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Long-term outcome of iatrogenic gas embolism

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Abstract *Objective:* To establish the incidence and long-term prognosis of iatrogenic gas embolism. *Methods:* This was a prospective inception cohort. We included all consecutive adults with proven iatrogenic gas embolism admitted to the sole referral academic hyperbaric center in Paris. Treatment was standardized as one hyperbaric session at 4 ATA for 15 min followed by two 45-min plateaus at 2.5 then 2 ATA. Inspired fraction of oxygen was set at 100% during the entire dive. Primary endpoint was 1-year mortality. All patients had evaluation by a neurologist, visual field tested by Goldman kinetic perimetry and brain MRI or CT scan at 6 months and 1 year. *Results:* From January 1993 to August 2004, 125 of 4,727,496 hospitalizations had proven iatrogenic gas embolism. The crude mortality was 25/119 (21%) at 1 year. Cardiac arrest at time of accident and ICU admission, and SAPS II of 33 or more were independent prognostic factors of 1-year mortality (OR = 4.39, 95% CI 1.46–12.20 and OR = 6.30, 1.71–23.21, respectively). Among ICU survivors, independent predictors of 1-year mortality were age (OR = 1.07, 1.01–1.14), Babinski sign (OR = 6.58, 1.14–38.20) and acute kidney failure (OR = 8.09, 1.28–51.21). Focal motor deficits (OR = 12.78, 3.98–41.09) and Babinski sign (OR = 6.76, 2.24–20.33) on ICU admission, and duration of mechanical ventilation of 5 days or more (OR = 15.14, 2.92–78.52) were independent predictors of long-term sequels. *Conclusions:* Gas embolism complicates 2.65 per 100,000 hospitalizations, and is associated with high mortality and morbidity. Babinski sign on ICU admission is associated with poor prognosis.

Keywords Iatrogenic · Gas embolism · Outcome · Mortality · Sequels · Glasgow Outcome Scale

Introduction

Gas embolism is a rare complication of invasive medical or surgical procedures [1]. Gas embolism may originate in the venous system or in the systemic arterial circulation. In the former case, the gaseous embolus may reach the systemic circulation via pulmonary shunting or via patent foramen ovale. When the gaseous embolus is in the arterial circulation, it may cause transient arterial obstruction with subsequent ischemia/reperfusion injuries. This accident is commonly recognized when sudden neurological, pulmonary or cardiac abnormalities occur during invasive procedures. More subtle cases may be diagnosed by echocardiography, transcranial Doppler, CT scan or other diagnostic procedures.

Gas embolism is considered as an emergency, and treatment includes interruption of the embolic procedure, attempt to extract intravascular gas, external cardiac

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massage and immediate oxygenation, at best under hyperbaric conditions. Hyperbaric oxygen therapy (HBO) is recommended, although randomized, controlled clinical trials are lacking [1–3]. Indeed, HBO may reduce gas bubble volume by increasing ambient pressure and by inducing blood denitrogenation, which facilitates oxygen diffusion from the emboli to the surrounding plasma. It also permits a better oxygenation of ischemic tissues by increasing dissolved-oxygen content in blood and tissues. Finally, HBO may decrease cerebral edema. Potential disadvantages of HBO include risks associated with the transport of critically ill patients, hyperoxic seizures, claustrophobic reactions and barotraumas.

Little is known about the morbidity and mortality associated with iatrogenic gas embolism. Indeed, the diagnosis of gas embolism may be difficult in conditions other than high risk surgery. In addition, when recognized, iatrogenic gas embolism requires a specific management and patient referral to a hyperbaric facility. The long-term follow-up of patients often does not involve the hyperbaric physicians. Thus, unsurprisingly, the few available retrospective studies showed a wide range of mortality from 5 to 23% and of sequels from 13 to 71% [4–14].

We took the opportunity, as a referral center in Paris and its suburb, to conduct a prospective cohort study with careful short-term and 1-year follow-up to determine the mortality and morbidity from proven iatrogenic gas embolism.

Materials and methods

This was a prospective single-center, inception cohort study performed at Raymond Poincaré University-affiliated Hospital. The intensive care unit (ICU) has a separate unit for HBO. This is the sole public hyperbaric oxygen facility for Paris and its suburb. Therefore, all cases of iatrogenic gas embolism in this area are referred to our center. The protocol was approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale of Saint-Germain en Laye (Yvelines, France), and informed consent was waived according to the observational nature of the study; all patients received routine standard of care for gas embolism (cardiopulmonary resuscitation, fluid therapy, mechanical ventilation and positive inotropic support whenever needed).

Patients

Patients of 18 years of age or above and hospitalized in our hyperbaric center were prospectively enrolled in the study if they met all eligibility criteria. Inclusion criteria included: (1) clinical condition at risk for iatrogenic gas embolism; (2) at least one of the following clinical sign: coma, focal motor deficit, seizures, cardiac arrest, cardiovascular collapse and acute dyspnea; (3) evidence of gas bubble entry in the systemic circulation as noticed during a surgical or radiological procedure, or presence of gas bubbles in left heart cavities at echocardiography or in cerebral arteries at transcranial Doppler or CT scan. Notable exclusion criteria included underlying disease with a life expectancy of less than 1 month, moribund patients likely to die within 24 h and patients with decompression sickness.

Hyperbaric oxygen therapy

An identical HBO procedure was used for all patients. We used a multiplace hyperbaric chamber (CxPRO, COMEX®, Marseille, France) pressurized with compressed air at 4 atmospheres absolute (ATA) for 15 min (30 msw depth, 405 kPa) followed by two 45-min plateaus at 2.5 then 2 ATA (Appendix 1). All intubated patients were mechanically ventilated in the chamber with 100% oxygen (RCH LAMA®). The remaining patients received 100% oxygen during the full session via a tight-fitting face mask. All patients received intravenous diazepam or midazolam, and phenobarbital to prevent hyperoxic seizures. The hyperbaric session was completed by 12 h of normobaric oxygen therapy.

Data collection

Data collection at inclusion

Clinical evaluation The following data were recorded: (1) general characteristics including demographics, diagnosis and recent surgery; (2) severity of illness assessed by vital signs, Glasgow Coma Scale score and Simplified Acute Physiology Score II (SAPS II) [15]; (3) neurological, cardiac and respiratory symptoms; (4) type and source of gas embolism; (5) time to HBO treatment; (6) presence of a patent foramen ovale (PFO); (7) interventions including type and doses of vasopressors, and mechanical ventilation.

Laboratory variables

Hematological and chemistry data, blood gas determinations, electroencephalography and whenever possible magnetic resonance imagings (MRI) or computerized tomography (CT scan) of the brain were recorded.

Follow-up

During the hospital stay, data were collected for vital signs, results from laboratory tests and any major

interventions performed. The neurological status, as established by a senior neurologist, and mortality were recorded at discharge from the ICU, at discharge from the hospital, at 6 months and at 1 year. All patients had visual field evaluation tested by Goldman kinetic perimetry and brain MRI or CT scan at 6 months and at 1 year following gas embolism.

Endpoints

The primary outcome was 1-year mortality. Secondary outcomes were neurological sequels similarly assessed at ICU discharge, then among ICU survivors at 6 months and 1 year using the Glasgow Outcome Score (1, death; 2, vegetative state; 3, severe disability, i.e., the patient is unable to live independently; 4, moderate disability, i.e. the patient is able to live independently but unable to return to work; 5, mild or no disability, i.e., the patient is able to return to work) [16].

Statistical analysis

Data are expressed as median and interquartile range for continuous variables and as number and percentage for binary variables. Comparisons were made using Student's *t* or Mann–Whitney tests for continuous variables (as appropriate), and chi-square of Fischer's exact test (as appropriate for binary variables).

The occurrences of death and sequels were analyzed independently, based on the same analysis plan, as described below.

They were considered as binary outcomes, for which the association with patient, disease and other characteristics was assessed through estimated odds ratio (OR) and 95 percent confidence intervals (95% CI) computed from fitted logistic regression models. Multivariate logistic models were fitted, with goodness of fit assessed by the Hosmer-Lemeshow test, where small *P* values indicate a lack of fit of the model [17]. All tests were two-sided, with *P* values of 0.05 or less denoting statistical significance.

Statistical analyses were performed on SAS 9.1 (SAS Inc, Cary, NC) and R 2.7.2 (http://www.R-project.org) software packages.

Results

Study population

From January 1993 to August 2004, a total of 4,727,496 patients were admitted at the Assistance Publique Hôpitaux de Paris, and 1,931 (0.04%) had suspicion of gas embolism. Among these patients, gas embolism was proven in only 125 cases that were referred to the hyperbaric unit for HBO (Table 1). Six patients (homeless) were lost to follow-up after hospital discharge. Almost all accidents were air embolism except nine cases of carbon dioxide gas embolism following coelioscopy or hysteroscopy (Table 2). The main clinical manifestations did not differ between venous and arterial gas embolism, except a higher rate of acute myocardial infarction in case of arterial gas embolism (26 vs. 10%, $P = 0.03$; Table 3).

Mortality

The crude mortality was 14/119 (12%) at ICU discharge, 19/119 (16%) at hospital discharge, 21/119 (17.6%) at 6 months and 25/119 (21%) at 1-year (Fig. 1).

Univariate analysis suggested that, immediately following gas embolism onset, non-survivors were more likely to present with cardiac arrest ($P = 0.0004$), cardiovascular collapse ($P = 0.005$), acute myocardial infarction ($P = 0.02$), acute kidney failure ($P = 0.01$) and disseminated intravascular coagulopathy ($P = 0.045$) (Table 4). At the time of ICU admission, non-survivors had lower Glasgow Coma Scale scores ($P < 0.0001$), higher SAPS II scores ($P < 0.0001$) and arterial lactate levels ($P = 0.001$), and were more likely receiving vasopressor therapy ($P = 0.03$) and on mechanical

Table 1 Population characteristics

Variables	$N = 119$ Median (quartiles), *N* (percentage)
Age (years)	53 (33–65)
Gender (male)	67 (56)
Type of gas embolism	
Venous	92 (77)
Arterial	27 (23)
Nature of gas	
Air	110 (92)
CO_2	9 (8)
Known patent foramen ovale	15 (13)
Brain imaging prior HBO: yes	51 (43)
Time from accident to HBO (h)	6 (5–10)
Admission severity of illness	
SAPS II	33 (21–55)
Glasgow Coma Score	8 (3–15)
Mechanical ventilation at admission	76 (64)
Vasopressor therapy	27 (23)
Outcome	
Duration of coma (h)	10 (0–48)
Duration of coma in survivors (h)	30 (12–120)
Duration of mechanical ventilation (days)	1 (0–5)
Duration of mechanical ventilation in survivors (days)	3 (1–8)
ICU length of stay (days)	3 (2–10)

Table 2 Causes of gas embolism

Clinical context	*N* (%)
Central venous catheterization	29 (24.3%)
Removal	9 (7.5%)
Accidental removal	8 (6.7%)
Manipulation and usual care	7 (5.9%)
Insertion	5 (4.2%)
Peripheral venous catheterization	2 (1.7%)
Thoracic procedures	25 (21%)
Pleural puncture or drainage	8 (6.7%)
Trans-thoracic biopsy	4 (3.3%)
Tumorectomy	4 (3.3%)
Bronchoscopy	3 (2.5%)
Pleuroscopy	2 (1.7%)
Miscellaneous	4 (3.4%)
Cardiac surgery	18 (15%)
Valve surgery	7 (5.9%)
Coronary bypass surgery	6 (5%)
Inter-auricular communication closure	3 (2.5%)
Inter-ventricular communication closure	2 (1.7%)
Abdominal surgery	14 (12%)
Laparoscopy	7 (5.9%)
Liver transplant	4 (3.3%)
Miscellaneous	3 (2.5%)
Neurosurgery–sitting position	7 (5.8%)
Spine surgery	2 (1.7%)
Facial surgery	1 (0.8%)
Interventional radiology	13 (10.8)
Arteriography	6 (5%)
Coronarography	4 (3.3%)
Miscellaneous	3 (2.5%)
During renal replacement therapy	5 (4.2%)
Gynecologic celioscopy	2 (1.7%)
Massive blood transfusion	3 (2.5%)
Suicide attempt (air auto-infusion)	2 (1.7%)
Miscellaneous	3 (2.5%)

ventilation ($P = 0.02$). Non-survivors had longer duration of coma ($P < 0.0001$), of mechanical ventilation ($P < 0.0001$) and of ICU stay ($P = 0.02$). Multivariate analysis suggested that cardiac arrest at time of gas embolism and an ICU admission SAPS II score of 33 or more were the only independent prognostic factors with an odds ratio of dying of 4.39 (95% CI 1.46–12.20) and 6.30 (95% CI 1.71–23.21), respectively (Table 5).

Among ICU survivors, 1-year non-survivors were older ($P = 0.01$), were more likely to present with Babinski sign, had a longer duration of coma ($P = 0.006$), of mechanical ventilation ($P = 0.005$) and of ICU stay ($P = 0.01$) (Table 4). Multivariate analysis suggested as independent prognostic factors age (OR = 1.07, 95% CI 1.01–1.14), presence of Babinski sign (OR = 6.58, 95% CI 1.14–38.20) and presence of acute kidney failure (OR = 8.09, 95% CI 1.28–51.21) (Table 5).

Neurological sequels

Among the 105 ICU survivors, 45 patients (42.9%) left the ICU with neurological sequels, including mainly 4 (8.9%) patients with vegetative state, 31 (6.7%) with focal motor deficits, 7 (15.6%) with restriction of the visual field, 3 (6.7%) with cognitive problems and 2 (4.4%) with seizures (Table 4). During follow-up, there was a substantial attenuation of sequels at 6 months with fewer patients having a GOS 2, GOS 3 and a GOS 4, and more patients who recovered and resumed to their previous social activity (GOS 5) (Fig. 1).

Univariate analysis suggested that patients with neurological sequels were older ($P = 0.01$), had a longer delay from accident to HBO therapy ($P = 0.03$) and were more likely to receive HBO more than 7 h from gas embolism ($P = 0.02$), were more likely to present at ICU admission with focal motor deficits ($P < 0.0001$), Babinski sign ($P < 0.0001$), cranial nerve paralysis

Table 3 Main clinical presentation in venous and arterial gas embolism

Symptoms	All patients ($N = 119$)	Venous gas embolism ($N = 92$)	Arterial gas embolism ($N = 27$)	*P* value
Neurological symptoms				
Motor deficit (%)	54 (45%)	44 (48%)	10 (37%)	0.32
Seizure (%)	36 (30%)	26 (28%)	10 (37%)	0.38
Babinski sign (%)	46 (39%)	39 (42%)	7 (26%)	0.12
Visual field abnormalities (%)	16 (13%)	13 (14%)	3 (11%)	0.68
Other cranial nerves abnormalities (%)	35 (29%)	27 (29%)	8 (30%)	0.98
Cardiac symptoms				
Cardiac arrest (%)	21 (18%)	18 (20%)	3 (11%)	0.32
Chest pain (%)	6 (5%)	6 (7%)	0	0.14
Shock (%)	33 (28%)	25 (27%)	8 (30%)	0.53
Acute myocardial infarction (%)	16 (13%)	9 (10%)	7 (26%)	0.03
Respiratory symptoms				
Dyspnea (%)	50 (42%)	40 (43%)	10 (37%)	0.48
Cardiogenic pulmonary edema (%)	14 (12%)	10 (11%)	4 (15%)	0.57
Acute lung injury/ARDS	7 (6%)	6 (7%)	1 (4%)	0.58
Others symptoms				
Acute renal failure (%)	15 (13%)	11 (12%)	4 (15%)	0.69
Disseminated intravascular coagulopathy (%)	11 (9%)	9 (10%)	2 (7%)	0.80

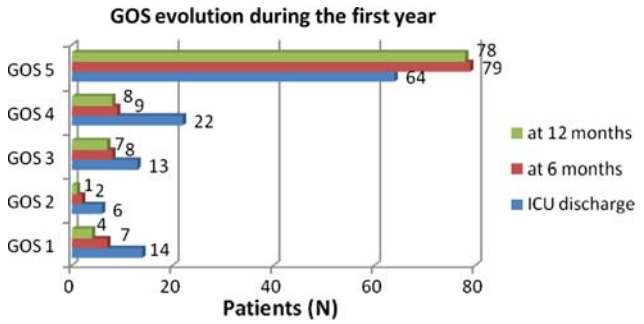

Fig. 1 Glasgow Outcome Score (GOS) at intensive care unit (ICU) discharge, 6 months and 1 year

($P = 0.02$), and had longer duration of mechanical ventilation ($P = 0.006$) and ICU stay ($P = 0.02$) (Table 4). Of note, more patients with neurological sequels had had brain imaging performed prior to HBO therapy ($P = 0.002$). Multivariate analysis showed that presence at ICU admission of focal motor deficits ($P < 0.0001$) and of Babinski sign ($P = 0.0007$), and duration of mechanical ventilation larger than 5 days ($P = 0.0012$) were independent predictors of long-term sequels (Table 5).

Adverse events and observance

All patients completed a single HBO session followed by 12 h of normobaric oxygen therapy, except one patient who had two consecutive HBO sessions because of persistent massive neurological dysfunction and CT scan evidence of remaining bubbles in the cerebral arteries after the first HBO session. There were no adverse events related to HBO, except one patients who experienced

Table 4 1-year outcome of 119 patients with iatrogenic gas embolism

Variable	All patients $N = 119$			ICU survivors only $N = 105$			1-year survivors		
	1-year Survivors ($N = 94$)	1-year Non-survivors ($N = 25$)	P value	ICU Survivors ($N = 94$)	1-year Non-survivors ($N = 11$)	P value	Without sequels ($N = 60$)	With sequels ($N = 45$)	P value
Age (years)	52 (31–63)	57 (44–67)	0.17	52 (31–63)	67 (52–79)	0.01	52 (31–61)	57 (45–70)	0.01
Gender (male)	53 (56)	14 (56)	1.00	53 (56)	5 (45)	0.54	34 (57)	24 (53)	0.84
Type of gas embolism (arterial)	25 (27)	2 (8)	0.06	25 (27)	1 (9)	0.29	17 (28)	9 (20)	0.37
Type of gas (air)	87 (73)	23 (19)	1.00	86 (92)	11 (100)	1.00	55 (92)	43 (96)	0.70
Brain imaging prior to HBO	52 (55)	9 (36)	0.48	52 (55)	3 (27)	0.62	24 (40)	31 (69)	0.002
Evidence for air bubbles at brain imaging	14 (29)	7 (78)	0.008	14 (29)	3 (100)	0.03	4 (18)	13 (43)	0.08
Time to HBO (h)	6 (4–10)	7 (5–10)	0.71	6 (4–10)	7 (4–12)	0.83	6 (4–9.5)	8 (5–12)	0.03
Time to HBO < 7 h[a]	–	–	–	–	–	–	39 (65)	19 (32)	0.02
Symptoms at time of accident									
Cardiac arrest	10 (11)	11 (44)	0.0004	10 (11)	2 (18)	0.61	6 (10)	5 (11)	1.00
Mean arterial pressure (mmHg)	60 (14–71)	55 (27–70)	0.98	60 (14–71)	65 (45–89)	0.40	54 (8–70)	69 (40–72)	0.13
Shock	20 (21)	13 (52)	0.005	20 (21)	3 (27)	0.70	14 (23)	9 (20)	0.81
Myocardial infarction	9 (10)	7 (29)	0.02	9 (10)	2 (18)	0.32	6 (10)	5 (11)	1.00
Chest pain	6 (5)	0 (0)	0.34	6 (5)	0 (0)	1.00	5 (8)	1 (2)	0.23
Dyspnea	38 (40)	13 (52)	0.37	38 (40)	8 (73)	0.06	28 (47)	18 (40)	0.55
Pulmonary edema	11 (12)	3 (13)	1.00	11 (12)	2 (18)	0.62	10 (17)	3 (7)	0.15
Focal motor deficit	43 (46)	11 (44)	1.00	43 (46)	8 (73)	0.12	15 (25)	36 (80)	<0.0001
Seizures	25 (27)	11 (44)	0.14	25 (27)	4 (36)	0.49	15 (25)	14 (31)	0.51
Babinski sign	36 (38)	10 (40)	1.00	36 (38)	8 (73)	0.05	13 (22)	31 (69)	<0.0001
Visual symptoms	15 (16)	1 (4)	0.19	15 (16)	0 (0)	0.19	7 (12)	8 (18)	0.19
Other cranial nerves	28 (30)	7 (28)	1.00	28 (30)	3 (27)	1.00	12 (20)	19 (42)	0.02
Symptoms at ICU admission									
Glasgow coma score	13 (4–15)	3 (3–6)	<0.0001	13 (4–15)	4 (3–15)	0.17	14.5 (4–15)	9 (4–15)	0.44
SAPS II	32 (20–43)	60 (47–68)	<0.0001	32 (20–30)	47 (22–63)	0.13	32 (20–39)	36 (22–56)	0.11
SAPS II < 33	50 (53)	3 (12)	0.0002	–	–	–	–	–	–
Shock	16 (17)	11 (44)	0.007	16 (17)	2 (18)	1.00	13 (22)	5 (11)	0.20
DIC	6 (6)	5 (21)	0.045	6 (6)	0 (0)	1.00	4 (7)	2 (4)	0.70
Acute kidney failure	8 (9)	7 (29)	0.01	8 (9)	0 (0)	0.59	3 (5)	5 (11)	0.28
Creatine kinase (× normal value)	1(1–4)	2 (1–7)	0.09	1 (1–4)	2 (1–6)	0.38	1 (1–3)	1 (1–4)	0.73
Lactates	1.8 (1.2–2.9)	6.2 (2.6–10)	0.001	1.8 (1.2–2.9)	4.2 (2.6–8.3)	0.05	1.3 (1.2–2.6)	2.7 (1.3–3.7)	0.15
Duration of coma (h)	7 (0–24)	96 (16–240)	<0.0001	7 (0–24)	96 (16–240)	0.006	8 (0–18)	20 (0–72)	0.08
Duration of coma <20 h	–	–	–	–	–	–	47 (78)	23 (51)	0.007
Duration of mechanical ventilation (days)	1 (0–3)	5 (2–20)	<0.0001	1 (0–3)	5 (2–20)	0.005	1 (0–2)	3 (0–8)	0.006
ICU length of stay (days)	3 (2–8)	7 (3–29)	0.01	3 (2–8)	9 (3–32)	0.01	3 (2–5)	7 (2–19)	0.002

[a] The value of 7 h was used as it corresponded to the median in non-survivors

Table 5 Multivariate analyses for death and neurological sequels in 119 patients with iatrogenic gas embolism

	Odds ratio, 95% confidence intervals	*P* value
All patients—crude 1-year mortality 25/119		
SAPS II >33	6.30 [1.71; 23.21]	0.006
Cardiac arrest	4.39 [1.46; 12.20]	0.008
Hosmer-Lemeshow goodness-of-fit test, $P = 0.91$		
ICU survivors—crude 1-year mortality 11/105		
Age (years)	1.07 [1.01; 1.14]	0.02
Duration of mechanical ventilation (days)	1.06 [0.99; 1.14]	0.07
Babinski sign	6.58 [1.14; 38.20]	0.04
Acute renal failure	8.09 [1.28; 51.21]	0.03
Hosmer-Lemeshow goodness-of-fit test, $P = 0.28$		
ICU survivors—crude rate of sequels at 1 year 45/105		
Duration of mechanical ventilation >5 days	15.14 [2.92; 78.52]	0.0012
Focal motor deficit	12.78 [3.98; 41.09]	<0.0001
Babinski sign	6.76 [2.24; 20.33]	0.0007
Hosmer-Lemeshow goodness-of-fit test, $P = 0.13$		

seizures during the HBO session, which resolved by shifting the patient from pure oxygen to air.

Discussion

This is the first prospective cohort study that included a 1-year follow-up of patients with documented iatrogenic gas embolism. In this study the crude prevalence of iatrogenic gas embolism was 2.65 cases per 100,000 hospital admissions. Our hyperbaric unit is the only public facility for the Paris great area, a region of nearly 13 millions inhabitants (20% of the French population). The observed prevalence of iatrogenic gas embolism is in line with recent reports from the Haute Autorité de Santé (HAS) in France [3]. This study also established that about one out of five patients with iatrogenic gas embolism died within 1 year, and that one out of five survivors had persistent neurological sequels at 1 year following the accident.

The design of this prospective inception cohort study differed markedly from previous reports on gas embolism [4–14]. We used strict criteria to define gas embolism including not only the onset of neurological, cardiovascular or respiratory symptoms during exposure to a medical or surgical procedure at risk of gas embolism, but also direct evidence of gas in the systemic circulation noticed during or immediately after the procedure. We included only patients with iatrogenic accident and not patients with decompression sickness. All patients were closely followed up for 1 year with a particular focus on neurological sequels as assessed by a senior neurologist from clinical examination, visual field tested by Goldman kinetic perimetry and brain imaging. All patients were treated in a hyperbaric chamber, according to recommendations from the European Committee for Hyperbaric Medicine or Undersea and Hyperbaric Medical Society [2]. Hyperbaric oxygen therapy should be delivered as soon as possible, and other treatments may have included cardiopulmonary resuscitation, volume expansion, mechanical ventilation and positive inotropic support [1, 18, 19]. There is no consensus on the practical modalities for HBO session in iatrogenic gas embolism [20]. Our treatment procedure consisted of achieving optimal mechanical reduction of bubbles size and optimizing blood denitrogenation. Thus, priority was given to the duration of oxygen exposure rather than to pressure. In addition, the mechanical effect on bubble size reduction may not be substantially influenced by increasing the pressure from 4 to 6 absolute atmospheres [21–23]. We used high oxygen pressure (3.8 ATA) and with careful prevention with benzodiazepine or barbiturates, we did not observe an increased risk of seizures. We did not observe any evidence for lung toxicity during the HBO session, and none of the hospital survivors had pulmonary sequels at the long term.

The study population shared most of the characteristics of previously reported cohorts [4–14], highlighting the still too high proportion of gas embolism following central venous catheterization [24, 25]. Of note, the clinical presentation was not significantly different between venous and arterial gas embolism except more myocardial ischemia in patients with arterial gas embolism. The observed large proportion of patients with neurological symptoms following venous gas embolism suggested right-to-left shunting via intrapulmonary shunt or patent foramen ovale, found in 15 out of 31 patients who had transesophageal echocardiography. This prevalence of patent foramen ovale is in line with previous reports [26].

Short-term mortality was about 12%, in keeping with mortality rates reported in retrospective studies [4–14]. However, after ICU discharge, there were still a significant number of deaths with a 1-year mortality of 21%, and almost 43% of ICU survivors had neurological sequels. The source of gas embolism, venous versus arterial, did not influence the risk of death or long-term neurological sequels, in contrast to previous observations [14].

Similarly, in contrast to common thoughts, the type of gas, air versus carbon dioxide, did not influence long-term mortality and morbidity. Patients with major arterial gas embolism during cardiac or vascular surgery may have died prior to being referred to the hyperbaric unit. This study confirmed that the time to HBO treatment is a prognostic factor [14], and in practice a delay of 7 h or less was associated with a better outcome. Of note, brain imaging was performed in 43% of patients prior to referral to the hyperbaric unit causing on average a 2½ h delay to HBO treatment. Then, unsurprisingly, these patients were more likely to present with long-term neurological sequels. These findings highlighted that when gas embolism is suspected, imaging should not be performed prior to HBO therapy.

Cardiac arrest at the time of accident was the main risk factor for short-term mortality, probably highlighting the large volume of gas that entered in the circulation. Among risk factors for long-term mortality and sequels, the presence of Babinski signs on ICU admission is probably the most interesting factor. Indeed, examination of toe reflexes is a very easy and robust test. It may allow rapid recognition of severe cases and prompt referral to hyperbaric units. To determine whether exposure to high oxygen pressure had contributed to neurological sequels would require comparing our HBO strategy to a strategy of lower depth and/or lower duration of exposure to oxygen.

In conclusion, iatrogenic gas embolism complicates 2.65 per 100,000 hospitalizations, and is associated with high long-term mortality and morbidity. The type and the source of gas embolism have little impact on outcome, whereas a time to hyperbaric oxygen therapy of 7 h or less reduced the risk of mortality and neurological sequels. Presence of Babinski signs at time of ICU admission is associated with poor long-term outcome.

Appendix

See Fig. 2.

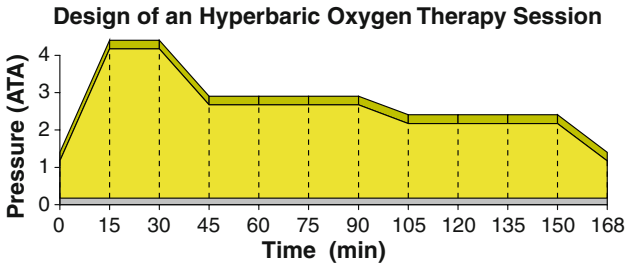

Fig. 2 Design of chamber session, showing the pressure and duration of oxygen exposure

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