The Role of Deep Hypothermic Cardiac Arrest in the Surgical Treatment of Complex Intracranial Aneurysms

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Abstract

Giant and complex intracranial aneurysms can be formidable lesions to tackle from a surgical standpoint. Their treatment has witnessed an enormous improvement in recent decades with the development of several technical refinements, both surgical and endovascular. By combining optimal cerebral protection with extended periods of circulatory control, deep hypothermic cardiac arrest (DHCA) is a useful adjunct for appropriately dealing with very select cases. In this article we discuss the rationale behind the use of DHCA and review the results of the most relevant series recently published. DHCA remains an important though exceptional way of surgically treating giant and complex intracranial aneurysms.

Keywords

Cardiac standstill, circulatory arrest, giant aneurysm, hypothermia

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The treatment of intracranial aneurysms, both ruptured and unruptured, has witnessed a dramatic improvement in outcomes made possible by continuous refinement in microsurgical technique alongside major technological developments and a growing understanding of the physiology of the brain under normal circumstances or when challenged. Even after the advent of endovascular aneurysm treatment, exclusion of giant or very complex aneurysms still remains a daunting task associated with considerable morbidity.

Because the natural history of such aneurysms left untreated is recognisably rather dismal, a therapeutic attitude is recommended. Poor prognosis associated with giant or large aneurysms is intimately related to their high risk of rupture, mass effect and the likelihood of emboli coming from the aneurysmal sac being washed down the distal circulation.[1] In the International Study of unruptured intracranial aneurysms (ISUIA),[2] published in 2003, the five-year incidence of rupture for giant anterior and posterior circulation aneurysms was 40 % and 50 %, respectively. In the series by Peerless et al.,[3] mortality rate for unruptured giant aneurysms was higher than 60 % following the index procedure, all surviving patients being left with marked neurological disability.

In recent decades improvement in surgical and endovascular techniques has significantly changed not only the outcome of treatment but also many of the considerations leading to the final therapeutic decision. Despite the immense ground covered in the last few years, current endovascular technology still has important limitations in the treatment of larger-sized or more complex-shaped aneurysms. Long-term efficacy of sub-optimal sac packing or exclusion remains a problem, currently being addressed with the deployment of more novel stenting devices. Microsurgical exclusion of large or giant aneurysms still to this day remains the gold standard for treatment.

Many factors have made possible the improvement in outcomes; wider, wiser and therefore safer use of surgical corridors, microsurgical control of the circulation, technological improvement enabling us to better monitor, understand and protect brain function, and safer and more efficacious pharmacological intervention are but a few.

Deep hypothermic cardiac arrest (DHCA) has been on the map for the treatment of aneurysms of the intracranial circulation for quite some time now. From its dawn it was used as an extraordinary measure of brain protection but at the same time one carrying a mighty risk for the patient. Using a paradigm equivalent to that used in cardiac surgery, DHCA applied to intracranial aneurysm surgery is justified if and when the estimated time of circulatory arrest needed for the repair of the aneurysm extends far beyond the time boundaries estimated safe by the current though sophisticated brain protective measures.

Historical Perspective

The use of hypothermia as a mechanism of neural protection was introduced over 50 years ago.[4] Several technological advances in the field of cardiac surgery in the 1940s–1950s led to the development and routine use of extracorporeal circulation and cardiac arrest. By decreasing cerebral metabolic needs, hypothermia considerably prolongs tolerance time to ischaemia, up to 60 minutes at the18–20 ºC range.

In the early 1960s, several neurosurgeons went as far as to use the technique for some more complex neurovascular pathology as well as some haemorrhagic metastatic tumours.[4] Early promising results were soon to be rebuffed by Drake's report from 1964,[5] with 10 consecutive cases of intracranial aneurysm treated with the help of DHCA. A mortality rate of 30 % occurred, mostly attributed to complications related to hypothermia and cardiac standstill, with post-operative coagulopathy emerging as the main culprit. Two years later, Uihlein et al.[6] published their series with 66 patients and a peri-operative mortality rate of 23 %, again evidencing great difficulty in dealing with post-operative coagulation diathesis.

These results, along with cumbersome and unsophisticated pump technology as well as prolonged anaesthesia time, led to a decline in the use of this technique.[4,7] At the same time a number of advances were being introduced in the field of neurosurgery, mainly the widespread use and potential of the microscope, new and more sophisticated clip technology, the concept of local circulatory control and temporary clipping and of course the use of drugs enabling intra-operative blood pressure control and brain protection. All these advances strongly pushed forward the field of vascular neurosurgery allowing for a vast number of intracranial aneurysms to be treated under meticulous microsurgical technique and normo- or mild hypothermia.

In the 1980s refinement in anaesthetic management of patients undergoing hypothermia and cardiac bypass, especially problems relating to disturbed coagulation, along with a clear upgrading of extracorporeal circulation techniques, encouraged a re-evaluation of DHCA for the treatment of giant or more complex intracranial aneurysms.[4] Several series were then reported in the literature disclosing a more favourable outcome and an acceptable morbidity given the enormous challenge of the lesions being treated. These results fuelled interest in the use of DHCA in the following years.

Rationale

Very large or otherwise very complex intracranial aneurysms pose several difficulties when treatment, both surgical and/or endovascular, is attempted. Size in itself remains a significant problem especially for aneurysms that cannot be deflated and shrunk by puncturing, suction techniques or temporary local circulatory arrest. Inability to secure proximal control, massive calcification of the aneurysm wall and the presence of significant intramural thrombosis all add up to an increased difficulty.

Systemic hypotension as a means to procure a drop in aneurysm turgor and flow has fallen out of favour due to its potential deleterious consequences to several organs including the brain. Focal circulatory arrest using temporary clips has subsequently become the answer, but the risk of infarction remains directly related to the length of time those clips are applied.[7]

By virtually abolishing the circulation (though in practical terms a minimal flow and pressure needs to be maintained in order to prevent migration of air emboli) and at the same time protecting the brain form ischaemia at very low core temperatures, DHCA combines ultimate cerebral protection and optimal surgical conditions.

DHCA can therefore be seen as an ultimate adjunct for the treatment of exceptional aneurysms that do not lend themselves to conventional surgical and anaesthetic techniques.

Table 1: Deep Hypothermic Circulatory Arrest Associated Morbidity[7]

Clinical coagulopathy
Deep vein thrombosis
Hypoperfusion
Myocardial infarction
Cerebral infarction
Temperature instability
Augmented fluid shifts
Delayed awakening

The decision to use DHCA in the treatment of an intracranial aneurysm is very elaborate and not devoid of some degree of subjectivity enclosed in the observation and weighing of several factors. The size of the aneurysm, its location along the cerebral vascular tree, characteristics of the local circulation (anastomotic, terminal, presence of collaterals), presence of calcification and mural thrombosis, and relationship to afferent and efferent arteries are all important. Appreciation of the difficulties implicated in each case remains subjective to each surgeon and tainted by their own track record and experience in past instances.

Because DHCA still carries a potential for complication far above that associated with conventional anaesthetic situations (see *Table 1*), other estimates such as patient age, medical co-morbidity (especially cardiac and pulmonary disease), neurological status and overall general condition[7] and the absolute need to secure a proficient multidisciplinary effort must all factor in for the final decision.

Literature Review

The most well-known fact transpiring from the review of all series on the use of DHCA in intracranial aneurysm surgery in the last 30 years[8–18] is the remarkable improvement in mortality and outcome in the more recent reports. We have therefore opted to focus our attention on the series published in the last four years accounting for the largest population of patients treated with this technique in North American and European institutions[19–21] (see *Table 2*).

The 15-year experience with the use of DHCA of the Neurological Institute of New York was reviewed in 2007.[19] In a group of 66 patients treated, with a mean age of 49 years (range 15–73 years), 77 % harboured unruptured aneurysms. In 20 % of cases a previous unsuccessful treatment had been attempted. In five cases an operation carried out under conventional measures was aborted in favour of a procedure utilising DHCA, which was deferred for another week. Half were posterior circulation aneurysms, basilar tip and proximal internal carotid artery (ICA) being the two most prevalent locations. Fifty-seven out of 66 were giant and 35 % were heavily thrombosed or calcified. Average time of cardiopulmonary bypass was 132 minutes (range 45–252 minutes) and the mean cooling time was 28.5 minutes (range 17–52 minutes). Time of circulatory arrest was 26.2 minutes (range 6–77 minutes) with a mean temperature of 17.6 ºC (range 15–21 ºC) at the end of hypothermia. The 30-day mortality was 12 % (seven patients) with two deaths attributed to the bypass procedure, secondary to cardiac tamponade and aortic root rupture. Six patients developed neurological problems, either ischaemia or temporal lobe haematoma, and 11 sustained medical complications such as cardiac arrhythmias, deep vein thrombosis, pulmonary embolism, pneumonia, urosepsis and syndrome of inappropriate secretion of antidiuretic hormone. An excellent or good outcome (Glasgow Outcome Scale [GOS] 4 or 5)

Table 2: Literature Review of Recent Studies Contemplating the Use of Deep Hypothermic Circulatory Arrest in the Treatment of Complex Intracranial Aneurysms

Study	Number of Patients (Female:Male)	Mean Age (Years) (Range)	Anterior: Posterior Circulation	Mean Size (cm) (Range)	Mean Core Temperature (ºC) (Range)	Mean Bypass Time (Minutes) (Range)	Mean Arrest Time (Minutes) (Range)	Morbidity (Minor:Major)	Peri-operative Mortality
Mack et al., 2007[19]	66 (41:25)	49 [15–73)	33:33	2.8 (0.8–3.5)	17.6 (15–21)	132 (45–252)	26.2 (6–77)	16 (10:6)	7
Schebesch et al., 2010[20]	26 (12:14)	45.6 (17–71)	17:9	2.48 (1.0–5.0)	18.4 (18–20)	136 (45–240)	23.4 (3–102)	14 (10:4)	3
Ponce et al., 2011[21]	103 (64:39)	44.8 (5–77)	7:97*	2.71 (1.2–5.0)	17.2 (12–20)	–	21.8 (2–72)	37 (18:19)	14

**Ninety-six patients had 97 posterior circulation aneurysms.*

was reported in 67 % of patients. Age and pre-operative neurological status correlated with functional outcome: age was related to clinical decline after surgery, with patients over 60 years showing the worst outcomes, a trend also observed with increased circulatory arrest time and in the group harbouring giant aneurysms. Interestingly, the authors compared their results in three consecutive five-year cohorts and noticed not only a decrease in the percentage of giant aneurysms treated at their institution, but also in the number of circulatory arrest procedures, diminishing from 34 between 1989 and 1993 to only 12 in the last five years of the study (1999–2003). Based on their results they defined the ideal candidate for DHCA to be under 60 years of age with little medical co-morbidity. The optimal time of circulatory arrest should be under 30 minutes; extreme hypothermia should be avoided and combined with rapid post-operative awakening to decrease the likelihood of post-operative haematomas. The authors conclude that DHCA is a relatively safe procedure to be carried out in centres with experience in this technique for the treatment of high-risk aneurysms, with large anterior communicating artery (ACoA), ICA bifurcation, posterior inferior cerebellar artery (PICA), midbasilar or from the vertebral artery, without thrombus or calcium, experiencing the most favourable outcomes.

In 2010, the largest European experience so far reported was published in *Acta*, also spanning a 15-year period. Schebesch et al.[20] treated 26 patients with a mean age of 45.6 years (range 17–71 years), with six of these patients having been previously submitted to an attempt at treatment under conventional circumstances. Nine aneurysms (34 %) were from the posterior circulation, and overall 42 % presented with subarachnoid haemorrhage (SAH). Patient selection was based on the senior author's appraisals, and included "the size of the aneurysm, wall properties, localisation, perforator anatomy, and the form and size of the aneurysmal neck." In fact the mean size of the lesions treated was 2.48 cm and calcification or thrombosis was found in 34 % overall. Of the non-giant aneurysms treated (46 %), all had dome-to-neck ratios less than one with the presence of atheroma, thrombus or adherence to the surrounding structures. Treatment-related mortality was 11.5 % and morbidity was 15 %. The mean cardiac arrest time was 23.4 minutes (range 3–102 minutes), achieved mean brain temperature was 18.4 ºC (range 18–20 ºC) and the mean time of cardiopulmonary bypass was 136 minutes (range 45–240 minutes). At six months 50 % of the patients improved their neurological symptoms compared with their pre-operative status. Age over 65 years, SAH, Hunt & Hess (H&H) and Fisher scores, pre-operative neurological symptoms and prolonged cardiac arrest time all correlated negatively with outcome at six months. The authors comment that with the progressive improvement in endovascular treatment, only in very special circumstances will such a surgical undertaking be needed.

The largest series published on this topic came in March 2011 from the Barrow Neurological Institute. Ponce et al.[21] updated their previous results to a remarkable cohort of 103 patients. This is a retrospective analysis of the cases treated in a 24-year period, with 96 patients harbouring 97 posterior circulation aneurysms (60 of them from the basilar tip) with only seven lesions from the anterior vascular tree. Interestingly, in the last 10 years of the study no aneurysm from the anterior part of the circle of Willis was treated with this technique. The authors argue that with the use of temporary clipping, mild hypothermia, barbiturate suppression, induced hypotension, perforator visualisation with indocyanine green and adenosine-induced transient cardiac arrest, a treatment solution was achieved obviating DHCA. The routine use of the orbitozygomatic approach with anterior clinoidectomy, ICA proximal control either at the neck or petrous region or temporary balloon occlusion were all instrumental for the final result.[16] These 105 patients represented only 1.9 % of the aneurysms treated by the senior author, with a mean age of 44.8 years (range 5–77 years), 16 of which having had some kind of previous treatment attempted. Most patients had multiple neurological signs secondary to mass effect and 47 (45 %) presented with SAH, of which 10 had an H&H grade IV or V. Mortality rate was 14 %, permanent morbidity occurred in 18.4 % of the cases and at late follow-up a favourable outcome was achieved in 77 % of the cohort. It must be stated that the combined rate of temporary and/or permanent morbidity and mortality ended at 49.5 %. It is the authors' belief that this high morbidity reflects the selection of predominantly giant and complex basilar tip aneurysms, a higher risk group compared with other locations. Patient selection is now limited to this type of lesion, predominantly those with posterior projection, dolichoectatic, with an abnormal base, calcified or thrombosed. Of utmost importance to the authors is the risk of intra-operative rupture and perforator stroke. The trend for a declining indication for this procedure is also distinctive, with only six patients treated in the last five years.

Conclusions

Deep hypothermia and cardiac arrest has been in the armamentarium of neurosurgeons for decades now and has been the subject of continuous improvements, mostly resulting from the increased sophistication of surgical and anaesthesiological techniques useful in heart and circulatory bypass peripheral surgery. Morbidity and mortality related to the procedure has been significantly reduced, making it an invaluable tool to be used with very precise indications, even in the environment of strong endovascular competition.

Its application can be found in the odd case of giant or more complex aneurysms for which the estimated time of local circulatory shutdown would surpass the range estimated safe when using conventional brain protection measures. Other than size, variables that the surgeon must bear in mind include perforator anatomy, posterior circulation location, wide neck and presence of calcium or thrombus. However, what is not accountable in any published series and therefore cannot be taken as a general recommendation is the personal view one has of each particular case, which is going to mould one's own attitude in each situation. The mere attribute of complexity encloses a non-negligible degree of subjectivity. The trend towards a reduction in the use of DHCA reflects the development of deconstructive options, bypass procedures, arterial re-implantation and new stent technology.[22] DHCA should be used preferentially in tertiary centres offering multidisciplinary comprehensive approaches to aneurysm treatment. The paucity of cases with indication for such a procedure certainly warrants a careful referral of patients aimed at optimising outcomes and maintaining expertise. ■

1. Hanel R, Spetzler RF, Surgical treatment of complex intracranial aneurysms, *Neurosurgery*, 2008;62 (6 Suppl. 3):1289–97.
2. Wiebers DO, Whisnant JP, Huston J 3rd, et al., Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment, *Lancet*, 2003;362(9378):103–10.
3. Peerless SJ, Wallace MD, Drake CG, Giant intracranial aneurysms, In Youmans JR, ed., *Neurological Surgery: A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems,* Philadelphia: WB Saunders, 1990;1742–63.
4. Rothoerl RD, Brawanski A, The history and present status of deep hypothermia and circulatory arrest in cerebrovascular surgery, *Neurosurg Focus*, 2006;20(6):E5.
5. Drake CG, Barr HW, Coles JC, et al., The use of extracorporeal circulation and profound hypothermia in the treatment of ruptured intracranial aneurysms, *J Neurosurg*, 1964;21:575–81.
6. Uihlein A, MacCarty CS, Michenfelder JD, et al., Deep hypothermia and surgical treatment of intracranial aneurysms. A five-year survey, *JAMA*, 1966;195(8):639–41.
7. Connolly ES, Heyer EJ, Solomon R, Cardiac standstill for giant cerebral aneurysms, In: Leroux PD, Winn HR, Newell DW, eds, *Management of Cerebral Aneurysms*, Philadelphia: WB Saunders, 2004;613–25.
8. Sundt TM Jr, Surgical technique for giant intracranial aneurysms, *Neurosurg Rev*, 1982;5(4):161–8.
9. Baumgartner WA, Silverberg GD, Ream AK, et al., Reappraisal of cardiopulmonary bypass with deep hypothermia and circulatory arrest for complex neurosurgical operations, *Surgery*, 1983;94(2):242–9.
10. Gonski A, Acedillo AT, Stacey RB, Profound hypothermia in the treatment of intracranial aneurysms, *Aust N Z J Surg*, 1986;56(8):639–43.
11. Richards PG, Marath A, Edwards JM, et al., Management of difficult intracranial aneurysms by deep hypothermia and elective cardiac arrest using cardiopulmonary bypass, *Br J Neurosurg*, 1987;1(2):261–9.
12. Solomon RA, Smith CR, Raps EC, et al., Deep hypothermic circulatory arrest for the management of complex anterior and posterior circulation aneurysms, *Neurosurgery*, 1991;29(5):732–8.
13. Williams MD, Rainer WG, Fieger HG Jr, et al., Cardiopulmonary bypass, profound hypothermia, and circulatory arrest for neurosurgery, *Ann Thorac Surg*, 1991;52(5):1069–74.
14. Ausman JI, Malik GM, Tomecek FJ, et al., Hypothermic circulatory arrest and the management of giant and large cerebral aneurysms, *Surg Neurol*, 1993;40(4):289–8.
15. Aebert H, Brawanski A, Philipp A, et al., Deep hypothermia and circulatory arrest for surgery of complex intracranial aneurysms, *Eur J Cardiothorac Surg*, 1998;13(3):223–9.
16. Lawton MT, Raudzens PA, Zabramski JM, et al., Hypothermic circulatory arrest in neurovascular surgery: evolving indications and predictors of patient outcome, *Neurosurgery*, 1998;43(1):10–21.
17. Sullivan BJ, Sekhar LN, Duong DH, et al., Profound hypothermia and circulatory arrest with skull base approaches for treatment of complex posterior circulation aneurysms, *Acta Neurochir*, 1999;141(1):1–12.
18. Massad MG, Charbel FT, Chaer AS, AUsman JI, Closed chest hypothermic circulatory arrest for complex intracranial aneurysms, *Ann Thorac Surg*, 2001;71(6):1900–4.
19. Mack WJ, Ducruet AF, Angevine PD, et al., Deep hypothermic circulatory arrest for complex cerebral aneurysms: lessons learned, *Neurosurgery*, 2007;60(5):815–27.
20. Schebesch KM, Proescholdt M, Ullrich OW, et al., Circulatory arrest and deep hypothermia for the treatment of complex intracranial aneurysms – results from a single European center, *Acta Neurochir*, 2010;152(5):783–92.
21. Ponce FA, Spetzler RF, Han PP, et al., Cardiac standstill for cerebral aneurysms in 103 patients: an update on the experience at the Barrow Neurological Institute, *J Neurosurg*, 2011;114(3):877–84.
22. Cunha e Sá M, The use of deep hypothermia and cardiac arrest in the surgical treatment of large and complex intracranial circulation aneurysms, *Acta Neurochir*, 2010;152(6):1089–90.