Netherlands Journal of Critical Care
Submitted October 2017 – Accepted November 2017

ORIGINAL ARTICLE

Use of cardiopulmonary bypass and full heparinisation in patients with an asymptomatic intracranial aneurysm

W.M. van den Bergh[1], J.M. Dieleman[2], A.J.C. Slooter[3], D. van Dijk[3]

[1]Department of Critical Care, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands;
[2]Department of Anesthesiology, University Medical Center Utrecht, Utrecht, the Netherlands
[3]Department of Intensive Care Medicine and Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

Correspondence
W.M. van den Bergh - w.m.van.den.bergh@umcg.nl

Keywords - **cardiopulmonary bypass; intracranial aneurysm; risk assessment; subarachnoid haemorrhage**

Abstract

Introduction: The overall prevalence of unruptured intracranial aneurysms is 3.2%. The rupture risk of an intracranial aneurysm during cardiopulmonary bypass requiring full heparinisation is unknown.

Patients and Methods: Rupture risk was assessed using data from a trial in which dexamethasone was compared with placebo in 4482 patients undergoing cardiac surgery with cardiopulmonary bypass.

Results: Not a single haemorrhagic stroke occurred during surgery and only one patient had a subarachnoid haemorrhage three weeks after cardiac surgery.

Discussion: Although the actual prevalence of intracranial aneurysms in the study population is unknown, based on patient characteristics, it is likely that the incidence is not below the average of 3.2% of the general population. So probably at least 143 patients with an intracranial aneurysm underwent surgery with full heparinisation without any rupture.

Conclusion: Cardiopulmonary bypass with heparinisation is not a risk factor for rupture of an intracranial aneurysm. An unruptured intracranial aneurysm should not hinder lifesaving surgery for which cardiopulmonary bypass is required.

Introduction

Intracranial saccular aneurysms, also known as berry aneurysms because of their shape, are common acquired lesions with an overall prevalence of 3.2%.[1] Subarachnoid haemorrhage due to a ruptured aneurysm has an incidence of 6-10 per 100,000 people with several factors regarded as potential predictors of rupture. It is clear and commonly accepted that a ruptured aneurysm should be secured as soon as possible and definitively before any major surgery, regardless of the use of cardiopulmonary bypass.

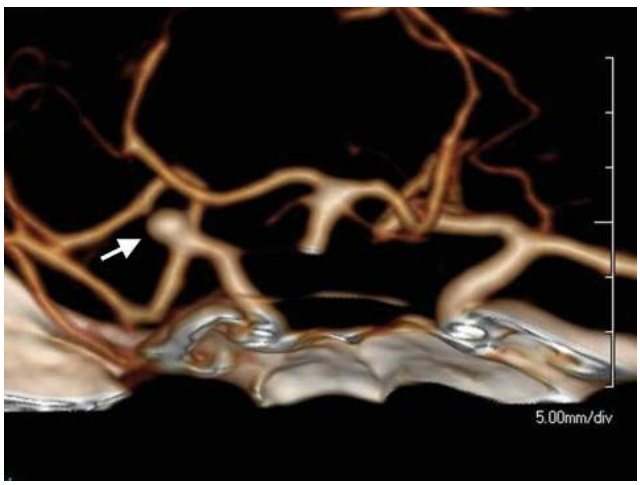

Figure 1. CT angiography of the candidate (Case 1) for lung transplantation showing an aneurysm at the left middle cerebral artery (arrow)

Physicians may consider an intracranial aneurysm to be an unacceptable risk during surgery requiring cardiopulmonary bypass with subsequent full heparinisation. Therefore, these procedures may be cancelled or postponed until the aneurysm is protected. However, the risk of aneurysm rupture during cardiopulmonary bypass procedures with full heparinisation has not yet been studied. This clinical challenge is illustrated by two candidates for lung transplantation. Data from a randomised controlled trial in 4482 patients undergoing cardiac surgery with cardiopulmonary bypass were used to estimate the risk for aneurysm rupture during such a procedure.

Case 1

A 48-year-old woman was screened for lung transplantation, because of severe chronic obstructive pulmonary disease. She had a history of hypertension and was a former smoker. Four years before, she had a subarachnoid haemorrhage from

a ruptured aneurysm of the right middle cerebral artery, from which she fully recovered. The ruptured aneurysm was surgically clipped, but an asymptomatic additional aneurysm of the left middle cerebral artery remained. Recent CT angiography showed an aneurysm with a 4 by 4 mm dome and a 2 mm neck, which was stable over time *(figure 1)*.

Case 2

A 56-year-old woman was screened for lung transplantation, because of severe lung emphysema. She had a history of hypertension and quit smoking when she was 50 years of age. Two years ago, she had a left-sided craniotomy for clipping of an unruptured middle cerebral artery bifurcation aneurysm. A small asymptomatic left-sided internal carotid artery aneurysm remained with a maximal diameter of 2.5 mm, which stayed stable over time according to follow-up CT angiographies.

Both patients are being considered for bilateral lung transplantation, which may require cardiopulmonary bypass with full heparinisation; final inclusion on the waiting list has been postponed to perform a risk assessment for perioperative aneurysm rupture.

Patients and methods

The study was approved by the appropriate Ethics authority. Written informed consent was obtained from all subjects, both from participants of the randomised clinical trial described below as well as from the patients described in the introduction. The study was registered before patient enrolment at Trial Registration clinicaltrials.gov; Identifier: NCT00293592.

The prevalence of unruptured intracranial aneurysms in the general population is 3.2%.[1] In our randomised clinical trial on dexamethasone in 4482 patients undergoing cardiac surgery with cardiopulmonary bypass and full heparinisation (DECS trial), we followed patients during the first year after surgery for major morbidity including stroke.[2]

Results

None of the participants had a haemorrhagic stroke during cardiac surgery. Only one of the 4482 patients had an aneurysmal subarachnoid haemorrhage during follow-up, but this occurred three weeks after cardiac surgery when the patient was already home. In our study population, 143 persons are expected to harbour an intracranial aneurysm. If we assume that the subarachnoid haemorrhage in the participants of the trial was still somehow related to the procedure, the cardiopulmonary bypass associated risk for aneurysm rupture would be 1/143 or 0.7% (95% confidence interval 0.1-4.9%). However, the patients were followed for one year, and a risk of rupture of 0.7% per year is comparable with the natural history of intracranial aneurysms.[3]

Discussion

We found no indication that cardiopulmonary bypass with full heparinisation is a risk factor for rupture of an intracranial aneurysm.

A limitation of our study is that the exact prevalence of intracranial aneurysm in participants of the DECS trial is unknown. In the meta-analysis by Vlak et al. that forms the basis of our analysis, the overall estimated prevalence of 3.2% (95% CI 1.9-5.2) is calculated for an average study population that was without comorbidity, consisted of 50% men, and had a mean age of 50 years.[1] However, both age above 50 (prevalence ratio 2.2; 95% CI 1.3-3.6) and atherosclerosis (prevalence ratio 1.7; 95% CI 0.9-3.0) increase the risk for harbouring an intracranial aneurysm. Our study population had a mean age of 66 years with risk factors for cardiovascular disease so it is unlikely that the prevalence of intracranial aneurysm is lower than estimated for the general population.

According to a meta-analysis in 4705 patients totalling 6556 unruptured aneurysms, the overall risk of rupture was assessed to be between 0.6% and 1.3% per patient-year at risk.[3] If the single subarachnoid haemorrhage in our study, three weeks after cardiac surgery, was related to the procedure, the cardiopulmonary bypass associated risk for aneurysm rupture would be estimated at 0.7% per patient at risk, which is comparable with the natural history of aneurysm rupture. However, based on the numbers of this meta-analysis and our study, the sample size for an unrelated matched cohort study exceeds 6000 per arm, so even in our large study population of 4482 patients, the results must be interpreted with caution.

Patient characteristics that increase the risk of aneurysmal rupture are smoking and migraine.[4] Postulated triggers for aneurysm rupture are coffee and cola consumption; physical exercise; nose blowing; straining for defecation; sexual intercourse; anger; and startling.[5]

The risk of aneurysm rupture during cardiopulmonary bypass procedures with full heparinisation has not yet been studied. We could only find one case report describing aneurysm rupture during neurosurgical clipping under the protection of hypothermic cardiac arrest with use of femoro-femoral cardiopulmonary bypass and heparinisation, but this occurred after neurosurgical dissection of the aneurysm and active external cooling to 32 °C.[6]

Although surgical clipping and endovascular coiling have shown to be effective in the prevention of rebleeding of *symptomatic* aneurysms (i.e. after aneurysmal subarachnoid haemorrhage),[7] their use for the treatment of *asymptomatic* aneurysms is not clear, since benefit of treatment cannot be seen until a follow-up of several decades. Meta-analyses on patients with unruptured intracranial aneurysms showed that the occurrence of an unfavourable outcome one year after treatment is not negligible and in general more frequent after clipping (6.7%) then after coiling (4.8%).[8-10]

Treatment should be considered for unruptured aneurysms in patients under 60 years of age, and possibly for aneurysms

larger than 7 mm in diameter in older patients, without comorbidity. The decision for or against intervention is actually more complex, as this further depends on other risk factors for spontaneous rupture, the risk of the intervention, life expectancy and comorbidity. The risk of rupture of the aneurysm is composed of patient-related (age, hypertension, race) and aneurysmal-related (size, location, previous rupture) factors.[11]

In conclusion, the risk of rupture of a small asymptomatic intracranial aneurysm located in the anterior circulation is relatively low while complications of treatment can be serious. Cardiopulmonary bypass is not a risk factor for rupture of an intracranial aneurysm, as illustrated by the absence of subarachnoid haemorrhage in any of our 4482 patients during cardiac surgery with full heparinisation. An unruptured intracranial aneurysm should not hinder life-saving surgery for which cardiopulmonary bypass is required.
Our patients are scheduled for bilateral lung transplantation. As median survival for double-lung transplantation is 7.4 years (source: www.ishlt.org) and in our institution more than 10 years and aneurysm treatment risk exceeds the aneurysm rupture risk for this period, we do not plan to perform aneurysm repair in these patients.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors; however we did extract information from our previously published study, which was supported by the Netherlands Organization for Health Research and Development (ZonMw), grant number 80-82310-98-08607 and the Dutch Heart Foundation, grant number 2007B125.

References

1. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. Lancet Neurol. 2011;10:626-36.
2. Dieleman JM, Nierich AP, Rosseel PM, et al. Intraoperative high-dose dexamethasone for cardiac surgery: a randomized controlled trial. JAMA. 2012;308:1761-7.
3. Wermer MJ, van der Schaaf IC, Algra A, Rinkel GJ. Risk of rupture of unruptured intracranial aneurysms in relation to patient and aneurysm characteristics: an updated meta-analysis. Stroke. 2007;38:1404-10.
4. Vlak MH, Rinkel GJ, Greebe P, Algra A. Risk of Rupture of an Intracranial Aneurysm Based on Patient Characteristics: A Case-Control Study. Stroke. 2013;44:1256-9.
5. Vlak MH, Rinkel GJ, Greebe P, et al. Trigger factors and their attributable risk for rupture of intracranial aneurysms: a case-crossover study. Stroke. 2011;42:1878-82.
6. Strebel S, Mendelowitsch A, Kindler C. Rupture of a giant intracranial aneurysm while starting cardiopulmonary bypass for hypothermic circulatory arrest. J Neurosurg Anesthesiol. 2004;16:263-5.
7. Molyneux A , Kerr R , Stratton I, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2,143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360:67-1274.
8. Kotowski M, Naggara O, Darsaut TE, Raymond J. Systematic reviews of the literature on clipping and coiling of unruptured intracranial aneurysms. Neurochirurgie. 2012;58:125-39.
9. Hwang JS, Hyun MK, Lee HJ, et al. Endovascular coiling versus neurosurgical clipping in patients with unruptured intracranial aneurysm: a systematic review. BMC Neurol. 2012;12:99.
10. Lawson MF, Neal DW, Mocco J, Hoh BL. Rationale for Treating Unruptured Intracranial Aneurysms: Actuarial Analysis of Natural History Risk versus Treatment Risk for Coiling or Clipping Based on 14,050 Patients in the Nationwide Inpatient Sample Database. World Neurosurg. 2013;79:472-8
11. Greving JP, Wermer MJ, Brown RD Jr, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. Lancet Neurol. 2014;13:59-66.