INTERACTIVE CARDIOVASCULAR AND THORACIC SURGERY

Interactive CardioVascular and Thoracic Surgery 9 (2009) 323-326

www.icvts.org

# Best evidence topic - Valves

# Does the use of carbon dioxide field flooding during heart valve surgery prevent postoperative cerebrovascular complications?

Salvatore Giordanoa,\*, Fausto Biancarib

<sup>a</sup>Department of Surgery, Vaasa Central Hospital, Hietalahdenkatu 2-4, 65130, Vaasa, Finland <sup>b</sup>Department of Surgery, Oulu University Hospital, Oulu, Finland

Received 1 March 2009; received in revised form 29 April 2009; accepted 30 April 2009

## Summary

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was whether there is any benefit with the use of carbon dioxide  $(CO_2)$  field flooding techniques in heart valve surgery, in order to reduce postoperative neurological complications. Altogether 202 articles were found using the reported search, and six of them were used to answer the clinical question. All but one trial, were prospective, randomised. Four studies reported a significantly lower intracardiac bubble count in the  $CO_2$  group. A significant reduction of p300 peak latencies in the  $CO_2$  group was observed in one study. Otherwise, neurocognitive test batteries did not reveal any advantages of  $CO_2$  field flooding in two studies. Three studies reported on postoperative cerebrovascular complications and the overall rate of stroke, transient ischemic attack (TIA) or prolonged reversible ischemic neurological deficit was 1.2% in the  $CO_2$  group and 2.5% in the control group (P=ns). Although the use of  $CO_2$  field flooding has been observed to be associated with a significantly lower count of intracardiac air bubbles, and improved survival in two small studies, so far there is no evidence of a sustained reduction of cerebrovascular complications with the use of this method.

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Keywords: Evidence-based medicine; Heart valve surgery; Carbon dioxide field flooding; Air embolisation; Stroke

# 1. Introduction

A best evidence topic was constructed according to a structured protocol, which is described in detail in the ICVTS [1]. This article updates a previous best evidence topic published in 2004 [2].

## 2. Three-part question

In [patients undergoing heart valve surgery] can [carbon dioxide field flooding] reduce [postoperative neurological complications]?

## 3. Clinical scenario

You are a resident and you notice that surgeons use carbon dioxide  $(CO_2)$  field flooding in order, they say, to reduce the risk of air embolism during heart valve surgery. Since  $CO_2$  is 25 times more soluble in blood and tissues than air [3], and  $CO_2$  emboli are better tolerated than air emboli [4], you resolve to check in the literature whether this method is neuroprotective.

## 4. Search strategy

Medline, Ovid and Cochrane databases were searched from date of inception to January 2009.

\*Corresponding author. Tel.: +358 443346119; fax: +358 6323152. E-mail address: salvatoregiordano@yahoo.it (S. Giordano). [CARBON DIOXID.mp AND VALVE SURGERY.mp]. In addition, the reference lists of all relevant articles were searched.

## 5. Search outcome

Two hundred and two abstracts were identified and ten were deemed to be relevant. Most of the papers were considered not relevant as none focused on its potential neuroprotective efficacy. Experimental studies were excluded from this analysis. Thus, we were able to review five prospective randomised trials and one prospective non-randomised study which we used to answer the question. Their results are summarised in Table 1.

#### 6. Results

Flooding the surgical field with  $CO_2$  reduces the incidence of intracardiac air by 85%, possibly because of the density and solubility of  $CO_2$  [5]. The density of  $CO_2$  is 1.5 times that of air, so that  $CO_2$  empirically and preferentially fills the dependent parts of the surgical field [6].

Webb et al. [5] observed that, among patients undergoing heart valve surgery, those who had not  $CO_2$  field flooding had persistent air bubbles for at least 30 min after resumption of heart beat and usually for 45 min. Patients who underwent surgery with  $CO_2$  field flooding had no air bubbles remaining <1 min in 48 out of 56 patients. These patients were not randomised and the trans-oesophageal echocardiographer was not blinded to the study group

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Table 1 Best evidence papers

Author, date, journal and country	Patient group	Outcomes	Key results	Study weakness
Webb et al., (1997), Ann Thorac Surg, USA, [5] Non-randomised, controlled study (level 2b)	CO <sub>2</sub> field flooding group (56 patients) vs. control group (22 patients) in heart valve surgery	Trans-oesophageal appearance of air bubbles inside the heart or the aorta	In the control group residual foam was detected inside the heart, aorta or both for at least 30 min  No foam was observed at the resumption of heart beat in 34/56 patients and in 14/56 patients all bubbles disappeared within the first minute. The remaining 8 patients had complete disappearance of bubbles in 1–24 min	Non-randomised study  The incidence of neurological complications was not reported
Martens et al., (2001), Ann Thorac Surg, Germany, [7] Randomised, controlled trial (level 1b)	CO <sub>2</sub> field flooding group (31 patients) vs. control group (31 patients) in heart valve surgery	Mortality  Myocardial damage  Neurocognitive function	Mortality: 3% in CO <sub>2</sub> group vs. 16.1% in control group ( <i>P</i> =not stated)  Creatinine kinase MB was significantly increased in the CO <sub>2</sub> group  Neurocognitive tests did not reveal a statistically significant difference  Two patients exhibited prolonged confusion in CO <sub>2</sub> group (6.4%) and 1 patient presented prolonged reversible ischemic neurologic deficit with hemiparesis in control group (3%)	Study groups too small to reveal differences in mortality or major neurologic adverse events
Kalpokas et al., (2003), Perfusion, Australia, [8] Randomised, controlled trial (level 1b)	CO <sub>2</sub> field flooding (10 patients) vs. mechanical de-airing (8 patients) during heart valve surgery	Trans-oesophageal assessment scores of air bubbles inside the cardiac cavities	Median score was 2.25 in mechanical de-airing group vs.  1.0 in the CO <sub>2</sub> field flooding group (P=0.01)  No neurological complication occurred in the study groups	Small size study (18 patients randomised, 8 in mechanical de-airing group and 10 in CO <sub>2</sub> field flooding group)
Svenarud et al., (2004), Circulation, Sweden, [9] Randomised, controlled trial (level 1b)	CO <sub>2</sub> field flooding (10 patients) vs. mechanical de-airing (10 patients) during heart valve surgery	Trans-oesophageal assessment of maximal number of gas emboli inside left atrium, left ventricle and ascending aorta  Myocardial damage assessed by troponin T and creatine kinase-MB	Median number of microemboli up to 20 min after the end of CPB was 161 in the $\mathrm{CO_2}$ group vs. 723 in the control group $(P < 0.001)$ Number of detectable microemboli after CPB fell to zero in 7 min in the $\mathrm{CO_2}$ group and in 19 min in the control group $(P < 0.001)$ Troponin T and creatine kinase-MB on day 1 did not differ between the groups	The incidence of neurological complications was not reported
Skidmore et al., (2006), J Extra Corpor Technol, USA, [10] Randomised, controlled trial (level 1b)	CO <sub>2</sub> field flooding group (21 patients) vs. control group/air flooding (22 patients) during heart valve surgery	Trans-oesophageal assessment of air bubbles inside the left atrium and left ventricle  Segmental wall motion at baseline, 1 min, 10 min and 60 min after aortic declamping  28 patients were evaluated with Trailmaking A and B and	Bubble count was higher in the control group $(3.06 \pm \text{ vs.} 1.78 \pm, P = 0.10)$ Segmental wall motion 1–60 min was better in the CO <sub>2</sub> group compared to the control group $(P = 0.4)$ . Particularly, the inferior wall tended better function in CO <sub>2</sub> group  Re-operation rate was significantly higher in the CO <sub>2</sub> group $(4.5\% \text{ vs. } 33.3\%, P = 0.02)$	The incidence of neurological complications was not reported

Table 1 (Continued)

Author, date, journal and country	Patient group	Outcomes	Key results	Study weakness
		Rey Auditory Verbal	No difference	
		Memory learning	in transient	
		preoperatively, 2 days	neurocognitive decline	
		and 2 weeks after surgery	was observed	
Martens et al.,	CO <sub>2</sub> field flooding group	Neurocognitive testing	On 5th postoperative day p300	_
(2008), Ann Thorac	(39 patients) vs. control	and p300 auditory evoked	peak latencies were significantly	
Surg, Germany, [11]	group (41 patients)	potential peak latencies	shorter in the CO <sub>2</sub> group	
	during heart valve	were performed	$(390 \pm 68 \text{ ms vs. } 429 \pm 75 \text{ ms,}$	
	surgery	preoperatively and on 5th	P = 0.02)	
Randomised,		postoperative day		
controlled trial			Neurocognitive tests did not	
(level 1b)		Neurocognitive deficit	reveal differences between study	
		was defined as a 20%	groups	
		decrement in two or	Mantalitus 2 (0) in the CO manua	
		more tests	Mortality: 2.6% in the CO <sub>2</sub> group	
		Other outcome end-	and 4.9% in the control group, <i>P</i> =0.56	
		points: mortality,	P=0.36	
		mortality, cerebrovascular	Stroke, TIA or PRIND: 0% in the	
		events or confusional	CO <sub>2</sub> group and 4.9% in the control	
		syndrome	group, $P=0.18$	
		•		
			Confusional syndrome: 12.8% in	
			the $CO_2$ group and 4.9% in the	
			control group, $P=0.26$	

assignment. In addition, the incidence of postoperative stroke or cerebrovascular complications were not reported. In 2001, Martens et al. [7] reported the results of a prospective randomised study on  $CO_2$  insufflation into the thoracic cavity compared to conventional de-airing techniques. They did not find any statistically significant differences between the two groups in terms of mortality or neurocognitive function. However, mortality rate was lower in the  $CO_2$  field flooding group (3% vs. 16%, P-value not stated) and the number of high-risk patients was higher in the experimental group. Furthermore, postoperatively and 24 h after surgery, creatinine kinase MB was higher in the  $CO_2$  field flooding group (38.0 $\pm$ 4.1 vs. 28.0 $\pm$ 2.1, P=0.02). In a prospective randomised trial, Kalpokas et al. [8]

recorded the amount of intracardiac bubbles during openheart valve surgery comparing mechanical de-airing and CO<sub>2</sub> field flooding. At transesophageal echocardiography, the bubble count was higher in the mechanical de-airing group compared with CO<sub>2</sub> flooding group and neurological complications were not detected in any of the study groups. The main problem with this study is its small size (only 18 patients randomised).

In 2004, Svenarud et al. [9] performed a prospective randomised trial including 20 patients undergoing first time single-valve replacement (mitral or aortic valve). Using transesophageal echocardiography, they observed a median number of microemboli of 161 in the  $\rm CO_2$  group vs. 723 in the control group (P < 0.001). No data on postoperative cerebrovascular complications have been reported by the authors and the study population was small.

In another randomised study, Skidmore et al. [10] recorded intracardiac bubbles and segmental wall motion in 43 patients who underwent heart valve surgery, 21 randomised to  $\mathrm{CO}_2$  field flooding and 22 to air field flooding. Bubbles count was higher in the air group than  $\mathrm{CO}_2$  group (mean:

3.06 vs. 1.78, P=0.10) and segmental wall motion at 1–60 min was better in the  $CO_2$  group (P=0.04), particularly in the inferior wall. The authors came to the conclusion that flooding surgical field with  $CO_2$  is associated to improved myocardial function and less air bubbles in the heart. They did not report any data regarding postoperative cerebrovascular complications, but they performed some neurocognitive testing in 28 patients, without detecting any significant difference.

More recently, Martens et al. [11] performed a prospective randomised trial on 80 patients undergoing open-heart valve surgery comparing CO<sub>2</sub> surgical field flooding with conventional de-airing. They used six battery neurocognitive tests and recorded p300 wave auditory-evoked potentials in order to evaluate the brain function. The authors observed a significant reduction of p300 peak latencies in the CO<sub>2</sub> group on the 5th postoperative day. Neurocognitive test batteries did not reveal any differences between groups. However, immediate postoperative mortality (2.6% vs. 4.9%, P=0.56), stroke, transient ischemic attack (TIA) or prolonged reversible ischemic neurological deficit (0% vs. 4.9%, P=0.18) were less frequently observed in the CO<sub>2</sub> group, except confusional syndrome, which was higher in the  $CO_2$  group (12.8% vs. 4.9%, P=0.26). These differences did not reach statistical significance.

Three studies reported on postoperative cerebrovascular complications [7, 8, 11]. When the results of these studies were summed, the rate of stroke, TIA or prolonged reversible ischemic neurological deficit was 1.2% in the  $CO_2$  group and 2.5% in the control group (P=ns).

#### 7. Clinical bottom line

In a previous best evidence topic on this issue [2], the authors concluded that the solubility of CO<sub>2</sub> emboli justifies

the efforts to replace intracavital air with  $CO_2$  in openheart surgery to reduce gaseous emboli. However, the present review of currently available studies shows that there is no evidence on the neuroprotective efficacy with this method. Beside the costs of this technique, it has been reported that elevated blood levels of  $CO_2$  can be reached with field flooding techniques and it may result in acidosis [12, 13].

Although the use of  $\mathrm{CO}_2$  field flooding has been observed to be associated with significantly lower count of intracardiac air bubbles, and improved survival in two small studies, so far there is no evidence of a sustained reduction of cerebrovascular complications with the use of this method.

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