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Experimental paper

Tracheal temperature for monitoring body temperature during mild hypothermia in pigs☆

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ABSTRACT

Aim of the study: Out-of-hospital induction of mild therapeutic hypothermia after cardiac arrest needs easy to use and accurate body temperature monitoring. The aim of the study was to evaluate the best temperature probe position on a specially designed tracheal tube, as compared to pulmonary artery temperature (Tpa) during cooling to mild hypothermia in pigs.
Methods: Eight swine (29–38 kg) were anesthetized and intubated with an endotracheal tube with three temperature probes: T1 was attached to the wall of the tube, 1 cm proximal to the cuff-balloon, without contact to the mucosa; T2 and T3 were placed on the cuff-balloon with tight contact to the mucosa, T3 was covered by a small plastic tube to protect the mucosa against mechanical alterations. Body temperature was measured with a pulmonary artery catheter. Pigs were cooled from Tpa 38.5 to 33.0 °C with fast surface and slow endovascular cooling in a crossover design. To assess hysteresis, areas under the curve (AUC) were compared. Data are presented as mean and 95% confidence intervals.
Results: Temperatures were not different either during fast surface (T1-Tpa: 0.1[−0.3 to 0.5] °C, T2-Tpa: 0.2[0.0 to 0.4] °C, T3-Tpa: 0.4[0.1 to 0.7] °C) or slow endovascular (T1-Tpa: −0.3[−0.5 to 0.2] °C, T2-Tpa: −0.1[−0.3 to 0.0] °C, T3-Tpa: −0.1[−0.5 to 0.3] °C) cooling. There was no difference in hysteresis related to the location of the temperature probes. Faster surface cooling correlated with a larger but not significantly different hysteresis between the probes.
Conclusions: Tracheal temperature is an accurate surrogate for body temperature during fast and slow cooling to mild hypothermia in pigs and regardless of the location of the temperature probe on the tube.

1. Introduction

Induced mild hypothermia after cardiac arrest has been shown to improve both neurologic recovery and survival and is recommended by current guidelines.[1,2] As novel cooling devices are introduced, that allow high cooling rates and cooling in the field, one important but still unanswered issue arises: which temperature site for monitoring of cooling allows optimal guidance of therapy while assuring patient safety.[3] As the brain is the target organ for cooling, brain temperature measurement would be desirable, but is not available in patients resuscitated from cardiac arrest. Pulmonary artery temperature (Tpa) might reflect body temperature[4–10] and brain temperature (Tbr) most accurately.[11] However, the routine use of a pulmonary artery catheter in intensive care patients is limited by its invasiveness.[12,13] In addition ease-of-use, accuracy and fast response time to rapid temperature changes of standard temperature measurement sites (tympanum, oesophagus, bladder, rectum, etc.) are still a matter of debate.[4–10] While these may reflect brain temperature during thermal stability or slow changes of body temperature, this may be different during rapid cooling. Body temperature measurement sites like rectum or bladder, where the probe can be surrounded by non-perfused materials, may show a clinically relevant delay in reflecting changes of Tpa, leading to the risk of overcooling and eliciting arrhythmias, more so in the less controlled out-of-hospital setting.[7,14–17] So we believe, that for the acute care setting more convenient to use and fast reacting temperature probes are needed, especially for rapid cooling and early achievement of mild hypothermia, which maximizes the potential benefit of hypothermia as has been shown in animal models[18,19] and some clinical trials.[20,21]

To assess the agreement between temperatures monitored at different sites the method of Bland–Altman[22,23] is consid-

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ered adequate by most of authors dealing with various modes of thermometry.[4–8,10,11,14,15,24] However, any evaluation of the accuracy of temperature measurements must also address the cooling strategy for which the respective temperature monitoring is used. When rapid cooling is used, hysteresis has to be addressed as well. Hysteresis is defined as the lagging of an effect behind its cause. In our case this would refer to lagging of tracheal temperature change behind temperature changes caused by the cooling device.

We therefore designed a study to determine the best temperature probe position on a specially designed tracheal tube, as compared to pulmonary artery temperature (Tpa) during the induction of mild hypothermia in pigs.

2. Methods

The experimental protocol was approved by our institutional animal investigation committee. Animal care and use was performed by qualified personnel and supervised by veterinarians. All animal facilities and transportations comply with the current legal requirements and guidelines.

2.1. Animal preparation

After an adaptation period of 14 days eight female pigs (Piétrain × Edelschwein) weighing 29–38 kg received premedication with atropine sulfate 0.5 mg/kg, acepromazine maleate 1.75 mg/kg, piritramide 15 mg and midazolam 1.25 mg. They were anesthetized with propofol 40 mg (repeated doses if necessary) and intubated with a specially designed endotracheal tube (SilkoClear Trachealtube, Rüsch Austria Ges.m.b.H., Wien, Austria), with three temperature probes (Fig. 1). The pressure of the high volume low pressure cuff was checked after intubation to be between 40 and 60 mmHg. The correct position of the tube and probes was confirmed by a chest X-ray via measuring the distance between the tip of the tracheal tube and the carina. Controlled mechanical ventilation was performed with tidal volumes of 10 ml/kg, positive end-expiratory pressure of 5 cm H_2O, FiO_2 of 0.3, a ratio of inspiration to expiration 1:2. No heated humidification and no gastric tube were used to avoid interference with the evaluation of the three different temperature probes placed on the tip of the tube (see below). To maintain anesthesia during preparation, propofol (20 mg/kg/h intravenously), and boluses of piritramid (30 mg intravenously) were given. For the maintenance of normovolemia animals received normal saline 5 ml/kg/h via a peripheral intravenous cannula (ear-vein, 18 G). Electrocardiogram electrodes were attached to the extremities, a pulse-oximeter probe was placed on the tail, and a gastric tube was inserted. An arterial catheter was placed in the left brachial artery by Seldinger technique for monitoring of arterial pressure, and for blood sampling.

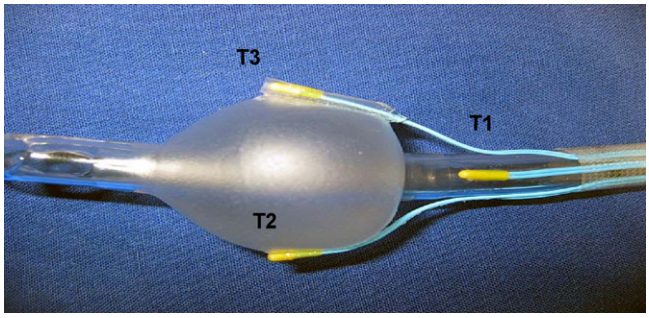

Fig. 1. Endotracheal tube with three temperature probes. T1, tracheal probe proximal to the cuff; T2, tracheal probe on the cuff without plastic covering; T3, tracheal probe on the cuff with plastic tube covering.

2.2. Temperature measurements

The endotracheal tube (SilkoClear Trachealtube, Rüsch Austria Ges.m.b.H., Wien, Austria; Fig. 1) was prepared 1 day before the experiment, so that the first temperature probe (T1) was attached to the wall of the tube 1 cm proximal to the cuff-balloon, supposed to have no contact to the mucosa of the trachea. The second (T2) and third (T3) probes were placed on the cuff-balloon with tight contact to the mucosa, whereas T3 was covered by a small plastic tube to protect the mucosa against mechanical alterations. These modified probes were taken from standard tympanic temperature probes (Mon-a-Therm, Tyco Healthcare, Gosport, UK) and checked in a water bath for accuracy before the experiment. A pulmonary artery catheter (CCO Pulmonary Artery Catheter, Edwards Lifesciences LLC, Irvine, CA) was inserted via the right jugular vein for monitoring of pulmonary artery blood temperature (Tpa) and administration of medications and infusions. Baseline Tpa was maintained at 38.5 ± 0.2 °C with a heating blanket or fans.[25] All the temperatures were recorded automatically at 1 min intervals.

2.3. Cooling

To investigate the effect of different cooling rates on temperature differences at various measurement sites, two different cooling methods were used in a crossover design, with rewarming between each cooling procedure. Surface cooling was performed with external cooling blankets (EmcoolsPads, Emcools®, Wien, Austria) covering neck, chest, abdomen and legs. Endovascular cooling was performed with a central venous catheter (Icy™, Alsius Corp., Irvine, CA) placed in the femoral vein. This venous catheter was connected to an external cooling device (CoolGard 3000, Alsius Corp., Irvine, CA).[26]

After baseline measurements, rocuronium (bolus of 0.5 mg/kg, then 0.5 mg/kg/h) was given and the pigs were cooled from 38.5 to 33.0 °C Tpa with the first device. After achieving the target temperature and 30 min of temperature stabilization, pigs were rewarmed as fast as possible. After allowing the temperature to reach a steady state for another 30 min, cooling was performed with the second cooling method. At the end of the experiment pigs were sacrificed with potassium. Autopsy with special focus on the mucosa of the trachea was not considered, because of the short duration of experiments we did not expect any mucosal membrane injury.

2.4. Statistical analysis

Data are presented as mean ± standard deviation (SD), or absolute and relative frequencies. We calculated areas under the curve (AUC) for the time-wise differences between temperature measurements at the different sites to assess hysteresis using a trapezoid method. To assess agreement we used the Bland–Altman approach.[22,23] Mean differences and 95% limits of agreement were calculated and a graphical display of differences vs. mean and standard vs. test was generated. The plot was used to inspect whether the difference and its variance was constant as a function of the average; a value near zero implied concordance. The limits of agreement were calculated as the mean bias ± two standard deviations. To allow for the experiment-wise repeated nature of measurements we intended to use linear random effects models, but these models were unstable. Therefore we calculated robust standard errors and 95% confidence intervals based on these standard errors. For the comparison between groups we used linear regression models with robust standard errors including several covariates. For explanatory analyses we used a matched pair Wilcoxon test. Data were analysed using Stata 8 (Stata Corp., College Statio, TX) and MS Excel 2003. A two-sided p-value of <0.05 was considered statistically significant.

3. Results

Data were collected on eight female pigs weighing 33.5 ± 4.5 kg. There was no significant difference between animals and cooling strategy in anesthesia doses and no significant effects of hypothermia were noted on hemodynamic in any phase. In all animals surface cooling showed a significant faster cooling rate than endovascular cooling. The time needed to reduce Tpa from 38.5 to 33 °C was 31 ± 10 min with surface cooling, as compared with 87 ± 14 min with endovascular cooling. This resulted in a cooling rate of 11.9 ± 3.8 °C/h with surface cooling, as compared to 3.9 ± 0.6 °C/h with endovascular cooling ($p < 0.0001$).

3.1. Comparison of hysteresis areas

To test for lagging of T1, T2 and T3 behind Tpa changes, hysteresis areas (AUC: areas under the curve) were calculated (Fig. 2). Results of the hysteresis areas under the curve during fast surface and slow endovascular cooling are presented in Table 1. Overall (surface pooled with endovascular cooling; T1 vs. T2 vs. T3) there was no statistically significant difference in hysteresis areas related to the measurement site ($p = 0.24$). However during fast cooling the mean difference between T3 and Tpa was 0.4 °C with a confidence interval of 0.1–0.7 °C. In contrast the faster cooling rate correlated with a significant larger hysteresis ($p = 0.0003$) than the slow cooling rate.

Table 1
Results of the hysteresis areas under the curve of tracheal temperature compared to pulmonary artery temperature during fast and slow cooling in eight pigs.

	Fast cooling, 11.9 ± 3.8 °C/h, $n = 8$	Slow cooling, 3.9 ± 0.6 °C/h, $n = 8$	p-Value
T1	2.6 ± 1.5	1.5 ± 0.8	$p = 0.09$
T2	2.0 ± 0.8	1.0 ± 0.7	$p = 0.02$
T3	2.4 ± 0.8	1.3 ± 0.5	$p = 0.01$
p-Value	$p = 0.5$	$p = 0.4$	

Data are given as mean ± SD; T1, tracheal temperature proximal to the cuff; T2, tracheal temperature on the cuff without plastic; T3, tracheal temperature on the cuff with plastic.

3.2. Agreement between pulmonary artery and tracheal temperatures

The mean baseline temperature for Tpa was 38.5 °C, for T1 37.8 ± 0.4 °C, for T2 38.2 ± 0.2 °C and T3 38.1 ± 0.4 °C. Mean differences during cooling with fast surface and slow endovascular cooling are shown in Table 2. There was no significant difference of bias related to the measurement site of the tracheal temperature probe (slow cooling group: $p = 0.24$, fast cooling group: $p = 0.15$), but there was a significant difference of bias with relation to the cooling rate ($p = 0.005$). The Bland–Altman plot was used to inspect whether the difference and its variance was constant as a function of the average; a value near zero implied concordance (Fig. 3).

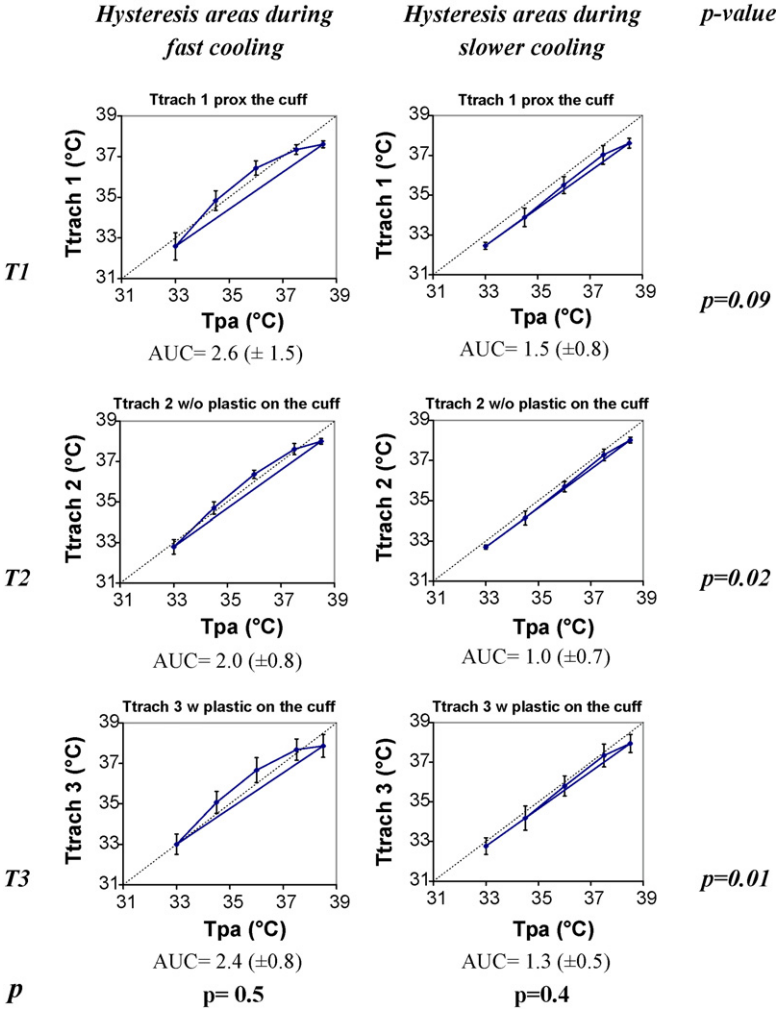

Fig. 2. Hysteresis areas during fast and slow cooling.

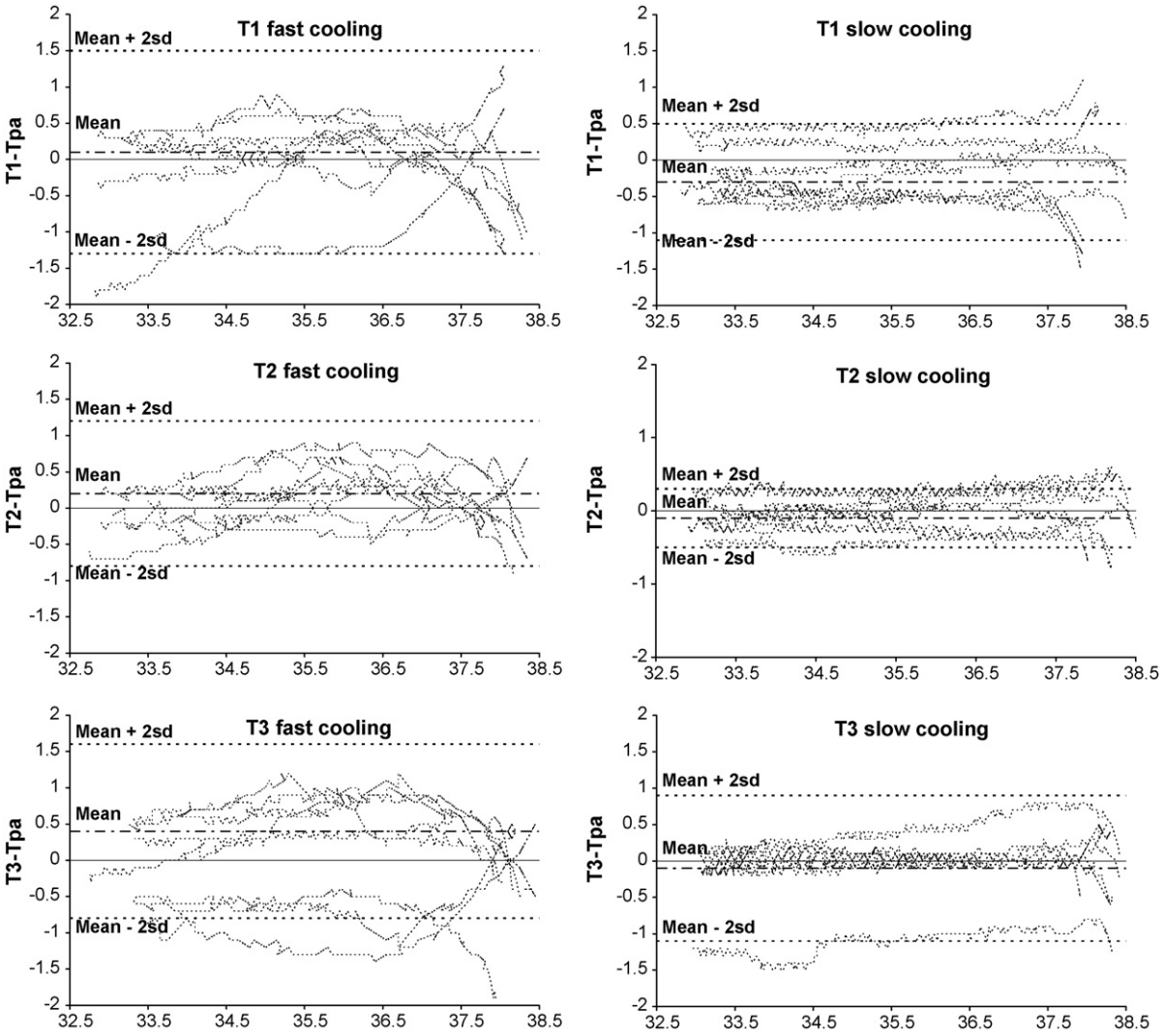

Fig. 3. Experiment-wise average vs. different plots (modified Bland–Altman plots) of temperature differences against averages during fast (Emcools®) and slow (Alsius®) cooling. T1, proximal tracheal temperature probe; T2, temperature probe on the cuff without plastic covering; T3, temperature probe on the cuff with plastic tube covering.

Table 2
Mean differences from tracheal to pulmonary artery temperature and 95% confidence intervals during fast and slow cooling in eight pigs.

	Fast cooling, 11.9 ± 3.8 °C/h, $n = 8$	Slow cooling, 3.9 ± 0.6 °C/h, $n = 8$	p-Value
T1-Tpa (°C)	0.1 (−0.3 to 0.5)	−0.3 (−0.5 to 0.2)	$p = 0.004$
T2-Tpa (°C)	0.2 (0.0–0.4)	−0.1 (−0.3 to 0.0)	$p = 0.013$
T3-Tpa (°C)	0.4 (0.1–0.7)	−0.1 (−0.5 to 0.3)	$p = 0.008$
p-Value	$p = 0.24$	$p = 0.15$	
Observations	$n = 288$	$n = 288$	

Tpa, pulmonary artery temperature; T1, tracheal temperature proximal to the cuff; T2, tracheal temperature on the cuff without plastic; T3, tracheal temperature on the cuff with plastic.

4. Discussion

This study compared three modes of tracheal temperature measurement, using pulmonary artery temperature for comparison. The results document the feasibility and accuracy of tracheal temperature measurements regardless of the location of the temperature probe on the tube as a surrogate of body temperature during fast and slow cooling to mild hypothermia in pigs.

Hypothermia should be induced as early and rapid as possible in order to improve outcome and survival.[18–21] To ensure that the beneficial effects of therapeutic hypothermia are not abolished, the consensus target temperature range of 32–34 °C should neither be over- nor under-run. Studies showed that overcooling is associated with the risk of severe complications, like atrial or ventricular fibrillation, coagulopathy and an increased risk of infections.[27–31] Furthermore there is evidence that at temperatures of less than 30 °C electric and pharmaceutic anti-arrhythmic therapies may be ineffective.[32] Merchant et al.[27] observed a trend for worse outcome in patients who were overcooled. Thus, precise temperature control is an important factor for the successful use of therapeutic hypothermia. Tracheal thermometry could facilitate the implementation of mild hypothermia and minimize the risk of overcooling by being an accurate and easy to use temperature monitoring. Another potential benefit of tracheal temperature measurements would be the redundancy for an additional temperature probe, therefore simplifying resuscitation especially in the out-of-hospital setting.[1,2]

There is still ongoing debate on the best temperature measurement site and the respective reliability reflecting body temperature. Some authors regard tracheal temperature as accurate in assessing body temperature,[33,34] whereas others consider a similar bias and variability as unacceptable for clinical use.[24] However, there is no generally established definition for the degree of bias and variability which can be considered clinically reliable, nor are there

generally used methods for analysing such data, which makes interpretation and direct comparison difficult. The statistical analysis should address the three components of agreement: (1) the degree of linear relationship between (two) measurements (hysteresis); (2) the differences in mean values and (3) the differences in variances. The better an individual measure addresses these three components, the better it evaluates agreement.[35] To judge the acceptability of a given bias and variability, it should be distinguished between steady state conditions or slow temperature changes – where most sites reflect body temperature[14] – and the new field of rapid cooling – where inertia of the measurement system plays a significant role. Various studies found that during steady state conditions and very slow temperature changes respectively, a bias between 0.03 and 0.9 °C and a variability between 0.2 and 1.0 °C,[4–8,10,14] and during slow cooling (~3 °C/h) a bias between 0.1 and 0.56 °C and a variability of 0.19–0.4 °C were considered reliable to reflect body temperature.[11,34,36] Therefore the results of our slower cooling group would imply reliability for all three tracheal probes with a bias between −0.4 and −0.1 °C and a variability ranging between 0.2 and 0.5 °C. During higher cooling rates (~10 °C/h) a bias between 0.05 and 0.2 °C and a variability between 0.46 and as high as 2.7 °C was considered accurate.[16,37] In our fast cooling group tracheal temperature probes showed a bias between 0.1 and 0.4 °C and a variability between 0.5 and 0.7 °C. During very high cooling rates of 30–50 °C/h with cardiopulmonary bypass, a bias between −0.21 and 2.1 °C, and a clearly higher variability between 1.7 and 2.1 °C were considered to reliably reflect body temperature.[14,15] Thus, the higher the cooling rate is, the bigger the bias will be, and, particularly the variance, which from our point of view is the crucial criteria for being clinically acceptable.

Besides bias and variance, the impact of the temperature probe response to changes is important, especially during rapid changes of temperature. Technical facts and issues reflecting a restricted perfusion to specific temperature sites[38] and/or poor sensor placement are reasons for the inertia of a measurement system. Consistent with other studies,[14,36] we found that a higher cooling rate correlates with an increased delay. In order to quantify this delay we calculated hysteresis areas which showed to be a good method for quantifying the inertia of a measurement system. A temperature probe or measurement site showing a very large hysteresis would imply a very long response time to temperature changes and would consequently be clinically unacceptable. At cooling rates that did not exceed 4.5 °C/h, tracheal temperatures showed only a very small hysteresis and good agreement with the pulmonary artery temperature. In these cases tracheal temperatures tend to slightly underestimate pulmonary artery temperature, showing a small bias. T2 was the best estimate of body temperature, because it lies within the limits of our opinion acceptable limits for the bias and variance of 0.3 °C during slow cooling and of 0.5 °C during fast cooling. During very high cooling rates tracheal temperature slightly overestimates pulmonary artery temperature, showing a bigger variance and hysteresis as an effect of a delayed response time. The experimental cooling rate of almost 13 °C/h in our fast cooling group is very high and was probably only possible because of the low weight of the pigs. At present such high cooling rates in adults are only being achieved with cardiopulmonary bypass. When induced after cardiac arrest, such high cooling rates for systemic hypothermia are still not practicable and it is questionable if they will get clinically relevant in the future. Yet we know that there are a lot of ongoing and maybe future studies with various cooling methods being evaluated, with the ambition of achieving high cooling rates. In these cases we have to keep in mind the bigger variance of probably any probe, as the hysteresis and consequently the mean difference might rise with higher cooling rates.

When evaluating data of only eight pigs, the presumably small explanatory power of statistical significance has to be considered. Though we found no statistically significant difference between tracheal measurement sites, we found that T2 tends to reflect pulmonary artery temperature best during both, fast and slow cooling, showing the smallest hysteresis and variance. When assessing hysteresis of tracheal temperature probes compared to the pulmonary artery temperature probe it has to be considered that the gold standard may also have a significant hysteresis. Keeping in mind that there is no other way of comparing the function of temperature change over time, and the fact that pulmonary artery temperature is considered the gold standard, we evaluated the hysteresis of tracheal temperature probes compared to pulmonary artery temperature, without knowing the potential hysteresis of pulmonary artery temperature itself. Further studies should look at possible tracheal mucosa damage due to the temperature probe on the cuff of the tube. However for those experiments the duration of having the tube in place needs to be longer at least 24 h. And for those experiments at its only necessary to check the temperature probe with the best results found in this study. The comparison to other temperature sites (tympanum, esophagus, bladder, rectum, etc.) was not the primary aim of this study and therefore will not be reported here. Another limitation, which should be mentioned was, that the present investigation was made in female pigs that had no cardiac arrest. Therefore the results may have limited value to predict circumstances in clinically induced hypothermia after cardiac arrest, which also can happen in male patients. However for proving the principal concept of tracheal temperature monitoring, we consider our results as first important step for further necessary investigations, especially in patients after cardiac arrest.

5. Conclusion

During steady state and at a cooling rate that does not exceed 4.5 °C/h, tracheal temperature measurement is feasible, shows a small bias in regards to faster cooling rates and accurately approximates pulmonary artery temperature with minimal underestimation. During very high cooling rates it shows a bigger hysteresis and a higher variability. Tracheal temperature is an accurate surrogate for body temperature during fast and slow cooling to mild hypothermia in pigs regardless of the location of the temperature probe on the tube.

Conflict of interest

There are no conflicts of interests.

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