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Isoflurane or propofol sedation in patients with targeted temperature management after cardiopulmonary resuscitation: A single center study

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ABSTRACT

Propose: Targeted temperature management improves outcomes in comatose patients after cardiac arrest. Short lasting sedatives might enable rapid awakening after targeted temperature management and therefore early prognostication and extubation. Aim of the present study was to compare sedation with volatile isoflurane to intravenous propofol.
Materials and methods: All patients after cardiopulmonary resuscitation undergoing targeted temperature management treated between 01/2014 and 02/2017 at a single tertiary referral hospital were screened. Exclusion criteria included extracorporeal support or a survival below 48 h.
Results: Data on 214 patients (median age 66.1 years, 62.6% shockable rhythm, survival 69.6%) are reported, 178 patients on propofol and sufentanil and 36 patients on isoflurane and sufentanil. Median time to first spontaneous breathing (9.3 h vs. 9.5 h, $p = .373$), median duration on mechanical ventilation in extubated patients (99.4 h vs. 105.7 h, $p = .692$) and median ICU stay (11.1d vs. 9.8d, $p = .320$) were similar in patients on propofol or isoflurane, respectively. Findings were confirmed by propensity score matching. Opioid dose was significantly lower in the isoflurane group ($p < .001$) while norepinephrine dose was significantly higher ($p = .004$).
Conclusion: Isoflurane sedation is feasible on during targeted temperature management. Time to spontaneous breathing, mechanical ventilation duration or ICU stay was not reduced by isoflurane.

1. Introduction

In comatose patients after out-of-hospital cardiac arrest (OHCA), return of spontaneous circulation (ROSC) and an initial shockable rhythm, current treatment guidelines recommend targeted temperature management (TTM) [1, 2] in order to improve outcome. The same treatment algorithm could also be considered for all other patients after cardiac arrest [1, 2]. During TTM, a constant core temperature of 32–36 °C is recommended for 24 h [1, 2]. Rewarming should be performed slowly with a rate of 0.25–0.5 °C/h [3]. During the 24 h of TTM (plus 4–20 h of rewarming in case of a TTM below 36 °C) a deep sedation is mandatory for multiple reasons, including shivering, reduced cerebral oxygen consumption and tracheal tube toleration [1].

After TTM, a discontinuation of sedation is indicated for neurological prognostication 72 h after cardiac arrest [1]. During TTM, half-life time of sedatives is increased by slowed metabolism [4, 5] and potential kidney and liver dysfunction after cardiac arrest. Current guidelines therefore suggest short-acting drugs for sedation and analgesia in patients after cardiac arrest [1, 4]. Volatile isoflurane has a very short context-sensitive half-life time and therefore appears to be an optimal candidate for sedation in patients after cardiac arrest [6]. Although several case series have demonstrated feasibility of volatile anesthetics in patients on intensive care units (ICU) [6] and in patients after cardiac arrest [7, 8], the risk-benefit ratio is not clear. A prospective randomized trial in a general population of critically ill patients is currently ongoing [9] however not focusing on patients on patients after cardiac arrest undergoing TTM. Potential side effects of volatile anesthetics have been reported, including vasodilation [6, 10], decreases shivering thresholds [10] and induces hypoxia and hypercapnia [11, 12].

The aim of our registry analysis was to compare time to spontaneous breathing and time on mechanical ventilation after cardiac arrest sedated with isoflurane plus sufentanil or propofol plus sufentanil.

2. Methods

We report data derived from a single-center retrospective registry of patients after cardiopulmonary resuscitation and return of spontaneous

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circulation. All patients presented at the medical ICU of the University Medical Center Freiburg between January 2014 and February 2017.

2.1. Targeted temperature management (TTM)

Following our local standard operating procedure, all comatose patients with ROSC after successful cardiopulmonary resuscitation (CPR) were treated with TTM (disregarding of initial rhythm or place of cardiac arrest). A core temperature of 33 °C was maintained for 24 h, followed by rewarming at 0.2 °C per hour. When a contraindication for a TTM with 33 °C was present or expected (like bleeding), a target temperature of 36 °C could be chosen at the caring physician's direction. Patients were either cooled by a catheter-based (Thermogard XP®, Zoll, Germany) or surface-based (Arctic Sun®, Medivance, Germany) feedback-controlled cooling device. The device was implicated once patients reached the ICU after routine pre-clinical initiation of cooling.

2.2. Patient selection

Using a computerized search, we identified a total of 294 patients after cardiopulmonary resuscitation whose medical reports included the search criteria for the German OPS code 8-607.0 to 8-607.3 (coding for a feedback-controlled cooling device) within January 2014 and February 2017. Several patient groups were pre-specified to be excluded for this research including those with a survival below 48 h (since the impact of sedation could not be investigated) and those with an extracorporeal support (since the severe underlying disease influences sedation strategy and timing of extubation rather than the sedative alone). Fig. 1 shows details on patients excluded.

2.3. Sedation and spontaneous breathing

Sedation of patients after ROSC was protocol based aiming at a Richmond Agitation Sedation Scale (RASS) of −5 during TTM. Sedation was stopped or at least significantly reduced aiming at a RASS of −1 to −2 once patients reached 36 °C (in case of TTM with 33 °C) or after 24 h of TTM (in the case of TTM with a targeted core temperature of 36 °C). Until 2015, standard sedation for patients after CPR on our ICU was a combination of propofol and sufentanil administered by continuous intravenous infusion. Starting in July 2015, volatile sedation using isoflurane with the AnaConDa device (AnaConDa®, Sedana Medical, Uppsala, Sweden) was introduced on our ICU. The standard operating procedure for sedation during TTM after CPR was amended with the volatile sedation isoflurane, which became the recommended primary sedative choice. Due to availability (only two AnaConDa® device monitors were available during the investigated time period) and caring physician's direction, isoflurane sedation was not initiated in all patients. Isoflurane was monitored continuously on a breath-by-breath basis aiming at an end-tidal isoflurane concentration of 0.5 to 1.0%. Time to first spontaneous breathing was calculated from the time point when patients with a TTM with 33 °C reached 36 °C (and sedation was aimed at RASS -1 to −2) or 24 h after reaching 36 °C in case of 36° TTM. Spontaneous breathing was defined by first spontaneous breathing episode of 30 min or longer.

2.4. Data processing and matching

Data analysis was blinded to patient identity and approved by the ethics committee of the University of Freiburg (Ethik-Kommission der Albert-Ludwigs-Universität Freiburg, Engelberger Straße 21, 79106 Freiburg, Germany). Ethics approval file number was 606/16. *t*-Test, Fisher's exact test, ANOVA or Mantel-Cox test were employed as applicable and a p-value of ≤0.05 was considered statistically significant. All data are given as median (interquartile range = IQR) if not otherwise stated. Propensity score matching was performed using SPSS 23.0 for baseline characteristics matching age, gender, CPR duration, in hospital cardiac arrest, targeted temperature management targeting 36 °C, preexisting pulmonary, kidney, liver or cerebral disease.

3. Results

3.1. Patient collective

A total of 294 patients were screened and after exclusion of 80 patients (32 due to survival <48 h and 41 due to an extracorporeal assist device) a total of 214 patients could be considered for analysis (Fig. 1). Median age at time of cardiac arrest was 66.1 years (IQR 64.2–67.9 years) and 71.0% were male. 78.5% of all patients were resuscitated

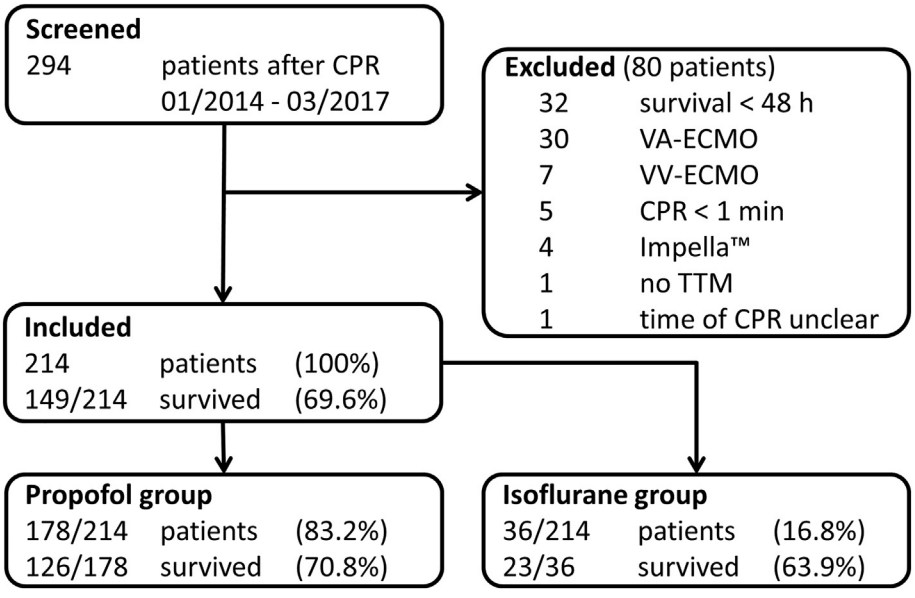

Fig. 1. Flow chart of patients included in study. Flow chart showing patients screened, excluded and included in the study. Abbreviations: CPR = cardiopulmonary resuscitation, VA-ECMO = venoarterial extracorporeal membrane oxygenation, VV-ECMO = venovenous extracorporeal membrane oxygenation, TTM = targeted temperature management.