■ CLINICAL INVESTIGATIONS

Efficacy of Continuous Insufflation of Oxygen Combined with Active Cardiac Compression–Decompression during Out-of-hospital Cardiorespiratory Arrest

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Background: During experimental cardiac arrest, continuous insufflation of air or oxygen (CIO) through microcannulas inserted into the inner wall of a modified intubation tube and generating a permanent positive intrathoracic pressure, combined with external cardiac massage, has previously been shown to be as effective as intermittent positive pressure ventilation (IPPV).

Methods: After basic cardiorespiratory resuscitation, the adult patients who experienced nontraumatic, out-of-hospital cardiac arrest with asystole, were randomized to two groups: an IPPV group tracheally intubated with a standard tube and ventilated with standard IPPV and a CIO group for whom a modified tube was inserted, and in which CIO at a flow rate of 15 l/min replaced IPPV (the tube was left open to atmosphere).

Both groups underwent active cardiac compression–decompression with a device. Resuscitation was continued for a maximum of 30 min. Blood gas analysis was performed as soon as stable spontaneous cardiac activity was restored, and a second blood gas analysis was performed at admission to the hospital.

Results: The two groups of patients (47 in the IPPV and 48 in the CIO group) were comparable. The percentages of patients who underwent successful resuscitation (stable cardiac activity; 21.3 in the IPPV group and 27.1% in the CIO group) and the time necessary for successful resuscitation (11.8 ± 1.8 and 12.8 ± 1.9 min) were also comparable. The blood gas analysis performed after resuscitation (8 patients in the IPPV and 10 in the CIO group) did not show significant differences. The arterial blood gases performed after admission to the hospital and ventilation using a transport ventilator (seven patients in the IPPV group and six in the CIO group) showed that the partial pressure of arterial carbon dioxide (Pa_{CO_2}) was significantly lower in the CIO group (35.7 ± 2.1 compared with 72.7 ± 7.4 mmHg), whereas the pH and the partial pressure of arterial oxygen (Pa_{O_2}) were significantly higher (all $P < 0.05$).

Conclusions: Continuous insufflation of air or oxygen alone through a multichannel open tube was as effective as IPPV during out-of-hospital cardiac arrest. A significantly greater elimination of carbon dioxide and a better level of oxygenation in the group previously treated with CIO probably reflected better lung mechanics. (Key words: Oxygenation; resuscitation; ventilation.)

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CONTINUOUS insufflation of oxygen (CIO) in the trachea is a method that has been used in different settings to maintain arterial oxygenation in the absence of respiratory movement. This method was shown to maintain adequate gas exchange using high flow rates in paralyzed dogs,[1,2] whereas the efficiency of the technique to improve carbon dioxide elimination was poorer in pigs, probably because of the absence of collateral ventilation.[3] In patients, Brochard et al.[4] demonstrated that CIO using microcannulas inserted into the inner wall of a modified standard endotracheal tube, maintained adequate oxygenation during periods of apnea or during

disconnection for tracheal suctioning. Using this method, CIO created a positive pressure in the endotracheal tube, to a level that depended on the amount of flow delivered and generated by the air entrainment mechanism.[5]

During cardiopulmonary resuscitation (CPR) for cardiorespiratory arrest, external cardiac massage must be delivered promptly in association with ventilation.[6] The hemodynamic effectiveness of external cardiac massage has been attributed to both the compression of the heart between the sternum and the vertebral column[7,8] and to the increase in intrathoracic pressure created by chest compression, which explains the blood flow from the thorax.[9-11] Using the properties of CIO, which generates a positive pressure in the lungs, several groups have previously shown in animals that external cardiac massage alone could be used to generate adequate ventilation during CIO because of the "bellows effect" of external chest compression.[12-14] Compression of the thorax generated active expiration through the open endotracheal tube, whereas passive decompression resulted in inspiratory flow entering the lungs, up to the level of positive pressure generated by the CIO.[12] Because the hemodynamic effectiveness of CIO-CPR was at least as good as the standard method, and even better for some hemodynamic variables, and because this method simplified the global approach of the resuscitation process, it seemed worthwhile to try it in patients.[15]

The aim of this prospective, randomized, controlled trial was therefore to evaluate the feasibility and effectiveness of CIO as the sole method of ventilation during cardiorespiratory arrest by comparing it with the reference method using IPPV, in patients with out-of-hospital cardiac arrest and with a poor prognosis.

Materials and Methods

The protocol was approved by the Ethics Committee of Pitié-Salpétrière Hospital, Paris (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale), which granted approval for the protocol to be conducted in several locations.

Patients

Adult patients (older than 16 yr) who experienced out-of-hospital cardiorespiratory arrest were prospectively included in the study. Criteria for disqualification from the study follow: cases of cardiorespiratory arrest that occurred within the context of trauma, polytrauma

or a catastrophe (massive influx of victims) and patients who presented with cardiorespiratory arrest caused by ventricular fibrillation.

Basic (Non-physician-based) Cardiopulmonary Resuscitation

A rapid response team of paramedics from the Paris Fire Brigade (Paris, France) was called to the scene. They had standard equipment, comprising a cardiopump (Cardiopump Ambu, Bordeaux, France) and an oxygen therapy case. This case contained an autofilling manual insufflation bag (IM 5 manual ventilator; Air Liquide Santé, Paris, France), a 3.4-l bottle of pressurized oxygen, with a manual regulator—allowing a fraction of inspired oxygen ($F_{I_{O_2}}$) close to 1 to be obtained for a flow rate of 15 l/min—face masks, Guedel airways of various sizes, and a mucus aspirator.

Cardiorespiratory arrest was confirmed by the absence of carotid artery (or femoral artery) pulse for 5-10 s in an unconscious, nonresponsive person who was no longer breathing (or who was in a state of agonal respiration). This process of diagnosis did not require more than 30 s. After the diagnosis was confirmed and the airway opened by standard methods, CPR was performed by two firemen, with the patient on a hard surface, with an alternation of five active cardiac compression-decompressions using the cardiopump (80-100 compressions/min) and of positive pressure breaths given by face mask (15-20 insufflations/min). This was continued until a carotid pulse appeared; checks were made for this every 2 min.

Specialized (Physician-based) Cardiopulmonary Resuscitation

A medical team was called by the first aid team. As soon as the team arrived, the electrocardiographic recording was assessed using the paddles of a defibrillator placed on the precordial area. The patients were then classified according to the type of rhythm observed: asystole, extreme bradycardia, or ventricular fibrillation. In the case of ventricular fibrillation, electric shocks of increasing intensity were delivered at 200, 300 and 360 J; these patients were not included in the study and were treated in a conventional manner. In the case of asystole or extreme bradycardia, the patients were included and randomized to two groups by the physician drawing lots on the scene: a control group and a CIO group were created.

Patients in the control group were intubated using a standard, cuffed endotracheal tube with an ID of 7.5 mm
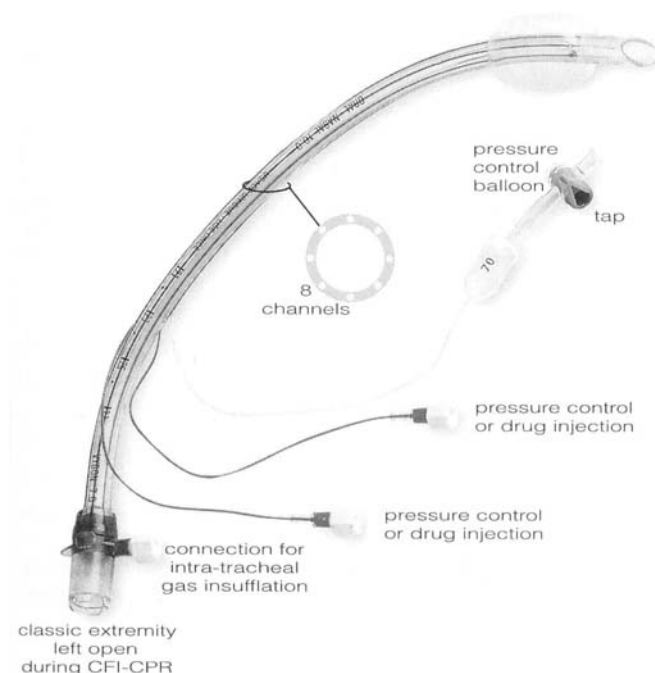
Fig. 1. Schema of the Boussignac-type multichannel endotracheal tube with the eight capillaries inserted in the wall of the tube. Note that the external extremity is left open to atmosphere during continuous insufflation of oxygen and cardiac massage.

(endotracheal tube, Vygon, Ecouen, France); 3 mg epinephrine diluted in 7 ml isotonic solution was injected into the tube; manual ventilation was continued.

Patients in the CIO group were intubated using a multichannel, cuffed endotracheal tube with an ID of 7.5 mm (Boussignac-type tube; Vygon). This tube has eight lateral capillaries with an ID less than 700 μm molded in the wall of the tube, opening slightly above the distal tip of the tube and joined together proximally. This tube is also fitted with two independent injection or pressure measuring sites that end at its distal tip (fig. 1). As soon as the patients were intubated, CIO was performed using the capillaries from the common proximal end at a flow rate of 15 l/min. This is known to generate a constant endotracheal pressure of approximately 10 cm H_2O.[5] The proximal end of the tube was left open to atmosphere with no other method of ventilation. Three milligrams of epinephrine diluted in 7 ml isotonic solution were injected into the trachea *via* one of the two injection sites. Active compression–decompression was then performed continuously at a rate of 80–100 compressions/min. The combination of chest movements generated by chest massage and CIO was the only means for delivering ventilation.

In both groups, the period between the time of the call and the arrival of the resuscitation medical team was noted. For patients in both groups electrocardiography was monitored and a stopwatch was started up as soon as the patient was intubated and ventilated (T_0) in both groups. Intravenous boluses of 3 mg epinephrine were injected every 3 min after a peripheral venous route linked to a bottle of isotonic solution was placed. The total quantity of epinephrine injected was noted. After intubation, pulse oximetry was started and oxygen saturation (Sp_{O_2}) was noted every 5 min for the next 30 min. As soon as spontaneous cardiac action was restored, defined by the restoration of a palpable carotid pulse,[6] the stopwatch was stopped, and the period of time between the start of specialized CPR and successful resuscitation was noted. After successful resuscitation was stable for 1 min, mechanical ventilation was started in the patients using a transport ventilator (AXR1a; MMS SA, Pau, France), with tidal volume (V_t) = 12 ml/kg, respiratory frequency = 12 cycles/min, and $F_{I_{O_2}}$ = 1. If successful resuscitation did not occur, specialized CPR was continued for a maximum of 30 min. The occurrence of gasping was not recorded.

If stable successful resuscitation occurred, an initial arterial blood sample was taken using a heparinized syringe (Arterial Blood Sampler; Chiron Ltd, Halstead, UK) by femoral puncture, as soon as mechanical ventilation was started (transport ventilator). The sample was placed in a cold container between 0 and 4° and transported to the laboratory of the Intensive Care Unit (ICU) of Hospital Bégin, where blood gas analysis (G_1) was performed within the next hour (ABL3 and hemoximeter; ABL, Copenhagen, Denmark). A subsequent blood gas analysis (G_2) was performed in the hospital in which the patient was transported, as soon as the patient was admitted to the ICU and standard ICU ventilation was begun. Heart rate and blood pressure were also monitored noninvasively every 5 min during transfer to the hospital. Patients were directly admitted to the ICU.

Statistical Analysis

End Points The effectiveness of ventilation was compared using arterial blood gas analysis after recovery of spontaneous cardiac activity and arrival in the ICU. The number of patients with an Sp_{O_2} more than 70% was compared during resuscitation and before successful resuscitation. The effectiveness of resuscitation was assessed by the time for initial recovery of spontaneous cardiac activity and the total dose of epinephrine needed in the two groups.
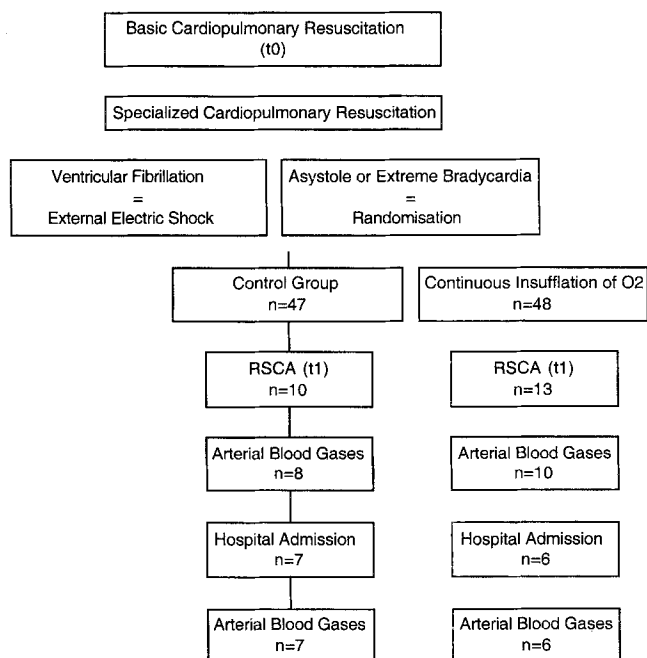
Fig. 2. Schema describing the protocol and the number of patients included at each step in the study. RSCA = resumption of spontaneous cardiac activity.

The results were expressed as the mean ± SD. Quantitative values were compared using the Kruskal-Wallis nonparametric test. Percentages in both groups were compared using the chi-square test. A value of $P < 0.05$ was necessary.

Results

Figure 2 illustrates the schema for inclusion in the study and the follow-up. Ninety-five patients were included in the study: 47 in the control group and 48 in the

Table 1. Comparison of the Control and CIO Groups Receiving Active Cardiac Compression/Decompression

	Control Group (n = 47)	CIO Group* (n = 48)
Age (yr)	63 ± 3	62 ± 3
Sex (male/female)	31/16	29/19
Period of basic CPR (min)	6.3 ± 2.4	6.7 ± 2.3
Period of specialized CPR (min)	20 ± 8.7	21 ± 9.7
$Sp_{O_2} > 70\%$ at t0 (%)	34	44
Cardiac/noncardiac etiologies	27/20	29/19

* No difference was observed between the two groups for any of these parameters.

CIO = continuous insufflation of oxygen; CPR = cardiopulmonary resuscitation.

Table 2. Comparison of Patients in the Control and CIO Groups with Resumption of Spontaneous Cardiac Activity

	Control Group (n = 10)	CIO Group* (n = 13)
Age (yr)	63 ± 21	65 ± 14
Sex (male/female)	5/5	11/2
Period of basic CPR (min)	8.4 ± 2.4	6.4 ± 1.8
Period of specialized CPR (min)	23 ± 10.1	19.6 ± 10.6
Total period of CPR for patients with resumption of cardiac activity (min)	29.2 ± 10.8	26.1 ± 11.7
Total period of CPR for patients admitted to the ICU (min)	29.9 ± 11.9	25.8 ± 17.5
$Sp_{O_2} > 70\%$ at t0 (min)	50	70
Cardiac/noncardiac etiologies	5/5	9/4
RSCA (%)	21.3	27.1
Time taken for RSCA (min)	11.8 ± 5.4	12.8 ± 6.7

* No difference was observed between the two groups for any of these parameters.

CIO = continuous insufflation of oxygen; CPR = cardiopulmonary resuscitation; ICU = intensive care unit; RSCA = resumption of spontaneous cardiac activity.

CIO group. The characteristics of the two groups are shown in table 1 and were strictly similar.

Successful resuscitation was accomplished after the onset of specialized CPR for a similar number of patients in the two groups: 10 and 13 patients in the control and CIO groups, respectively (table 2).

Figure 3 shows that there was no significant difference in the number of patients with an Sp_{O_2} more than 70% before Successful resuscitation in the two groups at any time in the first 30 min. There was no difference in the duration of basic, specialized, or total CPR between the two groups (tables 1 and 2).

Arterial blood gases immediately after successful resuscitation could be sampled in eight patients in the control

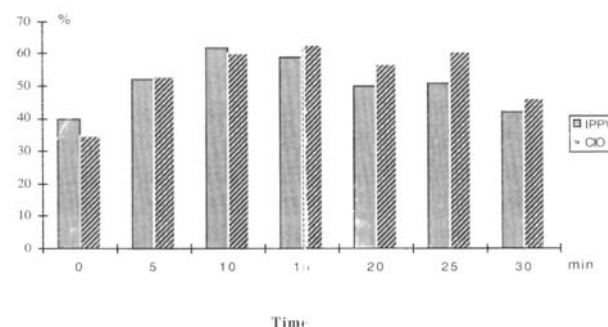Fig. 3. Comparison of the percentage of patients with an Sp_{O_2} more than 70% from T_0 to T_{30} in the patients in whom spontaneous cardiac activity did not resume in the two groups.

Table 3. Comparison of Blood Gas Analyses in the Control and CIO Groups after Resumption of Cardiac Activity

	Control Group (n = 8)	CIO Group* (n = 10)
pH	6.85 ± 0.11	6.88 ± 0.059
Pa_{CO_2} (mmHg)	86 ± 25	96 ± 42
Pa_{O_2} (mmHg)	162 ± 99	247 ± 162
HCO_3^- (mM)	14.1 ± 3.6	17.6 ± 5.2
Sa_{O_2} (%)	93.5 ± 5.9	95.1 ± 5.3

* No difference was observed between the two groups.

group and in 10 in the CIO group, with no significant difference in the results (table 3).

Lastly, seven patients in the control group and six in the CIO group could be admitted to the hospital and were able to undergo blood gas analysis performed at admission after a period of mechanical ventilation with the same transport ventilator and the same settings (V_t = 12 ml/kg, rate = 12/min, $F_{I_{O_2}}$ = 1, and maximum pressure = approximately 40 cm H_2O). Table 4 shows that Pa_{CO_2} was significantly lower and pH and Pa_{O_2} were significantly higher in the CIO group.

The quantities of epinephrine necessary to achieve resumption of cardiac activity were comparable for the two groups, and there was no difference between the two groups concerning hemodynamics after successful resuscitation. All the patients admitted to the hospital died between day 0 and day 7.

Discussion

This preliminary study suggests the possibility of treating cardiorespiratory arrest by replacing IPPV with a continuous insufflation of oxygen. The percentage of successful and stable successful resuscitation was comparable in the two groups in the current study. In addition, blood gas analysis performed at admission to the ICU suggests that the lungs of the patients previously treated with CIO and who received prolonged external cardiac compression–decompression may have been

Table 4. Comparison of Blood Gas Analyses in the Control and CIO Groups on Admission to the Intensive Care Unit

	Control Group (n = 7)	CIO Group (n = 6)
pH	7.01 ± 0.19	7.29 ± 0.147*
Pa_{CO_2} (mmHg)	64.9 ± 17.7	33.8 ± 2.6*
Pa_{O_2} (mmHg)	194.6 ± 101	374.8 ± 147*
HCO_3^- (mM)	18.1 ± 6.4	19.2 ± 4.4
Sa_{O_2} (%)	96.1 ± 5.3	99.2 ± 5.3

* $P < 0.05$.

less abnormal, as indicated by a more physiologic Pa_{CO_2} and pH level in this group, and better oxygenation.

The effectiveness of CIO delivered with a similar endotracheal tube combined with external cardiac massage in CPR was previously observed in a patient, in whom cardiorespiratory arrest occurred during a coronary angiography procedure, with satisfying neurologic and cardiovascular response.[15] The bellows effect of external chest compression during constant-flow transtracheal oxygen delivery has been shown in dogs by Branditz et al.[13] Kern et al. also used a modified pharyngeal–tracheal-lumened airway for the same purpose.[14] In an experimental study performed in paralyzed pigs, Brochard et al.[12] were able to maintain a normal Pa_{CO_2} using manual or mechanical thoracic compressions at a rate of 90 compressions/min. Oxygenation was maintained using a multichannel tube, which permitted continuous insufflation of 15 l/min air, with an endotracheal pressure of approximately 10 cm H_2O. During cardiorespiratory arrest secondary to ventricular fibrillation in the same study, the authors compared the respiratory and hemodynamic effectiveness of continuous insufflation of air using the multichannel tube combined with external cardiac massage, to the effectiveness of standard CPR with intermittent positive-pressure ventilation during two consecutive periods of 4 min. A significant difference, favoring continuous insufflation of gas, was observed for the systolic aortic pressure and the blood flow in the common carotid artery. There was a similar effectiveness regarding gas exchange and the coronary pressure gradient. Although the mechanisms of cardiac arrest were different, this preliminary study in patients confirms the possibility of using CIO as a method of ventilation during CPR, as observed in the animal models.

The blood samples taken as soon as cardiac activity resumed showed a substantial level of hypercapnia, which, together with a decrease in bicarbonate and lactic acidosis, was responsible for severe acidosis, as previously observed. The percentage of patients with a Sp_{O_2} more than 70% with no resumption of spontaneous cardiac activity was comparable in the two groups up to the 30th min. At admission to the ICU, although the number of patients was small, there was a striking difference between the two groups in terms of arterial blood gases. Because the mode and pattern of ventilation delivered by the transport ventilator were similar in the two groups between the two gas samples, this result probably reflects differences in the respiratory system mechanics of the two groups. During transportation, no adjustment of ventilation was made and the same set-

tings were used on a small portable ventilator. For these ventilators, known to have a limited ability to ventilate very sick lungs, the upper alarm pressure limit was set identically in the two groups, around 40 cm H_2O. In a model of cardiorespiratory arrest in pigs, Idris *et al.*[16] demonstrated that, with unaltered ventilatory parameters, the minute ventilation obtained using mechanical ventilation decreased after 10 min of cardiac massage, with the formation of progressive atelectasis and a reduction in pulmonary and thoracic compliance. Because CIO generates a positive pressure in the lungs, this positive end-expiratory pressure effect may have been protective against prolonged external chest massage-induced atelectasis. One may also hypothesize that it could protect against other forms of pulmonary injury, such as pulmonary contusion or pulmonary edema favored by the negative intrathoracic pressure generated by active decompression. Although no measurement of respiratory mechanics was available, the possibility of a protective effect of CIO against pulmonary lesions created by prolonged massage is a plausible hypothesis. We did not record the presence of gasping in the two groups, which can also influence gas exchange and outcome.[17-19] We cannot rule out that a difference in active gasping in the two groups explain part of the difference.

Normal ventilation at the initial stage of CPR may not be necessary. Tang *et al.*[20] conducted a randomized study in rats using a model of cardiorespiratory arrest by ventricular fibrillation, in which the effects of massage with IPPV and those of massage with no IPPV but with an $F_{I_{O_2}}$ of 1, were compared. They found that, although Pa_{O_2} was lower and Pa_{CO_2} higher, the absence of IPPV did not alter the percentage of success of CPR or survival at 24 h. Coronary perfusion was identical in the two groups. In the nonventilated group, only the animals with resumption of cardiac activity developed gasp-type respiration during cardiac massage. In another randomized study performed in pigs using a comparable protocol, Noc *et al.*[21] noted, after 8 min of external compression without ventilation, a moderate increase in Pa_{CO_2} and a higher Pa_{O_2} than with IPPV. Survival after 48 h was comparable. In this study, comparable gasp-type ventilation was noted initially in the two groups, but, later, the nonventilated animals only underwent gasp-type ventilation combined with a ventilation because of external massage. In the current study, we were not able to record gasp-type ventilation. Massage alone without positive pressure can only maintain alveolar ventilation for a limited period of time.[22] Using pigs that were paralyzed to suppress gasp ventilation, Idris *et al.*[16] demonstrated

that, after 10 min of massage with no ventilation, severe hypercapnia with respiratory acidosis occurred, with the minute ventilation decreasing.

Apneic oxygenation, which consists of placing the airway of an animal not experiencing spontaneous respiratory activity in contact with pure oxygen, has been shown to allow a subnormal Pa_{O_2} to be maintained, but is followed by to a significant accumulation of carbon dioxide.[1] In a study performed in patients not undergoing ventilation, CIO was performed through the channels of a multichannel tube similar to the one used in the current study, with an oxygen flow generating an intrathoracic pressure of 10 cm H_2O.[4] After 90 s, Pa_{O_2} remained stable, but Pa_{CO_2} increased significantly, showing that this method was not able to maintain alveolar ventilation. Several studies have shown that CIO, even at a low flow rate, allows Pa_{O_2} to be maintained at close to normal values but that the elimination of carbon dioxide, dependent on the gas flow rate, is only modest in patients.

Gas transportation processes in the lung are controlled by two mechanisms: convection in the airways proportional to the flow of fresh gas and diffusion in the alveoli.[5] The gas diffusion law accounts for the possibility of maintaining normal oxygenation, even when there is no respiratory movement,[5] but the carbon dioxide elimination mechanisms appear to depend on convection phenomena.[23] The multichannel tube used in the study allows the expired gas to be continuously replaced by inspired fresh gas and may help to produce better mixing in the distal part of the airway.[5] The cardiogenic oscillations that contribute to the gas transportation when the gas flow is delivered close to the carina would appear to have a negligible role.[24] The main reason for alveolar ventilation in this study, however, was probably the generation of tidal ventilation during the effects of chest compression and decompression. In their experimental study, Brochard *et al.*[12] demonstrated that CIO, combined with external cardiac massage performed manually or mechanically, generated a V_t of 52 $\pm$ 21 ml at a rate of 93 compressions/min (rate of compression); the minute volume obtained was one third lower than that observed for IPPV with a V_t of 10 ml/kg. Although the inspired V_t is produced passively by the CIO, the expired V_t is caused by external compression of the chest.

The endotracheal tube used in this study was previously tested in different conditions in animals[12,25] and in patients.[4] During mechanical ventilation, it can be used to maintain a lung positive pressure and adequate oxy-

genation during tracheal suctioning, to deliver ventilation[26] or to deliver tracheal gas insufflation to washout carbon dioxide in hypercapnic patients during mechanical ventilation.[27,28] Because of the small size of the capillaries molded in the wall of the tube, the inner diameter is kept constant and does not induce an increase in resistance.

The method of cardiac massage also affects ventilatory effectiveness; the various studies mentioned herein used manual or mechanical massage. Using active compression-decompression, Carli et al.[29] demonstrated that, in dogs, the negative pressure generated by the active decompression produced a minute ventilation twice that obtained with manual or mechanical compression. In a model of cardiorespiratory arrest in pigs, Hevesi et al.[22] compared the effects of combining mechanical massage with either IPPV or continuous positive airway pressure, to produce a minute ventilation equal to 75% of the basic spontaneous ventilation. They found that, although hemodynamic parameters and Pa_{CO_2} were comparable in the two groups, Pa_{O_2} was significantly higher in the continuous positive airway pressure group. The combination of active compression-decompression with a positive end-expiratory pressure effect probably facilitated to maintain ventilation in our study. Our method may therefore be very close to the combination of high-flow continuous positive airway pressure delivered to the lungs with a simple chest massage. The delivery of fresh gas at the tip of the tube may also help in decreasing dead space.[26,27]

This study was the first clinical human study to substitute a method of CIO for IPPV during CPR. CIO appears as a promising, simple technique to deliver ventilation during CPR. The results of this study did not show improvement in survival. It will be necessary to conduct larger studies to determine whether CIO may help to improve the prognosis of preadmission cardiorespiratory arrest.

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