Title:

Comparing anesthesia with isoflurane and fentanyl/fluanisone/midazolam in a rat model of cardiac arrest

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Contributions:

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Short Title:

Effect of anesthesia on resuscitation from cardiac arrest

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Abstract

Background: Only one in ten patients survives cardiac arrest (CA), underscoring the need to improve CA management. Isoflurane has shown cardio- and neuroprotective effects in animal models of ischemia/reperfusion injury. Therefore, beneficial effect of isoflurane should be tested in an experimental CA model. We hypothesize that isoflurane anesthesia improves short-term outcome following resuscitation from CA compared with a subcutaneous fentanyl/fluanisone/midazolam anesthesia.

Methods: Male Sprague Dawley rats were randomized to anesthesia with isoflurane (n=11) or fentanyl/fluanisone/midazolam (n=11). After 10 min of asphyxial CA, animals were resuscitated by mechanical chest compressions, ventilations, and epinephrine and observed for 30 min. Hemodynamics including coronary perfusion pressure, systemic O₂ consumption, and arterial blood gases were recorded throughout the study. Plasma samples for Endothelin-1 and catecholamines were drawn before and after CA.

Key findings: Compared with fentanyl/fluanisone/midazolam anesthesia, isoflurane resulted in a shorter time to return of spontaneous circulation (ROSC), less use of epinephrine, increased coronary perfusion pressure during CPR, higher mean arterial pressure post ROSC, increased plasma levels of Endothelin-1 and decreased levels of epinephrine. The choice of anesthesia did not affect ROSC rate or systemic O₂ consumption.

Conclusion: Isoflurane reduces time to ROSC, increases coronary perfusion pressure, and improves hemodynamic function, all of which are important parameters in CA models.

Keywords:
Cardiac arrest, isoflurane, catecholamines, oxygen consumption, anesthesia, fentanyl
New and noteworthy

The preconditioning effect of volatile anesthetics in studies of ischemia/reperfusion injury has been demonstrated in several studies. This study shows the importance of anesthesia in experimental cardiac arrest studies as isoflurane raised coronary perfusion pressure during resuscitation, reduced time to return of spontaneous circulation and increased arterial blood pressure in the post cardiac arrest period. These effects on key outcome measures in cardiac arrest research are important in the interpretation of results from animal studies.
1 Introduction

Although survival after cardiac arrest (CA) has improved over the past decades, overall mortality remains unacceptably high at 90% (34). In view of this dismal prognosis, it is crucial to examine whether certain resuscitation strategies have the potential to improve outcome. To this end, the pre- and postconditioning effects of volatile anesthetics are well known, and experimental research has shown improved cardiac function and diminished neurological injury following ischemia/reperfusion injury and CA (5, 14, 26, 27).

The study of protective resuscitation strategies after CA invariably involves the use of anesthetized animals, and the choice of anesthetics in animal models may interfere with factors of importance to subsequent recovery, both prior to the induction of CA, and during resuscitation (19). High coronary perfusion pressure (CPP) and cerebral blood flow (CBF) are known predictors of ROSC, and volatile anesthetics may, by their effect on these parameters, therefore increase the rate of ROSC (16, 23, 25). Endothelin-1 is a known predictor of resuscitation failure and a lack of response to epinephrine during CPR (30, 31), and the Endothelin-1 induced vasoconstriction is affected by volatile anesthetics (1). Finally, oxygen debt is a good predictor of outcome in animal models of shock (28). Oxygen debt is proportional to the duration of CA and to the systemic O₂ consumption (VO₂) before CA. Anesthetics affect VO₂ and the choice of anesthesia could therefore affect the ROSC rate (8, 24, 33).

1.1 Objective

The aims of the current study were to: 1) explore the potential beneficial effect on ROSC rate of isoflurane anesthesia when compared to fentanyl/fluanisone/midazolam (FFM) anesthesia
in an experimental model of cardiac arrest and 2) to investigate the impact of anesthesia on important outcome measures in experimental CA research.

1.2 Hypothesis

The primary hypothesis was that anesthesia with isoflurane improves the rate of ROSC when compared to anesthesia with FFM. The secondary hypotheses were that the potential effect on ROSC rate is attributable to changes in CPP, CBF, or VO₂ and that isoflurane anesthesia increases plasma levels of Endothelin-1 and catecholamines.
2 Material and methods

2.1 Ethical statement

The study was approved by the National Committee on Animal Research Ethics no. 2012-15-2934-0047 (Animal Experiments Inspectorate, Copenhagen, Denmark) and conducted in accordance with the “Principles of Laboratory Animal Care” (NIH publication Vol 25, No. 28 revised 1996).

2.2 Study design

A list randomizing the animals to either isoflurane or FFM anesthesia was prepared before starting the study (See Figure 1). It was not possible to blind the primary investigator during the experimental procedures, but all subsequent data analyses were carried out blinded.

Figure 1: Study design. Animals were divided into 2 groups: isoflurane (n=11) and FFM (n=11).

FFM=fentanyl/fluanisone/midazolam, BL=baseline, BS=blood sample, CA=cardiac arrest, CBF=carotid blood flow, CPP=coronary perfusion pressure, CPR=cardiopulmonary resuscitation, ROSC=return of spontaneous circulation, VO$_2$=systemic O$_2$ uptake.

2.3 Experimental animals and housing
Male Sprague Dawley rats (Taconic, Denmark) weighing 400g were used for this study. Rats were housed pairwise at room temperature and humidity (22-23°C, 45%), at 12-hour light/dark cycle, with free access to food and water. Cages were enriched with bedding material, tube for hiding, and toys.

2.4 Experimental procedures

2.4.1 Animal preparation

To make groups comparable the animals were anesthetized accordingly:

Induction: Anesthesia in the two groups was induced by either 5% isoflurane or subcutaneous (sc) injection of FFM (fentanyl 0.0788 mg/ml, fluanisone 2.5 mg/ml and midazolam 1.25 mg/ml) (2.4ml/kg). In the FFM group a single dose of Ketamine (100mg/kg) was administered intraperitoneally (ip) to prevent pharyngeal reflexes during intubation.

Surgery: During surgical preparation anesthesia was maintained with 2.5% isoflurane while anesthesia in the FFM group was maintained with sc injection of a lower FFM dose (0.6ml/kg) every 30 min.

Cardiac arrest: During cardiac arrest neither isoflurane nor FFM was administered.

Resuscitation: During resuscitation isoflurane was resumed at 1% in the isoflurane group, where as FFM administration was postponed to match the lower level of isoflurane.

Post-ROSC: Following ROSC, as no painful procedures were carried out, anesthesia was maintained with 1% isoflurane in the isoflurane group and administration of FFM was delayed corresponding to the time from start of asphyxia until ROSC resulting in an accordingly lower dose in the FFM group(32).
The level of anesthesia was monitored by, tail pinch, whisker stimulation, and changes in blood pressure and pulse throughout the study.

Before tracheotomy, animals were orally intubated using a 17-gauge venous catheter and ventilated with 30% O₂ and a tidal volume of 8ml/kg. For the VO₂ measurements, a tracheotomy was performed to prevent loss of expiratory gasses. After tracheotomy, tidal volume was reduced to 5ml/kg. The ventilation rate was adjusted to maintain PaCO₂ at 31-44mmHg. The temperature was kept at 36.5-37.5°C by a feedback-controlled heating pad.

Saline, 2ml/kg/h, was administered during preparation. The left femoral artery was catheterized for invasive blood pressure measurement and arterial sampling, using a PE90 tube connected to a 22-gauge venous catheter. The femoral vein was catheterized using a PE50 tube for fluid and drug administration. Pressure catheters (2F) (Millar, Huston, TX, USA) were placed in the right atrium via the right jugular vein and aortic arch via the right carotid artery to determine coronary perfusion pressure (CPP). A flow probe (Transonic Systems, Ithaca, NY, USA) was placed around the left carotid artery to measure carotid blood flow. CPP was calculated as the difference between aortic pressure and right atrial pressure just before compression, and CBF was calculated as the mean flow. Both were averaged over 10 compressions. Both measures are reported after 30 seconds of CPR.

Data on blood pressures, carotid blood flow, ECG, ETCO₂, hind paw saturation, and rectal temperature were continuously collected using PowerLab (AD instruments, Oxford, United Kingdom). Arterial blood samples (100μl) were analyzed at baseline, 5, 15, and 30 min after ROSC (Radiometer, Brønshøj, Denmark).

2.4.2 Cardiac arrest and resuscitation
CA was induced by asphyxia and defined as a mean arterial pressure (MAP) below 20mmHg. To prevent spontaneous respiration during induction of CA, rocuronium (2.4mg/kg) was administered 30 seconds before turning off the ventilator. After 10 min of CA, resuscitation was initiated by administration of epinephrine 0.01mg/kg. If ROSC (defined as MAP>40mmHg) was not achieved, adrenalin administration was repeated every two minutes. To prevent bias as the primary investigator was not blinded, chest compressions were delivered in a standardized fashion by a custom-made thumper at a rate of 200min⁻¹, a depth of 1.4cm (1/3 of anterior-posterior chest diameter), and with equal 1:1 compression/relaxation ratio. Animals were ventilated with 100% O₂ at a rate of 70min⁻¹. After ROSC, adrenalin (0.0015mg/kg) was administered if MAP dropped below 40mmHg (needed in 2 animals in the isoflurane group within the first 10 min). After a 30 min observation period, animals were euthanized with an iv. lethal dose of pentobarbital.

2.4.3 Systemic O₂ consumption (VO₂) and CO₂ production (VCO₂)

VO₂ and VCO₂ in steady state conditions were determined by respirometry by measuring oxygen and carbon dioxide concentrations in the inspiratory and expiratory air, using serially connected O₂ analyzer (Servomex, Crowborough, England), CO₂ sensor P-61B (AEI Technologies, Pittsburg, PA, USA), and CO₂ analyzer P-61B (AEI Technologies, Pittsburg, PA, USA). To collect all expiratory gas, a tube with a volume above the minute volume was connected to the expiratory line via a t-piece; and a pump to provide suction through the system was connected after the gas analyzers. VO₂ and VCO₂ were calculated as the product of the suction flow rate through the analyzers and the integrated area below or above baseline of the expiratory gas curves as a function of time and values were reported as ml(STPD)/min/kg. Data collection and subsequent integration was done using Biopac MP150.
and AcqKnowledge acquisition software (Biopac systems, Goleta, CA, USA) as previously described(21).

2.4.4 Blood samples

Blood samples (1.4ml ≈ 5% of total blood volume(32)) were collected in EDTA-coated tubes at baseline and 30 min after ROSC and centrifuged at 0°C and 1600g for 15 min. Plasma was stored at -80°C until analysis. Endothelin-1 (R&D systems, Minneapolis, MN, USA), and catecholamines (DRG international, Springfield, NJ, USA) were analyzed using an ELISA assay following the manufacturer's recommendation. Detection limits and intraassay variation were: Endothelin-1 (0.29pg/ml, 15%), epinephrine(5pg/ml, 33%), norepinephrine(16pg/ml, 5%), dopamine(29pg/ml, 5%).

2.5 Sample size

Based on pilot studies, we estimated a ROSC rate of 90% in the isoflurane group and 20% in the FFM group, requiring a sample size of 11 animals per group, with a power of 0.9 and a α of 0.05.

2.6 Experimental outcomes

2.6.1 Primary outcome

The primary outcome measure was ROSC defined as a MAP above 40mmHg.

2.6.2 Secondary outcomes

Secondary outcomes were time to ROSC, CPP and CBF during CPR, systemic oxygen consumption (VO₂) and carbon dioxide production (VCO₂) at baseline, plasma analysis of Endothelin-1 and catecholamines at baseline and 30 min after ROSC and physiological data.
2.7 Statistical methods

Normally distributed variables are presented as mean with 95\% confidence interval (CI) and non-normally distributed values are presented as median and interquartile range (IQR). Normality was determined by histogram and Q-Q plots.

Repeated measurements were analyzed using analysis of variance for repeated measurements to test for any time-dependent difference between the groups. The differences in baseline values and end of study values were analyzed using post hoc pairwise comparison. Non-normally distributed data were transformed on a logarithmic scale to ensure normality. All data are graphically presented on the original scale.

Not normally distributed continues variables were analyzed using Kruskal-Wallis one-way analysis of variance. Normally distributed continuous variables were analyzed using Students T-test. Dichotomous outcomes were compared using Fischer’s exact test. Two-tailed p-values less than 0.05 were considered statistically significant. Analyses were performed using the Stata 12.1 (StataCorp, TX, USA), and graphs were constructed in Prism 5.0 (GraphPad, California, USA).
3 Results

3.1 Animals included

A total of 23 animals (weight 400g ± 14, age 11 weeks) were used for this study. One animal was excluded due to technical error during preparation. The remaining 22 animals were evenly randomized to the two experimental groups, and none were excluded in the subsequent analysis.

3.2 Baseline data

Baseline data are shown in Table 1. Compared with the FFM group, the isoflurane group had a lower heart rate, a higher temperature, higher CBF, and increased levels of glucose and lactate at baseline. All other baseline parameters were comparable between the two groups, including time from asphyxia to CA (isoflurane vs FFM: 119 sec [110;129] 116 sec [81,150]).
Table 1: Physiologic parameters: Data are presented as mean and 95%CI. MAP=Mean arterial pressure, CBF=Carotid blood flow, Iso=Isoflurane group, FFM=Fentanyl/fluanisone/midazolam group. #=difference at baseline, *=difference at 30 min post ROSC between the two groups.

3.3 Outcomes and estimations

3.3.1 Primary outcome

No difference in ROSC rates between the two groups was found (p=0.6) (Table 2). However, time to ROSC was significantly shorter in the isoflurane group than in the FFM group (92sec [57;127] vs. 241sec [155;329], p<0.001). Furthermore, the resuscitated rats in the FFM group required a higher number of epinephrine doses during resuscitation (2doses [2;3] vs. 1dose [1;1], p<0.004) than the isoflurane group. There was no difference in the presenting rhythm at initiation of CPR among the groups (isoflurane group: PEA=6, asystoli=5; FFM group: PEA=4, asystoli=7; p=0.67)

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane</th>
<th>FFM</th>
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<tbody>
<tr>
<td>ROSC</td>
<td>9 (82%)</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>No</td>
<td>2 (18%)</td>
<td>4 (36%)</td>
</tr>
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</table>

Table 2: ROSC=return of spontaneous circulation, FFM=fentanyl/fluanisone/midazolam

3.3.2 Secondary outcomes

Physiologic data

Physiologic data are shown in Table 1. The isoflurane group showed a significant increase in MAP, CBF, pH, and hemoglobin during the post-resuscitation period compared with the FFM group. The two animals in the isoflurane group receiving epinephrine in the early post-ROSC
phase did not differ from animals not receiving epinephrine in regards to hemodynamic function. In the post-ROSC period, the heart rate increased in the isoflurane group, while the heart rate decreased in the FFM group. The higher lactate in the isoflurane group observed at baseline was also evident immediately after ROSC; however, at 30 min, no difference existed between groups.

Coronary perfusion pressure and carotid blood flow

Figure 2 shows the results of the CPP and CBF measurements after 30 seconds of CPR. The CPP was significantly higher in the isoflurane group than in the FFM group. When comparing CPP based on ROSC vs. no ROSC, CPP was higher in the animals achieving ROSC (Figure 2). During CPR, we observed no difference in the CBF between the two groups; however, when categorizing the data based on resuscitation outcome, we did see a higher CBF in the group achieving ROSC.
Figure 2: Coronary perfusion pressure and carotid blood flow during CPR: Data are presented as median and interquartile range and provided as numbers below each group. Isoflurane (n=11), FFM (n=11), ROSC (n=16) no ROSC (n=6). FFM=fentanyl/fluanisone/midazolam, ROSC=return of spontaneous circulation.

**Systemic O2 consumption and CO2 production.**

Data on VO2 and VCO2 are shown in Figure 3. We observed a trend towards a lower VO2 in the isoflurane group, however this was not significant (p=0.09). There was no difference in VO2 when groups were defined according to resuscitation outcome. We observed no difference in VCO2, either when groups were defined according to anesthesia received or on the basis of their resuscitation outcome.
Figure 3: Systemic O₂ consumption and CO₂ production. Data are presented as median and interquartile range and provided as numbers below each group. Isoflurane (n=11), FFM (n=11), ROSC (n=16) no ROSC (n=6).

FFM=fentanyl/fluanisone/midazolam, ROSC=return of spontaneous circulation.

Plasma analyses

The results of the plasma analyses are shown in Figure 4 and 5. The isoflurane group showed increased levels of Endothelin-1 at baseline and 30 min after ROSC compared with the FFM group. There was no difference in Endothelin-1 levels when ROSC was compared with no ROSC (Figure 4).

Compared with FFM, isoflurane decreases levels of epinephrine at baseline, however this difference was not found 30 min after ROSC. Norepinephrine and dopamine showed no
difference between the two groups (Figure 5). We observed no difference in any of the 
catecholamines when groups were defined according to resuscitation outcome (data not 
shown).

Figure 4: Plasma levels of Endothelin-1. Data are presented as median and interquartile range and provided as 
numbers below each group. Isoflurane (n=11), FFM (n=11), ROSC (n=16) no ROSC (n=6).

FFM=fentanyl/fluanisone/midazolam, ROSC=return of spontaneous circulation.
Figure 5: Plasma levels of catecholamines. One outlier in the FFM group with epinephrine levels 5 fold the mean of the group was excluded. Including this outlier in the dataset does not change the results. Data are presented as median and interquartile range and provided as numbers below each group. Isoflurane (n=11), FFM (n=11, for epinephrine n=10). FFM=fentanyl/fluanisone/midazolam, ROSC=return of spontaneous circulation.
4 Discussion

In this rat model of asphyxial CA, we demonstrate how two commonly used anesthetic regimes affect short term outcome measures traditionally used in resuscitation research (12, 32). Compared with FFM, isoflurane results in shorter time to ROSC, lower dose of epinephrine, higher CPP during CPR, higher MAP post ROSC, increased plasma levels of Endothelin-1 and decreased levels of epinephrine. Contrary to our hypothesis, this did, however, not translate into an increased ROSC rate.

The absence of any difference in ROSC rate between groups despite a higher CPP in the isoflurane group may be attributable to the high CPP in both groups. Despite the difference in CPP among groups, the median CPP in the FFM group was 15.2 mmHg, which leaves a large proportion of the animals in this group above the threshold where ROSC is possible. Had the insult been more severe, animals been older or had comorbidities, the CPP increase caused by isoflurane may have been sufficed to place this group above the critical threshold where ROSC is possible. In our data, the relationship between ROSC and CPP levels (Figure 2B) is in accordance with the literature, where a CPP below 15 mmHg is a strong predictor of unsuccessful resuscitation (25).

In a porcine model of asphyxial CA, Kurita et al showed a ROSC rate of 100% in the isoflurane group compared to 60% in the propofol/fentanyl group (19). Riess et al recently failed to show increased ROSC rates with the use of volatile anesthesia; however, sevoflurane in this study was compared with no anesthesia (27). In both studies, CPP during CPR was above 15 mmHg in all study groups. Likewise, other studies fail to show a benefit on survival or neurological outcome, but report improvement in secondary endpoints such as cardiac function, mitochondrial function, and inflammatory markers (15, 22, 27). The beneficial
effect on secondary outcomes is also seen in the present study where MAP and CBF in the post-ROSC phase were higher in the isoflurane group. These benefits may be caused by the increased CPP during CPR, which diminishes the post-resuscitation injury (9). A large proportion of patients resuscitated from cardiac arrest subsequently die in the ICU in part due to neurological and cardiovascular collapse. Improvement in post-ROSC hemodynamic, such as MAP and CBF, may prove important in ameliorating outcome, however a longer follow-up period is needed to investigate this. Previous studies using brief periods of sevoflurane during CPR or after ROSC, demonstrated similar effects on CPP and myocardial function. Hence the effects seen in this study by isoflurane may apply to volatile anesthetics in general (22, 27).

In a porcine model of ischemic-induced CA, Shah et al demonstrated that an increased level of Endothelin-1 at baseline predicts resuscitation failure and failure to respond hemodynamically to epinephrine (30, 31). These findings could not be reproduced in our study, as baseline Endothelin-1 levels did not differ between animals achieving ROSC and those that did not. Differently, the increased plasma levels of Endothelin-1 in the isoflurane group could explain the higher CPP during resuscitation in the isoflurane group, as the difference in CPP was driven by a higher aortic pressure. This is supported by the results of Hilwig et al. (10) showing an increase in CPP with Endothelin-1 treatment, and the study by Holzer et al. (11) demonstrating an increase in cerebral perfusion. The possible beneficial effect of Endothelin-1 administration during resuscitation may however not apply to the post ROSC period, where several studies have demonstrated detrimental effects of Endothelin-1 administration and beneficial effects of treatment with Endothelin antagonists. During the post ROSC period the vasoconstriction caused by Endothelin-1 is believed to increase the
afterload causing augmented myocardial dysfunction and worsen cerebrovascular reactivity causing neurological injury (10, 17, 18).

To our knowledge, this study is the first to report on VO$_2$ in isoflurane-anesthetized rats. We found a metabolism about seven times higher than in humans (3). Comparison of our data with those of other studies of isoflurane anesthesia in other species, shows that our data fit Brody’s equation which predicts a curvilinear decrease in mass specific VO$_2$ with body mass described by a power function (3, 4, 6, 24). Several of these studies show a reduction of VO$_2$ during isoflurane anesthesia comparable to the metabolic depression of sleep (2, 24).

However, as we found no significant difference between the groups in our study, isoflurane does not seem to suppress metabolism more than anesthesia in general. These results accordingly show that the beneficial effects of volatile anesthetics reported in other ischemia/reperfusion studies may be caused by other mechanisms than a reduction of the oxygen debt. Additionally, our VO$_2$ data show that rate of ROSC after CA cannot be predicted from baseline metabolism.

4.1 Limitations

The study was designed to investigate the effect on ROSC rate and therefore a short follow-up period of 30 min was chosen. However, after 30 min, the MAP in the FFM group was very low, and a longer follow-up may have revealed a higher mortality in this group. The route of administration was different for the two anesthetics, isoflurane given continuously and FFM given as a bolus every 30 min. When compared to continues isoflurane inhalation, the level of anesthesia varies more with subcutaneous bolus injections, causing a risk of difference in anesthetic level at the time of CA. As both FFM and isoflurane is know to reduce arterial blood pressure, the preparation was timed to ensure that no FFM bolus was given right before
asphyxia (mean time from FFM bolus to asphyxia 20min [16;24]). No bolus was given during asphyxia, CA, or CPR to avoid potential confounding by peak levels of fentanyl/fluanisone or midazolam during resuscitation, and to match the lower isoflurane level during CPR and in the post ROSC period. As anesthesia in the current study was induced prior to cardiac arrest, further studies are warranted to seek a similar protective effect when volatile anesthetics are initiated after the ischemic event. Even though we performed pilot studies and sample size calculations, we cannot entirely ignore the possibility of a type two error in the present study. Another common limitation in ischemia/reperfusion is the size of the insult. If the insult is not severe enough, a potentially protective effect might be missed, which is illustrated by the high ROSC rates in our study. In the present study, rats were subjected to 10 min of CA, which we consider a severe insult. However, the animals were young and healthy, not resembling the average CA patient. Applying the same insult to an aged rat may show different results. Our study did not evaluate neuronal injury, as the focus of our study was hemodynamic parameters and short term outcome. There are conflicting results about the effect of volatile anesthetics on cerebral injury. Several studies on cerebral ischemia/reperfusion injury have demonstrated neuroprotective effects(7, 20, 35) where as exposure of the developing brain to volatile anesthetics may be neurotoxic(13, 29).

4.2 Implications

The quality of CPR is not only important for the ROSC rate, but also for post resuscitation injury. The benefit of volatile anesthetics on CPP, time to ROSC, and adrenalin doses seen in the present and in other studies may prove important in reducing post-resuscitation injury. In the current study, this is illustrated by improved post-ROSC hemodynamics and supported by other studies demonstrating that higher CPP during CPR improves post-resuscitation
injury(9). Furthermore, with the improvement in CPR quality, possibility of prolonged
resuscitation attempts with mechanical compression devices, and availability of extracorporeal
membrane oxygenation, sedation of patients can be necessary during ongoing CPR. In this
situation volatile anesthetics could potentially be superior to fentanyl/midazolam anesthesia.
As anesthetics are inevitable in resuscitation research, it is crucial to examine their impact on
study design and outcome measures. Coronary perfusion pressure, a commonly used
outcome measure of CPR quality, cannot be compared among studies using different
anesthetic regimes because the CPP is affected by the anesthesia used. When designing
new or comparing past studies, we must keep the results of the present study in mind.

4.3 Conclusion

Compared with FFM, isoflurane anesthesia decreases time to ROSC, augments CPP during
CPR and MAP after resuscitation, increases plasma levels of Endothelin-1, and decreases
catecholamine levels. Even though these changes did not translate into an increased ROSC
rate, they are important outcome measures in experimental CA research.

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7 References


