Hypothermia and operative mortality during on-pump coronary artery bypass grafting

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Objective: Controversy surrounds the effect of hypothermia on operative mortality during cardiac surgery. The present study accessed a large clinical database of coronary artery bypass graft operations to address the issue.

Methods: A retrospective review of the Society of Thoracic Surgeons Adult Cardiac Surgery Database identified patients treated with isolated, nonemergency, on-pump coronary artery bypass grafting from July 2011 to December 2012. The patients were divided into 3 groups according to their lowest core temperature during the procedure: moderate hypothermia ($\leq 34^{\circ}\text{C}$), mild hypothermia ($>34^{\circ}\text{C}$ but $\leq 36^{\circ}\text{C}$), and normothermia ($>36^{\circ}\text{C}$). The primary endpoint of the study was operative mortality, defined according to the Database criteria.

Results: During the study period, 142,541 patients were available for analysis; 94,777 (66.5%) received moderate hypothermia, 42,750 (30.3%) mild hypothermia, and 5014 (3.5%) normothermia. Operative mortality occurred in 1394 patients (1.5%) in the moderate hypothermia, 534 (1.3%) in the mild hypothermia, and 105 (2.1%) in the normothermia group. Multivariate analysis identified hypothermia (both mild [odds ratio, 0.66; 95% confidence interval, 0.54-0.81; $P < .0001$] and moderate [odds ratio, 0.73; 95% confidence interval, 0.60-0.89; $P = .0015$]) was protective against operative mortality compared with normothermia. No incremental benefit was noted between the different hypothermia grades ($P = .0827$).

Conclusions: Most patients receive hypothermia during on-pump coronary artery bypass grafting. Hypothermia is protective against operative mortality compared with normothermia in such patients. Moderate hypothermia does not provide additional survival benefit. (*J Thorac Cardiovasc Surg* 2014;148:2712-8)

See related commentary on pages 2718-9.

Controversy exists about the risks and benefits of hypothermia during cardiac surgery.^{1,2} Ho and Tan³ reviewed the effect of hypothermia on cardiac operative mortality in a 2009 meta-analysis and identified 37 reports totaling 6444 patients. The general conclusion was that normothermia during cardiopulmonary bypass in adult cardiac surgery was as safe as that of hypothermia. Importantly, in that meta-analysis, more than one half of the studies contained <100 patients and therefore lacked an adequate sample size to address the issue. The Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database (STS-ACSD) began collecting lowest core

temperature data during the procedure in July 2011. The addition of this field to the database has offered an opportunity to study the effect of hypothermia on operative mortality during cardiac surgery in a large patient population.

METHODS

The Duke University Health System institutional review board declared this research exempt from review owing to the de-identified nature of the STS-ACSD. Funding limitations allowed analysis of only on-pump coronary artery bypass grafting (CABG). The STS-ACSD was reviewed for all patients treated with isolated CABG from July 1, 2011 to December 31, 2012. Of the 216,321 patients identified, 73,780 patients (34.1%) were excluded to develop a more homogenous cohort of stable, nonemergency patients for evaluation (Figure 1). No exclusion criteria were used at the hospital level; however, some hospitals were excluded from the analysis on the basis of the applied patient exclusion criteria.

The patients were divided into 3 groups according to the lowest core temperature during the procedure (STS-ACSD, version 2.73, sequence no. 2780): moderate hypothermia ($\leq 34^{\circ}\text{C}$), mild hypothermia ($>34^{\circ}\text{C}$ and $\leq 36^{\circ}\text{C}$), or normothermia ($>36^{\circ}\text{C}$). The distinction between mild and moderate hypothermia was determined by institutional practice. The patient characteristics studied were the standard STS risk model covariates (ie, risk calculator variables) and additional non-risk model covariates (Table 1), which also included the hospital CABG volume.⁴

The primary endpoint of the present study was operative mortality, which was defined as operative death (sequence no. 6390), discharge death (no. 6370), or death at 30 days after surgery (no. 6380). The secondary individual endpoints were permanent stroke (no. 6030) and reoperation for bleeding or tamponade (no. 5760). A combined infection endpoint was also used and consisted of the individual endpoints of deep sternal

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Abbreviations and Acronyms

CABG

= coronary artery bypass grafting

CI

= confidence interval

OR

= odds ratio

STS

= Society of Thoracic Surgeons

STS-ACSD

= Society of Thoracic Surgeons Adult Cardiac Surgery Database

infection (no. 5860), mediastinitis (no. 5870), pneumonia (no. 6150), and sepsis (no. 6010).

Descriptive statistics for categorical variables are reported as counts and percentages and continuous variables as the mean ± standard deviation and/or median and interquartile range. Categorical variables were compared using the chi-square test and continuous variables using the Kruskal-Wallis test.

Univariate and multivariate associations between the 4 endpoints and the 3 perfusion temperature groups were assessed using logistic regression analysis with the generalized estimating equation. To compare mild or moderate hypothermia with normothermia on each outcome, multivariate models were adjusted for the STS risk model covariates and non-risk model covariates, in addition to the 3 perfusion temperature groups. Missing covariates were imputed using most common category for categorical covariates and group-specific medians for continuous covariates. All continuous covariates were tested for linearity, and nonlinear relationships were accounted for using flexible splines, including linear splines or quadratic polynomial. All statistical tests were 2-sided, with the α level set at 0.05 for statistical significance. All analyses were performed using SAS, version 9.3 (SAS Institute, Cary, NC).

RESULTS

The study group included 142,541 patients treated with on-pump, nonemergency, isolated CABG. During cardiopulmonary bypass, 94,777 patients (66.5%) received moderate hypothermia, 42,750 (30.0%) mild hypothermia, and 5014 (3.5%) normothermia. A histogram of the lowest core temperature of the study group during the procedure is shown in Figure 2. The STS patient risk model covariates are listed as patient characteristics in Table 2. The operative data are reported in Table 3.

Operative mortality occurred in 1394 patients (1.5%) in the moderate hypothermia group, 534 (1.3%) in the mild hypothermia group, and 105 (2.1%) in the normothermia group. Stroke occurred in 1257 patients (1.3%) in the moderate group, 495 (1.2%) in the mild group, and 57 (1.1%) in the normothermia group. Reoperation occurred in 1662 (1.8%) in the moderate group, 716 (1.7%) in the mild group, and 99 (2.0%) in the normothermia group ($P = .025$). Finally, infection occurred in 3189 (3.4%) in the moderate group, 1318 (3.1%) in the mild group, and 161 (3.2%) in the normothermia group.

Univariate analysis identified mild hypothermia to be protective against operative mortality compared with normothermia (odds ratio [OR], 0.60; 95% confidence interval [CI], 0.49-0.72; $P < .0001$) and moderate

FIGURE 1. Algorithm describing patient exclusion process. CABG, Coronary artery bypass grafting; STS-ACSD, Society of Thoracic Surgeons Adult Cardiac Surgery Database.

ACD

TABLE 1. Society of Thoracic Surgeons non-risk model covariates

Age by group: <55, 55-64, 65-74, and ≥ 75 y (STS-ACSD no. 140)
History of smoking (STS-ACSD nos. 650 and 661)
No. of distal anastomoses with venous conduit (STS-ACSD no. 3200)
No. of distal anastomoses with arterial conduit (STS-ACSD no. 3190)
Dyslipidemia (STS-ACSD no. 800)
Radial arterial used for grafts (STS-ACSD no. 3260)
Preoperative medication, β -blocker (STS-ACSD no. 1710)
Preoperative medication, ACE inhibitor or ARB within 48 h (STS-ACSD no. 1730)
Preoperative medication, anticoagulant (STS-ACSD nos. 1750, 1780, 1850, 1880, 1900)
Preoperative medication, aspirin (STS-ACSD no. 1820)
Preoperative medication, lipid lowering (STS-ACSD no. 1830)
Proper antibiotic administration (STS-ACSD nos. 2710 and 2720)
STS-ACSD, Society Thoracic Surgeons Adult Cardiac Surgery Database, version 2.73; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

hypothermia (OR, 0.86; 95% CI, 0.77-0.95; $P = .0028$). Furthermore, mild hypothermia was protective against stroke compared with moderate hypothermia (OR, 0.87; 95% CI, 0.77-0.97; $P = .0125$). Moderate hypothermia was protective against operative mortality compared with normothermia (OR, 0.70; 95% CI, 0.58-0.84; $P = .0002$). Additional univariate analyses of perfusion temperature and endpoints are reported in Table 4.

Multivariate analysis identified mild hypothermia was protective against operative mortality compared with normothermia (OR, 0.66; 95% CI, 0.54-0.81; $P < .0001$). Moderate hypothermia was also protective against mortality compared with normothermia (OR, 0.73; 95% CI, 0.60-0.89; $P = .0015$). Mild hypothermia was not significantly protective against operative mortality compared with moderate hypothermia ($P = .0827$). No other perfusion temperature-related variables were protective of the primary or secondary endpoints (Table 5).

DISCUSSION

The effect of hypothermia during cardiac surgery is controversial, and current data have provided conflicting guidance. With a small anticipated effect size, most studies have lacked an adequate sample size to evaluate the question. The present study leveraged the large patient volume in the STS-ACSD to evaluate the effect of hypothermia in patients undergoing on-pump CABG. In a group of 142,541 patients, 96.5% of the patients received hypothermia ($\leq 36^\circ\text{C}$), which was protective against mortality compared with normothermia. This held true in multivariate analysis of both mild hypothermia ($>34^\circ\text{C}$ and $\leq 36^\circ\text{C}$; OR, 0.66; 95% CI, 0.54-0.81; $P < .0001$) and moderate hypothermia ($\leq 34^\circ\text{C}$; OR, 0.73; 95% CI, 0.60-0.89; $P = .0015$). No benefit was seen for operative mortality, however, in the comparison of mild and moderate hypothermia ($P = .0827$).

An attempt was made to create study cohorts that were as homogeneous as possible. In doing so, 73,780 patients (34.1%) and 29 hospitals (2.7%) were excluded from the present study. These are significant numbers; however, the covariates used to exclude the patients and hospitals were clearly variables that would have confounded our analysis. Most are known to be clinically significant predictors of operative mortality, and, hence, their presence could have contaminated the outcome analysis. Examples of such variables include reoperation (operative mortality, OR, 3.13), shock (OR, 2.9), and emergency status with resuscitation or salvage (OR, 8.00).⁴ Exclusion of these types of patients from the analysis seemed reasonable and still left a study group of >142,000 patients.

An important issue to consider is what constitutes normothermia. Mackowiak and colleagues⁵ studied 700 temperature recordings from 148 healthy patients. They reported a mean temperature of $36.8^\circ\text{C} \pm 0.4^\circ\text{C}$. Thus,

FIGURE 2. Histogram of lowest patient temperature during on-pump coronary artery bypass grafting for the entire study group ($n = 142,541$ patients). Std Dev, Standard deviation.

TABLE 2. Society of Thoracic Surgeons risk model covariates according to lowest core temperature during the procedure

Variable	Moderate hypothermia (n = 94,777)	Mild hypothermia (n = 42,750)	Normothermia (n = 5014)	P value
Continuous variables				
Age (y)				<.0001
Mean $\pm$ SD	65.1 $\pm$ 10.3	64.3 $\pm$ 10.4	63.7 $\pm$ 10.7	
Median (IQR)	65 (58-73)	65 (57-72)	64 (56-71)	
BSA (m ²)				<.0001
Mean $\pm$ SD	2.00 $\pm$ 0.24	2.03 $\pm$ 0.25	2.05 $\pm$ 0.25	
Median (IQR)	2.00 (1.84-2.16)	2.03 (1.87-2.19)	2.05 (1.87-2.21)	
Last preoperative creatinine (mg/dL)				.0150
Mean $\pm$ SD	1.17 $\pm$ 0.99	1.16 $\pm$ 0.98	1.16 $\pm$ 0.94	
Median (IQR)	1.0 (0.80-1.2)	1.00 (0.80-1.20)	1.00 (0.80-1.20)	
Ejection fraction (%)				<.0001
Mean $\pm$ SD	52.5 $\pm$ 12.1	52.5 $\pm$ 11.9	51.0 $\pm$ 12.9	
Median (IQR)	55 (45-60)	55 (45-60)	55 (44-60)	
Categorical variables				
Female sex	24,887 (26.26)	10,443 (24.43)	1252 (24.97)	<.0001
White race	76,777 (81.01)	35,665 (83.43)	4237 (84.50)	<.0001
Smoking history*	31,803 (33.56)	14,284 (33.41)	1666 (33.23)	.8332
Diabetes				.0065
Insulin treated	15,360 (16.21)	6807 (15.92)	873 (17.41)	
Non-insulin treated	27,595 (29.12)	12,504 (29.25)	1518 (30.28)	
Dialysis	2521 (2.66)	1093 (2.56)	136 (2.71)	.4932
Hypertension	83,198 (87.78)	37,497 (87.71)	4418 (88.11)	.7012
Chronic lung disease				<.0001
Moderate	5803 (6.12)	2590 (6.06)	346 (6.90)	
Severe	3900 (4.11)	1814 (4.24)	251 (5.01)	
Immunosuppression	2304 (2.43)	1011 (2.36)	139 (2.77)	.1995
PVD	13,283 (14.02)	5658 (13.24)	672 (13.40)	.0003
CVD				.0005
Stroke	6778 (7.15)	2821 (6.60)	334 (6.66)	
No stroke	6702 (7.07)	2906 (6.80)	337 (6.72)	
Previous PCI	23,660 (93.78)	11,216 (94.05)	1361 (94.32)	.4388
Myocardial infarction				<.0001
<24 h	1269 (1.34)	588 (1.38)	135 (2.69)	
1-21 d	25,947 (27.38)	11,320 (26.48)	1569 (31.29)	
>21 d	17,435 (18.40)	7913 (18.51)	846 (16.87)	
Unstable angina	35,224 (37.17)	16,375 (38.30)	1924 (38.37)	.0001
NYHA functional classification				<.0001
Class I-III	11,324 (11.95)	4698 (10.99)	629 (12.54)	
Class IV	2817 (2.97)	1172 (2.74)	190 (3.79)	
Atrial fibrillation/flutter	5820 (6.14)	2508 (5.87)	360 (7.18)	.0008
Inotropes	578 (0.61)	244 (0.57)	36 (0.72)	.3833
No. of diseased coronary vessels				<.0001
2	16,281 (17.18)	9627 (22.52)	1133 (22.60)	
3	76,590 (80.81)	31,058 (72.65)	3508 (69.96)	
Left main disease >50% stenosis	29,757 (31.40)	13,219 (30.92)	1523 (30.37)	.0948
Aortic valve stenosis	2121 (2.24)	1005 (2.35)	105 (2.09)	.3137
Mitral valve stenosis	249 (0.26)	117 (0.27)	15 (0.30)	.8631
Aortic valve regurgitation, moderate plus	956 (1.01)	443 (1.04)	49 (0.98)	.8711
Mitral valve regurgitation, moderate plus	4250 (4.48)	1854 (4.34)	261 (5.21)	.0193
Tricuspid valve regurgitation, moderate plus	1790 (1.89)	885 (2.07)	128 (2.55)	.0011
Status, urgent	54,559 (57.57)	24,424 (57.13)	3156 (62.94)	<.0001

Data presented as mean $\pm$ SD, median (IQR), or n (%). SD, Standard deviation; IQR, interquartile range; BSA, body surface area; PVD, peripheral vascular disease; CVD, cerebrovascular disease; PCI, percutaneous coronary intervention; NYHA, New York Heart Association. *Smoking is not a risk model covariate but was included as a significant patient characteristic.

TABLE 3. Operative characteristics

Variable	Moderate hypothermia (n = 94,777)	Mild hypothermia (n = 42,750)	Normothermia (n = 5014)	P value
Continuous variables				
Blood products transfused intraoperatively (U)				
PRBCs				<.0001
Mean $\pm$ SD	1.81 $\pm$ 1.58	1.72 $\pm$ 1.61	1.82 $\pm$ 1.73	
Median (IQR)	2 (1-2)	2 (1-2)	2 (1-2)	
FFP				.0040
Mean $\pm$ SD	0.63 $\pm$ 1.25	0.64 $\pm$ 1.26	0.66 $\pm$ 1.25	
Median (IQR)	0 (0-1)	0 (0-0)	0 (0-1)	
Platelets				.0618
Mean $\pm$ SD	1.01 $\pm$ 2.36	1.07 $\pm$ 2.44	0.93 $\pm$ 1.86	
Median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	
Cryoprecipitate				<.0001
Mean $\pm$ SD	0.15 $\pm$ 1.06	0.31 $\pm$ 1.81	0.22 $\pm$ 1.27	
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	
Blood products transfused postoperatively (U)				
PRBCs				.7006
Mean $\pm$ SD	2.34 $\pm$ 2.33	2.34 $\pm$ 2.42	2.38 $\pm$ 2.28	
Median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	
FFP				.0001
Mean $\pm$ SD	0.59 $\pm$ 1.64	0.55 $\pm$ 1.61	0.55 $\pm$ 1.44	
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	
Platelets				.2295
Mean $\pm$ SD	0.52 $\pm$ 1.78	0.46 $\pm$ 1.68	0.48 $\pm$ 1.79	
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	
Cryoprecipitate				.0014
Mean $\pm$ SD	0.18 $\pm$ 1.16	0.23 $\pm$ 1.48	0.26 $\pm$ 1.81	
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	
Skin incision time (min)				<.0001
Mean $\pm$ SD	243 $\pm$ 71.6	224 $\pm$ 68.8	216 $\pm$ 74.7	
Median (IQR)	235 (194-285)	216 (177-262)	206 (165-258)	
Total ventilation time (h)				<.0001
Mean $\pm$ SD	17.8 $\pm$ 63.8	15.9 $\pm$ 55.8	17.0 $\pm$ 53.5	
Median (IQR)	6.95 (4.58-12.30)	6.32 (4.25-11.25)	6.33 (4.08-12.33)	
Total ICU time (h)				<.0001
Mean $\pm$ SD	67.5 $\pm$ 94.3	62.1 $\pm$ 85.7	65.0 $\pm$ 110.2	
Median (IQR)	46.5 (25.0-73.7)	44.0 (24.0-71.0)	43.7 (23.8-72.0)	
Categorical variables				
Intraoperative blood transfusion	33,678 (35.53)	12,523 (29.29)	1532 (30.55)	<.0001
Postoperative blood transfusion	36,472 (38.48)	14,719 (34.43)	1801 (35.92)	<.0001
Readmission to ICU	2801 (2.96)	1160 (2.71)	153 (3.05)	.0395

Data presented as mean $\pm$ SD, median (IQR), or n (%). PRBCs, Packed red blood cells; SD, standard deviation; IQR, interquartile range; FFP, fresh frozen plasma; ICU, intensive care unit.

95% of healthy patients would have a temperature of 36.0°C to 37.6°C, and the lower limit of normothermia would be 36.0°C, such as was used in the present study. In the meta-analysis of 37 studies by Ho and colleagues,³ normothermia was reported to be a temperature of 33.0°C to 38.0°C. Furthermore, hypothermia was variously worded as hypothermia, mild, moderate, moderate-deep, or deep, usually with 1 break point of temperature that ranged from 20.0°C to 37.0°C. The present study adhered to a clear definition of normothermia and has provided a reasonable distinction between the hypothermia levels.

The 3 cohorts in the present study were significantly different in baseline patient characteristics. Many of these factors are known to affect operative mortality. Recognizing this, each of the STS risk model covariates reported in Table 2, in addition to those non-risk model covariates listed in Table 1, was entered into the multivariate analysis of the effect of temperature on the primary and secondary outcomes. A total of 39 clinically relevant patient characteristics were entered into the analysis. Given the large number of patients in the present study and the robust nature of the multivariate analysis, additional statistical

TABLE 4. Univariate logistic regression analysis of lowest core temperature levels during the procedure and endpoint outcomes

Outcome	Mild vs normothermia		Moderate vs normothermia		Mild vs moderate hypothermia	
	Unadjusted OR (95% CI)	P value	Unadjusted OR (95% CI)	P value	Unadjusted OR (95% CI)	P value
Operative mortality	0.60 (0.49-0.72)	<.0001	0.70 (0.58-0.84)	.0002	0.86 (0.77-0.95)	.0028
Stroke	1.03 (0.76-1.39)	.8645	1.19 (0.90-1.57)	.2307	0.87 (0.77-0.97)	.0125
Infection	1.02 (0.85-1.21)	.8680	1.09 (0.91-1.30)	.3634	0.93 (0.86-1.01)	.0818
Reoperation	0.86 (0.69-1.07)	.1809	0.91 (0.73-1.14)	.4205	0.94 (0.85-1.04)	.2180

OR, Odds ratio; CI, confidence interval.

assessment using propensity matching or other methods was thought not to be indicated.

The effect of hypothermia during cardiac surgery has been controversial in the reported studies. Ho and colleagues³ thoroughly reviewed the worldwide published data on the topic. In their review of 37 studies, they reported that hypothermia was harmful in 16 studies, not estimable in 13, and beneficial in 8. However, more than one half of the studies reported on <100 patients. The largest study contained 1732 patients and used a combined endpoint of mortality and nonfatal Q-wave myocardial infarction in its power calculation to determine the sample size.⁶ That study showed no difference in the individual or combined endpoint. The investigators rightly pointed out that hypothermia can reduce the oxygen demand.⁶ It is precisely that which was most likely the source of the association of hypothermia and reduced operative mortality reported in the present study.

The strength of the present study was evident in the large number of subjects in each study group, allowing for vigorous statistical assessment. The importance of this statement can be found in a review of the data reported by Ho and colleagues.³ For comparison, a sample size of >10,189 patients per group would be required to detect the difference in their reported mortality rates for hypothermia (1.9%) versus normothermia (1.4%). This is assuming 80% power under mortality rate assumptions consistent with their findings (test of independent proportions; 2-sided $\alpha = 0.05$). No other studies have provided such numbers, apart from the present evaluation.

The main limitations of the present study were selection bias, unmeasured confounders, and retrospective data collection. These limitations were most evident in that the patient characteristics were not equally distributed among the study groups. Although multivariate analysis

was used with an extensive list of potential confounders, unmeasured variables remained a potential bias. The method of hypothermia grouping was also a concern.

The intent of the present analysis was to address the treatment decision of the degree of hypothermia as broad strategies of moderate, mild, and no hypothermia. Although surgeons often choose an exact temperature goal, the actual temperature achieved will often be determined by a number of other factors about the case (eg, patient size, duration of bypass time). Although a continuous analysis could be used to identify temperature cutpoints, the estimation of such cutpoints could be unreliable and subject to overinterpretation. Finally, a continuous analysis could lead to extreme estimates in the tails of the distribution where the data are sparse.

Funding for our project was limited and prevented additional data analysis and hypothesis testing, with its attendant implications. To be clear, the data and analysis established an association between temperature and operative mortality; however, causality remains speculative. Also of importance was that the minority of patients (3.5%) received normothermic perfusion. The reasoning for such a choice remains unknown and certainly could have implications on the measured endpoints. Finally, the findings in our report apply only to select patients treated with isolated, nonemergency, on-pump CABG and should not be generalized to other operative groups (eg, emergency CABG, valve repair or replacement).

CONCLUSIONS

Most patients in the STS-ACD who underwent on-pump CABG had a core temperature during the procedure of $\leq 36^{\circ}\text{C}$. Patients who received hypothermia demonstrated a significant mortality benefit compared

TABLE 5. Multivariate logistic regression analysis of lowest core temperature levels during the procedure and endpoint outcomes

Outcome	Mild vs normothermia		Moderate vs normothermia		Mild vs moderate hypothermia	
	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Operative mortality	0.66 (0.54-0.81)	<.0001	0.73 (0.60-0.89)	.0015	0.91 (0.82-1.01)	.0827
Stroke	1.08 (0.80-1.46)	.6211	1.13 (0.85-1.49)	.4063	0.96 (0.85-1.08)	.4723
Infection	1.09 (0.91-1.30)	.3541	1.13 (0.94-1.36)	.1823	0.96 (0.89-1.04)	.3253
Reoperation	0.86 (0.69-1.08)	.2033	0.89 (0.71-1.11)	.2952	0.97 (0.88-1.07)	.6025

OR, Odds ratio; CI, confidence interval.

ACD

with those who maintained a normal temperature (ie, $>36^{\circ}\text{C}$). Greater degrees of hypothermia (ie, $<34^{\circ}\text{C}$ vs $\geq 34^{\circ}\text{C}$) did not result in more benefit. The strength of our analysis was the large number of subjects in the database. Additional examination of the data is indicated to better identify the breakpoint temperature at which benefit will be derived.

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EDITORIAL COMMENTARY

To cool or not to cool?

Jennifer S. Lawton, MD

See related article on pages 2712-8.

To cool or not to cool—that is the question that is raised by the recent study by Greason and colleagues¹ appearing in this issue of the *Journal*. Greason and colleagues¹ used the Society of Thoracic Surgeons database to evaluate patients undergoing nonemergency on-pump isolated coronary artery bypass grafting (CABG) with specific attention to the effect of lowest intraoperative recorded core body temperature on the primary end point of operative mortality and secondary end points of stroke, reoperation for bleeding, and a combined infection end point.

The main strength of the study is in the large number of patients included in the analysis ($N = 142,541$), because previous studies have had too few patients to demonstrate meaningful statistical differences between groups. Patients were categorized into temperature groups according to the lowest recorded intraoperative temperature: moderate hypothermia ($\leq 34^{\circ}\text{C}$; $N = 94,777$), mild hypothermia ($>34^{\circ}\text{C}$ and $\leq 36^{\circ}\text{C}$; $N = 42,750$), and normothermia ($>36^{\circ}\text{C}$; $N = 5014$). The study spanned an 18-month period.

Univariate analysis demonstrated that mild hypothermia was better than moderate hypothermia which in turn was better than normothermia for the end point of operative mortality; however, operative mortality was 1.5% in the moderate hypothermia group, 1.3% in the mild hypothermia group, and 2.1% in the normothermia group. After multivariate analysis, mild and moderate hypothermia were protective relative to normothermia for the primary end point of operative mortality; however, mild hypothermia was not protective relative to moderate hypothermia.

Unfortunately, this large study was retrospective in nature and involved very different populations and enrollment biases. Clearly, the normothermic group was the sickest of all groups; it had more patients with lower ejection fraction, diabetes mellitus, chronic lung disease, recent myocardial infarction, unstable angina, higher New York Heart Association classification, atrial fibrillation or flutter, and urgent status. The normothermic patient group also had a higher incidence of readmission to the intensive care unit. In addition, Greason and colleagues¹ excluded patients with known predictors of operative mortality ($N = 73,780$), including reoperation, shock, emergency status with resuscitation, or salvage, to “create study cohorts that were as homogeneous as possible.” This may have introduced additional bias, despite multivariate adjustment attempts.

Do the results of this study indicate that hypothermia is good, hyperthermia is bad, or both? Greason and colleagues¹ speculated that hypothermia is protective as a result of reduced oxygen demand during CABG; however, does this really affect operative mortality? Hypothermia may also be detrimental because it is known to be associated

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