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ORIGINAL ARTICLE

# Hypothermia during CRRT, a comparative analysis

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**Background:** One of the most common adverse events during continuous renal replacement therapy (CRRT) is hypothermia, reported to occur in over 4/10 cases. In turn, hypothermia is known to be associated with higher mortality rates among patients treated in intensive care units (ICU). The present study examined if a novel warming device in the current generation of CRRT systems could lower incidence of hypothermia compared to previous generation technology.

**Methods:** We included ICU patients >18 years, at Skåne University Hospital, Lund from November 2006 to August 2019 and treated with CRRT. Temperature measurements were recorded from the CRRT systems and from the patients hourly.

**Results:** In total, 310 patients treated with the older system vs 32 patients treated using the newer CRRT system were included. We found that historic Prismaflex patients spent 11.43% of their time in hypothermia, as compared to the novel Prismax CRRT system, where 10.06% of patient hours were below 36.0°C (Chi-Square $P = .0063$).

The novel blood warmer is associated with less heat loss compared to the older warmer: mean patient temperature was 37°C vs 36.5°C for these two groups and mean set return temperature was 37.9°C vs 40.9°C (both $P < .001$).

**Conclusions:** The current generation CRRT system and blood warmer significantly decreases the risk of hypothermia among critically ill patients treated with continuous renal replacement therapy as compared to historic controls. Achieving target temperature is easier with the new system.

## 1 | INTRODUCTION

Adverse events during continuous renal replacement therapy (CRRT) have been studied. One of the most common was severe hypothermia, <35.0°C, reported in 44% of all cases.[1] Recent literature shows that hypothermia may be less common now, but data on the subject are scarce.[2]

Hypothermia is associated with risks of bradycardia/arrythmia, impaired pharmacodynamics, coagulopathy and transfusion requirements.[3] It is associated with higher mortality rates: In a time-series analysis of over 15 000 admissions during 8.5 years, incidence of hypothermia (<36.0°C) decreased from 29% to 21% during the study period and was associated with ICU mortality in both medical and surgical patients.[4] Laupland et al reported hypothermia (<36°C) occurring in 18% of 10 962 medical and surgical admissions within the first 24 hours of admission to ICUs in France. In this study hypothermia was more common in surgical patients but was only an independent predictor of ICU mortality in medical patients.[5] Other research groups have reported similar findings; hypothermia predicts mortality in elderly patients with sepsis.[6] A study of 636 051 critically ill patients using two large, independent, multinational databases found increasing degrees of hypothermia to be associated with progressively increasing mortality.[7]

The Prismaflex CRRT system uses the Barkey blood warmer, also known as Prismacomfort. It operates by covering the blood return flow with a silicon tube heat exchanger; the heat is thus transferred by the contact of the resistance heating system. The

Thermax blood warmer responds to changing treatment parameters by repeatedly adjusting heating to fulfil the prescribed return blood temperature.

We hypothesized that hypothermia during CRRT could be avoided using newer blood warmers. Specifically, the present study primarily aims at assessing if the novel Thermax blood warmer, used for the Prismax system, is associated with fewer events of hypothermia than its predecessor. Secondarily, is the new warmer more accurate and reliable in reaching and maintaining chosen target temperature during CRRT as compared to the blood warmer used for the Prismaflex system?

**Editorial Comment:**

Hypothermia is associated with increased risks of complications in critically ill patients. This retrospective cohort study showed that the use of the TherMax continuous renal replacement therapy warming device was associated with lower risk of hypothermia as compared to the previously used system, the PrismaFlex, and its warming technology.

## 2 | METHODS

### 2.1 | Cohort

The study is registered at Clinical Trials.gov: NCT03973814. After approval from Swedish Ethical Review Authority (*Dnr 2019-04388*), a total of 9046 patients admitted to the Intensive Care Unit at Skåne University Hospital, Lund during the years 2006-2019 were screened and 342 patients undergoing CRRT were identified and included. The old Prismaflex with the Barkey warmer was used until November 2018, thereafter the Prismax with the Thermax was used. We extracted data from the electronic patient database management system ICCA (IntelliSpace Critical Care and Anesthesia, Philips, the Netherlands) which contains complete clinical datasets generated during the ICU stay. Descriptive data of the two groups are presented in Table 1. Inclusion criteria: >18 years of age and admission to the adult intensive care unit at Skåne University Hospital, Lund during the period from November 2006 to August 2019 and treatment with CRRT during the ICU stay. Hypothermia was described as elsewhere in the literature: <36.0°C.

The temperature value set at the warmer in question was recorded in the ICCA system hourly. Patient temperature was also recorded hourly, either from ear, oesophagus, from invasive hemodynamic monitoring or from urinary bladder temperature catheter according to department routines. Additionally, the set temperature of the so-called Bairhugger body-warmer blanket was recorded, if used.

### 2.2 | Technical details

Both the historic and present CRRT warming systems works by a basic principle of creating a temperature gradient towards the blood compartment. In contrast to the Barkey warmer, the Thermax has a feedback system allowing for continuous changes in heating/cooling dependent on treatment parameters.

A sensitivity analysis was performed, where we excluded the first 2 hours of CRRT treatment; this was done to test if the phase of starting continuous renal replacement therapy was the main driver of overall hypothermia.

### 2.3 | Statistics

Continuous data were described by means and standard deviations. Significance was tested by using the chi-squared test. For all calculations the SAS software version 9.4 (Statistical Analysis Software) was used. Significance level was defined as $P < .05$.

## 3 | RESULTS

In total, 57 741 hours were available for evaluation in this cohort. When comparing the historic and novel CRRT systems, we found that Prismaflex patients spent 11.43% (6112 treatment hours below 36°C /53465 treatment hours in total) of their time in hypothermia, as compared to the novel Prismax CRRT system, where 10.06%

**TABLE 1** Descriptive data of the historic Prismaflex control group and novel Prismax study group in the cohort

| Characteristics | PrismaFlex | PrisMax | *P* value |
|---|---|---|---|
| Treatments, n | 310 | 32 | |
| Age | 65.39 ± 12.53 | 65.45 ± 14.66 | not significant |
| Gender | 42.5% female | 40.9% female | not significant |
| SAPS3 | 74.09 ± 13.63 | 75.72 ± 14.85 | not significant |
| KDIGO class upon CRRT start | 3 | 3 | not significant |
| Blood flow | 184.45 ± 50.40 | 136.64 ± 33.89 | $P < .05$ |
| Effluent flow | 42.18 26.72 | 63.44 83.99 | $P < .05$ |
| Haemoglobin | 108.48 ± 22.17 | 110.62 ± 19.76 | not significant |

(430 treatment hours below 36°C /4276 treatment hours in total) of patient hours were below 36.0°C (Chi-Square $P = .0063$) (Figure 1).

A sensitivity analysis was performed (data not shown in figure), where the temperatures recorded during the first 2 hours of CRRT were excluded. Significant differences between the historic and novel systems prevailed; more hypothermia for the Prismaflex patients, with patient temperatures <36.0°C during 12.7% as compared to 11.2% of the treatment time ($P = .0216$).

The Thermax blood warmer is associated with less heat loss compared to the Barkey warmer. This is highlighted by a mean patient temperature of 37°C vs 36.5°C for these two groups but also by the fact that the mean set return temperature was 37.9°C vs 40.9°C.

This difference in mean set return temperature translates to a significant ($P < .001$) difference in the historic Barkey system compared to the new Thermax system (Table 2, Figure 2). Seemingly, an overcorrection was needed in the old system probably because of its insufficiency to maintain the sought blood temperature in the patient.

Use of the adjacent Bairhugger body-warmer blanket was significantly less common in the Thermax group compared to the Barkey group; 17/32 (53.1%) patients used the blanket as compared to 285/310 (91.9%) ($P < .001$). For those patients with adjacent warming there were more Bairhugger-free hours in the Thermax group compared to the Barkey group; 99.7 ± 93.4 hours without (16.7 ± 16.4 hours with) in the Thermax group compared to 73.2 ± 107.3 hours without (40.3 ± 45.7 hours with) in the Barkey group ($P < .01$).

## 4 | DISCUSSION

This large cohort study shows the Thermax CRRT warming device to be associated with lower risk of hypothermia as compared to the previously used CRRT system, the Prismaflex and its' warming technology. These differences remained significant even after exclusion of the first 2 CRRT treatment hours, done to test if starting continuous renal replacement therapy was the main driver of overall hypothermia. We further demonstrate how mean temperatures are closer to the 37-degree Celsius target temperature in patients treated with the novel technology and how heat loss is less of an issue.

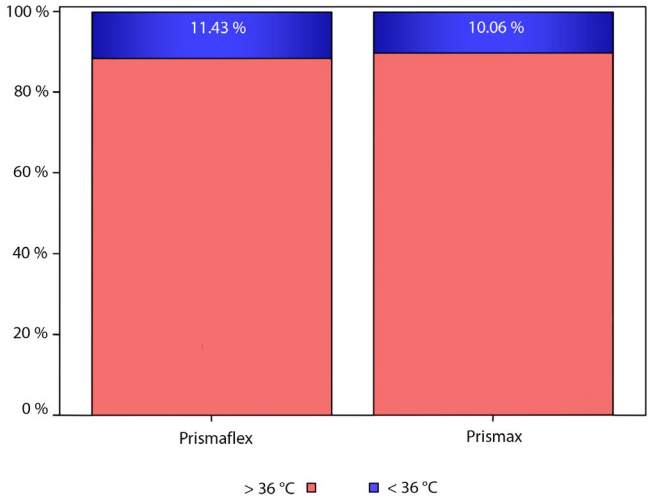


**FIGURE 1** Percentages of total treatment hours spent below 36.0°C in the historic Prismaflex system with its Barkey warmer and the novel Prismax system with its Thermax warmer. Prismaflex patients spent 11.43% of their time in hypothermia, as compared to the Prismax system, where 10.06% of patient hours were below 36.0°C ($P = .0063$)

**TABLE 2** Comparison of the set temperatures of the Prismaflex-Barkey and the Prismax-Thermax systems as well as the real measured patient temperatures

| Characteristics | PrismaFlex | PrisMax | *P* value |
|---|---|---|---|
| Treatments, n | 310 | 32 | |
| Set temperature | 40.9°± 0.6°C | 37.9°C ± 1.9°C | $P < .001$ |
| Real temperature | 36.5°C ± 0.7°C | 37.0°C ± 0.9°C | $P < .001$ |
| Difference | -4.4°C ± 1.0°C | -0.9°C ± 2.5°C | $P < .001$ |

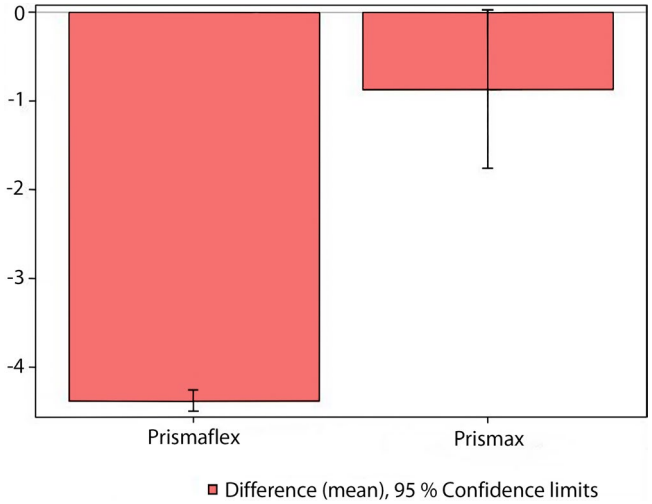


**FIGURE 2** Graphic presentation of the mean differences with 95% confidence intervals between the set warmer temperatures compared to the measured temperature in the patient, for the older Prismaflex-Barkey system and the newer Prismax-Thermax system

Some concerning cases of hypothermia have been reported, using the Prismaflex and its blood warmer.[8] Even more problematic issues have been raised with regards to the overall warming capacity of other manufacturers' devices.[9] Very few studies have specifically investigated CRRT and hypothermia, especially during the latest decade. In the mid to late 1990s, incidence of CRRT-related hypothermia was reported at 25%-55%.[10,11] Notably, hypothermia was not uniformly defined at this time and both arteriovenous and venovenous modalities were in use.

One small randomized controlled trial from 2004 exists. Circuits were randomized to an intravenous fluid warmer set at 38.5°C on the dialysate and to the replacement fluid lines or no fluid warmer. Patient core temperature was recorded at baseline and then hourly and hypothermia was defined as a core temperature <36.0°C. In this study, intravenous fluid warmers did not prevent hypothermia during

CRRT.[12] In contrast to the scarce evidence regarding blood warmers during CRRT, numerous studies exist with regards to peri-operative intravenous fluid warming; these include patients undergoing general surgery, cardiac surgery and caesarean section.[13-15]

As mentioned in the methods, both tested systems warm returning blood by creating a temperature gradient. The main factors determining the efficacy of the warmer are the blood flow through the warmer and the temperature gradient between the warming surface and blood. For instance, modern citrate protocols use lower blood flows compared to heparin anti-coagulated circuits, requiring a more exact determining of the set temperature. In theory, the patient's own temperature regulatory mechanism could detect that energy is either lost or added to the blood compartment and interfere with the warmer. Full knowledge about temperature regulation in the heterogeneous critically ill patient population is lacking. These patients can be young or old, with low or high body mass index and reasons for ICU admission can obviously range from septic shock, via post-operative adverse events to major trauma. Both pre-ICU demographic and co-morbid properties, via intra-ICU events will have an impact on patients' endogenous temperature control.

The implications of our study results are hard to assess. It is likely beneficial to mitigate the risk of hypothermia, and as previously mentioned, the association between hypothermia and increased mortality has been shown in the ICU setting.[4-7] A single center study from Brussels investigating body temperature showed patients with hypothermia to have a worse prognosis than those with fever.[16] Avoiding hypothermia in the peri-operative period may reduce the incidence of cardiac events,[17] lower risk of surgical wound infection and decrease duration of hospital stay.[18] However, despite the findings of the present study and previous data on temperature and outcomes, we cannot be certain that actively avoiding hypothermia among CRRT patients would lower mortality or other adverse events. From a bed side nursing standpoint, our findings, however, have an immediate impact. No longer do they have to guesstimate how much they need to overcompensate the return blood temperature during CRRT to (almost) reach target temperature. They might not need other external warmers such as warming blankets to ensure correct patient temperature. This reduces both workload and additional costs.

### 4.1 | Limitations of the study

This study has strengths and weaknesses. We used a large, independent, high-resolution ICU database and included 342 patients with 57 741 measured temperatures. The granularity of the data was high, it included both temperature data from the patients and from the historic Prismaflex CRRT system as well as the novel Prismax and their respective warming systems Barkey and Thermax. No manual inputs were needed, data were transferred machine to machine. Weaknesses include the fact that confounding factors such as varying room temperature, covering of the patients and use of external warmers exist. Bairhugger usage data were available, showing that external blanket warming was more used in the Prismaflex group. The decision to use this device is nurse driven and complex. External warming is by no means a rescue method when the CRRT warmer fails. Naturally, patients can undergo surgery or radiologic examinations exposing them to (risk of) hypothermia and we lack these data. Moreover, the historic group is much larger and spanned over 12 years, whereas the Thermax/study group contains patients from 10 months. The sizes of the two samples are large due to the hours of use of the both machines, but the difference in sample sizes is also large. However, the standard deviations in real patient temperature (Table 2) are quite similar in the two groups, implying that statistical significance testing still is valid and meaningful.

The study is retrospective; however, the data were collected prospectively, and the analysis was undertaken independent of our study hypothesis. Lastly, this is a single center study, decreasing the external validity of our study findings.

## 5 | CONCLUSIONS

The Prismax CRRT system and the Thermax blood warmer significantly decrease the risk of hypothermia among critically ill patients treated with continuous renal replacement therapy as compared to historic controls. Furthermore, achieving target temperature is easier with the new system.

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### CONFLICT OF INTEREST

The authors Bell and Broman have an IIR Grant from Baxter Medical, but not for this study. So, no COI to be reported.

### AUTHORS' CONTRIBUTIONS

The Max Bell and Marcus Broman designed the protocol, conducted the study and wrote the manuscript. Claudio Ronco supervised the study and participated in writing of the manuscript.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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