Research Article

Prophylactic peritoneal dialysis improves post-surgical outcomes in high-risk pediatric cardiac patients

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AIM: To evaluate early peritoneal dialysis (PD) in high risk patients after pediatric cardiac surgery and compare it with standard care of post pediatric cardiac surgery.

METHODS: A retrospective study done on patients operated between Jan 2014 and Dec 2018, a total of 1163 pediatric patients underwent different cardiac surgical procedures, and we adopted early peritoneal dialysis protocol since Jan 2014 in a subgroup of patients. This protocol entails routine intraoperative peritoneal dialysis catheter (Peritoneal Dialysis) insertion through the peritoneal lining in the sub-xiphoid space and starting peritoneal dialysis in the ICU when certain criteria were met, this group of patients was compared to the standard care (Not initiating. to maintain negative fluid balance). The Study groups included 40 patients who had pediatric cardiac surgery, of whom 25 had the standard postoperative care and their mean age was 10.4 ± 6.27 months, the other 15 patients had early peritoneal dialysis (started within 6 hours after surgery) and their mean age was 9.29 ± 5.37 months; where the P value was 0.570.

RESULTS The mean Body Surface Area (BSA) of the standard group was 0.327 ± 0.059 m^2 and in the early peritoneal dialysis group was 0.323 ± 0.054 m^2; p-value was 0.805. In the standard peritoneal dialysis group, the mean cross clamp time was 163.12 ± 18.27 minutes and it was 167.73 ± 19.58 hours in the early peritoneal dialysis group and the p value was 0.456. The mean ventilation time in the standard peritoneal dialysis group was 7.82 ± 3.50 days compared to 5.40 ± 2.26 days in the early peritoneal dialysis group, the p value was 0.022. The mortality in the standard group was 4 (16%) and in the early peritoneal dialysis group was 2 (13.3%) and the p value was 0.819.

CONCLUSION: Initiation of early peritoneal dialysis in selected high-risk patients after pediatric cardiac surgery had beneficial effect on postoperative conditions; it significantly reduces the ventilation time and hence improves the postoperative outcome.

Key Words: *Peritoneal dialysis*; *Pediatric cardiac surgery*

INTRODUCTION

Children who undergo cardiac surgery are at risk for complications e.g. acute kidney insufficiency (AKI), venous congestion and low cardiac output which may lead to the development of ascites, abdominal compartment syndrome, decreased renal blood flow, and renal failure which affects less than 10% of pediatric patients undergoing cardiopulmonary bypass (CBP), it leads to increase fluid overload and extravasation. The cardiopulmonary bypass used in pediatric cardiac surgery is accompanied by an inflammatory reaction and leaky capillary syndrome [1-3]. Fluid overload is a predictor of prolonged hospital stay, also it carries the risk of other adverse outcomes e.g. mortality [4,5]. Fluid restriction and diuretics comprise the standard management of fluid balance in postoperative cardiac surgery patients [6]. Ultrafiltration in cardiopulmonary bypass is a one of the measures to help patients having fluid overload and inflammatory reactions and another method is post-operative peritoneal dialysis (PD) [7-10].

We compared outcomes in infants who had a peritoneal dialysis catheter (PDC) placed during surgery and undergone early PD in the cardiac surgery intensive care unit (CSICU) starting within 6 hours postoperative with those of age-matched infants having similar surgeries who received the standard care of postcardiac surgery.

METHODS

Participants and study design

This study is a retrospective cross-sectional study done between Jan 2014 and Dec 2018, at pediatric cardiac surgery unit at National Heart Institute (Giza), Egypt. Pediatric patients underwent different cardiac surgical procedures; we adopted early peritoneal dialysis protocol since Jan 2014 in a subgroup of patients. This protocol entails routine intraoperative peritoneal dialysis catheter insertion through the peritoneal lining in the sub-xiphoid space and starting peritoneal dialysis in the ICU when certain criteria were met, this group of patients was compared to the standard care of post pediatric cardiac surgery care with no early peritoneal dialysis to maintain negative fluid balance, depending mainly in fluid restriction and diuretics.

The Study groups included 40 pediatric patients who had cardiac surgery, of whom 25 had the standard care, the remaining 15 patients entailed routine intraoperative peritoneal dialysis catheter. This study was approved by our institutional ethics committee.

Group I: (Patients with standard postoperative care)

Twenty-five patients 17 (68%) males and 8 (32%) females. Their ages ranged between 0.5 and 21 months. All the patients in group I have standard management of post pediatric cardiac surgery care maintaining negative fluid balance without initiating peritoneal dialysis depending mainly on fluid restriction and diuretics in the ICU. The targeted negative balance was -10 to -30 ml/Kg/day.

Group II (Patients having early peritoneal dialysis)

This group included 15 patients 10 (66.7%) males and 5 (33.3%) females, their ages ranged between 0.6 and 20 months. They had PDC insertion through the peritoneal lining in the sub-xiphoid space during operation and started early peritoneal dialysis in the ICU within 6 hours, the subjects of this group were matched in age and gender to the standard care group.

Intraoperative insertion of Medtronic DLP Left Heart Vent Catheter routinely via sternotomy in the peritoneal cavity after complex operation in early PD group (Figure 1), it is used instead of Amicath (Acute Peritoneal Catheter Kit, Ameco Medical Industries) (Figure 2), which is used in cases of peritoneal dialysis in the ICU following acute kidney injury for its much lower cost, as well as its feasibility. In all children after surgical repair, epicardial echocardiographic examinations were performed using (Phillips EPIQ7C) using higher frequency probes (5-12 MHz) after disconnection of cardiopulmonary bypass machine to detecting residual lesions and assess

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residual pressure gradient using pulsed and continuous wave Doppler in multiple epicardial views. Epicardial images may only be obtained by an operator who is wearing a sterile gown and gloves within the operative field as described in the guidelines.

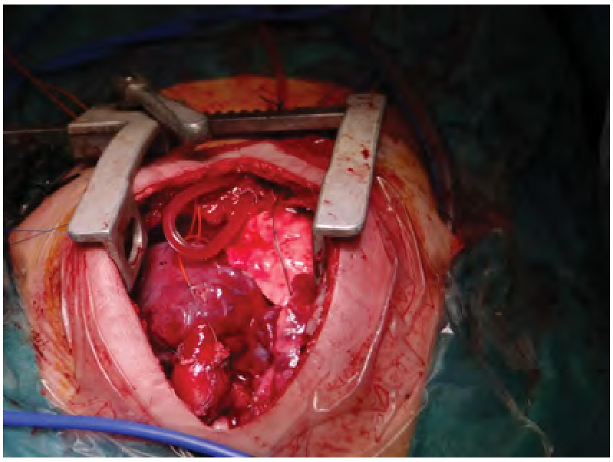

Figure 1) *Intraoperative insertion of Medtronic DLP Left Heart Vent Catheter routinely via sternotomy in the peritoneal cavity after complex operation in early peritoneal dialysis.*

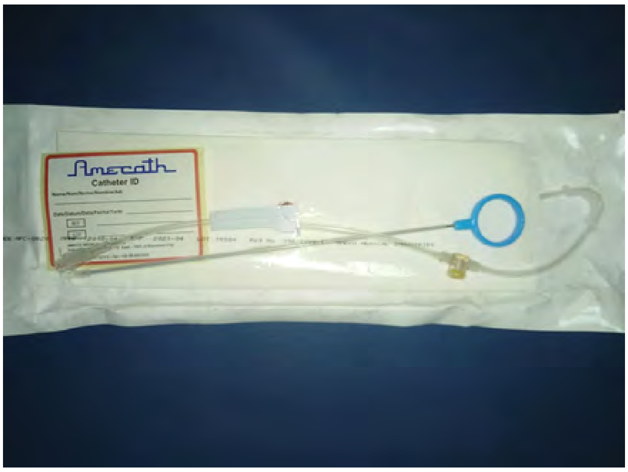

Figure 2) *Amicath (Acute Peritoneal Catheter Kit, Ameco Medical Industries) is used in cases of standard PD in the ICU following acute kidney injury.*

The inclusion criteria for all patients in both groups:

-Aortic cross clamping time more than 120 minutes.

-Cardiopulmonary bypass time more 160 minutes.

-Neonatal total corrections: Arterial switch, truncus arteriosus, Ebstein anomaly.

-Significant right ventricular outflow tract (RVOT) obstruction after Fallot.

-Significant left ventricular outflow tract (LVOT) obstruction after Rastelli like repair if PG > 40 mmHg.

-Right ventricle/left ventricle pressure ratio > 0.6.

-Single ventricle associated with severe atrioventricular valve (AVV) regurge.

Exclusion criteria

-Body weight more than 30 Kg.

-Age more than 14 years.

-Acute kidney injury

According to Acute Kidney Injury Network (AKIN) classification, AKI was classified into stages I to III on the basis of increases in serum creatinine or decreases in urine output (Table 1) [11].

TABLE 1
Indications for PDA closure.

Stage	Serum Creatinine	Urine Output
1	Increase in serum creatinine level by ≥0.3 mg/dl or increase to 150-200% of reference value in 48 h	<0.5 ml/Kg/h for 8 h
2	Increase of serum creatinine level to 200-300% of reference value in 48 h	<0.5 ml/Kg/h for 16 h
3	Increase of serum creatinine level to >300% of reference value or serum creatinine level ≥4.0 mg/dl with acute rise of ≥ 0.5 mg/dl in 48 h	<0.3 ml/Kg/h for 24 h, or anuria for □ 16h

Diagnoses and operations in the patient's groups

<u>**Surgical procedures**</u>

Surgical procedures were done under general anesthesia with modified neurolept. Through midline sternotomy, the pericardial cavity was entered after partial thymectomy. If required a large piece of pericardium was harvested and treated with 2% glutaraldehyde for 5 minutes. The ascending aorta, proximal arch, the root of the neck vessels and both pulmonary artery and its branches were dissected to full mobilization. After going on bypass, a state of moderate hypothermia is maintained during a state of cardioplegic arrest. The state of cardioplegic arrest was achieved by a single dose of Custidiol. The dose is effective for three hours of continuous cardioplegic arrest.

The group of early peritoneal dialysis included 7 (46.7%) cases of tetralogy of Fallot (TOF), 2 (13.3%) cases of atrioventricular canal (AVC), 2 (13.3%) cases of total anomalous pulmonary venous return (TAPVR), one case (6.7%) of transposition of great arteries having arterial switch operation (D-TGA, ASO), one case (6.7%) of truncus arteriosus, one case (6.7%) of transposition of great arteries with ventricular septal defect and pulmonary stenosis (D-TGA, VSD, PS), and one case (6.7%) of Glenn procedure associated with AVV repair.

The group of standard care included 31 (52%) cases tetralogy of Fallot (TOF), 3 (12%) cases of atrioventricular canal (AVC), 2 (8%) cases of total anomalous pulmonary venous return (TAPVR), one (4%) case of transposition of great arteries and arterial switch (D-TGA and ASO), one (4%) case of truncus arteriosus, 2 (8%) cases of transposition of great arteries with ventricular septal defect and pulmonary stenosis (D-TGA, VSD, PS), one (4%) case of neonatal Ebstein anomaly, and 2 (8%) cases of Glenn procedure, septectomy with AVV repair.

The patients' group who started early peritoneal dialysis (within 6 hours postoperative) was selected according to the previously described inclusion criteria and irrespective of developing oliguria. The applied regimen of peritoneal dialysis at our ICU was performed by pediatricians with the help of nursing care and pediatric nephrology consultation was needed in some situations. The dialysis solution 10 mL/kg 1.5%, was used (Dianeal; Baxter Healthcare), 2 to 3 mEq/L of potassium chloride and unfractionated heparin 200 U/L were added. The peritoneal cavity at the start is filled with the PD solution during 5 minutes; dwell time was 45 minutes, then draining the peritoneal fluid passively over 10 minutes. This cycle was repeated during the period of peritoneal dialysis. Termination of peritoneal dialysis and removal of the PDC occurred when the patient was in a weaning phase defined as a net negative fluid balance for a at least 2 consecutive days, decreasing mechanical ventilation settings and withdrawal of inotropes, normal serum potassium (<4.0 mEq/L), and adequate urine output (1 mL/kg/hour).

Standard postsurgical care regarding fluid balance was applied in the form of furosemide 1mg/kg intravenously every 6 hours for 2 doses, then according to clinical evaluation. Also, chlorothiazide sodium was sometimes added.

Decrease of urine output with increase in serum creatinine following the criteria of AKI allow to initiate peritoneal dialysis in the ICU using Amicath (Acute Peritoneal Catheter Kit, Ameco Medical Industries), and these patients are excluded from the study protocol.

All patients were given inotropes and vasoactive medications according to clinical evaluation. Maintenance fluids were restricted to two-thirds initially, then adjusted according to clinical status and fluid balance. Electrolytes and blood sugar were regularly monitored and adjusted. Outcome variables in the form of duration of mechanical ventilation to the first extubation, ICU stay duration and in-hospital mortality were compared between the two groups. Cases of AKI were not involved in the study protocol to avoid the confounding effect of renal injury.

STATISTICAL METHODS

All data were collected, tabulated and statistically analyzed using the Statistical Package for the Social Sciences (IBM SPSS version 25). Continuous variables were summarized as mean +/- standard deviation if normally distributed. Non-normally distributed continuous variables were summarized as median and inter-quartile range (IQR). Categorical variables were summarized as proportions and frequencies. Normality was assessed by the Shaprio-Wilk test. Student t-test was used for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. Chi-Square test (X^2) was used to test categorical variables (results were presented as percentages and the corresponding P-value). All tests were two-sided, $p < 0.05$ was considered statistically significant, and $p \geq 0.05$ was considered non-statistically significant.

RESULTS

The Study groups included 40 pediatric patients who had cardiac surgery under certain inclusion/exclusion criteriae, 15 patients randomized to early/prophylactic peritoneal dialysis (PPD) with mean age 9.29 ± 5.37 months, and 25 patients randomized to standard medical treatment (no PPD) with mean age 10.4 ± 6.27 months. Baseline characteristics (age, gender, and body weight and body surface area) showed no statistically significant difference between the two groups (Table 2).

TABLE 2

Baseline demographic and clinical characteristics for prophylactic peritoneal dialysis and no prophylactic peritoneal dialysis patients

Variables	Group	No PPD (n=25)	PPD (N= 15)	P-value
Age (months)	-Mean ± SD	10.4 ± 6.27	9.29 ± 5.37	0.57
Gender	-Males	17 (68%)	10 (66.7%)	0.931
	-Females	8 (32%)	5 (33.3%)	
Body weight (Kg)	-Mean ± SD	6.44 ± 1.41	5.84 ± 1.4	0.087
Height (cm)	-Mean ± SD	61.00 ± 6.03	62.03 ± 5.76	0.597
Body surface area (m^2)	-Mean ± SD	0.327 ± 0.059	0.323 ± 0.054	0.805
Cross clamping time (min)	-Mean ± SD	163.12 ± 18.27	167.73 ± 19.58	0.456
CARDIOPULMONARY BYPASS time (min)	-Mean ± SD	194.80 ± 17.11	200.00 ± 18.03	0.367

As regard cross clamping time and cardiopulmonary bypass (CBP) time, both showed no statistically significant difference between the two groups of the study. In PPD group, the mean cross clamping time was 167.73 ± 19.58 minutes, while in no PPD group it was 163.12 ± 18.27 minutes, and the p value was 0.456. The cardiopulmonary bypass time mean in PPD group was 200.00 ± 18.03 minutes, while in no PPD group it was 194.80 ± 17.11 minutes, and the p value was 0.367 (Table 2).

We found that the time of mechanical ventilation showed a statistically significant decrease in the PPD group in comparison to standard care group. The mean ventilation time of PPD group was 5.40 ± 2.26 days, while in no PPD group the mean ventilation time was 7.82 ± 3.50 days, and the P value was 0.022. In contrast, cardiac intensive care unit (CICU) time of stay and mortality did not show statistically significant difference between the two groups (Table 3) (Figure 3).

TABLE 3

Comparison of outcome variables between prophylactic peritoneal dialysis and no prophylactic peritoneal dialysis patients

Variables		No PPD (n=42)	PPD (N= 40)	P value
Ventilation time (days)	-Mean ± SD	7.82 ± 3.50	5.40 ± 2.26	0.022*
CSICU time (days)	-Median	18	20	0.581
	-Range	(6 - 80)	(10-72)	
Mortality	-Deaths	4 (16%)	2 (13.3%)	0.819
	- Living	21 (84%)	13 (86.7%)	

There were no statistically significant differences between groups as regard of congenital cardiac anomalies requiring surgery (Tetralogy of Fallot, atrioventricular canal, total anomalous pulmonary venous drainage, transposition of great arteries with arterial switch operation, truncus arteriosus, transposition of great arteries with ventricular septal defect and pulmonary stenosis, neonatal Ebstein anomaly and single ventricle pathway) (Table 4 and Figure 3).

TABLE 4

Patients and diagnoses

Variables	No PPD (n=25)		PPD (n=15)		P-value
	N	%	N	%	
TOF	13	52	7	46.7	0.744
AV Canal	3	12	2	13.3	0.902
TAPVD	2	8	2	13.3	0.586
TGA, ASO	1	4	1	6.7	0.708
Truncus Arteriosus	1	4	1	6.7	0.708
TGA, VSD, PS	2	8	1	6.7	0.877
Neonatal Ebstein Anomaly	1	4	0	0	0.433
Single Ventricle Pathway	2	8	1	6.7	0.877

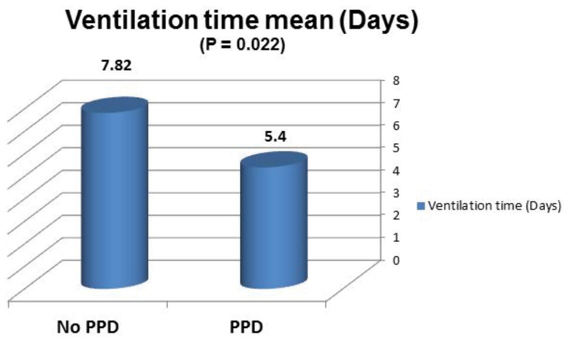

Figure 3) *Ventilation time mean in study groups.*

DISCUSSION

Fluid overload pediatric cardiac surgery is one of the major problems associated with adverse outcome; this makes both treatment and prevention equally a cornerstone of management in pediatric post cardiac surgery ICU. This study reveals that initiation of prophylactic peritoneal dialysis is a reliable maneuver for fluid management with a very low risk for adverse events and it is associated with significant decrease in mechanical ventilation time.

Positive fluid balance leads to decreased lung compliance and interferes with gas exchange [12]. So to improve gas exchange and tissue oxygenation achieving drainage of free peritoneal fluid was found to be effective [13]. Also there is decrease in cardiac output in hypervolemic states which can be relieved by ultrafilteration [14]. Ventilator acquired pneumonia is a common complication of mechanical ventilation and associated with increased mortality rate. The use of sedation and muscle relaxants during mechanical ventilation can also be associated by inevitable hazards and costs [15-18].

Peritoneal dialysis achieves drainage of free peritoneal fluids, avoiding volume overload and preventing electrolytes disturbances which leads to arrhythmias and other morbidities and increased mortality in the ICU patients [19]. Ventricular arrhythmias and cardiac arrest may occur as complications for hypokalemia [20]. Also, the use of diuretics is complicated by metabolic alkalosis which suppresses spontaneous respiration and delays weaning from mechanical ventilation [21].

Prophylactic peritoneal dialysis carries many suggested mechanisms of action for improving outcome, it limits volume overload and edema by direct drainage of extravascular fluid which may increase lymphatic drainage and improve renal blood flow [22]. Peritoneal dialysis also adjusts cytokines following cardiopulmonary bypass and associated with capillary leak syndrome which may prevent nephron damage and protect renal functions [23].

In our study, there was statistically significant decrease in ventilation time in prophylactic peritoneal dialysis group in comparison to no peritoneal dialysis group, while ICU stay time and mortality did not show statistically significant differences between the prophylactic peritoneal dialysis group and no peritoneal dialysis group, this may require larger sample size, as well as the progress in surgical techniques had an impact on overall mortality rate.

Cases of AKI –by definition according to guidelines- requiring therapeutic peritoneal dialysis were not included in this study, as peritoneal dialysis alters urine output and serum creatinine and to avoid overlap of results between suggested benefit of prophylactic peritoneal dialysis and adverse outcome of renal failure.

In comparison to our study, Kwiatkowski et al. reported a retrospective case-matched cohort study in patients having high risk for development of AKI following pediatric cardiac surgery. Their patients were matched before and after peritoneal dialysis catheter placements. There was statistically significant decrease in time to negative fluid balance, duration of mechanical ventilation, inotrope scores and electrolyte disturbances in peritoneal dialysis catheters placement. There were no significant differences in the duration of cardiac ICU stay, hospital stay and mortality. They also carried an unmatched subgroup analysis to compare between patients having passive peritoneal dialysis drainage and those having renal replacement therapy (RRT) using peritoneal dialysis. There was no significant difference between the subgroups regarding time to extubation and time to negative fluid balance.

Quietly similar to our study, Kwiatkowski et al. also had a single-center, unblended, and randomized clinical trial on patients less than 6 months of age having cardiac surgery. Infants received intravenous furosemide (1mg/kg every 6 hours) or a standardized peritoneal dialysis regimen. There was no statistically significant difference between the peritoneal dialysis and furosemide groups regarding the achievement of negative fluid balance on the first postoperative day. In the furosemide group, there was statistically significant increase in having 10% fluid overload, mechanical ventilation time, duration of inotrope uses and electrolyte abnormality scores in comparison to the peritoneal dialysis group. There were no statistically significant differences in mortality in, duration of cardiac ICU stay and duration of hospital stay between the two groups [24].

Pan et al. performed a retrospective observational study including patients with RVOT obstruction who had anatomical repair. All patients were at high-risk of fluid overload, with RVOT obstructive lesions [TOF, pulmonary artery atresia with VSD and the double-outlet right ventricle with pulmonary stenosis] and younger than 3 years were included in the study. They compared between two types of strategies for starting peritoneal dialysis. Aggressive peritoneal dialysis strategy was started directly in the operating room or in pediatric cardiac ICU within 6 h of admission in a group of patients who met high risk criteria for fluid overload according to clinical experience. The other relatively more conservative strategy for peritoneal dialysis depends on clinical factors such as positive fluid balance, oliguria or presence of AKI was applied in another group. A comparison between early peritoneal dialysis group, and the control group without early peritoneal dialysis in 45 matched patient pairs (totally 90) was done. After propensity matching, there where was a statistically significant decrease in mechanical ventilation time, vasoactive-inotropic score (VIS) [25]. There was statistically significant increase in rate of negative fluid balance in the early peritoneal dialysis group.

In contrast, Ryerson et al. found that prophylactic PDC with or without peritoneal dialysis after the Norwood procedure did not show decrease the time to reach to negative fluid balance and it showed severe side effects. This may be due to the age of their patients and post-surgery differences in physiology [26].

Some studies reported major complications following PDC insertion e.g. peritonitis, small bowel obstruction, bowel perforation, wound dehiscence and omental herniation (about 5% to 7%) and the incidence of complications is less (4.3% to 4.8%) in patients who had intraoperative peritoneal dialysis catheter insertion [27-32]. In our study minor complication of peritoneal dialysis were reported and instantly treated, e.g. obliteration of the dialysis catheter and oozing around the catheter, which were controlled rapidly and did not affect outcome. No cases reported peritonitis, perforation or other major adverse event.

LIMITATIONS

Our study is a single-center retrospective study, and this is a major limitation. Although we tried to avoid confounding factors by matching in age, gender and cardiac defects requiring surgery in the two groups of the study, but there were inevitable confounders as our patients were selected from different time periods, which might be affected by differences in ICU management protocols, changing of physicians and available resources.

Our study recommends prophylactic peritoneal dialysis after pediatric cardiac surgery for high risk patients to decrease fluid overload and to decrease ventilation time with very limited complications, but further multicenter studies and use of biomarkers are needed to confirm or deny the feasibility of prophylactic peritoneal dialysis in pediatric post cardiac surgery.

CONCLUSION

Early/prophylactic peritoneal dialysis proved to reduce the duration of mechanical ventilation after pediatric cardiac surgery, by improvement of fluid drainage and preventing volume overload which minimizes the adverse effects and hazards of mechanical ventilation (e.g. ventilator associated pneumonias, barotrauma and hazards of sedation). We recommend early peritoneal dialysis in high risk patients to achieve more effective fluid management and obtain better clinical outcomes, and we suggest a multicenter prospective randomized trial for further evaluation of early peritoneal dialysis.

CONFLICT OF INTEREST

We have no disclosures, no refunds or personal interest direct or indirect for this research, generally or regarding Medtronic and Ameco Medical Industries.

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