

ORIGINAL ARTICLE

Prevention of Early Ventilator-Associated Pneumonia after Cardiac Arrest

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ABSTRACT

BACKGROUND

Patients who are treated with targeted temperature management after out-of-hospital cardiac arrest with shockable rhythm are at increased risk for ventilator-associated pneumonia. The benefit of preventive short-term antibiotic therapy has not been shown.

METHODS

We conducted a multicenter, double-blind, randomized, placebo-controlled trial involving adult patients (>18 years of age) in intensive care units (ICUs) who were being mechanically ventilated after out-of-hospital cardiac arrest related to initial shockable rhythm and treated with targeted temperature management at 32 to 34°C. Patients with ongoing antibiotic therapy, chronic colonization with multidrug-resistant bacteria, or moribund status were excluded. Either intravenous amoxicillin-clavulanate (at doses of 1 g and 200 mg, respectively) or placebo was administered three times a day for 2 days, starting less than 6 hours after the cardiac arrest. The primary outcome was early ventilator-associated pneumonia (during the first 7 days of hospitalization). An independent adjudication committee determined diagnoses of ventilator-associated pneumonia.

RESULTS

A total of 198 patients underwent randomization, and 194 were included in the analysis. After adjudication, 60 cases of ventilator-associated pneumonia were confirmed, including 51 of early ventilator-associated pneumonia. The incidence of early ventilator-associated pneumonia was lower with antibiotic prophylaxis than with placebo (19 patients [19%] vs. 32 [34%]; hazard ratio, 0.53; 95% confidence interval, 0.31 to 0.92; $P=0.03$). No significant differences between the antibiotic group and the control group were observed with respect to the incidence of late ventilator-associated pneumonia (4% and 5%, respectively), the number of ventilator-free days (21 days and 19 days), ICU length of stay (5 days and 8 days if patients were discharged and 7 days and 7 days if patients had died), and mortality at day 28 (41% and 37%). At day 7, no increase in resistant bacteria was identified. Serious adverse events did not differ significantly between the two groups.

CONCLUSIONS

A 2-day course of antibiotic therapy with amoxicillin-clavulanate in patients receiving a 32-to-34°C targeted temperature management strategy after out-of-hospital cardiac arrest with initial shockable rhythm resulted in a lower incidence of early ventilator-associated pneumonia than placebo. No significant between-group differences were observed for other key clinical variables, such as ventilator-free days and mortality at day 28. (Funded by the French Ministry of Health; ANTHARTIC ClinicalTrials.gov number, NCT02186951.)

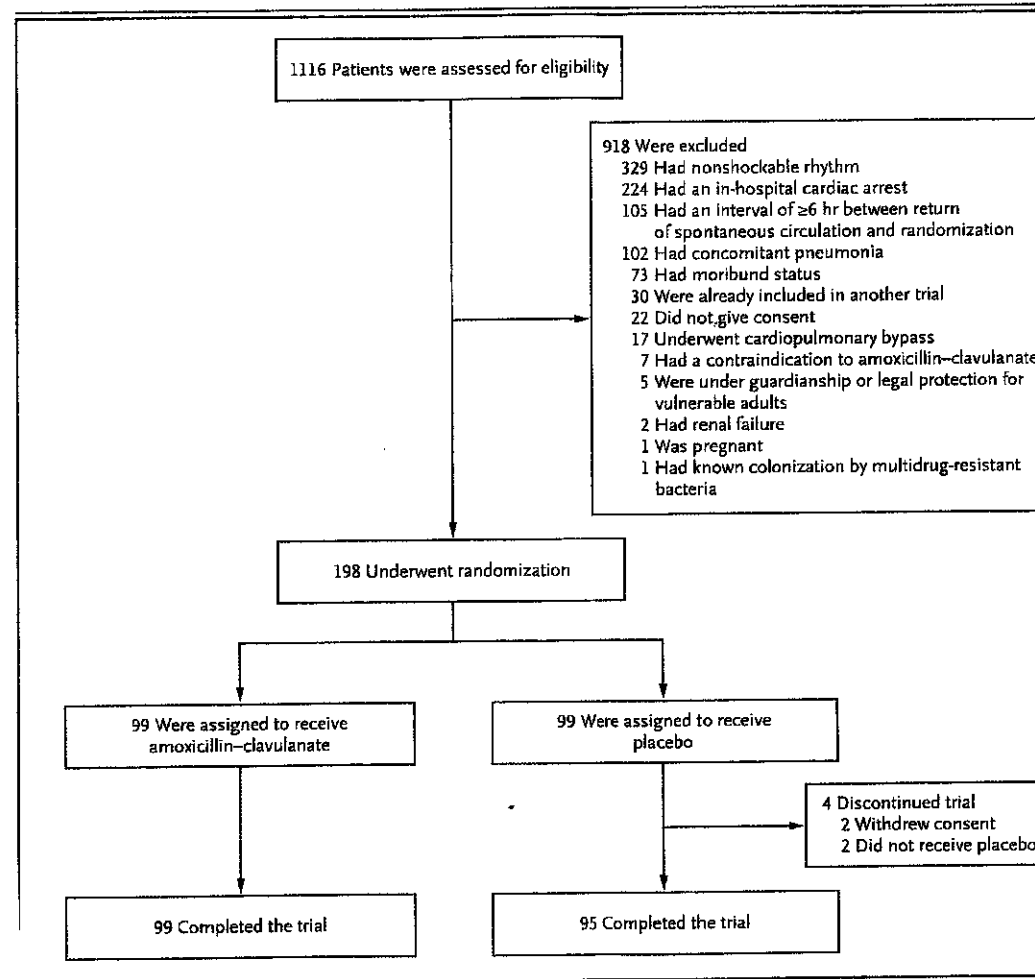


Figure 1. Screening and Randomization.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Antibiotic Group (N=99)	Control Group (N=95)
Median age (IQR) — yr	61 (50–73)	60 (51–72)
Male sex — no. (%)	76 (77)	80 (84)
Median body-mass index (IQR)†	26 (24–29)	27 (24–29)
Medical history		
Median score on the Charlson Comorbidity Index (IQR)‡	2 (1–4)	2 (1–4)
Chronic lung disease — no. (%)	6 (6)	9 (9)
Immunosuppression — no. (%)	3 (3)	0
Chronic heart disease — no. (%)	23 (23)	28 (29)
Diabetes — no. (%)	10 (10)	6 (6)
Out-of-hospital cardiac arrest		
Witnessed — no. (%)	94 (95)	90 (95)
Median no-flow time (IQR) — min§	2 (0–5)	3 (0–6)
Median low-flow time (IQR) — min§	20 (10–28)	18 (12–25)
Median time to intubation (IQR) — min	20 (12–34)	22 (13–33)
Initial shockable rhythm — no. (%)		
Ventricular fibrillation	84 (85)	74 (78)
Ventricular tachycardia without pulse	13 (13)	10 (11)
Other	2 (2)	11 (12)
Median no. of electric shocks (IQR)	3 (2–4)	2 (1–3)
Catecholamine support — no. (%)	73 (74)	67 (71)
Antiarrhythmic drugs — no. (%)	39 (39)	45 (47)
Suspected aspiration — no. (%)	3 (3)	8 (8)
Median baseline temperature (IQR) — °C	35 (35–36)	36 (35–36)
Median score on the Glasgow Coma Scale (IQR)¶	3 (3–3)	3 (3–3)
Median SOFA score (IQR)‖	8 (7–12)	9 (6–11)
Median APACHE II score (IQR)**	24 (22–28)	24 (20–28)
Mild therapeutic hypothermia		
Median interval between out-of-hospital cardiac arrest and hypothermia (IQR) — hr	6 (4–6)	5 (5–6)
Median duration of hypothermia (IQR) — hr	30 (24–34)	29 (23–33)
Median target temperature (IQR) — °C	34 (33–35)	34 (33–34)

* Percentages may not total 100 because of rounding. IQR denotes interquartile range.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ Scores on the Charlson Comorbidity Index range from 0 to 37, with higher scores indicating more coexisting conditions.

§ No-flow time refers to the period without any cardiopulmonary resuscitation procedure, and low-flow time refers to the total period with active cardiopulmonary resuscitation but without sustained spontaneous circulation.

¶ Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating a reduced level of consciousness.

‖ Scores on the Sequential Organ Failure Assessment (SOFA) range from 0 to 24 (from 0 to 4 for each of six organ systems), with higher scores indicating more severe organ dysfunction.

** Scores on the Acute Physiology and Chronic Health Evaluation (APACHE) II range from 0 to 71, with higher scores indicating a higher risk of death.