Large amounts of gas were seen in the venous circulation in all of these cases. If we postulate that, in a rapid ascent,barotrauma causes expanding gas in the alveoli to leak into the pulmonary veins, then one would expect most of the gas to be in the arterial system, but this is not the case. This pattern of distribution of the gas may indicate that the lungs trap gas bubbles more effectively than other tissues, such as the brain,[4] once the gas has passed thought the systemic circulation. Alternatively the gas may enter the venous circulation through the pulmonary lymphatic system as has been suggested in neonatal systemic air embolism.[5]

Conclusions

Decomposition and resuscitation can result in intravascular gas at autopsy. In view of the possible confusion arising from the production of decompositional gas, in performing diving autopsies it is important to autopsy the body as soon as possible after death. Analysis of the gas for hydrogen and carbon dioxide may indicate whether the gas is due to decomposition or not. In deep diving fatalities some gas formation due to decompression does occur.[2,3] It is not clear whether decompression makes any contribution to intra-vascular gas formation in diving fatalities during more superficial dives.

References

1 Hayman JA. *Postmortem technique in fatal diving accidents. Broadsheet No. 27.* Sydney: Royal College of Pathologists of Australasia, 1987

2. Edmonds C. Investigation of diving fatalities. In *Diving and subaquatic medicine. 3rd ed.* Edmonds C, Lowry C and Pennefather J. Eds. Oxford: Butterworth-Heineman Ltd, 1992: 438-447

3. Elliott DH and Bennett PB. Underwater Accidents. In *The physiology and medicine of diving. 4th ed.* Bennett PB and Elliott DH. Eds. Philadelphia: W.B. Saunders, 1993: 250-251

4 Gorman D. The pathology of decompression illness. In *Diving and hyperbaric medicine. 2nd ed.* Gorman D. Ed. Adelaide: Hyperbaric Medical Unit, Royal Adelaide Hospital, 1993; 9.1

5 Booth TN, Royal SA and Allen BA. Lymphatic air embolism: a new hypothesis regarding the pathogenesis of neonatal systemic air embolism. *Pediatr Radiol* 1995; 25: S220-S227

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OPEN CHAMBER CARDIAC SURGERY: A CLINICAL INJURY MODEL FOR ARTERIAL GAS EMBOLISM

Simon Mitchell, Ora Pellett and Des Gorman

Summary

Cerebral arterial gas embolism (CAGE) can occur in divers breathing compressed gas and as a consequence of some medical procedures. Open chamber left heart surgery, in particular, is invariably complicated by CAGE, although manifestations may be "subclinical". This paper discusses the utility of open chamber left heart surgery as a clinical injury model for CAGE in divers and other groups.

Key Words

Bubbles, CAGE, cardiovascular, investigations, research.

Review

Cerebral arterial gas embolism (CAGE) may occur in compressed gas diving following either pulmonary barotrauma or right to left shunting of venous inert gas bubbles.[1] Clinically, in divers, there is rapid onset of neurological phenomena such as altered consciousness, visual changes, cognitive changes, and sensorimotor deficits. The natural history of CAGE in divers is complex and may include death (often by drowning), persistent neurological symptoms, spontaneous recovery and relapse despite initial spontaneous recovery. CAGE is one of several mechanisms of bubble-induced injury collectively referred to as decompression illness (DCI).[2] The contribution of CAGE to morbidity in many cases of DCI is difficult to assess since several injury mechanisms may be involved simultaneously. This difficulty complicates the study of therapeutic intervention targeted at CAGE and is compounded by the usual absence of any pre-morbid data, a variable extent of injury and an even greater variation in the time from onset of illness in divers to presentation for treatment.

Cerebral arterial gas embolism also occurs in cardiac surgery. Any operation supported by a cardiopulmonary bypass (CPB) circuit carries the risk of CAGE as there are numerous ways in which air can be introduced into the body from the circuit. These include: incomplete pre-bypass de-airing of the circuit;[3] the use of a bubble oxygenator;[4] low blood volume in the venous reservoir;[5] high blood flow rates and entrainment of air into the venous inflow to the CPB machine.[6] In operations where the heart is not opened (closed chamber procedures), such as coronary artery bypass grafting (CABG), the CPB circuit is the main source of emboli. However, there is much

greater risk of CAGE in those procedures involving open chamber surgery of the left heart, such as valve replacement and repair of congenital defects. Air introduced to the heart chambers during these procedures may be ejected into the aorta when the heart is closed, resuscitated and allowed to work. Surgeons attempt to remove intracardiac air before cardiac ejection using "de-airing" techniques. However, studies utilising echocardiographic or Doppler techniques have documented that conventional de-airing techniques are not completely effective.[7-12] Recent studies have suggested that these conventional techniques fail because air is trapped in the pulmonary veins during surgery[7,11] and is not dislodged until the heart is resuscitated and pulmonary blood flow increases to normal levels.[7] These bubbles will pass to the left heart and in turn into the aorta. A novel and effective de-airing technique which allows the heart to develop physiological output without ejection into the systemic circulation has been reported[13] but is not yet widely used.

The use of cardiac surgery patients in a study of CAGE pathophysiology or treatment confers the following significant advantages over a group of divers with DCI: premorbid neurological and neurocognitive function can be assessed so that each patient can serve as their own control; the exposure to bubbles can be quantified using Doppler devices; and any treatment can be given at the same time in relation to the emboli exposure. However, before cardiac surgical patients are used in this way, a relationship between bubble exposure and outcome must be demonstrated. Moreover, to allow for reasonable group sizes in a trial of different treatments, adverse outcomes must occur frequently.

There is a plethora of studies showing adverse neurocognitive outcomes in patients after cardiac surgery. Many (50-70%) cardiac surgical patients are reported as suffering from post-operative cognitive deficits of some type, and 2-5% are said to suffer a peri-operative stroke.[14] It is known that the incidence of post-operative neurocognitive deficit is higher in coronary artery bypass graft (CABG) patients than in patients undergoing forms of vascular surgery which do not involve CPB,[15] and it is generally agreed that embolism of the cerebral circulation is an important contributing factor to such deficits.[16]

The argument that embolic brain injury is common and important in closed heart cardiac surgery such as CABG is supported by studies in which any deterioration in post-operative neurocognitive performance has been correlated against emboli exposure measured using Doppler devices. Stump and colleagues[17] reported a mean left common carotid artery emboli count of 130 in patients with neurocognitive deficit 5-7 days after CABG surgery and of only 63 in patients without deficit. Pugsley and colleagues[18] reported the percentage incidence of neurocognitive deficit at 8 weeks after CABG surgery as 9, 23, 31, and 43 in patients exposed to <200, 201-500, 501-1000 and >1000 middle cerebral artery (MCA) emboli respectively. Clarke and colleagues[19] reported cerebral complications after CABG surgery in 70% of patients exposed to greater than 60 (mean 118) MCA emboli and in only 30% of patients exposed to less than 60 MCA emboli.

Although these studies support the hypothesis of embolic brain injury during surgical procedures involving CPB, attribution of these injuries solely to bubbles is not possible. Although the Doppler devices used are more likely to detect bubbles than solid emboli of the same size,[20] CPB does generate non-gaseous emboli such as antifoam particles[21] and fibrin-platelet aggregates.[22] Indeed, there is still a considerable uncertainty about the relative importance of the different emboli generated by CPB. Moody and his colleagues used an alkaline phosphatase staining technique to demonstrate small capillary and arteriolar dilatations (SCADs) in the brains of patients who died after CPB and in dogs sacrificed after experimental CPB.[23,24] No SCADs could be demonstrated in control patients or animals who had not undergone CPB. The SCADs exhibited menisci at their ends and appeared empty. They were initially postulated to be air or fat emboli,[23] but subsequent work has shown that some of these lesions exhibit granular birefringence. Others have stained positive for glycoproteins and glycolipids.[24] These would be unusual findings in bubbles, although a bubble may acquire a lipid content as it strips surfactant from the vessel endothelium.[25]

In view of this confusion, closed chamber cardiosurgical procedures in which CPB is the principal source of emboli are probably not a suitable clinical injury model for CAGE in divers and other groups primarily injured by bubbles.

A much greater degree of cerebral embolism in open chamber procedures has been documented using Doppler devices. Stump and his colleagues[26] recorded a mean of 1339 left common carotid artery emboli (range 38-4455) throughout open chamber valve replacement surgery. In contrast, closed chamber CABG patients were only exposed to a mean of 62 emboli (range 23 - 107). Other researchers have recorded similar results.[7,9] This greater exposure in valve surgery patients is almost certainly accounted for by bubbles ejected from the left heart at the end of the procedure. Studies using transoesophageal echocardiography in the investigation of de-airing techniques support this contention. Bubbles have been observed emerging from the pulmonary veins soon after heart ejection is resumed,[7] or being trapped in sites like the left ventricular apex and right upper pulmonary vein under the influence of buoyancy, only to be "stirred up and expelled away" with the resumption of cardiac ejection.[11]

Despite the greater bubble exposure in open chamber surgery patients, comparisons of neurological outcome between this group and closed chamber (CABG)

surgery patients are confusing.[27] However, such comparisons are tenuous since CABG patients are usually older and affected by other risk factors for poor outcome such as carotid artery and cerebrovascular disease. The most recent review of this issue suggests that, on balance, open chamber patients are at greater risk of adverse neurological outcome.[27]

Nevertheless, for open chamber heart surgery patients to be used as a model of CAGE, it is still important to show a correlation exists between neurological outcome and bubble exposure. Surprisingly, there are no relevant published studies. However, we have produced some relevant preliminary data from our randomised prospective double blinded trial of lignocaine in cerebral protection in open chamber left heart surgery at Green Lane Hospital, Auckland, New Zealand.

Methods

The subjects were 23 patients undergoing left heart valve replacement surgery and who were enrolled in the lignocaine trial. This trial was approved by the North Health Ethics Committee in August 1994. There were 15 males and 8 females, and the mean age was 54.9 (SD 10.1). All patients underwent a battery of 11 neurocognitive tests before surgery. All tests were performed by the same research psychologist and in most cases were conducted within the same designated office at the hospital.

The right common carotid artery was continuously monitored for emboli activity from 5 minutes before cardiac cannulation until 20 minutes after withdrawal of CPB, using a Rimed Flowlink 300 colour flow Doppler (Rimed, Tel Aviv, Israel) interfaced to a purpose built emboli counting microprocessor. The nature and use of this device has been described in more detail elsewhere.[5] Doppler signal processors may be confounded in many ways,[28] and emboli "counts" are not exact. We therefore refer to the count as an "index of microembolic activity" (IMA). Nevertheless, calibration of our device has shown that increases in IMA are directly proportional to emboli numbers.[5]

The neurocognitive tests were repeated for all patients at 6 to 8 days, eight weeks and six months after surgery. Once again, all tests were conducted by the same research psychologist. Both the patients and the psychologist were blinded to the emboli exposure.

Only the change between the pre-operative and eight day performance in a computer generated test of reaction time (psychomotor speed) was analysed before the 1997 SPUMS Annual Scientific Meeting. A univariate linear regression was performed for the relationship between emboli exposure and any change in reaction time at eight days after surgery using the Systat statistical package.

Results

IMA ranged from 247 to 6,959 with a mean of 2,334 (SD 1694) for the 23 patients. Most emboli (mean fraction of total = 0.73 (SD 0.26) were recorded at the end of the procedure when the heart began to eject. Almost all signals were ultrasonically typical of bubbles. The regression plot for the relationship between IMA and change in reaction time at 8 days post surgery is shown in Figure 1. Note that an increase in reaction time (indicating a in performance) is plotted as a *negative* value. There was a significant decline in performance as IMA increased ($p < 0.025$).

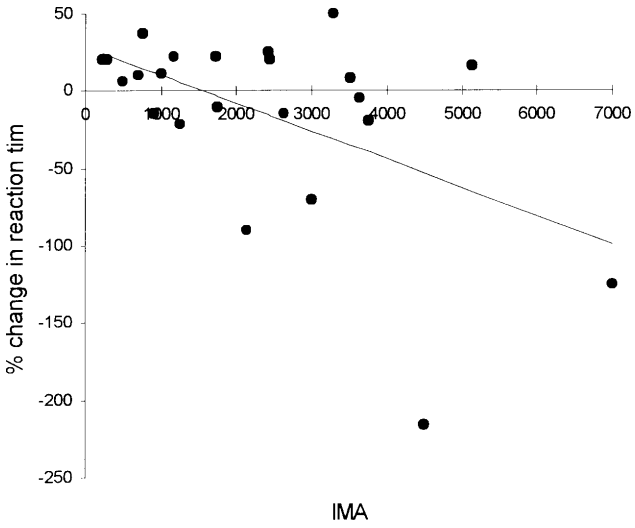

Figure 1. Relationship between change in reaction time at 8 days after surgery and perioperative emboli exposure An increase in reaction time is plotted as a negative value. R=0.52. p<0.025.

Discussion

These preliminary results suggest that increased exposure to emboli in open chamber left heart surgery is associated with a decline in neurocognitive performance. Given that the vast majority of the emboli are bubbles, this finding would support the use of open chamber cardiac surgery as a clinical injury model for CAGE in divers and other groups. However, this preliminary data must be interpreted with caution. First, all patients were part of a randomised, double blinded trial of lignocaine in cerebral protection during cardiac surgery which was not unblinded for this analysis. It follows that approximately half of these patients have received a drug which may have modified their neurocognitive outcome. Second, this analysis describes outcome in 1 of 11 tests, at 1 of 3 points in time, for 23 of 60 patients. We must wait for completion of all patient follow up, for unblinding of the lignocaine trial and the analysis of results for all tests at each follow up before drawing firm conclusions. This data will be reported in due course.

References

1 Francis TJR and Gorman DF. Pathogenesis of the decompression disorders. In *The physiology and medicine of diving (4th edition).* Bennett PB and Elliott DH. Eds. London: WB Saunders, 1993; 454-480

2 Francis TJR and Smith DH. Eds. *Describing decompression illness: The forty-second Undersea and Hyperbaric Medical Society workshop*. Bethesda, Maryland: Undersea and Hyperbaric Medical Society, 1991

3 Stump DA. Etiologic factors affecting brain function after cardiopulmonary bypass. *Proceedings of the 15th Annual San Diego Cardiothoracic Surgery Symposium* 1995: 106-113

4 Blauth CI, Smith PL, Arnold JV, Jagoe JR, Wootton R and Taylor KM. Influence of oxygenator type on the prevalence and extent of microembolic retinal ischaemia during cardiopulmonary bypass - assessment by digital image analysis. *J Thorac Cardiovasc Surg* 1990; 99: 61-69

5 Mitchell SJ, Willcox T, McDougall C and Gorman DF. Emboli generation by the Medtronic Maxima hard-shell adult venous reservoir in cardiopulmonary bypass circuits: a preliminary report. *Perfusion* 1996; 11: 145-155

6 Mitchell SJ, Willcox T and Gorman DF. Bubble generation and venous air filtration by hard shell venous reservoirs: a comparative study. *Perfusion* 1997; 12: 325-333

7 Tingleff J, Joyce FS and Pettersson G. Intraoperative echocardiographic study of air embolism during cardiac operations. *Ann Thorac Surg* 1995; 60: 673-677

8 Van der Linden J and Casimir-Ahn H. When do cerebral emboli appear during open heart operations? A transcranial Doppler study. *Ann Thorac Surg* 1991; 51: 237-241

9 Ohnishi Y, Uchida O, Hayashi Y, Kuro M, Sugimoto K and Kuriyama Y. Relationship between retained microbubbles and neuropsychologic alterations after cardiac operation. *Masui* 1995; 44: 1327-1333

10 Oka Y, Inoue T, Hong Y, Sisto DA, Strom JA and Frater RW. Retained intracardiac air - Transesophageal echocardiography for definition of incidence and monitoring removal by improved techniques. *J Thorac Cardiovasc Surg* 1986; 91: 329-338

11 Orihashi K, Matsuura Y, Hamanaka Y, Sueda T, Shikata H and Nomimura T. Retained intracardiac air in open heart operations examined by transesophageal echocardiography. *Ann Thorac Surg* 1993; 55: 1467-1471

12 Rescigno G, Riom H, Hallali P, Nottin R and Arnaud-Crozat E. Doppler analysis of the left venting line: an effective and simple technique to control heart de-airing. *Cardiovasc Surg* 1995; 3: 65-69

13 Milsom FP and Mitchell SJ. A superior heart de-airing technique reduces cerebral arterial gas embolism following left heart surgery. *Undersea Hyperbaric Med* 1997; 24 (Suppl): 24 (Abstract reprinted on page 111)

14 Stump DA, Rogers AT, Hammon JW and Newman SP. Cerebral emboli and cognitive outcome after cardiac surgery. *J Cardiothorac Vasc Anesth* 1996; 10: 113-119

15 Shaw PJ, Bates D, Cartlidge NEF, French JM, Heaviside D, Julian DG and Shaw DA. Neurologic and neuropsychological morbidity following major surgery: comparison of coronary artery bypass and peripheral vascular surgery. *Stroke* 1987; 18: 700-706

16 Treasure T. Interventions to reduce cerebral injury during cardiac surgery - the effect of arterial line filtration. *Perfusion* 1989; 4: 147-152

17 Stump DA, Tegeler CH, Rogers AT, Coker LH, Newman SP, Wallenhaupt SL and Hammon JW. Neuropsychological deficits are associated with the number of emboli detected during cardiac surgery. *Stroke* 1993; 24: 509

18 Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M and Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. *Stroke* 1994; 25: 1393-1399

19 Clark RE, Brillman J, Davis DA, Lovell MR, Price TRP and Magovern GJ. Microemboli during coronary bypass grafting - genesis and effect on outcome. *J Thorac Cardiovasc Surg* 1995; 109: 249-258

20 Moehring MA and Klepper JR. Pulse Doppler ultrasound detection, characterisation and size estimation of emboli in flowing blood. *IEEE Trans Biomed Engineering* 1994; 41: 35-44

21 Orenstein JM, Sato N, Aaron B, Buchholz B and Bloom S. Microemboli observed in deaths following cardiopulmonary bypass surgery: silicone antifoam agents and polyvinyl chloride tubing as sources of emboli. *Hum Pathol* 1982; 13: 1082-1090

22 Blauth CI, Arnold JV, Schulenberg WE, McCartney AC, Taylor KM and Loop FD. Cerebral microembolism during cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1988; 95: 668-676

23 Moody DM, Bell MA, Challa VR, Johnston WE and Prough DS. Brain microemboli during cardiac surgery or aortography. *Ann Neurol* 1990; 28: 477-486

24 Challa VR, Moody DM and Troost BT. Brain embolic phenomena associated with cardiopulmonary bypass. *J Neurol Sci* 1993; 117: 224-231

25 Hills BA and James PB. Microbubble damage to the blood brain barrier: Relevance to decompression sickness. *Undersea Biomed Res* 1991; 18: 111-116

26 Stump DA, Stein CS, Tegeler CH, Hitchings LP, Hager R, Eicke M and Burke GL. Validity and reliability

of an ultrasound device for detecting carotid emboli. *J Neuroimag* 1991; 1: 18-22

27 Nussmeier N. Adverse neurologic events: risks of intracardiac vs extracardiac surgery. *J Cardiothorac Vasc Anesth* 1996; 10: 31-7

28 Kurusz M and Butler BD. Embolic events and cardiopulmonary bypass. In *Cardiopulmonary bypass: Principles and practice*. Gravlee GP, Davis RF and Utley JR. Eds. Baltimore: Williams and Wilkins, 1993: 267-281

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A superior heart de-airing technique reduces cerebral arterial gas embolism following left heart valve surgery. Milson FP and Mitchell SJ. *Undersea Hyperbaric Med* 1997; 24 (Suppl): 24

Abstract

Background

Cerebral arterial gas embolism (CAGE) invariably occurs at termination of cardiopulmonary bypass (CPB) in left heart valve surgery. CAGE is not prevented by conventional left heart "de-airing" methods and has been linked to post-operative stroke and neurocognitive deficits. We have developed and assessed a novel de-airing technique which utilises high flow left ventricular and aortic venting from the working heart into the CPB venous line, prior to aortic declamping. This technique allows the heart to establish physiological output before the aortic clamp is removed. Ejected emboli pass to the CPB circuit, rather than the systemic circulation, and are removed by the circuit's protective elements.

Methods

The right common carotid artery was monitored throughout the left heart valve surgery using a colour flow Doppler interfaced to an emboli counting microprocessor in 21 consecutive patients de-aired conventionally (group 1), 9 consecutive patients de-aired by the novel technique (group 2) and 4 coronary artery bypass graft patients who did not require de-airing (group 3).

Results

The mean emboli count recorded after aortic declamping was 2,580 ± 321 (SEM) and 293 ± 110 in the group 1 and group 2 patients respectively (p=<0.001). The efficacy of the novel technique improved during the series: four of the last five group 2 patients were exposed to similar trivial numbers of emboli after aortic declamping (less than 20) as the group 3 patients.

Conclusions

Cerebral arterial gas embolism associated with left heart valve surgery is significantly reduced by the novel de-airing technique.

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Key Words

Bubbles, CAGE, cardiovascular, investigations, research.