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Early jugular bulb oxygenation monitoring in comatose patients after an out-of-hospital cardiac arrest

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Abstract *Objective:* To determine the role of early jugular bulb oxygenation monitoring in comatose patients after cardiac arrest.
Design: Prospective sequential study.
Setting: Medical intensive care unit in a university hospital.
Patients: Thirteen patients comatose after out-of-hospital cardiac arrest.
Interventions: A standard hemodynamic protocol.
Measurements and results: Jugular bulb oxygen saturation levels and oxygen extraction ratios could not discriminate between patients with good (6) and poor (7) cerebral outcome. This was also true for the jugular bulb-arterial lactate difference. Survivors had significantly higher overall oxygen transport values than non-survivors.
Conclusions: Jugular bulb oxygenation monitoring during the first few hours after cardiac arrest cannot reliably discriminate between comatose patients with a good and poor cerebral outcome. Further studies with an extended monitoring period are thus required.

Key words Cardiopulmonary resuscitation · Cerebral resuscitation · Out-of-hospital cardiac arrest · Coma · Jugular bulb oxygenation monitoring

Introduction

Jugular bulb oxygenation monitoring is frequently used in patients with severe traumatic brain injury [1–3]. The cerebral extraction of oxygen provides information about the degree of adequacy of cerebral blood flow relative to cerebral oxygen consumption [4]. Normal jugular bulb oxygen saturation (SbO_2) is ±65% [5]. The main criticism against its general use is that SbO_2 values reflect global brain oxygenation and may be normal in the case of regional disturbances.

Cardiac arrest is a form of global brain hypoxia and may result in extensive cerebral damage. Calcium shifts, brain tissue lactic acidosis, and increases in brain free fatty acid levels and extracellular excitatory amino acids are a few features of its extremely complex pathogenesis [6]. Due to its complex nature, specific measures have not proven to be useful in comatose patients resuscitated after cardiac arrest [7–9]. Therefore, in practice, general measures that raise mean arterial pressure and increase overall cerebral blood flow are frequently recommended, although no proof of their efficacy exists [6–10]. Due to a possible defect in cerebral blood flow autoregulation, it is not completely clear whether an increase in systemic blood flow will result in an increase in cerebral blood flow. Furthermore, studies during the immediate post-resuscitation phase are difficult to perform due to frequent hemodynamic instability [11–12]. We tried to define the role of jugular bulb oxygenation monitoring in the early resuscitation phase of comatose patients after an out-of-hospital cardiac arrest.

Materials and methods

We studied 13 comatose patients (Glasgow Coma Score ≤ 6) who had been successfully resuscitated after an out-of-hospital cardiac

arrest. The study was approved by the hospital ethical committee, and written informed consent obtained from the closest relative.

Immediately after admission to the emergency department and restoration of a stable heart rate, the patients were transferred to the medical intensive care unit (MICU). All patients were placed on mechanical ventilation (Bear 2, 3, 5, Bear Medical Systems, Riverside, Calif.), with the aim of keeping P_aCO_2 around 4.0 kPa and ensuring adequate arterial oxygenation. P_aO_2 never exceeded 20 kPa. All patients were monitored by continuous-pulse oximetry to ensure arterial oxygen saturation above 95%. Hemoglobin levels were constantly above 7 mmol/l. Ventilator settings were not changed during the investigation. A 7.5-F flow-directed pulmonary artery catheter with a fast-response thermistor (Baxter Healthcare Corp., Irvine, Calif.) was inserted via the right internal jugular vein. Cardiac output was measured by standard thermodilution methods. We calculated the mean of four 10-cc ice-cold saline injections randomly spread over the mechanical ventilation cycle. The radial or femoral artery was cannulated for the monitoring of arterial blood pressure.

Jugular monitoring

The left jugular bulb was cannulated with a 20-cm pediatric venous catheter (Careflow, Becton Dickinson, Sandy, Utah) for intermittent blood sampling as described by Goetting and Preston [13]. An oximetry catheter was not used. The exact location of the catheter tip was confirmed by a routine chest radiograph by expanding the exposure part to above the ears with the head slightly rotated to the contralateral side. Afterwards, the position of the patient's head was left unchanged for the duration of the entire investigation to minimize catheter displacement. Since the venous effluent from both hemispheres is mixed approximately two-thirds of the blood sampled from the left jugular originated from the left cerebral hemisphere and one-third from the right. However, this is less likely to be a problem in the case of global cerebral ischemia.

The patients were studied at four regular time points: (1) baseline, (2) after a 7-ml/kg standard colloidal fluid challenge, (3) during optimal fluid loading, defined as no further increase in cardiac output with further fluid challenges, and (4) after a 30-minute infusion of dobutamine 10 μg/kg per minute. If the cardiac index did not increase after the first 7-ml/kg standard fluid challenge, dobutamine was infused as the next step. Baseline measurements were always performed within 90 min after restoration of a stable cardiac rhythm and the study was usually finished within 3–4 h. Our resuscitation protocol aimed to achieve a cardiac index >3.0–3.5 min per square meter and a mean arterial pressure (MAP) between 90 and 110 mmHg.

In addition to standard hemodynamic measurements, blood was taken from the arterial, pulmonary artery and jugular bulb catheters for blood gas analysis. Blood sampling was conducted by discarding the first 3 ml. The mixed venous blood sample was withdrawn very slowly to avoid contamination with capillary blood. Samples were immediately placed on ice and analyzed within 15 min. Pulmonary artery and jugular bulb saturation levels were measured directly by cooximetry. The cerebral extraction ratio for oxygen was calculated as the difference between arterial and jugular bulb saturation divided by arterial saturation $[(SaO_2 - SbO_2)SaO_2]$. The jugular bulb-arterial CO_2 difference was calculated as a marker for tissue hypoxia associated with low blood flow. Arterial and jugular bulb lactate levels were determined by standard methods. We calculated the jugular bulb-arterial lactate difference as a measure of cerebral ischemia.

Good cerebral outcome was defined as the state of a conscious, alert patient, able to work and lead a normal life, despite any minor neurological or psychological deficiencies (Glasgow-Pittsburgh Cerebral Performance Score of 1). Poor cerebral outcome was defined as the state of a patient in a coma or a persistent vegetative state or certified brain dead (Glasgow-Pittsburgh Cerebral Performance Score 4 or 5) [14].

Statistical analysis was performed using a commercial software package (SPSS for Windows Release 5.0.2, SPSS Inc.). Data are expressed as means ± SD unless stated otherwise. Categorical data between survivors and non-survivors were compared using the Chi-square or Fisher exact test. Paired and unpaired *t*-tests or analysis of variance were used to compare continuous data and changes over time. A *P*-value ≤ 0.05 was considered statistically significant.

Results

Demographic and pre-hospital resuscitation data for the 13 patients are shown in Table 1. All patients were comatose on admission to the MICU. Six patients survived until discharged from hospital without neurological sequelae. None of the non-survivors ever regained consciousness: 2 of them died in cardiogenic shock, while the other 5 showed a persistent vegetative state resulting in withdrawal of life support measures. Catheterization of the jugular bulb was successful in all patients and without complications. Table 2 shows the hemodynamic parameters in the survivors and non-survivors. There was no difference in baseline values (time point 1). Fluid therapy did not increase cardiac index, stroke volume index or left ventricular stroke work index in either survivors or non-survivors as a group, although individual differences in response were observed. After infusion of dobutamine, cardiac index, stroke volume index and left and right ventricular stroke work indexes were significantly higher in the survivors than in the non-survivors. Cardiac index in the survivors increased over the baseline values after dobutamine infusion ($p = 0.032$), but this was not the case in the non-survivors. Figures 1 and 2 show the individual SbO_2 values for the survivors and non-survivors respectively. Although SbO_2 tended to be lower in the survivors, there was a wide overlap and it was not possible

Table 1 Demographic and pre-hospital resuscitation data [*C-R* call response (interval in minutes between the call receipt and the arrival at the patient's address, *MI* myocardial infarction, *VF* ventricular fibrillation, *EMD* electromechanical dissociation]

Pt	Sex (M/F)	Age	C-R interval	Initial heart rate	MI	Outcome (D/S)
1	M	86	4	Asystole	–	D
2	M	64	4	VF	+	S
3	M	43	9	Asystole	–	D
4	M	63	3	VF	+	S
5	M	52	3	VF	+	S
6	F	85	4	VF	+	D
7	M	54	0	EMD	–	D
8	M	49	5	VF	+	D
9	M	59	4	VF	–	S
10	M	52	9	VF	–	D
11	M	71	7	VF	+	S
12	M	79	7	Asysole	–	D
13	M	72	2	VF	–	S

Table 2 Hemodynamic data in the survivors and non-survivors (*S* survivors, *NS* non-survivors, *MAP* mean arterial pressure, *MPAP* mean pulmonary arterial pressure, *PAOP* pulmonary arterial occlusion pressure, *SVI* stroke volume index, *SVRI* systemic vascular resistance index, *PVRI* pulmonary vascular resistance index, *LVSWI* left ventricular stroke work index, *RVSWI* right ventricular stroke work index)

Variable		Time point[a]			
		1	2	3	4
Heart rate (bpm)	S	84±23	84±23	82±20	105±35
	NS	96±18	103±25	106±22	117±24
MAP (mmHg)	S	82±27	89±28	87±25	93±24
	NS	76±18	80±31	84±34	76±36
MPAP (mmHg)	S	21±5	23±6	25±3	23±4
	NS	23±7	25±10	27±9	22±8
PAOP (mmHg)	S	11±2	14±4	16±3	13±4
	NS	12±4	15±7	15±5	13±7
Cardiac index	S	2.6±0.6	2.8±1.0	2.5±0.8	4.2±1.4***
($l \cdot min^{-1} \cdot m^{-2}$)	NS	2.7±1.0	2.5±1.0	2.7±1.1	2.5±1.1
SVI	S	33±11	33±7	31±9	40±7**
($ml/beat^{-1} \cdot m^{-2}$)	NS	30±13	26±11	27±13	22±11
SVRI	S	2309±832	2432±886	2586±911	1690±478
($dyne \cdot s \cdot cm^{-5}$)	NS	2276±1021	2400±1138	2331±1175	1901±1424
PVRI	S	313±138	301±103	301±95	204±21**
($dyne \cdot s \cdot cm^{-5}$)	NS	391±306	354±188	373±170	358±86
LVSWI	S	35.6±14.3	40.2±16.5	36.2±14.6	50.7±12.7
($gxm \cdot m^{-2}$)	NS	28.7±8.7	29.3±17.4	33.0±19.8	25.2±19.2
RVSWI	S	9.7±4.8	10.7±3.9	10.5±3.2	13.0±2.6*
($gxm \cdot m^{-2}$)	NS	8.7±3.1	8.6±4.7	9.9±5.7	7.0±5.1

*$p<0.05$ for survivors compared with non-survivors, **$p<0.01$ survivors compared with non-survivors, ***$p<0.05$ time point 1 compard with time point 4

[a] Time point *1* baseline, time point *2* after 7-ml/kg fluid challenge, time point *3* optimal fluid loading, time point *4* after 30-min infusion of dobutamine

to distinguish between survivors and non-survivors based upon the measurements. Furthermore, individual changes in SbO_2 during the resuscitation protocol did not enable discrimination between survivors and non-survivors, as increasing and decreasing patterns were observed in both groups. Three of the survivors had persistent SbO_2 levels below 55%. Two of the non-survivors had SbO_2 levels between arterial (SaO_2) and mixed venous ($SmvO_2$) oxygen saturation, probably reflecting arterial blood bypassing the metabolically inactive brain. When we compared the means of the SbO_2 levels for the survivors and non-survivors, there was again no significant difference ($p = 0.127$).

Figures 3 and 4 show the cerebral oxygen extraction ratios for both survivors and non-survivors. Oxygen extraction ratios again showed a considerable overlap both initially and during the resuscitation protocol. The means of the oxygen extraction ratios for the survivors and non-survivors were not significantly different ($p = 0.125$). After infusion of dobutamine, there was a decrease in the oxygen extraction ratio in the survivors but not in the non-survivors.

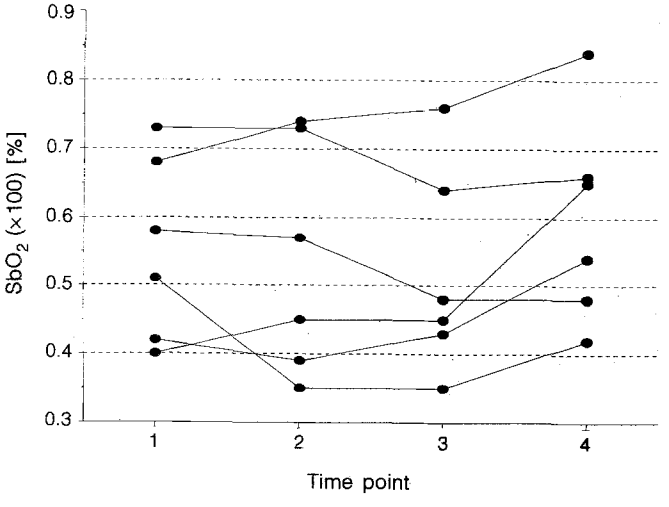

Fig. 1 Jugular bulb oxygen saturation (SbO_2) in the survivors

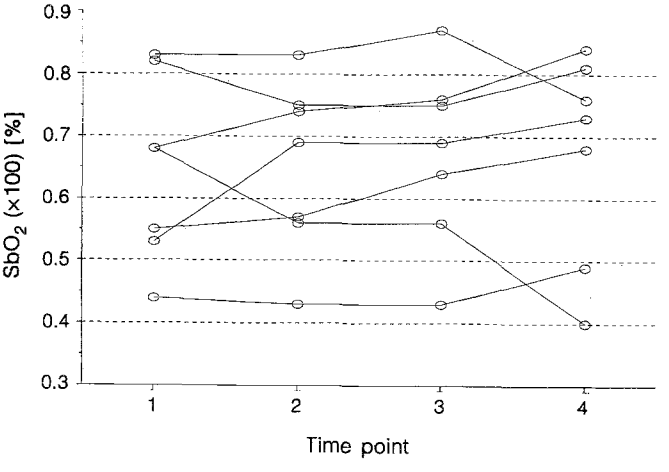

Fig. 2 Jugular bulb oxygen saturation (SbO_2) in the non-survivors

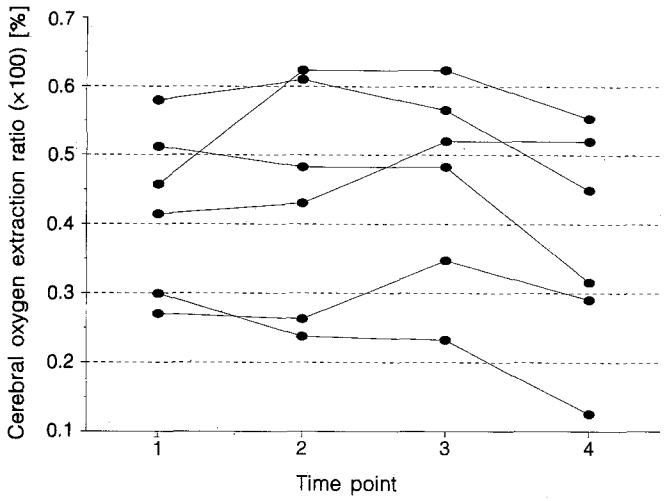

Fig. 3 Cerebral oxygen extraction ratio in the survivors

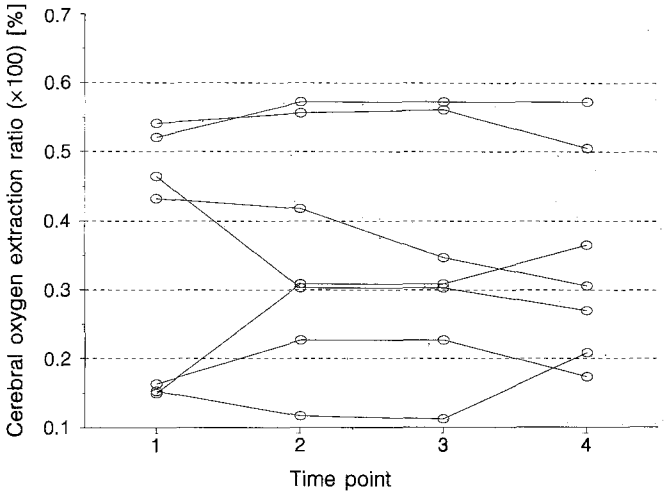

Fig. 4 Cerebral oxygen extraction ratio in the non-survivors

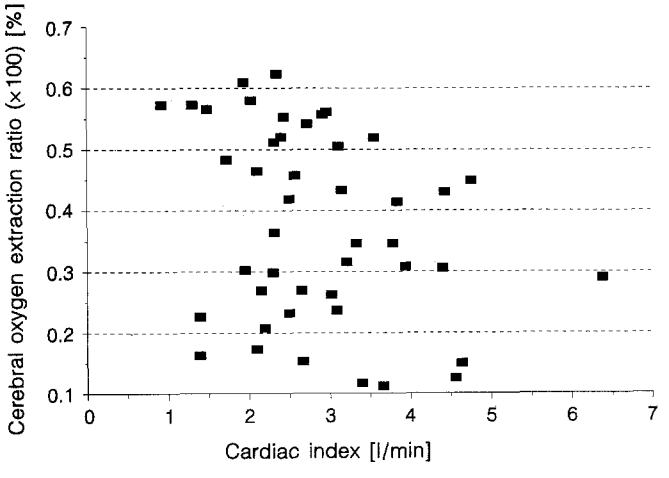

Fig. 5 Correlation between cardiac index and cerebral oxygen extraction ratio for the entire study population ($r = -0.276$, $p = 0.047$)

Figure 5 shows the relationship between the cardiac index and the cerebral oxygen extraction ratio. There was a slight but significant inverse correlation between the cardiac index and the oxygen extraction ratio for the entire study group ($r = -0.276$, $p = 0.047$). On further analysis, this correlation was significant for the survivors ($r = -0.451$, 95% CI -0.707 to -0.195, $p = 0.027$), but not for the non-survivors ($r = -0.245$, 95% CI -0.55 to 0.06, $p = 0.210$). In the survivors, there was a correlation between the cardiac index and the jugular bulb-arterial CO_2 difference ($r = -0.592$, $p = 0.002$), but this was not the case in the non-survivors ($r = -0.276$, $p = 0.155$). However, the overlap in 95% confidence intervals of the correlation coefficients, was even wider.

Systemic and jugular bulb lactate levels were obtained in all patients. Non-survivors had higher baseline and end-point systemic lactate levels than the survivors (7.4 versus 3.0 and 5.1 vs 2.3 mmol/l, respectively). However, when we calculated the difference between jugular bulb and arterial lactate levels (B-A) lactate), it was not possible to differentiate between survivors and non-survivors. Figure 6 shows the correlation between the cardiac index and the B-A lactate difference for the whole group ($r = 0.235$, $p = 0.112$). There was a correlation between cardiac index and B-A lactate in survivors ($r = 0.564$, 95% CI 0.204 to 0.924, $p = 0.004$), but this was not the case in the non-survivors $r = -0.04$, 95% CI -0.524 to 0.444, $p = 0.846$).

Discussion

The aim of the study was to determine the extent to which jugular bulb oxygenation monitoring may help to improve hemodynamic therapy during the early resuscitation phase after cardiac arrest. A decrease in cerebral

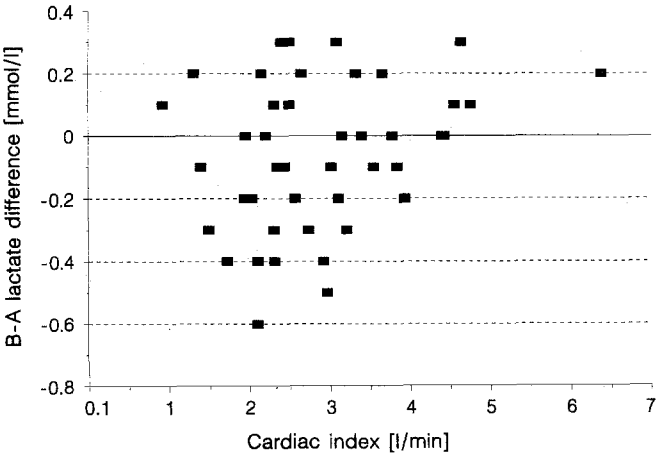

Fig. 6 Jugular bulb-arterial lactate difference versus cardiac index in the entiry study population ($r = 0.235$, $p = 0.112$)

blood flow with constant cerebral oxygen consumption will result in increased oxygen extraction and a consequently lower SbO_2, which also assumes constant arterial oxyhemoglobin saturation and hemoglobin levels. SbO_2 levels below 55% are usually regarded as indicative of a critical decrease in cerebral oxygen supply due to a reduction in blood flow, hemoglobin level or arterial oxygenation [15, 16]. SbO_2 levels above 75% are sometimes referred to as "luxury perfusion" [17] and may point to blood bypassing a metabolically inactive brain. All 13 patients were successfully resuscitated after an out-of-hospital cardiac arrest, but were comatose on admission to the MICU. We included patients with asystolic cardiac arrest, who have a generally poor prognosis, but this did not influence the results as we only aimed to study changes in jugular bulb oximetry in relation to the final outcome. All patients were treated with the same hemodynamic protocol, with the aim of increasing cardiac index to above 3.5 l/min and obtaining an MAP between 90 and 110 mmHg. SbO_2 levels and cerebral oxygen extraction ratios did not enable us to differentiate between survivors and non-survivors during the first few hours. Only 2 non-survivors showed very high SbO_2 levels that were between SaO_2 and mixed venous oxygen saturation ($S\bar{v}O_2$), together with very low extraction ratios. On the other hand, survivors had either very low (below 50%) or very high (above 80%) SbO_2 levels. Likewise, the jugular bulb-arterial lactate difference did not enable us to discriminate between the survivors and non-survivors. When we excluded the 2 patients who died in cardiogenic shock, the results remained the same.

There are several possible explanations for our findings. First, improper positioning of the jugular bulb catheter may result in contamination with extracranial blood. Furthermore, the normally small percentage of extracranial contamination may become higher in pathologic conditions, in which case SbO_2 levels are falsely elevated. We tried to ensure correct catheter position by control X-ray after insertion and by keeping the patient's head in the same position during the study [3], but the possibility of increased extracranial contamination due to the underlying condition cannot be totally excluded. The most likely explanation for our findings is that, although cardiac arrest is a global ischemic insult to the brain, the ischemic changes are heterogeneous. Highly metabolic regions, such as the hippocampus, cerebral cortex, and basal ganglia, are the most susceptible to ischemic injury [18]. As jugular bulb oxygen measurements only reflect the relationship between overall cerebral blood flow and overall cerebral metabolism, severe ischemic damage may exist despite normal measurements. In the survivors, there was an inverse correlation between the cardiac index and both the cerebral oxygen extraction ratio and the jugular bulb-arterial CO_2 difference. The venous-arterial CO_2 difference is regarded as a marker for tissue hypoxia associated with low blood flow [19–21]. This suggests that at least in the survivors an increase in cardiac output will result in an increase in cerebral blood flow. Furthermore, 5 out of 6 survivors showed a marked decrease in the cerebral oxygen extraction ratio after infusion of dobutamine. In accordance to the general circulation, this suggests a normal reaction in response to an increase in cerebral blood flow relative to a possible dobutamine-induced increase in overall cerebral oxygen consumption. As arterial oxygen saturation levels and hemoglobin levels remained constant, we believe that the decrease in the cerebral oxygen extraction ratio was the result of an increase in cerebral blood flow. It also suggests that cerebral oxygen consumption in these patients was flow independent. On the other hand, the cerebral oxygen extraction ratio and the jugular bulb-arterial CO_2 difference did not show any correlation with the cardiac index in the non-survivors. On the one hand, this could mean that a higher cardiac index in non-survivors does not automatically result in a higher cerebral blood flow. This may be explained by extreme cerebral vasoconstriction [22] or by blood cell aggregation [23, 24]. On the other hand, cerebral oxygen consumption could be flow dependent (suggesting ischemia) in which case increases in blood flow are not immediately reflected in changes in the oxygen extraction ratio. The jugular bulb-arterial lactate difference did not prove to be useful in discriminating between these possibilities. The positive correlation between the jugular bulb-arterial lactate difference and cardiac index in the survivors could be explained by a washout phenomenon.

Only a few studies on cerebral blood flow in humans following resuscitation after cardiac arrest have been reported. Beckstead et al. found that cerebral blood flow and cerebral oxygen consumption were below normal 2–6 h after resuscitation. Cerebral hyperemia was observed after 6–60 h [25]. In a more recent study, Cohan et al. described 13 comatose patients after cardiac arrest. Using the xenon-133 inhalation method, they found cerebral hyperemia in the non-survivors but not in the survivors [26]. However, definite conclusions from this study cannot be drawn. Although the authors tried to study these patients as early as possible, no patient was studied until <6 h after resuscitation. Jugular venous catheterization was not performed because the precarious clinical state of the patients precluded such invasive measurements. Other methods to quantitate cerebral blood flow in these patients, such as xenon-enhanced CT scanning, positron emission tomography (PET) and single photon emission computed tomography (SPECT) are difficult to apply during the first few hours. Transcranial Doppler ultrasonography does not provide quantitative cerebral blood flow estimates but may allow serial assessment of vasoconstriction, cerebral perfusion pressure reduction and impaired autoregulation. Furthermore, this technique is easily applied at the bedside. Near-infrared spectroscopy can be used to continuously monitor cerebrovascular hemoglobin saturation and allows for a qualitative esti-

mate of brain oxygenation. This could be very helpful during the early resuscitation phase [27].

We acknowledge that our study has several obvious shortcomings. First, only 13 patients are described, and a study of this size cannot completely determine the role of jugular bulb oxygenation monitoring in this patient group; this means that false-negative results are possible. Furthermore, the sample size is insufficient to make a formal assessment of its prognostic value relative to other, established, parameters, such as the Glasgow Coma Score. The intermittent sampling procedure is another shortcoming, since episodes of jugular bulb desaturation may be missed [28]. There is a correlation between the number of episodes of jugular desaturation and the final outcome in patients with severe head injury. However, as the aim of our study was to assess the changes in oxygenation levels immediately after a change in therapy (fluid infusion or inotropics), continuous monitoring was not absolutely necessary.

We have come to the conclusion that jugular bulb catheterization is safe and easy to perform in comatose patients after cardiac arrest. However, early jugular bulb oxygenation monitoring does not enable reliable discrimination between patients with a good and with a bad cerebral outcome. Further studies, with an extended monitoring period are necessary to assess its prognostic value.

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