J Extra Corpor Technol. 2018;50:44–52
The Journal of ExtraCorporeal Technology

Does the Type of Cardioplegia Solution Affect Intraoperative Glucose Levels? A Propensity-Matched Analysis

Linda B. Mongero, BS, CCP; Eric A. Tesdahl, PhD; Alfred H. Stammers, MSA, CCP; Andrew J. Stasko, MS, CCP, RRT; Samuel Weinstein, MD, MBA

Medical Department, SpecialtyCare, Inc., Nashville, Tennessee

Abstract: Myocardial protection during cardiac surgery is a multifaceted process that is structured to limit injury and preserve function. Evolving techniques use solutions with varying constituents that enter the systemic circulation and alter intrinsic systemic concentrations. This study compared two distinct cardioplegia solutions on affecting intraoperative glucose levels. Data were abstracted from a multi-institutional perfusion registry, including a total of 1,188 propensity-matched cases performed from January through October 2016, at 17 cardiac surgical centers across the United States in which both del Nido and 4:1 cardioplegia were used during the study period. Covariate data included insulin administration, crystalloid cardioplegia volume, diabetes history, glucose at operating room entry, and nine additional variables. Primary and secondary endpoints were the highest intraoperative glucose level and maximum glucose in excess of 180 mg/dL. Mixed-effects multivariable linear and logistic regression models were used to assess the primary and secondary endpoints, respectively, allowing for statistical control of center and surgeon effects. Greater median crystalloid cardioplegia volume was given in the del Nido group (n = 594) 1,040 mL [interquartile range (IQR) = {800, 1,339}] compared with the 4:1 group (n = 594) 466 mL [IQR = {360, 660}] in the 4:1 group ($p < .001$) despite these groups being statistically indistinguishable in terms of bypass and cross-clamp times as well as seven other patient covariates. More patients required intraoperative insulin drip in the 4:1 group compared with del Nido (65.7% vs. 56.2%, $p < .001$). Multivariable linear mixed-effects analysis yielded an estimated maximum intraoperative glucose for the del Nido group of 177.8 mg/dL compared with that of the 4:1 group, 183.5 mg/dL—a statistically significant reduction of 5.7 mg/dL ($p = .03$). Multivariable logistic mixed-effects analysis showed a statistically nonsignificant reduction in the likelihood of crossing the 180 mg/dL threshold for del Nido compared with 4:1 (odds ratio [OR] = .79, $p = .214$). After controlling for known confounding variables, intraoperative maximum glucose levels for the del Nido group were 5.7 mg/dL lower than that of the 4:1 group; there was limited evidence suggesting a difference between methods in the likelihood of exceeding the threshold of 180 mg/dL intraoperatively. Further research is warranted to examine the differential effects of cardioplegia solution on intraoperative glucose levels. **Keywords:** cardioplegia, glucose, propensity analysis. *J Extra Corpor Technol. 2018;50:44–52*

Myocardial protection during cardiac surgery is a multifaceted process that is structured to limit injury and preserve function. Evolving techniques use solutions with varying constituents that enter the systemic circulation and alter intrinsic systemic concentrations. Cardioplegia solutions vary in their electrolyte and solute configurations and a better understanding of the regulation of delivery and uptake of nutrients in the heart is required to optimize myocardial metabolic balance (1). The association between perioperative hyperglycemia and adverse outcomes after cardiac surgery is well established and efforts have been made to tightly control blood glucose during the cardiac procedure which has in turn led to hypoglycemia in the postoperative period (2). Bearing in mind that cardioplegia solutions may or may not contain glucose as an additive constituent in the delivery solution, this study compared the effect of two distinct cardioplegia solutions on intraoperative glucose levels.

METHODS

Data were abstracted from a multi-institutional perfusion registry, drawing on perfusion pump records for cases performed from January through October 2016, at 17 cardiac surgical centers across the United States. Information available for each patient included gender; height (cm); weight (kg); age; procedure type; procedure acuity; reoperation; total cross-clamp time (minutes); total duration of cardiopulmonary bypass (CPB) (minutes); three glucose level measures: on entry to the operating

Received for publication June 23, 2017; accepted November 17, 2017.
Address correspondence to: Linda B. Mongero, BS, CCP, Department of Clinical Perfusion, SpecialtyCare, 3100 West End Avenue, Nashville, TN 37203. E-mails: linda.mongero@specialtycare.net and lbmongero@aol.com
The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

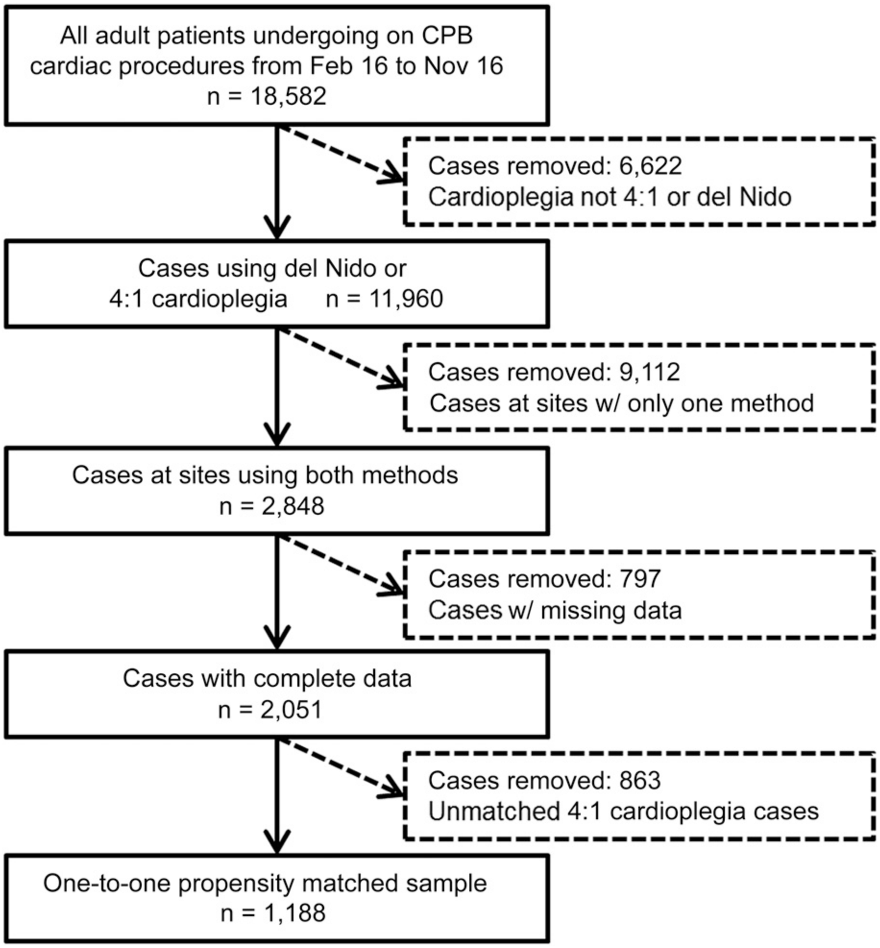

Figure 1. Sample selection criteria.

room, at the initiation of CPB, and the maximum intraoperative glucose level (mg/dL); history of diabetes; whether or not insulin was used intraoperatively; and volume of crystalloid cardioplegia administered intraoperatively.

Sample Selection and Propensity Matching

Sample selection and inclusion criteria are depicted in Figure 1. These included the use of either del Nido or 4:1 cardioplegia solution, surgery taking place at a site making use of "both" of these methods, and having complete outcome and covariate data. This process yielded an unmatched sample of 2,051 cases which was reduced to 1,188 after one-to-one nearest-neighbor propensity matching.

One key assumption in the application of propensity score methods is that of strong ignorability of treatment assignment (3–7), which states that each subject has a non-zero probability of receiving either treatment option. In our own sample, a large proportion of patients (9,112 as shown in Figure 1) underwent surgery at sites that provided only one type of cardioplegia, but not both. Thus, for the current analysis, we opted to focus only on those patients receiving treatment in centers where both forms of cardioplegia were available and administered during the study period.[1]

A propensity score was estimated for each patient using a linear mixed-effects model that included patient-level variables: preoperative blood glucose level, diabetes history, procedure type, gender, body surface area, estimated blood volume, body mass index, cross-clamp time, and total time on CPB, as well as random intercept for site of surgery to control for differing overall tendencies in the use of one method or another by site. Matching was carried out using a nearest-neighbor one-to-one matching algorithm as implemented in the R package "MatchIt" (8). Propensity score distributions and balance statistics are given in Table A1 and Figure A1. These methods yielded 1,188 one-to-

[1]Various strategies for calculating propensity scores at the hospital level were pursued; however, the matched samples that this process yielded had propensity scores with relatively poor balance and common support. Thus, out of caution, observations from these sites were not included in the current analysis. The authors note that future addition of detailed site-level variables may provide a fruitful avenue forward in balancing observations across centers where treatment assignment is best described as a site-level rather than patient-level phenomenon.

Table 1. Operative and demographic characteristics.

	Four to One Blood Crystalloid Ratio	del Nido	p-Value
n	594	594	
Procedure type [count {%}]			.003
Isolated CABG	303 (51.0)	251 (42.3)	
Aortic surgery	26 (4.4)	27 (4.5)	
AV surgery + CABG	70 (11.8)	59 (9.9)	
Combined AV/MV surgery	15 (2.5)	16 (2.7)	
Isolated AV surgery	103 (17.3)	126 (21.2)	.003
Isolated MV surgery	45 (7.6)	83 (14.0)	.003
MV surgery + CABG	32 (5.4)	32 (5.4)	
Nonelective procedure [count {%}]	143 (24.1)	147 (24.7)	.839
Female gender [count {%}]	194 (32.7)	200 (33.7)	.758
BMI (kg/m^2) [median {IQR}]	28.61 (25.09, 31.98)	28.40 (25.15, 32.44)	.804
BSA (m^2) [median {IQR}]	1.98 (1.81, 2.14)	1.97 (1.79, 2.13)	.333
Nadler estimated blood volume (L) [median {IQR}]	5.14 (4.42, 5.75)	5.05 (4.40, 5.73)	.380
Cross-clamp duration (minute) [median {IQR}]	81.0 (63.00, 111.00)	83.00 (63.00, 110.75)	.927
CPB duration (minute) [median {IQR}]	106.50 (83.00, 148.75)	108.00 (85.00, 144.75)	.916

IQR, interquartile range.

one propensity-matched patients for analysis; the median contribution of patients from each of the 17 sites was 40, with a minimum of 16 and a maximum of 166.

Statistical Methods

Patient demographic and operative characteristics were calculated according to the cardioplegia type received. All values reported for continuous variables are given as median and interquartile range, with count and percentage given for categorical variables. Group differences on continuous variables were conducted using Wilcoxon rank-sum tests, and differences on categorical variables were assessed using chi-squared tests. The primary endpoint, maximum intraoperative glucose level, was assessed using linear mixed-effects modeling as implemented in the R package "lme4" (9). This approach allowed us to estimate the effect of cardioplegia method while controlling for patient-level factors and accounting for similarity of outcomes by surgeon and hospital through the inclusion of a random-intercept term for each. The secondary endpoint, maximum glucose level greater than 180 mg/dL was similarly assessed using a binary logistic mixed-effects model which also allowed for the control of similarities by the surgeon and hospital. p values reported from both mixed-effects models were computed using the Kenward–Roger approximation. All analyses were carried out using the R statistical computing environment (10) and the "data.table" (11), "lme4" (9), "MatchIt" (8), "sjPlot" (12), and "tableone" (13) packages.

RESULTS

Descriptive statistics for operative and demographic variables are given in Table 1. These findings demonstrate, on the whole, very good covariate balance resulting from our propensity matching method. Groupwise comparisons of proportion of patients with diabetes history, female gender, and nonelective procedure were all statistically nonsignificant. Comparisons of first glucose on entry to the operating room, body mass index (BMI), body surface area (BSA). Nadler estimated blood volume (14), cross-clamp time, and total duration on CPB were all likewise statistically nonsignificant. Relatively more of the 4:1 patients underwent coronary artery bypass graft surgery (CABG) procedures (51.0% vs. 42.3%), whereas isolated aortic valve (AV) and mitral valve (MV) surgery were more common among del Nido patients (21.2% vs. 17.3%; 14.0% vs. 7.6%) (p = .003). Further details regarding the covariate balance are given in the Appendix.

Table 2. Glucose management characteristics.

	Four to One Blood Crystalloid Ratio	del Nido	p-Value
n	594	594	
Highest intraoperative glucose (mg/dL) [median {IQR}]	179.00 (155.00, 212.75)	168.00 (142.25, 203.00)	<.001
Highest glucose exceeded 180 mg/dL [count {%}]	294 (49.5)	229 (38.6)	<.001
Glucose at O.R. entry (mg/dL) [median {IQR}]	115.00 (01.00, 140.00)	115.00 (101.00, 140.00)	.976
First glucose on CPB (mg/dL) [median {IQR}]	146.00 (122.00, 184.75)	128.50 (110.00, 151.75)	<.001
Insulin administered in O.R. [count {%}]	390 (65.7)	334 (56.2)	.001
History of diabetes [count {%}]	216 (36.4)	204 (34.3)	.504
Volume of crystalloid cardioplegia administered (mL) [median {IQR}]	466.40 (360.00, 660.00)	1,040.00 (800.00, 1,339.25)	<.001

O.R., operating room.

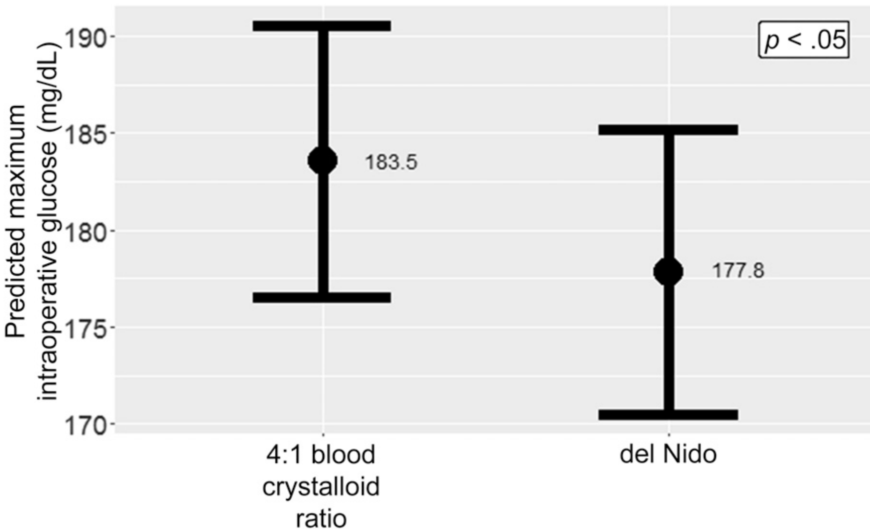

Figure 2. Mixed-effects estimates of maximum intraoperative glucose, by cardioplegia type.

More patients required intraoperative insulin in the 4:1 group compared with del Nido (Table 2, 65.7% vs. 56.2%, $p < .001$). Of patients given del Nido, the median volume of crystalloid cardioplegia administered intraoperatively was 1,040 mL (IQR = [800, 1,339]) compared with 466 mL (IQR = [360, 660]) in the 4:1 group ($p < .001$). Median first glucose on CPB for the del Nido group was 129 mg/dL (IQR = [110, 152]) compared with 146 mg/dL (IQR = [122, 185]) for the 4:1 group ($p < .001$). Median maximum intraoperative glucose was higher for the 4:1 group than del Nido (179 mg/dL vs. 168 mg/dL, $p < .001$). Similarly, the proportion of patients receiving 4:1 that also exceeded the threshold of 180 mg/dL was higher than that of patients receiving del Nido solution (49.5% vs. 38.6%, $p < .001$).

A multivariable linear mixed-effects model was estimated to assess the primary outcome, effect of cardioplegia method on maximum intraoperative glucose (full results reported in Table A2). This model included controls for patient demographic covariates, with random-intercept terms for the hospital and surgeon. Post hoc calculation of the intraclass correlation coefficient according to the surgeon and hospital revealed that the variation in maximum intraoperative glucose uniquely attributable to each was 10.3% and 7.5%, respectively. These figures highlight the utility of a linear mixed-effects approach as this technique allows for the adjustment of standard errors due to correlation in outcomes due to the hospital and/or surgeon.

Figure 2 gives the predicted maximum intraoperative glucose level and 95% confidence intervals for each cardioplegia method while holding all other covariates at their respective median values. We found that after controlling

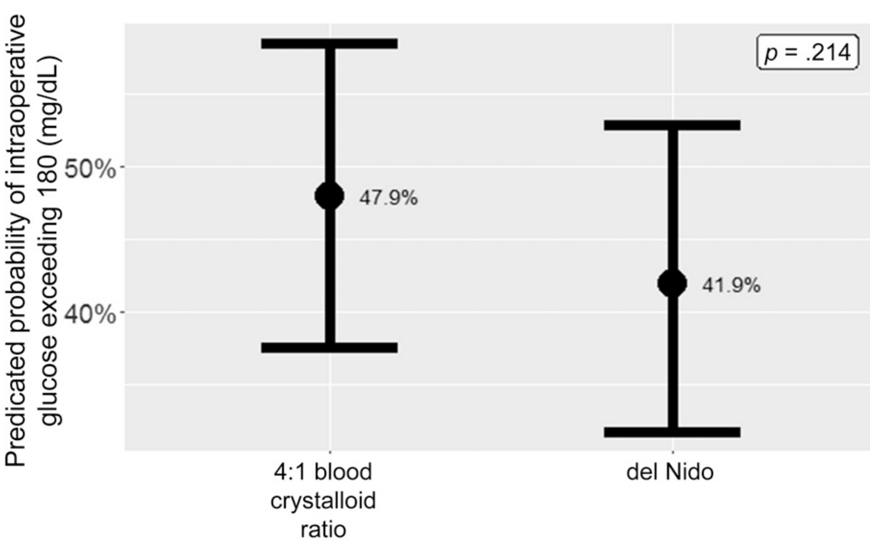

Figure 3. Mixed-effects estimates of probability of maximum intraoperative glucose exceeding 180 mg/dL.

for all demographic and operative variables, as well as surgeon and hospital, the del Nido group had a lower predicted maximum intraoperative glucose by 5.7 mg/dL (177.8 mg/dL vs. 183.5 mg/dL, $p = .035$).

A binary logistic mixed-effects model was estimated to assess secondary outcome, maximum intraoperative glucose greater than the threshold of 180 mg/dL (full results Table A3). After controlling for all demographic and operative variables, including the hospital and surgeon, we found that del Nido patients did not necessarily have a lower predicted probability of crossing this threshold for compared with the 4:1 patients (47.9% vs. 41.9%, $p = .214$, see Figure 3).

DISCUSSION

History of Glycemic Control

The scientific literature first recognized the importance of perioperative blood glucose control in the surgical patient in the early 1970s. During the 1980s, a mass of evidence was acquired that linked poor glucose control in diabetics with poor wound healing and increased rates of infection. In the 1990s, a large number of outcome-oriented clinical trials addressing diabetes in cardiothoracic surgery patients were reported with convincing evidence that diabetics were more likely to have wound infections, prolonged intensive care unit (ICU) length of stay, and mortality after cardiac surgery (15). At this time, there was no established ideal target range for blood glucose measurements for clinicians to follow. Van den Berghe et al. (16) in the early 2000 conducted a prospective, randomized, controlled trial on intensive insulin therapy in critically ill patients. Blood glucose levels were maintained in the 80–110 mg/dL range as compared with 180–200 mg/dL, and mortality was 4.6% in the control group vs. 8.0% in the standard control group and showed less multiple organ failure associated with sepsis. Over the next several years, many clinicians did studies that agreed that tight control of glucose in the range of 80–110 mg/dL was also the ideal range for surgical patients in the perioperative period. Finfer et al. (17) published that they found a greater incidence of mortality at 90 days after surgery in 6,104 patients randomly assigned to either intensive control (target 81–108 mg/dL) or standard control (target 180 mg/dL or less). In 2011, Lazar et al. compared aggressive glycemic control (90–120 mg/dL) against moderate control (120–180 mg/dL) in 82 patients undergoing CABG. In this report, there was no difference in the incidence of adverse events between the groups. This prompted the 2009 Society of Thoracic Surgeons' Practice Guidelines to recommend: IV. Management of Hyperglycemia Using Insulin Protocols in the Perioperative Period as a Class I recommendation stating "Glycemic control is best achieved with continuous insulin infusions rather than intermittent subcutaneous insulin injections or intermittent IV insulin boluses (level of evidence A)." All patients with diabetes undergoing cardiac surgical procedures should receive an insulin infusion in the operating room and for at least 24 hours postoperatively to maintain serum glucose levels 180 mg/dL (level of evidence B) (18).

There is a wide body of evidence that shows hyperglycemia is associated with longer stays in the ICU and other deleterious effects such as cerebral edema, increased risk of cardiac arrhythmia, and ischemic preconditioning leading to myocardial infarction. The "surgical stress" and release of gluconeogenic catecholamines is exacerbated during CPB and glucose homeostasis is disturbed which prompts an understanding of how to aid in controlling glucose levels during CPB (19). Certainly, eliminating glucose substrate from the CPB circuit is one avenue that may be used by the perfusionist.

Considering the fact that del Nido cardioplegia solution has been introduced recently to adult cardiac procedures and slow in adoption for patients that undergo coronary revascularization vs. valve surgery, we also report the patients with isolated AV and MV surgery more common among the del Nido group. Although it has been shown that short-term outcomes in adult cardiac surgery using del Nido solution have been found to be acceptable and comparable with conventional multidose whole blood cardioplegia (BC). As more centers begin using del Nido cardioplegia, it will be important to note that glucose levels were lower in our study and less insulin is given intraoperatively (20–22).

In another propensity-matched analysis of del Nido cardioplegia in adults, on leaving the operating room, the glucose levels in the del Nido group vs. BC were lower despite the fact that preoperative glucose were higher, and the level of insulin infusion was significantly higher in the BC group (23). In this study, with respect to the higher median glucose levels on CPB for multidose cardioplegia vs. the del Nido group may be because of the fact that these solutions contain glucose in the crystalloid component whereas del Nido has no glucose additive. In addition, it was more common to give intraoperative insulin in the 4:1 group compared with del Nido, even though this group has less crystalloid-containing glucose delivered. Consideration of any glucose-containing medications warrants review before use as it may impact the final glucose levels intraoperatively.

This is the first study to compare 4:1 and del Nido cardioplegia intraoperative glucose levels. Whether this is of importance to the patients' overall postoperative outcome, the authors have ascertained that limiting delivery of glucose-containing solutions intraoperatively does have an effect that shows a propensity for higher glucose levels although it did not statistical significance.

LIMITATIONS

We did not account for other additives that may have contained glucose during the intraoperative period. Most whole blood 4:1 cardioplegia solutions are dextrose-containing; however, we do not account for site-specific methods, and protocols for administering CP were hospital- and surgeon-specific and were not standardized throughout the study groups. The glucometer models are not known from institution to institution; however, we do know that all the institutions are using a glucose monitor approved by Clinical Laboratory Improvement Amendments which require clinical laboratories to be certificated by their state as well as the Center for Medicare and Medicaid Services before they can accept human samples for diagnostic testing.

CONCLUSION

After controlling for known confounding variables, maximum intraoperative glucose levels were estimated to be 5.7 mg/dL lower for del Nido cardioplegia patients (p = .035) compared with 4:1 patients. Descriptive analysis showed a reduced rate maximum intraoperative glucose greater than the 180 mg/dL threshold for del Nido patients which was unsupported by regression analysis. Further research is warranted to examine the differential effects of cardioplegia solution on intraoperative glucose levels.

REFERENCES

1. Kennergren C, Mantovani V, Strindberg L, et al. Myocardial interstitial glucose and lactate before, during, and after cardioplegic heart arrest. Am J Physiol Endocrinol Metab. 2003;284:E788–94.
2. Chaney MA, Nikolov MP, Blakeman BP, et al. Attempting to maintain normoglycemia during cardiopulmonary bypass with insulin may initiate postoperative hypoglycemia. Anesth Analg. 1999;89:1091–5.
3. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 1983;70:41–55.
4. McMurry TL, Hu Y, Blackstone EH, et al. Propensity scores: methods, considerations, and applications. J Thorac Cardiovasc Surg. 2015;150:14–9.
5. Deb S, Austin PC, Tu JV, et al. A review of propensity-score methods and their use in cardiovascular research. Can J Cardiol. 2016;32:259–5.
6. Brookhart MA. Variable selection for propensity score models. Am J Epidemiol. 2006;163:1149–56.
7. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivar Behav Res. 2011;46:399–424.
8. Ho DE, Imai K, King G, et al. MatchIt: nonparametric preprocessing for parametric causal inference. J Stat Softw. 2011;42:1–28.
9. Bates D, Maechler M, Bolker B, et al. Fitting linear mixed-effects models using lme4. J Stat Softw. 2015;67:1–48.
10. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2016.
11. Dowle M, Srinivasan A. Data.table: extension of 'data.frame'. R package version 1.10.0. 2016. Available at: https://CRAN.R-project.org/package=data.table.
12. Lüdecke D. sjPlot: data visualization for statistics in social science. R package version 2.3.1. 2017. Available at: https://CRAN.R-project.org/package=sjPlot.
13. Yoshida K, Bohn J. Tableone: create "table 1" to describe baseline characteristics. R package version 0.7.3. 2015. Available at: https://CRAN.R-project.org/package=tableone.
14. Nadler SB, Hidalgo JU, Block TB. Prediction of blood volume in normal human adults. Surgery. 1962;51:224–32.
15. Reddy P, Duggar B, Butterworth J. Blood glucose management in the patient undergoing cardiac surgery: a review. World J Cardiol. 2014;6:1209–17.
16. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. NEJM. 2001;345:1359–67.
17. Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360:1283–97.
18. Lazar HL, McDonnell M, Chipkin SR, et al. The society of thoracic surgeons practice guideline series: blood glucose management during adult cardiac surgery. Ann Thorac Surg. 2009;87:663–9.
19. Girish G, Agarwal S, Satsangi DK, et al. Glycemic control in cardiac surgery: rationale and current evidence. Ann Card Anesth. 2014;17:222–8.
20. Ota T, Yerebakan H, Neely RC, et al. Short-term outcomes in adult cardiac surgery in the use of del Nido cardioplegia solution. Perfusion. 2016;31:27–33.
21. Valooran GJ, Nair SK, Chandrasekharan K, et al. del Nido cardioplegia in adult cardiac surgery-scopes and concerns. Perfusion. 2016;31:6–14.
22. Sorabella RA, Akashi H, Yerebakan H, et al. Myocardial protection using del Nido cardioplegia solution in adult reoperative aortic valve surgery. J Card Surg. 2014;29:445–9.
23. Timek T, Willekes C, Hulme O, et al. Propensity matched analysis of del Nido cardioplegia in adult coronary artery bypass grafting: initial experience with 100 consecutive patients. Ann Thorac Surg. 2016;101:2237–42.

METHODOLOGICAL APPENDIX

Propensity Score Calculation and Matching

Propensity scores were calculated using logistic mixed-effects model to calculate the propensity to receive del Nido vs. 4:1 cardioplegia, as a function of patient diabetes status, preoperative glucose level, gender, body mass index, body surface area, estimated blood volume, procedure type, cross-clamp time, and total time on cardiopulmonary bypass. In addition to patient-level variables, we added a random-intercept term for the hospital to the propensity model to account for similarities in propensity to use del Nido according to the hospital.

Figure A1 depicts the distribution of resulting propensity scores in both the del Nido (listed as the "treatment" group in the figure) and 4:1 (listed as the control group in figure). Overlap and balance appear to be reasonably good among matched patients in both groups. Table A1 confirms this by giving the standardized mean difference between groups on all variables included in the propensity score model.

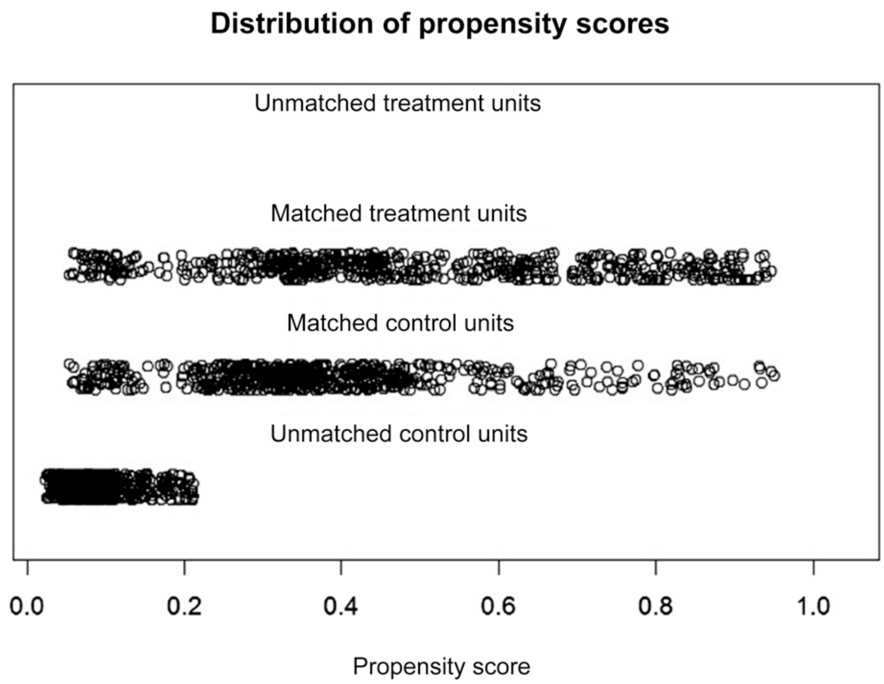

Figure A1. Distribution of propensity scores.

Table A1. Matching procedure balance summary.

	Summary of Balance for All Data			Summary of Balance for Matched Data			Percent Balance Improvement
	Means Treated	Means Control	Std. Mean Diff.	Means Treated	Means Control	Std. Mean Diff.	Std. Mean Diff.
Overall propensity score	.4875	.2088	1.1861	.4875	.3813	.452	61.8894
Diabetes status	.3434	.4173	−.1554	.3434	.3636	−.0425	72.6488
Gender (men)	.6633	.7049	−.0879	.6633	.6734	−.0214	75.7032
Gender (women)	.3367	.2951	.0879	.3367	.3266	.0214	75.7032
First glucose in O.R.	−.0951	.0388	−.1515	−.0951	−.0761	−.0215	85.8164
Procedure: aortic surgery	.0455	.0364	.0435	.0455	.0438	.0081	81.456
Procedure: AV surgery + CABG	.0993	.0611	.1277	.0993	.1178	−.0619	51.5757
Procedure: combined AV/MV surgery	.0269	.0124	.09	.0269	.0253	.0104	88.4548
Procedure: isolated AV surgery	.2121	.0714	.344	.2121	.1734	.0946	72.4882
Procedure: isolated MV surgery	.1397	.0309	.3137	.1397	.0758	.1844	41.2257
Procedure: MV surgery + CABG	.0539	.0309	.1017	.0539	.0539	0	100
Nadler estimated blood volume	−.1189	.0485	−.1685	−.1189	−.0563	−.063	62.6367
Body surface area	−.1124	.0458	−.1587	−.1124	−.0476	−.065	59.0593
Body mass index	−.1055	.043	−.1873	−.1055	−.0884	−.0216	88.4537
Cross-clamp time	.1263	−.0515	.1645	.1263	.1242	.002	98.8035
Total CPB time	.0579	−.0236	.0778	.0579	.0631	−.0049	93.7316

Primary Outcome Full Model Results

Table A2. Linear mixed-effects model estimating maximum intraoperative glucose.

Fixed Effects	B Estimate	95% Confidence Interval	*p*-Value
Intercept	73.537	49.89 to 97.19	<.001
Cardioplegia type = del Nido*	−5.709	−11.02 to −.40	.035
Glucose insulin given in O.R.	6.360	.99 to 11.73	.021
First glucose in O.R.	.613	.55 to .67	<.001
History of diabetes	−1.190	−6.31 to 3.93	.649
Intraoperative RBCs administered	.922	−.79 to 2.63	.291
Aortic surgery	−5.831	−17.55 to 5.89	.33
AV surgery + CABG†	−2.198	−10.22 to 5.82	.591
Combined AV/MV surgery†	−10.17	−24.51 to 4.17	.165
Isolated AV surgery†	−3.715	−10.23 to 2.80	.264
Isolated MV surgery†	−2.571	−10.91 to 5.77	.546
MV surgery + CABG†	−9.203	−19.60 to 1.20	.083
Nonelective procedure	−.795	−6.29 to 4.70	.777
Female gender	4.768	−1.28 to 10.82	.123
BMI	.007	−.51 to .53	.98
BSA	1.392	−13.23 to 16.01	.852
Cross-clamp time	.073	−.06 to .21	.293
Total time on CPB	.159	.06 to .26	.002
Random Effects			
Residual variance		1,198	
Variance attributable to surgeons		150.168	
Variance attributable to hospitals		109.667	
Number of surgeons		59	
Number of hospitals		19	
Intraclass correlation coefficient: surgeons		.103	
Intraclass correlation coefficient: hospitals		.075	
Observations		1,188	

*Effect defined relative to 4:1.
†Effect defined relative to CABG procedure.

Secondary Outcome Full Model Results

Table A3. Logistic mixed-effects model estimating odds of maximum intraoperative glucose exceeding 180 mg/dL.

Fixed Effects	Odds Ratio	95% Confidence Interval	*p*-Value
Intercept	.0018	.00–.01	<.001
Cardioplegia type = del Nido*	.7852	.54–1.15	.214
Glucose insulin given in O.R.	2.0397	1.34–3.09	<.001
First glucose in O.R.	1.0351	1.03–1.04	<.001
History of diabetes	1.0042	.70–1.45	.982
Intraoperative RBCs administered	1.1119	.96–1.29	.159
Aortic surgery	.3435	.14–.82	.017
AV surgery + CABG†	.6313	.36–1.11	.108
Combined AV/MV surgery†	.1872	.06–.55	.002
Isolated AV surgery†	.7083	.44–1.14	.154
Isolated MV surgery†	.5990	.33–1.10	.099
MV surgery + CABG†	.4123	.20–.87	.020
Nonelective procedure	.8216	.55–1.23	.336
Female gender	1.4104	.90–2.22	.136
BMI	.9868	.95–1.03	.497
BSA	1.1153	.37–3.33	.845
Cross-clamp time	1.0088	1.00–1.02	.093
Total time on CPB	1.0081	1.00–1.02	.045
Random Effects			
Variance attributable to surgeons		.397	
Variance attributable to hospitals		.362	
Number of surgeons		59	
Number of hospitals		19	
Intraclass correlation coefficient: surgeons		.098	
Intraclass correlation coefficient: hospitals		.089	
Observations		1,188	

*Effect defined relative to 4:1.
†Effect defined relative to CABG procedure.