Pulmonary endarterectomy is possible and effective without the use of complete circulatory arrest—the UK experience in over 150 patients

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Abstract

Objective: Pulmonary endarterectomy is the best treatment for patients with chronic thromboembolic pulmonary hypertension. Traditionally pulmonary endarterectomy has been performed utilising deep hypothermic circulatory arrest to provide a bloodless field, but some recent reports have challenged this concept. We reviewed our experience with selective antegrade cerebral perfusion as the initial strategy of controlling bronchial collateral flow to avoid complete circulatory arrest in patients undergoing pulmonary endarterectomy.

Methods: A retrospective review of all patients meeting the above criteria between July 2003 and June 2006. Selective antegrade cerebral perfusion at 20 °C was used as the initial means of reducing blood flow to the operative field.

Results: One hundred and fifty-one patients (83 male, 68 female, mean age 56 ± 16 years) were operated on using this strategy. The preoperative New York Heart Association class distribution showed the majority to be in class III or IV (142 of 151). At initial assessment, mean pulmonary artery pressure was 49 ± 12 mmHg and mean pulmonary vascular resistance was 851 ± 391 dynes s cm⁻⁵. Selective antegrade cerebral perfusion was required in 145 for a total period of 63 ± 24 min. Thirteen (9%) patients required conversion to deep hypothermic arrest for completion of the operation. In-hospital mortality was 22 (15%). There were no instances of focal neurological deficit. Prearranged clinical follow-up for 3 and 12 months was 97% complete with one late death by 3 months and one more by 12 months. The majority were in New York Heart Association class I or II at 3 months (102 of 115) and 12 months (65 of 74). At 3-month follow-up the mean pulmonary artery pressure was 27 ± 10 mmHg and pulmonary vascular resistance was 304 ± 220 dynes s cm⁻⁵.

Conclusions: Overall results improved with era and institutional experience. The use of selective antegrade cerebral perfusion for pulmonary endarterectomy appears to be technically feasible in the majority of patients and is an alternative to complete circulatory arrest. To clarify its role further, comparison with deep hypothermic circulatory arrest in a randomised controlled trial is necessary.

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1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) develops in approximately 1–4% of patients who sustain an acute pulmonary embolism [1–3]. As with other forms of pulmonary hypertension, CTEPH confers a poor prognosis when established and severe [1]. It is increasingly recognised as an important cause of pulmonary hypertension but is still under diagnosed. The recognition of CTEPH is important as many patients are treatable by pulmonary endarterectomy (PTE) with dramatic improvement in symptoms and prognosis [4,5]. This condition has recently been comprehensively reviewed [6].

For PTE to be successful, a complete and true endarterectomy must be performed in the correct plane. This requires a clear and bloodless operative field to allow for precise distal dissection and maximal clearance [7]. This in turn, necessitates the use of cardiopulmonary bypass (CPB) plus some additional method of reducing the collateral return to the pulmonary circulation from bronchial arteries. The most commonly used method is deep hypothermic circulatory arrest (DHCA) [7]. Much of our current knowledge and understanding of the surgical treatment comes from the University of California San Diego (UCSD). UCSD have...
performed the most procedures in the world and have set the
standards reporting excellent results [7,8]. Recently Jamie-
son has robustly reiterated the absolute need for DHCA to
perform PTE successfully [9]. However, other centres have
used various techniques to maintain selective antegrade
cerebral perfusion (SACP) whilst interrupting bronchial
artery blood flow return [10—12]. There has been recent
vigorous debate over the need for DHCA in this journal [9,12].

Since 2000, Papworth Hospital has been in the unique
position of being the only designated centre for PTE surgery
in the UK and therefore we are referred patients from the
whole country. As of August 2006 we have performed 300
procedures. We felt it was time to contribute our results to
the debate and report our experience of performing PTE with
hypothermia, but without routinely relying on complete
circulatory arrest. We developed the technique of aortic arch
clamping to reduce collateral pulmonary blood flow but
maintain SACP in the light of evolving techniques to maintain
cerebral perfusion in aortic surgery with superior results. At
the beginning of our experience we had noted delirium and
some permanent neurological damage when the cumulative
circulatory arrest times exceeded 60 min, but we knew that a
full distal dissection was obligatory for a successful outcome.
Therefore this technique was developed to give us more time
for full endarterectomy dissection compared with that
available under complete DHCA.

2. Patients and methods

2.1. Patient population

From July 2003, an operative strategy of SACP as the initial
technique for reduction of pulmonary collateral blood flow
for PTE was routinely employed. We reviewed the con-
secutive cohort of 151 such patients from 1 July 2003 to 30
June 2006. Patients were referred from the five UK national
pulmonary hypertension centres. The indication for opera-
tion was established from a clinical assessment of the patient
as well as a review of relevant investigations at a multi-
disciplinary meeting of surgeons, physicians and radiologists.
The decision to proceed was based on haemodynamic (right
heart catheter and/or echocardiogram) and anatomic (CT
pulmonary angiogram, pulmonary angiogram and/or MR
pulmonary angiogram showing sufficient operable disease
to suggest surgical clearance was feasible) grounds as well as
taking into consideration potential comorbidities. An inferior
vena cava (IVC) filter was placed preoperatively. All patients
were investigated with carotid Doppler scans and contrast CT
scans to image the aortic arch and carotid arteries pre
operation. A transoesophageal echocardiogram was utilised
during the operation.

All data were collected contemporaneously and entered
into a dedicated database prospectively.

2.2. Operative techniques

General anaesthesia was induced with placement of right
radial and femoral arterial, central venous and Swan Ganz
catheters for haemodynamic monitoring. A transoesophageal
echocardiograph probe was also inserted. Nasopharyngeal and
bladder thermometers monitored temperature. Near-infrared
spectroscopy was used to monitor cerebral oxygenation (INVOS
Cerebral Oximeter, Somanetics, Michigan, USA). Following
anaesthetic induction, a median sternotomy and inverted ‘T’
ventral pericardiotomy was performed. Tapes were placed
around the ascending aorta, main pulmonary artery, superior
vena cava (SVC) and around the aortic arch between the left
common carotid and left subclavian arteries. These tapes were
used to facilitate the application of the cross-clamps and
exposure of the pulmonary arteries for endarterectomy.

Systemic heparin was administered to achieve an
activated clotting time (ACT) of greater than 400 s. Aprotinin
was routinely used. The patient was placed on cardiopul-
monary bypass via an ascending aortic arterial cannula and
two venous cannulae (one two-stage cannula inserted in the
right atrial appendage and a right-angled superior vena caval
cannula) and cooled slowly with a gradient of less than 10
°C to core temperature of 20 °C using pH-stat management.
Vents were placed in the right superior pulmonary vein and
main pulmonary artery. A cardioplegia cannula was placed in
the aortic root. A cooling water jacket was placed over the
right ventricle. Ice was placed around the patient’s head and
1 g IV methylprednisolone was administered.

Once a core temperature of 20 °C was reached, with the
help of a self-retaining retractor, the main right pulmonary
artery was exposed between the ascending aorta and SVC. A
longitudinal right pulmonary arteriotomy was then per-
formed from the aorta medially to beneath the SVC laterally.
Care was specifically taken to avoid denuding the artery of
adventitial tissue to facilitate secure haemostasis when
suturing it closed following endarterectomy.

With the use of stay sutures and hand-held retractors, the
lumen of the right pulmonary arterial system was exposed
and the endarterectomy plane was raised using a scalpel and
spatula. By the use of a nerve hook, forceps and a sucker-
dissector, the plane was extended circumferentially and then
distally as far as possible with the intention of tracing the
specimen into all the affected segmental or subsegmental
vessels till it ended as a tail. The lungs were intermittently
hand ventilated to expel blood into the sucker-dissector
when necessary.

While the initial dissection was performed on hypothermic
vented CPB, once visualisation was at all compromised by
return of bronchial collateral blood flow, an angled clamp was
placed between the left common carotid and left subclavian
arteries (Fig. 1) and a cross-clamp was placed on the
ascending aorta below the arterial inflow cannula (CPB flow
was therefore confined to the brachiocephalic and left
carotid arteries). Use of gentle traction on the tape
previously placed between the left common carotid and left
subclavian artery was used to improve access for clamp
application. Cold blood cardioplegia was then administered.
SACP was maintained at approximately 1.0—1.5 litres per
minute (l/min) and perfusion pressure of 40—50 mmHg in the
right radial artery. During this time, femoral arterial pressure
was usually between 10 and 15 mmHg. The endarterectomy
was then completed with the above perfusion strategy. The
arteriotomy was closed with 5/0 Prolene (Ethicon, Johnson &
Johnson, Livingston, United Kingdom). The previously placed
arch clamp and aortic cross-clamp were then released and
attention was directed to the left side.
The left pulmonary arteriotomy was extended from the vent insertion site in the main pulmonary artery into the main left pulmonary artery. The left-sided endarterectomy was then completed with the same surgical technique and perfusion strategy as for the right side. An example of an endarterectomy specimen removed during SACP is illustrated below (Fig. 2).

If at any stage during SACP collateral flow continued to interfere with safe surgical dissection, the strategy was switched to DHCA. DHCA was instituted for periods of up to 20 min at a time. A recovery period of 10 min was used between arrest periods when more dissection time was required.

After completion of the endarterectomies, proximal and distal aortic clamps were removed and the patient was rewarmed slowly on full CPB flow to a core temperature of at least 36.5 °C. Any concomitant cardiothoracic surgical procedures were completed during this phase of the operation. The patient was then weaned from CPB guided by invasive haemodynamic and echocardiogram monitoring. Particular attention was paid to the provision of appropriate right ventricular support, avoidance of excessive filling pressures and minimisation of pulmonary barotrauma and oxygen toxicity.

On return to the intensive care unit, patients were routinely ventilated overnight. Avoidance of any hypoxaemia and provocation of a vigorous diuresis were key elements in management. Extubation was usually achieved on the first postoperative day for uncomplicated cases.

Data were recorded at fixed time points pre and post surgery to allow rigorous comparison. Initial assessment data were from right heart catheters performed by the pulmonary hypertension-referring centre within a year of surgery. Pre and post CPB haemodynamic data were obtained under general anaesthesia from a pulmonary artery catheter immediately prior and post CPB in the operating room. Wedge pressure was assumed to be 10 mmHg for these calculations. This was used to allow standardised comparison of pulmonary vascular resistance (PVR) pre and post surgery as wedging a pulmonary arterial catheter pre endarterectomy can be misleading in diseased vessels and immediately post surgery is potentially dangerous. The next time point for data collection was between 6 and 8 a.m. on the morning of the first postoperative day. Finally, a right heart catheter was performed at Papworth Hospital at 3 months post operation.

2.3. Follow-up

Outpatient follow-up was performed at 3 months and 1 year postoperatively. This comprised a clinical review, chest radiology (chest X-ray, CT) and 6-min walk test. Additionally, at the 3-month visit, a right heart catheter was performed.

2.4. Statistical analysis

Data are summarised as mean ± standard deviation for continuous variables and as number (or percentage) for categorical variables. Median was used to summarise data with significant outliers. Comparison between pre- and postoperative variables was performed for continuous variables using paired two-tailed Student’s t-test and for categorical variables using χ² analysis. A p value of less than 0.05 was considered statistically significant. The statistical analytic software used was Microsoft Excel.

3. Results

Of the 151 patients (83 male, 68 female, mean age 56 ± 16 years, range 20—80 years), 9 were in NYHA class I or II and 142 in class III or IV. One hundred and thirty-two patients were able to complete a 6-min walk as part of the initial assessment, with a mean distance of 256 ± 134 m.

Initial right heart catheter data were available for the majority of patients, revealing a mean pulmonary artery pressure of 49 ± 12 mmHg (n = 147). The remaining four patients were acutely ill or had echocardiographic evidence of a large right atrial thrombus, precluding a right heart catheter. These patients had transthoracic echocardiograms all showing pulmonary arterial systolic pressures over
80 mmHg. Cardiac output studies were available on 141 patients. Pulmonary vascular resistance was calculated for these patients, assuming a wedge pressure of 10 mmHg, and was $851 \pm 391$ dynes s cm$^{-5}$.

The mean duration of total cardiopulmonary bypass was $335 \pm 53$ min (including the time of SACP and DHCA). In six patients, PTE could be completed on full CPB without recourse to measures to control bronchial collateral flow. SACP was needed to control collateral blood flow in 145 patients with a mean total time of $63 \pm 24$ min. Thirteen patients (9%) required conversion to DHCA at some stage, with a total duration of $21 \pm 15$ min. Using the classification proposed by Thistlethwaite et al. [13], the most common type of disease encountered was type 2 (Table 1). Concomitant surgical procedures were performed in 19 patients (7 coronary bypasses, 3 aortic valve replacements, 2 patent foramen ovale closures, 5 right atrial thrombectomy, 1 left ventricular lipoma excision and 1 lung biopsy).

A pulmonary artery catheter could be floated before surgery in the majority, allowing intraoperative measurement of mean pulmonary artery pressure and pulmonary vascular resistance. Both demonstrated a significant fall post surgery (see Fig. 3 for paired data comparison). Mean pulmonary artery pressure and pulmonary vascular resistance on the first postoperative day were $25 \pm 7$ mmHg and $283 \pm 177$ dynes s cm$^{-5}$, respectively.

In-hospital mortality was 22 (15%) for the whole series. In the last 50 patients, the in-hospital mortality was 5 (10%) and for the last 25 it was 1 (4%). The leading causes of death were reperfusion pulmonary oedema and/or persistent pulmonary hypertension (Table 2). The one death due to perforation of the pulmonary artery was in a patient with severely calcified vessels, making the dissection difficult. Other causes of death included one each of late intracranial haemorrhage, mesenteric ischaemia and retroperitoneal haemorrhage (after intra-aortic balloon pump removal). Major early morbidity is listed in Table 3. Many of these complications occurred in the same patients and are not mutually exclusive, e.g. patients deteriorating with multiorgan failure who subsequently accounted for the deaths. Two patients had early postoperative seizure activity that subsided spontaneously and 11 had mild transient confusion. There were no instances of focal neurological deficit or delirium. For survivors, the median length of ICU stay was 4 days (range 2–69) and hospital stay 16 days (range 6–109). The absence of a high dependency unit sometimes necessitated a slightly longer stay in ICU for administration of continuous positive airway pressure support. Discharge directly to home was achieved in over 90% of patients.

At the time of analysis, 115 of 119 (97%) patients had returned for 3-month clinical follow-up by the Papworth pulmonary hypertension service. Of the remaining four, three were confirmed alive, with one death due to cerebrovascular accident. At 3 months, 102 of 115 patients were in NYHA class I or II; a significant improvement compared to initial assessment ($\chi^2 = 183.7, p < 0.001$). At 3-month follow-up the mean pulmonary artery pressure was $27 \pm 10$ mmHg and pulmonary vascular resistance was $304 \pm 220$ dynes s cm$^{-5}$.

Paired haemodynamic variables and 6-min walk distances were available for 101 patients. Mean pulmonary artery pressure and pulmonary vascular resistance were both significantly lower compared to pre-CPB values ($p < 0.001$). The absence of a high dependency unit sometimes necessitated a slightly longer stay in ICU for administration of continuous positive airway pressure support. Discharge directly to home was achieved in over 90% of patients.
Compromises both survival and functional outcome [5]. Our chronic thromboembolic pulmonary hypertension seriously of an incomplete clearance of disease in patients with operative field visualisation was compromised. Acceptance of optimal result, recourse to DHCA was undertaken whenever DHCA in over 90% of cases. Importantly, to avoid a less than performing pulmonary endarterectomy without the use of SACP techniques in PTE, different perfusion strategies have been developed to (i) preoperative definition of surgically accessible disease in proportion to the haemodynamic parameters, (ii) intraoperative technical success whilst providing optimal organ protection and (iii) meticulous postoperative care. Importantly, the risks are higher in those patients with distal disease and a high pulmonary vascular resistance, especially when the pulmonary vascular resistance is out of proportion to the degree of disease seen on imaging. There are very clear and steep learning curves for all aspects of this process and accrued experience in all three is vital. By way of illustration, the mortality was 17% in the first 200 patients operated on at UCSD during the period of establishment of that programme, followed by a fall to <5% for more recent subsets of patients [7]. Paralleling this, we have observed a trend towards falling mortality in the later patients in our cohort as a result of increased institutional experience and improved case selection. The series reported here includes some of our early experience with PTE and the mortality and morbidity reported in full are relatively high compared with current standards. Much of the morbidity documented occurred in the same patients who ultimately did not survive because patients with reperfusion injury and residual pulmonary hypertension were fully supported with haemofiltration and IABP as they deteriorated and developed multiorgan failure.

There were no major clinically detected permanent focal neurological deficits seen in these patients but some evidence of postoperative seizure activity and of confusion. The imprecision of basic clinical neurocognitive functional assessment precludes any definite conclusions being reached, especially with only the temporally separate DHCA group being available for comparison within the institution. The role of SACP techniques in PTE hinges critically on this issue of neurological morbidity as well as the issue of optimising operative conditions for surgical disease clearance.

As increasing numbers of units have begun undertaking PTE, different perfusion strategies have been developed to either avoid/reduce circulatory arrest (as in this patient cohort) and/or avoid deep hypothermia [10–12]. One of these groups has reported a technique conceptually similar to ours, using endoluminal balloon occlusion of the proximal descending thoracic aorta [10]. In contrast to our technique of cooling to 20 °C, they only cooled to 28–32 °C. The relative significantly reduced at 3 months (Fig. 4) whilst 6-min walk distance significantly increased (268 ± 135 m to 371 ± 96 m; n = 101; p < 0.001).

Clinical follow-up was available for 74 of 76 (97%) eligible patients at 12 months. One of those failing to attend follow-up was confirmed to have died (cause not known) with the remaining patient being alive but with NYHA status not known. Therefore the 1-year survival for patients discharged from hospital was 98%. The 12-month NYHA class (65 of 74 in class I or II) showed sustained improvement compared with preoperative assessment (χ² = 150.8, p < 0.001). Six-min walk distance also showed sustained improvement (256 ± 131 m to 381 ± 103 m; n = 63; p < 0.01) for those where paired distances were available.

4. Discussion

This study demonstrates the technical feasibility of performing pulmonary endarterectomy without the use of DHCA in over 90% of cases. Importantly, to avoid a less than optimal result, recourse to DHCA was undertaken whenever operative field visualisation was compromised. Acceptance of an incomplete clearance of disease in patients with chronic thromboembolic pulmonary hypertension seriously compromises both survival and functional outcome [5]. Our technique allows continued dissection to proceed uninter rupted beyond 20 min (which has been the conventionally practised time limit for DHCA in PTE [7]). Therefore, it allows additional time to perform a complete endarterectomy without the need to interrupt the dissection and restart perfusion for a period of time.

Fundamental to the use of any technique other than DHCA is the adoption of a strategy to ensure that when necessary, DHCA can be easily and expeditiously employed. Since we cool all the patients down to 20 °C on CPB, we can easily and rapidly convert to DHCA when required.

There was sustained clinical and functional benefit observed in survivors to 1 year. This is consistent with previously published results [4]. Further long-term follow-up will hopefully confirm the durability of the result.

The in-hospital mortality in this series was 15%, with the principal causes being reperfusion pulmonary oedema and persistent pulmonary hypertension. The complexity of the process of surgical management of chronic thromboembolic pulmonary hypertension most importantly relates to (i) preoperative definition of surgically accessible disease in proportion to the haemodynamic parameters, (ii) intraoperative technical success whilst providing optimal organ protection and (iii) meticulous postoperative care. Importantly, the risks are higher in those patients with distal disease and a high pulmonary vascular resistance, especially when the pulmonary vascular resistance is out of proportion to the degree of disease seen on imaging. There are very clear and steep learning curves for all aspects of this process and accrued experience in all three is vital. By way of illustration, the mortality was 17% in the first 200 patients operated on at UCSD during the period of establishment of that programme, followed by a fall to <5% for more recent subsets of patients [7]. Paralleling this, we have observed a trend towards falling mortality in the later patients in our cohort as a result of increased institutional experience and improved case selection. The series reported here includes some of our early experience with PTE and the mortality and morbidity reported in full are relatively high compared with current standards. Much of the morbidity documented occurred in the same patients who ultimately did not survive because patients with reperfusion injury and residual pulmonary hypertension were fully supported with haemofiltration and IABP as they deteriorated and developed multiorgan failure.

There were no major clinically detected permanent focal neurological deficits seen in these patients but some evidence of postoperative seizure activity and of confusion. The imprecision of basic clinical neurocognitive functional assessment precludes any definite conclusions being reached, especially with only the temporally separate DHCA group being available for comparison within the institution. The role of SACP techniques in PTE hinges critically on this issue of neurological morbidity as well as the issue of optimising operative conditions for surgical disease clearance.

As increasing numbers of units have begun undertaking PTE, different perfusion strategies have been developed to either avoid/reduce circulatory arrest (as in this patient cohort) and/or avoid deep hypothermia [10–12]. One of these groups has reported a technique conceptually similar to ours, using endoluminal balloon occlusion of the proximal descending thoracic aorta [10]. In contrast to our technique of cooling to 20 °C, they only cooled to 28–32 °C. The relative
advantage of their technique is of shorter total cardiopulmonary bypass time whilst our technique would provide a greater degree of hypothermic distal visceral and spinal cord protection. Additionally, this group has reported the use of short periods (approximately 10 min) of total circulatory arrest at 30 °C to complete the PTE [12]. As clearly expressed by Jamieson [9], the safety margin for cerebral protection and time pressure for thorough completion of the endarterectomy may become issues.

All of these techniques to avoid DHCA in PTE have been developed out of experience in cardiac surgical management of other pathologies requiring complex perfusion management. Evolution of aortic arch surgical techniques has provided evidence and opinion suggesting an advantage by maintaining antegrade cerebral perfusion [14–16]. Whilst it is important to consider this evidence, it is equally important not to generalise from it too greatly. For example, Griep has emphasised the specific importance of using antegrade cerebral perfusion techniques when one would otherwise be interrupting the cerebral circulation for more than 25 min during aortic arch surgery [15]. If during the conduct of PTE, DHCA is limited to 20 min periods, then it is unwise to infer too much from the aortic arch surgery cohort where the potential time of obligatory circulatory arrest may well exceed 25 min. With regard to conduct of PTE, the benchmark against which alternatives are compared has been and currently remains the use of DHCA. In fact, there is some evidence, again from the aortic arch surgery population, to suggest that DHCA is not a risk factor for neurological morbidity or mortality [17], although it is important to distinguish patient populations with atherosclerotic disease and the PTE population with normal aortas. In light of conflicting opinion and evidence, we propose to conduct a randomised controlled trial of our technique versus DHCA with accurate longitudinal measures of neuropsychological function along with haemodynamic, functional and survival outcomes.

In summary, the use of SACP for PTE appears to be technically feasible in the majority of patients. We feel that our technique may provide some distinct advantages, with reference to both potentially optimising cerebral protection and completeness of endarterectomy. Firstly, there is at least some theoretical advantage to maintaining antegrade cerebral perfusion. Secondly, the maintenance of this perfusion may allow a greater period of continuous time to complete the endarterectomy, thus optimising disease clearance. Thirdly, when necessary, easy and rapid recourse to DHCA is possible.

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References


Appendix A. Conference discussion

Dr P. Dartevelle (Le Plessis-Robinson, France): Congratulations on your presentation.

However I don’t agree with you. It’s true, it’s possible to perform this operation without circulatory arrest, but your results demonstrate a mortality rate which is three times more than the other teams who perform this kind of surgery. Your mortality rate is 15% and the mortality rate of the other teams is 5%. And the reason is probably because you don’t go far enough into the pulmonary arteries.

I think that I have tried everything in respect to this surgery, but I am now sure that total circulatory arrest is necessary. Moreover total circulatory arrest
is not a drawback in this surgery, because it's a short circulatory arrest for 20 min. The patients, 1 day after surgery, are extubated without neurological deficit, even in patients who are older than 80 years. Therefore let me iterate I totally disagree with the absence of circulatory arrest for this surgery. My question is: Why do you have so long cardiopulmonary bypass time? Because your cardiopulmonary bypass time is more than 5 h. Why is it so long? Because in my experience, cardiopulmonary bypass time should be less than 4 h.

Dr Thomson: To answer those two aspects, firstly, the operative in-hospital mortality rate and, secondly, the bypass duration.

To start with the latter, the cardiopulmonary bypass time was long, as you say. The reason we have a relatively long bypass time is that we ensure homogenous cooling of the patient and usually have a gradient between central and peripheral temperatures of under 10 °C and make sure the patient is homogenously cooled to 20 °C.

With regard to the operative mortality, an important point to make is the impact, as Jamieson has indicated, of the aspect of the learning curve on outcome in this operation. To consider the San Diego series, if you look at the first 200 patients that they did, the operative mortality was 17%, with, as you rightly point out, a very pleasing reduction over the time course of their whole patient cohort which they have reviewed.

With regard to our series, a similar pattern has been seen with the last 50 patients in our series, in this series, having a 10% mortality, and the last 25 there being only 1 death, i.e., a 4% mortality. So I think they are important points to make.

Additionally, what our technique allows us to do is to dissect carefully with antegrade cerebral perfusion, but, importantly, with the caveat that if we find that the dissection in the distal vessels, as you point out, which are very important, is difficult, then recourse to deep hypothermic arrest is possible.

So it’s in that context that we’re saying that yes, it’s possible, but the deep hypothermic arrest is an option which we need to have available to us to insure complete disease clearance.