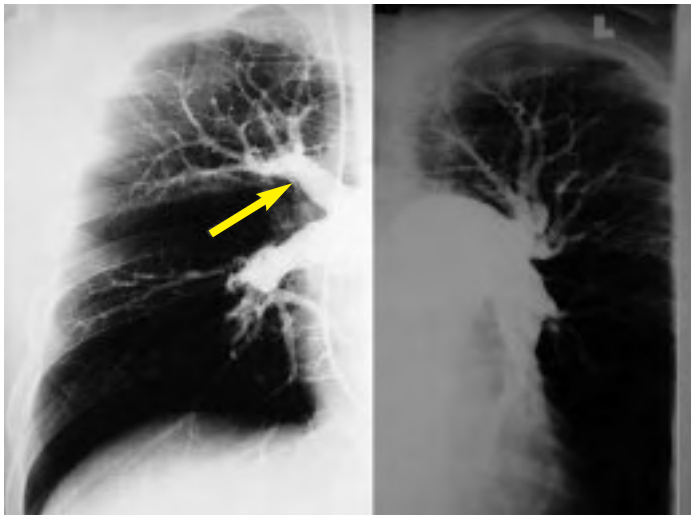

Figure 2. Right and left pulmonary angiograms demonstrate enlarged pulmonary arteries, poststenotic dilatation of vessels, lack of filling to the periphery in many areas, and abrupt cut-offs of branches. The yellow arrow points to intraluminal filling defects representative of a web or band.

In addition to pulmonary angiography, patients over 40 undergo coronary arteriography and other cardiac investigation as necessary. If significant disease is found, additional cardiac surgery is performed at the time of pulmonary thromboendarterectomy.

In approximately 15% of cases, the differential diagnosis between primary pulmonary hypertension and distal and small vessel pulmonary thromboembolic disease remains unclear and hard to establish. In these patients, pulmonary angioscopy is often helpful. The pulmonary angioscope is a fiberoptic telescope that is placed through a central line into the pulmonary artery. The presence of embolic disease, occlusion of vessels, or the presence of thrombotic material is diagnostic.

Medical Treatment

Chronic anticoagulation represents the mainstay of the medical regimen. Anticoagulation is primarily used to prevent future embolic episodes, but it also serves to limit the development of thrombus in regions of low flow within the pulmonary vasculature. Inferior vena caval filters are used routinely to prevent recurrent embolization. If caval filtration and anticoagulation fail to prevent recurrent emboli, immediate thrombolysis may be beneficial, but lytic agents are incapable of altering the chronic component of the disease.

Right ventricular failure is treated with diuretics and vasodilators, and although some improvement may result, the effect is generally transient because the failure is due to a mechanical obstruction and will not resolve until the obstruction is removed. Similarly, the prognosis is unaffected by medical therapy,[6,7] which should be regarded as only supportive. Because of the bronchial circulation, pulmonary embolization seldom results in tissue necrosis. Surgical endarterectomy therefore will allow distal pulmonary tissue

to be used once more in gas exchange.

In recent years there have been a few additions of pulmonary vasodilators to the medical armamentarium. These medications have shown to be quite effective in the treatment of idiopathic or primary pulmonary hypertension but there are no clear data supporting their use in patients with CTEPH. Obviously, one should not expect a change in the pulmonary resistance when the cause is obstruction from thromboembolic material. However, occasionally there may be a slight improvement in pulmonary vascular resistance of patients with CTEPH, who have developed chronic arteriopathy in vessels unaffected by clot. This temporary decline in hemodynamic measurements should in no way defer referral of such patient for surgical management. Unfortunately, we have now started to see a trend in delaying referral for patients with CTEPH, where the referring clinicians have resorted to the use of pulmonary vasodilators as temporizing measures. It is extremely important to recognize that no medical treatment will resolve the obstruction in the pulmonary vasculature and although there may be a transient improvement in pulmonary vascular resistance, the chronic arteriopathy will carry on and worsening resistance and severe right heart failure will follow. By the time the patient is finally referred for surgery, the operative risk is significantly increased and the overall benefit even after pulmonary endarterectomy is diminished. Although it is perfectly reasonable to temporarily manage patients using different pharmaceutical agents, this should not delay their referral for surgery that is curative

Pulmonary Thromboendarterectomy

Indications

When the diagnosis of thromboembolic pulmonary hypertension has been established, the decision for operation is made based on the severity of symptoms and the general condition of the patient. Early in the pulmonary endarterectomy experience, Moser and colleagues[8] 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 caused by pulmonary hypertension. The respiratory objective is to improve respiratory function by the removal of a large ventilated but unperfused physiologic dead space, regardless of the severity of pulmonary hypertension. The prophylactic goal is to prevent progressive right ventricular dysfunction or retrograde extension of the obstruction, which might result in further cardiorespiratory deterioration or death.[8] Our subsequent experience has added another prophylactic goal: the prevention of secondary arteriopathic changes in the remaining patent vessels.

Although most patients have a pulmonary vascular resistance level in the range of 800 to 1000 dynes/sec/cm^{-5} and pulmonary artery pressures less than systemic, the hypertrophy of the right ventricle that occurs over time makes pulmonary hypertension to suprasystemic levels quite possible. There is no upper limit of pulmonary vascular resistance level, pulmonary artery pressure, or degree of right ventricular dysfunction that excludes patients from an operation. We would offer surgical treatment to all patients who have evidence of thromboembolic material and have reasonable operative risk.

We have become increasingly aware of the changes that can occur in the remaining patent (unaffected by clot) pulmonary vascular bed subjected to the higher pressures and flow that result from obstruction in other areas. Therefore, with the increasing experience and safety of the operation, we are tending to offer surgery to symptomatic patients with mild to moderately elevated pulmonary vascular resistance, whenever the angiogram demonstrates thromboembolic disease. A rare patient might even have a pulmonary vascular resistance level that is normal at rest, although elevated with minimal exercise. This is usually a young patient with total unilateral pulmonary artery occlusion and unacceptable exertional dyspnea because of an elevation in dead space ventilation. Operation in this circumstance is performed not only to reperfuse lung tissue, but to reestablish a more normal ventilation perfusion relationship (thereby reducing minute ventilatory requirements during rest and exercise), and also to preserve the integrity of the contralateral circulation and prevent chronic arterial changes associated with long-term exposure to pulmonary hypertension.

Operation

Guiding Principles

There are several guiding principles for the operation. This is a bilateral disease in the vast majority of patients and, as such, surgical treatment and endarterectomy must be bilateral. The only reasonable approach to both pulmonary arteries is through a median sternotomy incision.

Cardiopulmonary bypass is essential to ensure cardiovascular stability when the operation is performed and to cool the patient to allow circulatory arrest. Excellent visibility is required, in a bloodless field. Because of the copious bronchial blood flow usually present in these cases, periods of circulatory arrest are necessary to ensure perfect visibility. It should be emphasized that although some endarterectomy is possible without circulatory arrest, a complete endarterectomy is not. The circulatory arrest periods are limited to 20 minutes, with restoration of flow between each arrest. With experience, the endarterectomy usually can be performed with a single period of circulatory arrest on each side.

It is essential to appreciate that the removal of visible thrombus is largely incidental to this operation. A true endarterectomy in the plane of the media must be accomplished. This plane of dissection should be then followed into all distal vessels.

Surgical Technique

A median sternotomy is performed in the standard fashion. Typically the right heart is enlarged, with a tense right atrium and a variable degree of tricuspid regurgitation. There is usually severe right ventricular hypertrophy, and with critical degrees of obstruction, the patient's condition may become unstable with the manipulation of the heart.

Full cardiopulmonary bypass is instituted with high ascending aortic cannulation and two caval cannulae. Once on bypass, surface cooling with both the head jacket and the cooling blanket is begun. The blood is cooled with the

pump-oxygenator. Cooling generally takes 45 minutes to an hour. During the cooling period, some preliminary dissection can be performed, with full mobilization of the right pulmonary artery from the ascending aorta. The superior vena cava is also fully mobilized. The approach to the right pulmonary artery is made medial, not lateral, to the superior vena cava.

When the patient's temperature reaches 20°C, the aorta is crossclamped and a single dose of cold cardioplegic solution (1 L) is administered. A modified cerebellar retractor is placed between the aorta and superior vena cava. Pulmonary arteriotomy is then performed. Any residual loose, thrombotic debris encountered is removed. Then, a microtome knife is used to develop the endarterectomy plane posteriorly, because any inadvertent egress in this site could be repaired readily, or simply left alone. Dissection in the correct plane is critical because if the plane is too deep the pulmonary artery may perforate, with fatal results, and if the dissection plane is not deep enough, inadequate amounts of the chronically thromboembolic material will be removed.

It is important that each subsegmental branch is followed and freed individually until it ends in a "tail," beyond which there is no further obstruction. Residual material should never be cut free; the entire specimen should "tail off' and come free spontaneously.

Once the right-sided endarterectomy is completed, circulation is restarted, and the arteriotomy is repaired. The surgeon then moves to the patient's right side. The pulmonary vent catheter is withdrawn, and an arteriotomy is made from the site of the pulmonary vent hole laterally to the pericardial reflection, avoiding entry into the left pleural space. The left-sided dissection is virtually analogous in all respects to that accomplished on the right. The duration of circulatory arrest intervals during the performance of the left-sided dissection is subject to the same restriction as the right.

After the completion of the endarterectomy, cardiopulmonary bypass is reinstituted and warming is commenced. The rewarming period generally takes approximately 90 to 120 minutes but varies according to the body mass of the patient.

The right atrium is then opened and examined. Any intra-atrial communication is closed. Although tricuspid valve regurgitation is invariable in these patients and is often severe, tricuspid valve repair is not performed. Right ventricular remodeling occurs within a few days, with the return of tricuspid competence. If other cardiac procedures are required, such as coronary artery or mitral or aortic valve surgery, these are conveniently performed during the systemic rewarming period. Myocardial cooling is discontinued once all cardiac procedures have been concluded.

When the patient has rewarmed, cardiopulmonary bypass is discontinued. Dopamine hydrochloride is routinely administered at renal doses, and other inotropic agents and vasodilators are titrated as necessary to sustain acceptable hemodynamics. The cardiac output is generally high, with a low systemic vascular resistance. Temporary atrial and ventricular epicardial pacing wires are placed.

Despite the duration of extracorporeal circulation, hemostasis is readily achieved, and the administration of platelets or coagulation factors is generally unnecessary. Wound closure is routine. A vigorous diuresis is usual for the next few hours, also a result of the previous systemic hypothermia.

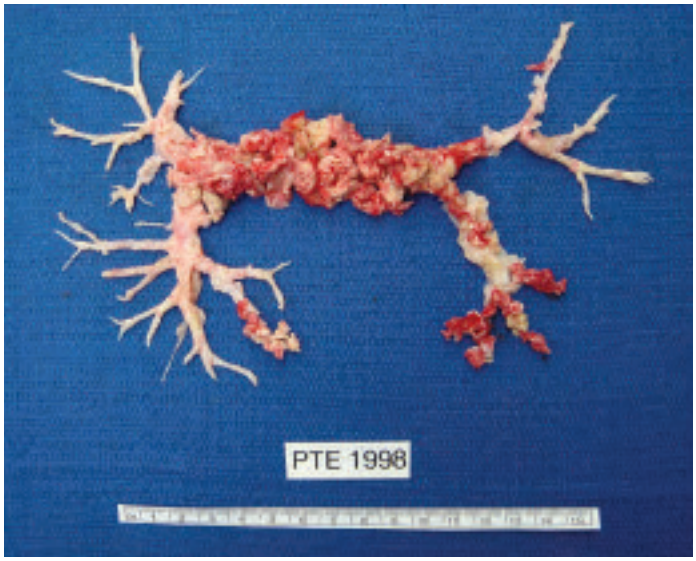

Figure 3. Surgical specimen removed from a patient showing evidence of some fresh and some old thrombus in the main and both right and left pulmonary arteries. It is important to note that simple removal of the gross disease initially encountered upon pulmonary arteriotomy will not be therapeutic, and will certainly result in the patient's death unless a full endarterectomy is performed.

Surgical Classification of Thromboembolic Material

There are four broad types of pulmonary occlusive disease related to thrombus that can be appreciated, and we use the following classification: [5,9] type I disease (approximately 10% of cases of thromboembolic pulmonary hypertension; **Figure 3**) refers to the situation in which major vessel clot is present and readily visible on the opening of the pulmonary arteries. As mentioned earlier, all central thrombotic material has to be completely removed before the endarterectomy. In type II disease (approximately 70% of cases; **Figure 4**), no major vessel thrombus can be appreciated. In these cases only thickened intima can be seen, occasionally with webs, and the endarterectomy plane is raised in the main, lobar, or segmental vessels. Type III disease (approximately 20% of cases; **Figure 5**) presents the most challenging surgical situation. The disease is very distal and confined to the segmental and subsegmental branches. No occlusion of vessels can be seen initially. The endarterectomy plane must be carefully and painstakingly raised in each segmental and subsegmental branch. Type III disease is most often associated with presumed repetitive thrombi from indwelling catheters (such as pacemaker wires) or ventriculoatrial shunts. Type IV disease does not represent primary thromboembolic pulmonary hypertension and is inoperable. Patients in this group are essentially misdiagnosed and have the poorest outcome. In this entity there is intrinsic small vessel disease, although secondary thrombus may occur as a result of stasis. Small-vessel disease may be unrelated to thromboembolic events ("primary" pulmonary hypertension) or occur in relation to thromboembolic hypertension as a result of a high flow or high pressure state in previously

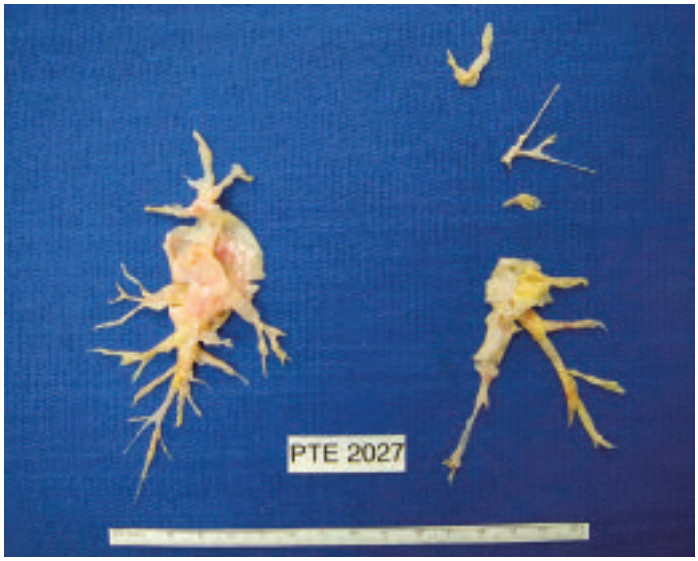

Figure 4. Specimen removed in a patient with type II disease. Both pulmonary arteries have evidence of chronic thromboembolic material, but there is no evidence of fresh thromboembolic material. Note the distal tails of the specimen in each branch. Full resolution of pulmonary hypertension is dependent on complete removal of all the distal tails.

Figure 5. Specimen removed from a patient with type III disease. Note that in this group of patients the disease is more distal, and the plane of dissection has to be raised individually at each segmental level.

unaffected vessels similar to the generation of Eisenmenger syndrome. We believe that there may also be sympathetic "cross-talk" from an affected contralateral side or stenotic areas in the same lung.

Postoperative Care

Meticulous postoperative management is essential to the success of this operation. All patients are mechanically ventilated for at least 24 hours, and all patients are subjected to a maintained diuresis with the goal of reaching the patient's preoperative weight within 24 hours. Although much of the postoperative care is common to more ordinary open heart surgery patients, there are some important differences.

The electrocardiogram, systemic and pulmonary arterial and central venous pressures, temperature, urine output, arterial oxygen saturation, chest tube drainage, and fluid balance are monitored. A pulse oximeter is used to continuously monitor peripheral oxygen saturation. Management of cardiac arrhythmias and output and treatment of wound bleeding are identical to other open heart operations. In addition, higher minute ventilation is often required early after the operation to compensate for the temporary metabolic acidosis that develops after the long period of circulatory arrest, hypothermia, and cardiopulmonary bypass. Tidal volumes and frequencies higher than those normally recommended after cardiac surgery are therefore generally used to obtain optimal gas exchange. The maximum inspiratory pressure is maintained below 30 cm of water if possible.

Although we used to believe that prolonged sedation and ventilation was beneficial and led to less pulmonary edema, subsequent experience has shown this not to be so. Extubation should be performed on the first postoperative day, whenever possible.

Patients have considerable positive fluid balance after operation. After hypothermic circulatory arrest, patients initiate an early spontaneous aggressive diuresis for unknown reasons, but this may, in part, be related to the increased cardiac output related to a now lower pulmonary vascular resistance level, and improved right ventricular function. This should be augmented with diuretics, however, with the aim of returning the patient to the preoperative fluid balance within 24 hours of operation. Fluid administration is minimized, and the patient's hematocrit level should be maintained above 30% to increase oxygen carrying capacity and mitigate against the pulmonary reperfusion phenomenon.

The development of atrial arrhythmias, at approximately 10%, is no more common than that encountered in patients who undergo other types of nonvalvular heart surgery.

Postoperative venous thrombosis prophylaxis with intermittent pneumatic compression devices is used, and the use of subcutaneous heparin is begun on the evening of surgery. Anticoagulation with warfarin is begun as soon as the pacing wires and mediastinal drainage tubes are removed, with a target international normalized ratio of 2.5 to 3.

Complications

Patients are subject to all complications associated with open heart and major lung surgery (arrhythmias, atelectasis, wound infection, pneumonia, mediastinal bleeding, etc) but also may develop complications specific to this operation. These include persistent pulmonary hypertension, reperfusion pulmonary response, and very rarely, neurologic disorders related to deep hypothermia.

Persistent Pulmonary Hypertension

In the vast majority of patients, the decrease in pulmonary vascular resistance level usually results in an immediate and sustained restoration of pulmonary artery pressures to normal levels, with a marked increase in cardiac output. In a few patients, an immediately normal pulmonary vascular tone is not achieved, but an additional substantial reduction may occur over the next few days because of the subsequent

relaxation of small vessels and the resolution of intraoperative factors such as pulmonary edema. In such patients, it is usual to see a large pulmonary artery pulse pressure, the low diastolic pressure indicating good runoff, yet persistent pulmonary arterial inflexibility still resulting in a high systolic pressure.

There are a few patients in whom the pulmonary artery pressures do not resolve substantially. We do operate on some patients with severe pulmonary hypertension but equivocal embolic disease. Despite the considerable risk of attempted endarterectomy in these patients, since transplantation is the only other avenue of therapy, there may be a point when it is unlikely that a patient will survive until a donor is found. In our most recent 500 patients, more than one third of all perioperative deaths were directly attributable to the problem of inadequate relief of pulmonary artery hypertension. This was a diagnostic rather than an operative technical problem. Attempts at pharmacological manipulation of high residual pulmonary vascular resistance levels with sodium nitroprusside, epoprostenol sodium, or inhaled nitric oxide are generally not effective. Because the residual hypertensive defect is fixed, it is not appropriate to use mechanical circulatory support or extracorporeal membrane oxygenation in these patients if they deteriorate subsequently.

The Reperfusion Response

A specific complication that occurs in most patients to some degree is localized pulmonary edema, or the reperfusion response. Reperfusion response or reperfusion injury is defined as a radiologic opacity seen in the lungs within 72 hours of pulmonary endarterectomy. This unfortunately loose definition may therefore encompass many causes, such as fluid overload and infection.

True reperfusion injury that directly adversely impacts the clinical course of the patient now occurs in approximately 10% of patients. In its most dramatic form, it occurs soon after operation (within a few hours) and is associated with profound desaturation. Edemalike fluid, sometimes with a bloody tinge, is suctioned from the endotracheal tube.[10]

One common cause of the reperfusion pulmonary edema is persistent high pulmonary artery pressures after operation when a thorough endarterectomy has been performed in certain areas, but there remains a large part of the pulmonary vascular bed affected by type IV change. However, the reperfusion phenomenon is often encountered in patients after a seemingly technically perfect operation with complete resolution of high pulmonary artery pressures. In these cases the response may be one of reactive hyperemia, after the revascularization of segments of the pulmonary arterial bed that have long experienced no flow. Other contributing factors may include perioperative pulmonary ischemia and conditions associated with high permeability lung injury in the area of the now denuded endothelium. Fortunately, this complication is much less common now in our series, probably as a result of the more complete and expeditious removal of the endarterectomy specimen that has come with the large experience over the last two decades.

Management of the Reperfusion Response

Early measures should be taken to minimize the development of pulmonary edema with diuresis, maintenance of the hematocrit levels, and the early use of peak end-expiratory pressure. Once the capillary leak has been established, treatment is supportive because reperfusion pulmonary edema will eventually resolve if satisfactory hemodynamics and oxygenation can be maintained. Careful management of ventilation and fluid balance is required. The hematocrit is kept high (30% to 35%), and the patient undergoes aggressive diuresis, even if this requires ultrafiltration. The patient's ventilatory status may be dramatically position-sensitive. The FiO_2 level is kept as low as is compatible with an oxygen saturation of 90%. A careful titration of positive end-expiratory pressure is carried out, with a progressive transition from volume-limited to pressure-limited inverse ratio ventilation and the acceptance of moderate hypercapnia.[10] The use of steroids is discouraged because they are generally ineffective and may lead to infection. Infrequently, inhaled nitric oxide at 20 to 40 parts per million can improve the gas exchange. On occasion we have used extracorporeal perfusion support (extracorporeal membrane oxygenator or, more commonly, extracorporeal carbon dioxide removal) until ventilation can be resumed satisfactorily, usually after 7 to 10 days. However, their use is limited to patients who have benefited from hemodynamic improvement, but are suffering from significant reperfusion response. Extracorporeal devices should not be used if there is no evidence or hope of subsequent hemodynamic improvement, since it carries mortality rates of close to 100% and will not play a role in improving irreversible pulmonary pressures.

Pericardial Effusion

Probably because of the lymphatic tissue that is encountered during the dissection of the hilum and the mobilization of the superior vena cava, possibly combined with the diminution of cardiac size that occurs immediately after the operation, we have encountered significant pericardial effusions in several patients. It is now our practice to either create a posterior pericardial window at the end of the operation or place a posterior pericardial drain, which we usually keep longer. These techniques have essentially eliminated the problem, and in general it is much easier to treat the pleural effusion on the left side in the occasional patient who may develop this complication.

Results

Approximately 2200 pulmonary thromboendarterectomies have been performed at UCSD Medical Center since 1970. Most of these cases (over 2000) have been completed since 1990, when the surgical procedure was modified as described above. The mean patient age in our group is about 52 years, with a range of 7 to 85 years. There is a very slight male predominance. In nearly one third of the cases, at least one additional cardiac procedure was performed at the time of operation. Most commonly, the adjunct procedure was closure of a persistent foramen ovale or atrial septal defect (26%) or coronary artery bypass grafting (8%).[5]

Hemodynamic Results

A reduction in pulmonary pressures and resistance to normal levels and a corresponding improvement in pulmonary blood flow and cardiac output are generally immediate and sus-

tained.[11,12] In general, these changes can be assumed to be permanent. Whereas before the operation, more than 95% of the patients are in NYHA functional class III or IV; at 1 year after the operation, 95% of patients remain in NYHA functional class I or II.[12,13] In addition, echocardiographic studies have demonstrated that, with the elimination of chronic pressure overload, right ventricular geometry rapidly reverts toward normal. Right atrial and right ventricular enlargement regresses. Tricuspid valve function returns to normal within a few days as a result of restoration of tricuspid annular geometry after the remodeling of the right ventricle, and tricuspid repair is not therefore part of the operation.

Operative Morbidity

Severe reperfusion injury was the single most frequent complication in our series, occurring in 10% of patients. Some of these patients did not survive, and others required prolonged mechanical ventilatory support. A few patients were salvaged only by the use of extracorporeal support and blood carbon dioxide removal. Neurological complications from circulatory arrest appear to have been eliminated, probably as a result of the shorter circulatory arrest periods now experienced, and perioperative confusion and stroke are now no more frequent than with conventional open heart surgery. Early postoperative hemorrhage required reexploration in 2.5% of patients, and only 50% of patients required intra- or postoperative blood transfusion. Despite the prolonged operation, wound infections are relatively infrequent. Only 1.8% experienced the development of any sternal wound complications, including sterile dehiscence or mediastinitis.

Deaths

In our experience, the overall mortality rate (30-day or in-hospital if the hospital course is prolonged) is about 7% for the entire patient group, which encompasses a time span of over 35 years. The mortality rate was 9.4% in 1989 and has been about 5% to 6% for the more than 1800 patients who have undergone the operation since 1990. Looking at our most recent experience over the last 10 years, the mortality rate is about 4% to 4.5%. We generally quote an operative risk of 2% to 5%, but some patients predictably fall within a much higher risk. With our increasing experience and many referrals, we continue to accept some patients who, in retrospect, were unsuitable candidates for the procedure (type IV disease). We also accept patients in whom we know that the entire degree of pulmonary hypertension cannot be explained by the occlusive disease detected by angiography but feel that they will be benefited by operation, albeit at higher risk. Residual causes of death are operation on patients in whom thromboembolic disease was not the cause of the pulmonary hypertension (approximately 50% of all deaths) and the rare case of reperfusion pulmonary edema that progresses to a respiratory distress syndrome of long standing, which is not reversible (25%).

Conclusion

It is increasingly apparent that pulmonary hypertension caused by chronic pulmonary embolism is a condition that is underrecognized and carries a poor prognosis. Medical therapy is ineffective in prolonging life and at best only transiently improves the symptoms. The only therapeutic alternative to pulmonary thromboendarterectomy is lung transplantation. The advantages of thromboendarterectomy include a lower operative mortality and excellent long-term results without the risks associated with chronic immunosuppression and chronic allograft rejection. The overall mortality for thromboendarterectomy at our institution is now in the range of 4% to 4.5%, with sustained benefit. These results are clearly superior to those for transplantation in both the short and long term.

Although pulmonary thromboendarterectomy is technically demanding for the surgeon and requires careful dissection of the pulmonary artery planes and the use of circulatory arrest; excellent short- and long-term results can be achieved. The successive improvements in operative technique developed over the last four decades allow pulmonary endarterectomy to be offered to patients with an acceptable mortality rate and excellent anticipation of clinical improvement. With this growing experience, it has also become clear that unilateral operation is obsolete and that circulatory arrest is essential.

The primary problem remains that this is an underrecognized condition. Increased awareness of both the prevalence of this condition and the possibility of a surgical cure should avail more patients of the opportunity for relief from this debilitating and ultimately fatal disease.

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