Duration of Hypothermia, Rewarming Rate and Temperature Influence Surgical Outcomes for On-Pump Coronary Artery Bypass Grafting

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Abstract

Objectives: Temperature management during cardiopulmonary bypass (CPB) has an established influence on surgical outcomes. The purpose of this study was to examine the relationship of the minimum temperature, duration of hypothermia, rewarming rate and peak rewarming temperature to post-surgical outcomes.

Methods: Analysis of 2259 patients undergoing isolated on-pump CABG. Outcomes included 30-day mortality, myocardial infarction, stroke, infection, prolonged ventilation, renal failure, return to theatre, 24-hour blood loss and post-operative length of stay. Regression analyses were used to compare temperature management with outcomes.

Results: Higher rewarming temperatures were associated with increased mortality, myocardial infarction and 24-hour blood loss; longer duration of temperatures below 34°C with increased 24-hour blood loss; and faster rewarming rates with increased incidence of stroke and 24-hour blood loss.

Conclusions: Rewarming temperature and rate, and the duration of temperature <34°C should be limited to reduce the incidence of adverse outcomes.

Key words: cardiopulmonary bypass (CPB), coronary artery bypass grafting (CABG), peak temperature, rewarming rate, surgical outcomes

Introduction

While rates of mortality, stroke and myocardial infarction have declined in recent decades [1, 2], evidence suggests that on-pump coronary artery bypass graft surgery (CABG) is still associated with post-operative cognitive dysfunction, coagulopathy and acute kidney injury [3, 4]. These outcomes are at least partly dependent on CPB temperature management, [5-9] and despite the evolution of bypass technology and on-going investigation, a consensus on the optimal CPB management strategy continues to elude investigators.

Hypothermia was initially introduced as a means of protection from ischaemic injury during CPB [10]. However evidence suggesting that warm bypass could reduce temperature after-drop and conduction abnormalities led to support for normothermic temperatures, raising concerns about neurological protection and tissue ischaemia in the absence of hypothermia [7, 11-13]. Currently, tepid bypass temperatures (32-35°C) appear to be an adequate compromise, permitting
the use of hypothermia while negating the
detriment of lower bypass temperatures.
Further evidence is however required to val-
idate this technique and identify any previ-
ously unforeseen complications.

More recently, the rewarming rate and
peak rewarming temperature have also come
under scrutiny. Evidence has emerged sug-
gest that an increase in these parameters
increases the incidence of post-operative re-
nal dysfunction [14], and decreases 30-day
and 3-year survival [15, 16]. Additional in-
vestigation is also justified to explore the ef-
effects of the rewarming rate and peak rewarm-
ing temperature on surgical outcomes for on-
pump CABG patients.

The objective of this study is to investi-
gate the effects of current temperature man-
agement strategies on adverse post-operative
outcomes. It is hypothesised that by optimis-
ing the duration and degree of induced hy-
pothemia, as well as the rate and final tem-
perature of rewarming during CPB, the inci-
dence of adverse post-surgical outcomes will
be reduced.

Methods

Following hospital Human Research Ethics
Committee approval, all 2779 patients who
underwent isolated on-pump coronary artery
bypass grafting (CABG) from June 2000 to
May 2013 were considered as potential sub-
jects for this study. Exclusions were 75 pa-
tients who received additional cardiotho-
racic procedures at the time of surgery, 163
who had previous exposure to CPB, and 282
for whom surgical outcome data were un-
available; 2259 patients were deemed eligi-
able for analysis.

Perioperative observations were collect-
ed at five-minute intervals throughout the
procedure by a computer interfaced with the
heart-lung machine. Patient co-morbidities
and outcomes were recorded into a cen-
tralised database. Medical record numbers
were used to correlate data from these
sources and compile a database comprising
patient co-morbidities, perfusion data and
surgical outcomes.

Non-pulsatile perfusion was performed
using Maquet Jostra HL-20 half-inch roller
pumps with membrane oxygenation via a
Terumo Capiox® oxygenator with an integra-
ted venous reservoir. Temperature was col-
lected on the arterial line and at the nasopha-
ryngeal site at 5-minute intervals. The bypass
circuit was primed with 1.6L of Hartman’s
solution, 0.5L of 4% albumin, 25 000 U of
heparin and 20mL of Frusemide.

Anticoagulation was achieved by the ad-
dition of heparin to maintain an activated
partial thromboplastin time (APTT) of ap-
proximately 999 seconds, reversed at termi-
nation of bypass.

Mean haemoglobin during bypass was
8.0g/dL (range 3.4-13.2g/dL), with transfu-
sion considered at approximately 6.0 -
7.0g/dL. Average arterial pressure was
56mmHg (range 40-90mmHg) and average
arterial line pressure 80mmHg (range 61-
97mmHg). The pH-Stat method of acid-base
management was used, aiming for a pH of
7.32, with pH maintained at an average of
7.30 in this patient cohort (range 7.13-7.49).

All procedures were performed through a
standard median sternotomy with CPB estab-
lished via a two-stage right atrial venous can-
nula with arterial return to the ascending aor-
ta. Standard cold blood cardioplegia was
used for myocardial protection, solely ante-
grade in 72.5% of cases, both ante- and ret-
rograde in 22.8% of cases and either warm
blood or cold crystalloid in the remainder.
Blood from the surgical field was salvaged
and returned to the venous reservoir via car-
diotomy suction.

The predictor variables for this study in-
cluded the minimum temperature attained
during CPB, the peak rewarming tempera-
ture, the duration of hypothermia (<34°C)
and the rewarming rate, selected based on
literature review and clinical observation.
The latter two variables were calculated from
the temperature recordings.

The outcome variables included 30-day
mortality, myocardial infarction, stroke, in-
fection, the development of post-operative renal failure, prolonged ventilation, return to theatre, requirement for blood products, post-operative length of stay and the volume of blood lost via the chest drain in the first 24 post-operative hours.

Several covariates were also included: age, gender, operation status (elective, urgent, emergency or salvage), EuroSCORE, bypass time, aortic cross-clamp time and the number of bypass grafts, with renal dysfunction as an additional co-morbidity in assessing the development of post-operative renal failure.

Multivariate regression analyses were used to analyse the association between the predictor variables and each of the surgical outcomes. Results were considered significant for \( P < 0.05 \). Statistical analysis was performed using IBM® SPSS® Statistics Version 21.

**Results**

Demographics of the patient population are presented in Table 1. Of 2259 patients eligible for analysis, data for blood products was unavailable for 553 (24.5%) patients and data for 24-hour blood loss was unavailable for 523 (23.2%) patients. This was either due to a failure to collect this information during the admission or omission of data from the database for those patients who either received no blood products or had no significant blood loss via the chest drain. EuroSCORE was unavailable for 160 (7%) patients due to missing data required for calculation of this score. The averages and incidences of predictors and outcomes for the study are displayed in Table 2.

**A: 30-Day Mortality**

The peak rewarming temperature was the strongest predictor of 30-day mortality (Table 3), with an odds ratio of 4.20 \( (P = 0.022) \). Higher EuroSCORE, indicating more co-morbidities, was also associated with an increase in the likelihood of mortality, as was a fewer number of bypass grafts.

**B: Post-Operative Myocardial Infarction**

Multivariate analysis reported an association of post-operative myocardial infarction with the peak rewarming temperature and EuroSCORE. The peak rewarming temperature was the strongest predictor of post-operative myocardial infarction \( (OR = 6.94; P = 0.011) \).

**C: Coagulopathy**

The multivariate analysis for 24-hour blood loss reported a positive association with increased rewarming rate \( (B = 1.156, P < 0.001) \), higher peak rewarming temperatures \( (B = 0.198; P < 0.001) \), and longer duration of hypothermia \( (B = 0.002, P = 0.001) \). The administration of blood products was similarly associated with higher peak rewarming temperatures \( (OR = 2.299, P < 0.001) \) and longer duration of hypothermia \( (OR = 1.011, P < 0.001) \).

**D: Renal Failure**

The duration of hypothermia was mildly associated with renal failure \( (OR = 1.011, P = 0.039) \). Of 118 patients who developed renal failure after CABG, 16 (13.6%) had pre-operative renal dysfunction. On multivariate analysis, patients with pre-operative renal dysfunction were three times more likely \( (OR = 3.164, P < 0.001) \) to develop post-operative renal failure than their counterparts with no pre-operative renal dysfunction.

**E: Post-Operative Length of Stay**

The multivariate analysis for post-operative length of stay also demonstrated a correlation with the duration of hypothermia \( (B = 0.001, P = 0.012) \). However further investigation with linear regression identified by-
### Table 1: Demographics of Patient Cohort

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Average for Patient Cohort (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Operation (years)</td>
<td>64.99 ± 2.18; (31-90)</td>
</tr>
<tr>
<td>BMI (kg.m⁻²)</td>
<td>28.4 ± 0.1 (14.4- 62.1)</td>
</tr>
<tr>
<td>BSA¹ (m²)</td>
<td>1.97 ± 0.01 (1.20 – 3.04)</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>7.39 ± 10.60 (0.88 – 87.33)</td>
</tr>
<tr>
<td>Number of Grafts</td>
<td>3.5 ± 0.9 (1-9)</td>
</tr>
<tr>
<td>Bypass Time (minutes)</td>
<td>99.24 ± 29.58 (25 – 306)</td>
</tr>
<tr>
<td>Aortic Cross Clamp Time (minutes)</td>
<td>60.96 ± 19.73 (16 – 190)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Frequency in Patient Cohort (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender [male/female]</td>
<td>78/22</td>
</tr>
</tbody>
</table>

#### Ethnicity

- Caucasian: 87.4%
- East/South East Asian: 2.7%
- ATSI²: 1.1%
- Pacific Islander: 0.6%
- South Asian: 0.5%
- Southern European: 0.2%
- African: 0.2%
- Middle Eastern: 0.1%
- Hispanic: 0.1%
- Other/Not Recorded: 7.1%

#### Medical History

- Diabetes: 30.5%
- Renal Dysfunction: 5.1%
- Peripheral Vascular Disease: 10.6%
- Respiratory Disease: 12.7%
- Cerebrovascular Disease: 9.0%
- Hypertension: 78.0%
- Hypercholesterolemia: 76.8%
- Smoking History: 61.9%
- Current Smoker: 13.5%
- Family History CAD³: 38.2%
- Angina: 65.3%
- Congestive Cardiac Failure: 20.3%
- Myocardial Infarction: 47.5%
- Previous CT Surgery: 3.5%
- Previous PCI: 11.6%

#### Operation Status

- Elective: 69.3%
- Urgent: 29.3%
- Emergency: 1.2%
- Salvage: 0.2%

¹ Body Surface Area; ² Aboriginal or Torres Straight Islander; ³ Coronary Artery Disease
Table 2: Averages and incidences of predictors and outcomes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum Bypass Temperature</td>
<td>32.2°C</td>
<td>28.4-35.3°C</td>
</tr>
<tr>
<td>Peak Rewarming Temperature</td>
<td>37.0°C</td>
<td>35.4-37.9°C</td>
</tr>
<tr>
<td>Duration of Hypothermia</td>
<td>50.4 minutes</td>
<td>0-170 minutes</td>
</tr>
<tr>
<td>Rewarming Rate</td>
<td>0.13°C/minute</td>
<td>0.02-0.35°C/minute</td>
</tr>
<tr>
<td>Average 24-hour Blood Loss</td>
<td>291.6mL</td>
<td>0.0 – 3700mL</td>
</tr>
<tr>
<td>Post-operative Length of Stay</td>
<td>8.4 days</td>
<td>0-140 days</td>
</tr>
<tr>
<td>Incidence</td>
<td></td>
<td>Absolute number</td>
</tr>
<tr>
<td>30-Day mortality</td>
<td>1.2%</td>
<td>27</td>
</tr>
<tr>
<td>Postoperative Myocardial Infarction</td>
<td>0.8%</td>
<td>19</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2%</td>
<td>28</td>
</tr>
<tr>
<td>Wound infection or Septicaemia</td>
<td>1.6%</td>
<td>16</td>
</tr>
<tr>
<td>Renal Failure¹</td>
<td>5.2%</td>
<td>118</td>
</tr>
<tr>
<td>Prolonged Ventilation (&gt; 24 hours)</td>
<td>4.5%</td>
<td>102</td>
</tr>
<tr>
<td>Return to Theatre (Any Cause)</td>
<td>3.6%</td>
<td>81</td>
</tr>
<tr>
<td>Administration of Blood Products</td>
<td>27.8%</td>
<td>627</td>
</tr>
</tbody>
</table>

¹Doubling of first post-operative serum creatinine or serum creatinine > 200U/L; ²platelets, packed cells and/or FFP

Table 3: Univariate and Multivariate Predictors of Mortality

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>P-value</td>
</tr>
<tr>
<td>Minimum Temperature</td>
<td>0.805</td>
<td>0.498</td>
</tr>
<tr>
<td>Peak Temperature</td>
<td>3.159</td>
<td>0.052</td>
</tr>
<tr>
<td>Duration of Hypothermia</td>
<td>1.002</td>
<td>0.831</td>
</tr>
<tr>
<td>Rewarming Rate</td>
<td>6.968</td>
<td>0.611</td>
</tr>
<tr>
<td>Age</td>
<td>1.03</td>
<td>0.135</td>
</tr>
<tr>
<td>Male Gender</td>
<td>0.649</td>
<td>0.309</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>1.048</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Elective Operation</td>
<td>0.472</td>
<td>0.053</td>
</tr>
<tr>
<td>Number of Grafts</td>
<td>0.637</td>
<td>0.028</td>
</tr>
<tr>
<td>Bypass Time</td>
<td>1.009</td>
<td>0.112</td>
</tr>
<tr>
<td>Cross-Clamp Time</td>
<td>0.990</td>
<td>0.326</td>
</tr>
</tbody>
</table>

*χ² = 29.825; P < 0.001; Hosmer-Lemeshow Statistic: χ² = 8.021; P = 0.431; Nagelkerke R² = 0.113
pass time as a stronger predictor for post-operative length of stay than the duration of hypothermia ($R^2 = 0.070$ and $R^2 = 0.079$ respectively).

**F: Stroke**

A more rapid rate of rewarming during CPB was shown to be positively associated with an increased likelihood of stroke (Table 4). Univariate analyses for stroke showed a significant association between stroke and aortic cross-clamp time. However multivariate analysis showed that aortic cross-clamp time was not significantly associated with stroke, nor did it provide a stronger predictive model.

**G: Minimum Hypothermic Temperature and Significant Negative Findings**

Although minimum temperature was identified as a significant predictor for the use of blood products (OR = 0.634; $P < 0.001$) and 24-hour blood loss ($B = -0.053$, $P < 0.001$) in the univariate analyses, the results of the multivariate regression analyses reported no significant associations between minimum bypass temperature and any of the adverse outcomes.

Prolonged ventilation, infection and return to theatre were not significantly associated with any of the variables considered in this study.

**H: Changes in Temperature Management**

Owing to the possibility of variations in temperature management technique during CPB over the time course of this study, a simple correlation was used to investigate the relationship between surgery date and temperature management strategy (Table 5). This indicated a marginal but significant increase in minimum bypass temperature over the period June 2000 – May 2013. There was a decline in the average peak rewarming temperature from approximately 37.4°C to 36.7°C, in the rewarming rate from 0.17°C/minute to 0.11°C/minute, and in the duration of hypothermia from 57 to 47 minutes over the same period.

The results of this study demonstrated a strong correlation between bypass time and

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**Table 4: Univariate and Multivariate Predictors of Stroke**

<table>
<thead>
<tr>
<th></th>
<th>Stroke</th>
<th></th>
<th>95% C.I.</th>
<th>Stroke</th>
<th>P-value</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td></td>
<td></td>
<td>Multivariate*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>P-value</td>
<td>(lower, upper)</td>
<td>OR</td>
<td>P-value</td>
<td>(lower, upper)</td>
</tr>
<tr>
<td>Minimum Temperature</td>
<td>1.185</td>
<td>0.584</td>
<td>0.646, 2.175</td>
<td>1.389</td>
<td>0.413</td>
<td>0.632, 3.052</td>
</tr>
<tr>
<td>Final Temperature</td>
<td>0.605</td>
<td>0.307</td>
<td>0.230, 1.589</td>
<td>0.640</td>
<td>0.387</td>
<td>0.233, 1.758</td>
</tr>
<tr>
<td>Duration of Hypothermia</td>
<td>0.992</td>
<td>0.399</td>
<td>0.975, 1.010</td>
<td>1.006</td>
<td>0.598</td>
<td>0.984, 1.029</td>
</tr>
<tr>
<td>Rewarming Rate</td>
<td>621.503</td>
<td>0.065</td>
<td>0.673, 574340</td>
<td>4483</td>
<td>0.026</td>
<td>2.759, 7287</td>
</tr>
<tr>
<td>Age</td>
<td>1.009</td>
<td>0.642</td>
<td>0.972, 1.046</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Male Gender</td>
<td>0.684</td>
<td>0.367</td>
<td>0.299, 1.561</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>1.002</td>
<td>0.900</td>
<td>0.968, 1.038</td>
<td>1.004</td>
<td>0.831</td>
<td>0.970, 1.039</td>
</tr>
<tr>
<td>Elective Operation Status</td>
<td>0.933</td>
<td>0.866</td>
<td>0.420, 2.074</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Number of Grafts</td>
<td>0.688</td>
<td>0.062</td>
<td>0.465, 1.019</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bypass Time</td>
<td>0.990</td>
<td>0.169</td>
<td>0.976, 1.004</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cross-Clamp Time</td>
<td>0.978</td>
<td>0.049</td>
<td>0.957, 1.000</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

$\chi^2 = 5.171$; $P = 0.395$; Hosmer-Lemeshow Statistic: $\chi^2 = 6.966$; $P = 0.540$; Nagelkerke $R^2 = 0.020$
duration of hypothermia ($r = 0.766; P < 0.001$). Therefore due to the modest reduction in the duration of hypothermia over the course of this study, the trend in the average bypass time over the same period was also investigated. Unlike the average duration of hypothermia, the average bypass time remained unchanged at approximately 100 minutes ($r = 0.008; P = 0.707$).

Additionally, a relationship between bypass time and the rate of rewarming has previously been established, with slower rates of rewarming resulting in extended bypass times, which are independently associated with adverse outcomes [17, 18]. Investigation of the relationship between rewarming rate and bypass time reported a significant increase in the bypass time with a reduction in the rate of rewarming ($R^2 = 0.150; P < 0.001$).

**Discussion**

Temperature management plays an important role in determining adverse surgical outcomes for patients receiving isolated CABG surgery. On a background of ongoing research into the optimisation of temperature management strategies, these results provide additional evidence to support several temperature management practices that are emerging as efficacious in the peri-operative management of CABG patients.

The aim of this study was to determine whether the current temperature management strategy for CPB influences adverse post-surgical outcomes in patients undergoing CABG. Results demonstrated an increase in the incidence of adverse outcomes for patients exposed to faster rates of rewarming, higher peak rewarming temperatures and longer durations of hypothermia.

**Rewarming Rate and Peak Rewarming Temperature**

Faster rates of rewarming have been associated with jugular bulb ($S_jV_O_2$) desaturation [15], which has been shown to predict cognitive decline as well as longer hospital stay and reduced 30-day and 3-year survival [16, 19]. Higher peak rewarming temperatures of 37°C compared to 34°C have additionally been associated with an increased incidence of post-operative renal dysfunction [14].

We demonstrated that an increase in peak rewarming temperature is positively associated with an increase in a range of adverse outcomes. Furthermore, faster rewarming rates were positively associated with a higher incidence of stroke and increased 24-hour blood loss. The lowest likelihood of adverse outcomes was therefore reported in patients who were rewarmed to lower temperatures at slower rewarming rates.

Although current practice continues to implement a peak rewarming temperature of approximately 37°C, there has been a gradual and modest reduction in peak rewarming temperatures. Increased awareness of the detriments of hyperthermia has likely culminated in a reduction of maximum rewarming temperatures [20]. The reduction in peak rewarming temperatures has probably also occurred as a consequence of the shift towards

<table>
<thead>
<tr>
<th></th>
<th>Pearson Correlation*</th>
<th>R^2 Value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum Temperature</td>
<td>0.072</td>
<td>0.005</td>
<td>0.001</td>
</tr>
<tr>
<td>Peak Rewarming Temperature</td>
<td>-0.454</td>
<td>0.206</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rewarming Rate</td>
<td>-0.324</td>
<td>0.105</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Duration of Hypothermia</td>
<td>-0.110</td>
<td>0.012</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.01 level (2-tailed); n = 2259
tepids CPB temperatures, ameliorating the need for aggressive rewarming that exposes patients to rapid rewarming rates and an ‘over-shoot’ to hyperthermic temperatures ≥ 38°C [20].

Discrepancies in Temperature Measurement at Monitored Sites

When compared to continuous jugular venous monitoring, measurements at other body sites, including the nasopharynx, underestimates temperature during the rewarming phase, increasing the risk of neurological injury, renal dysfunction and, as reported in this study, mortality, post-operative myocardial infarction and coagulopathy [21, 22].

A combination of nasopharyngeal and arterial outlet temperature monitoring is often implemented to gain the most accurate measurement of core temperature in the absence of jugular bulb temperature, which is considered too invasive for routine temperature measurement. However, there is a reported disparity of 3.4-4.9°C between the nasopharynx and the jugular bulb [22-24]. Furthermore, a jugular bulb temperature of 37°C has been shown to correspond to a nasopharyngeal temperature of just 34°C ± 2.9°C during rewarming, hence rewarming to peak nasopharyngeal temperatures of approximately 34°C could be efficacious [5, 14, 24, 25]. The average peak nasopharyngeal temperature attained in this study was 37.0°C, and was associated with increased adverse outcomes, supporting a reduction in the peak nasopharyngeal temperature during the rewarming phase.

Rewarming Rate and Bypass Time

Extended bypass time has been associated with reduced rewarming rates however also increased neurological morbidity [17, 18], and was demonstrated by this study to be a factor in determining post-operative renal failure and length of stay. A potential avenue for reducing the bypass time is to reduce the peak rewarming temperature, as discussed above, hence reducing the required duration of the rewarming phase.

A reduction in the peak rewarming temperature alone, without altering the rewarming rate would be beneficial in reducing the likelihood of adverse outcomes. However, by aiming for lower peak temperatures, slower rewarming rates could also be introduced without significantly prolonging the rewarming period. The results from this study demonstrate that although slower rewarming rates were correlated with longer bypass times, the general trend over the time course of the study was a reduction in the rewarming rate and peak rewarming temperature, while the bypass time remained constant.

Minimum Temperature and Warm Bypass

Tepid bypass temperatures (32 - 35°C) have curtailed the adverse outcomes reported in more severe hypothermia as well as reducing tissue metabolism and therefore oxygen demand, offering increased protection against ischaemic injury [26].

The average minimum temperature of 32.2°C in this patient cohort reflects the trend towards the use of tepid bypass temperatures for on-pump CABG. There was no relationship between adverse outcomes and the minimum bypass temperature, lending significant support to the current practice of tepid CPB.

Limitations

As a retrospective data analysis, the main limitations include the reliance on the accuracy of the database, as well as the exclusion of incomplete records that cannot be included for analysis. Excluded cases were not associated with any specific time period or patient group.

Errors in data entry were limited by designation of a single record keeper for adverse events, as well as by identification of values
outside the relative narrow temperature ranges used for this patient cohort.

Although the surgical and bypass techniques used at our institution follow concepts and techniques of standard practice, this was a single-centre study, which may impact the external validity of the results. Additionally, this study did not investigate any adverse neurocognitive outcomes other than stroke. As this is an area of significant current interest, an assessment of pre- and post-surgical neurocognitive status would have been a valuable addition to the results of this study.

**Conclusion**

Rewarming rate, peak rewarming temperature and duration of hypothermia all contribute to the adverse outcomes described in this study. Our results support a reduction in rewarming rate and peak rewarming temperature to achieve better outcomes in this patient population. The minimum bypass temperature was not associated with any adverse outcomes in this patient cohort, validating the current practice of tepid bypass techniques.

A reduction in these parameters is therefore recommended, with continued observation of the subsequent effect on outcomes. Additionally, by reducing the peak rewarming temperature, slower rewarming rates could be implemented without significantly prolonging the bypass time, however due to the known detriments of prolonged bypass time, continued observation of this association is warranted.

**Speculations**

Although in the past decade there has been a gradual shift towards reducing the rewarming rate and peak rewarming temperature, a further reduction in these parameters is warranted, with continued observation to determine whether this will cause a subsequent decline in adverse outcomes. Additionally, by reducing the peak rewarming temperature, slower rewarming rates could be implemented without significantly prolonging the bypass time, however continued observation of this association is recommended.

Finally, the phenomenon of increased coagulopathy with a longer duration of hypothermia has, to the best of our knowledge, never before been reported. Closer examination of the effects of this aspect of temperature management on coagulopathy is therefore also warranted.

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**References**


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