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ORIGINAL ARTICLE

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Buckberg versus Del Nido in isolated aortic valve replacement: a prospective, two-centre, randomized trial

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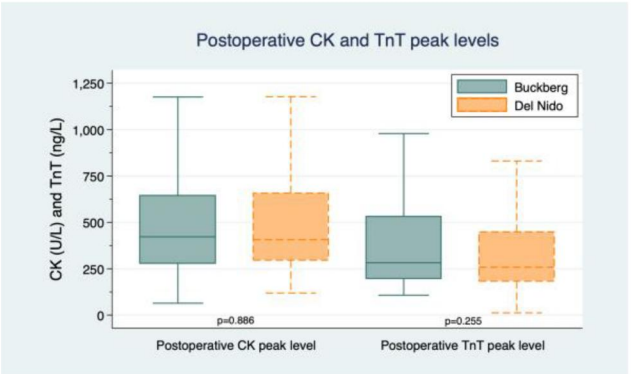
Bukcberg vs Del Nido in isolated aortic valve replacement: a prospective, multicentric, randomized trial

Summary

311 isolated AVR patients were randomized to BS or DNS in two different centers. Postoperative CK and TnT levels were determined. No differences in myocardial injury biomarkers were found. DNS group showed better glycemic control and less defibrillation after cross-clamp removal. No differences in haemodilution or red blood cell package transfusions were found.



Legend: AVR: aortic valve replacement, BS: Buckberg solution, DNS: Del Nido solution, CK: creatine kinase, TnT: ultrasensitive troponin T

Abstract

OBJECTIVES: Interest in Del Nido solution is increasing in adult cardiac surgery. This study compared Del Nido with Buckberg cardioplegia in patients undergoing isolated aortic valve replacement.

METHODS: A prospective, two-centre, randomized trial was conducted from July 2019 to August 2023, with adult patients undergoing first-time isolated aortic valve replacement, and were randomized to receive Buckberg (n = 159) or Del Nido (n = 152) solution. Primary end-point was Creatine Kinase and ultrasensitive Troponin T postoperative peak level.

RESULTS: A total of 311 patients were recruited. Total cardioplegia volume was higher in Del Nido group (1000 ml vs 374.5 ml, $P < 0.001$). No differences were observed in peak Creatine Kinase or Troponin T levels (422 vs 407 U/L and 282 vs 258 ng/L for Buckberg and Del Nido, respectively) or during postoperative days 1–5. After cross-clamp removal, patients in Del Nido group showed higher rates of spontaneous rhythm (66.7% vs 43.1%, $P < 0.001$) and less ventricular fibrillation requiring defibrillation (23.6% vs 49.7%, $P < 0.001$). Peak intraoperative glucose levels (128 mg/dl vs 198 mg/dl, $P < 0.001$) and insulin administration (18.1% vs 51.0%, $P < 0.001$) were lower in the Del Nido group. No other differences were found.

CONCLUSIONS: No differences between Del Nido and Buckberg solutions were detected. Del Nido presents better intraoperative glycaemic control, higher spontaneous rhythm, less ventricular fibrillation requiring defibrillation after cross-clamp removal, and more comfortable surgical workflow due to less re-dose interruptions.

CLINICAL REGISTRATION NUMBER: EU-CTR number: 2018-002701-59.

Keywords: cardioplegia • myocardial protection • Buckberg solution • Del Nido solution • aortic valve replacement

ABBREVIATIONS

AKIN	Acute Kidney Injury Network
AVR	Aortic valve replacement
BS	Buckberg solution
CK	Creatine kinase MB isoenzyme
CPB	Cardiopulmonary bypass
DNS	Del Nido solution
LVEDD	Left ventricle end diastolic diameter
LVEF	Left ventricle ejection fraction
TnT	Ultrasensitive troponin T

INTRODUCTION

Cardioplegia is crucial for myocardial protection during cardiac surgeries requiring heart arrest. At our institution, the Buckberg cardioplegic solution (BS) has long been the standard choice for cardioplegia.

Del Nido solution (DNS) was initially developed as a single-dose cardioplegic solution for paediatric cardiac surgery [1]. It is a calcium-free, potassium-rich, non-glucose-based cardioplegia, with an electrolyte composition similar to extracellular fluid [2]. Since 2017, DNS has been available at our hospitals and has progressively become the preferred solution for most isolated and combined procedures.

Interest in DNS has been increasing in adult cardiac surgery, and multiple studies have compared its use with blood cold cardioplegia solutions in adult cardiac procedures [3–8]. However, most studies are unicentric, include different procedures, or have a small number of patients.

This two-centre, prospective, randomized trial aims to compare DNS with BS in elective isolated aortic valve replacement (AVR).

PATIENTS AND METHODS

Ethical considerations

The study followed the Declaration of Helsinki and was approved by each site's Ethical Committee and the Spanish Medical and Sanitary Products Agency (April 12, 2019). The coordinating centre's Ethical Committee approval code was IIBSP-CAR-2018-71 (March 23, 2019). It was registered in EU-CTR (2018–002701-59) and Clinical Trials (NCT04259515). All patients provided written informed consent before participation.

Patients and methods

The authors declare that this manuscript has been elaborated according the CONSORT 2010 Statement methods [9].

A prospective, two-centre, randomized trial comparing BS and DNS in isolated AVR was designed and conducted in two Spanish hospitals. Eligible patients were over 18 and required first-time isolated AVR surgery. Exclusion criteria included urgent or emergent procedures according to EuroSCORE-II definitions [10], prior cardiac surgery and patients refusing blood transfusions.

Randomization was performed by the members of research team using central, secure, web-based randomization system with concealed allocation (Clinapsis®, Barcelona, Spain). Blocked randomization used blocks of 30 patients. Participants were randomized 1:1 to receive BS or DNS. Participants were blinded to treatment, but the surgical team (surgeons, perfusionists, and anaesthesiologists) could not be blinded due to cardioprotection protocol differences.

Surgical technique and cardioplegic solutions

Conventional general anaesthesia was used according to each centre's standard (see the Supplementary Material). Surgical approach (full sternotomy or partial upper ministernotomy) and prostheses insertion technique were at surgeon's discretion.

DNS and BS were both standardized commercial solutions. BS was administered in a 4:1 blood:cardioplegia ratio, with an induction dose at 4°C after aortic cross-clamp, followed by maintenance doses every 15–20 min or when myocardial activity was observed. A warm reperfusion dose was given before cross-clamp removal [11]. DNS was administered in a 1:4 blood:cardioplegia ratio, with a single 20 ml/kg (max 1000 ml) dose at 4°C after cross-clamping. An additional 500 ml dose was given if the ischaemic period exceeded 90 min or when myocardial activity restarted (see the Supplementary Material for detailed cardioplegia administration protocols).

Intraoperative fluid administration, transfusion, insulin administration, and inotropes or vasopressors followed the standard clinical practice and protocols of each centre.

End-points

Creatine Kinase (CK) and ultrasensitive Troponin T (TnT) levels at postoperative day 1 to 5 were determined daily. Primary endpoint was CK and TnT peak postoperative levels. Normal

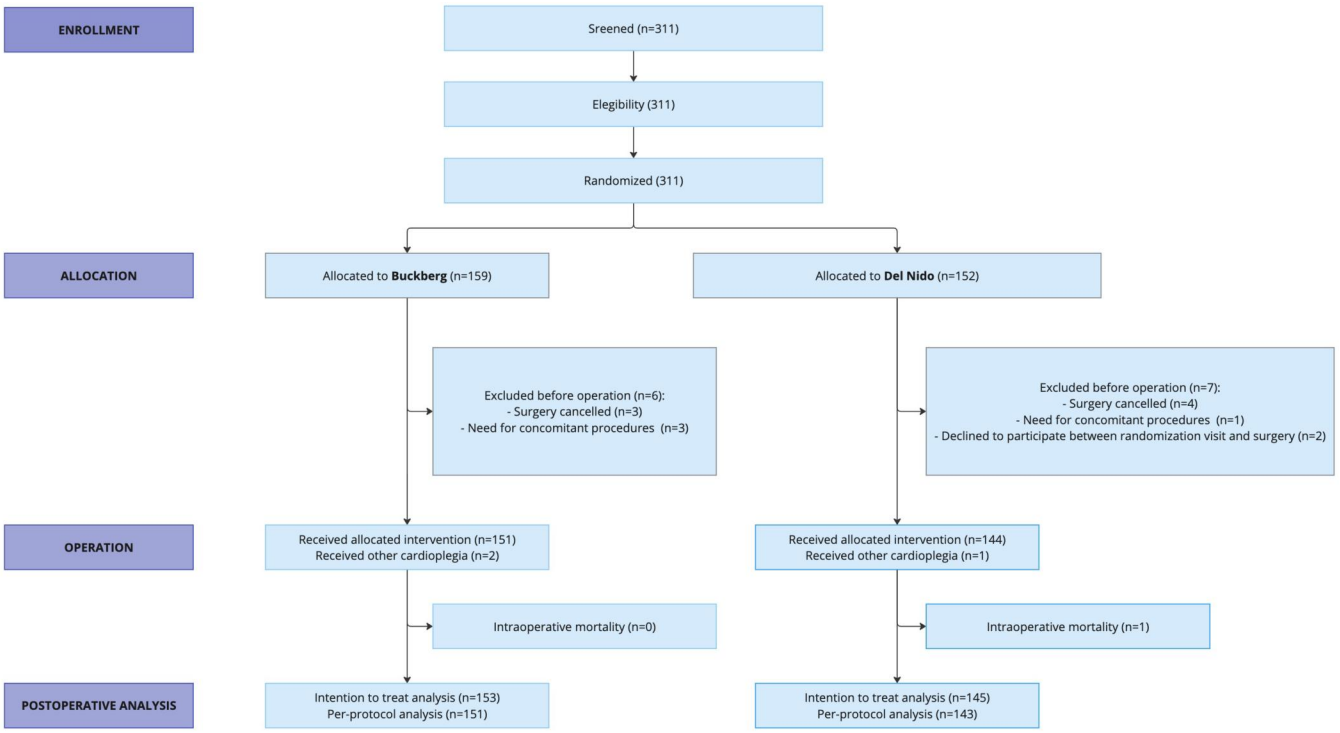


Figure 1: Enrollment flow diagram

laboratory reference values were 30 to 200 U/l for CK and <13 ng/l for TnT.

Secondary end-points included biomarker levels from day 1 to 5, cardiopulmonary bypass (CPB) and cross-clamp times, intra or postoperative inotropic support requirements, spontaneous rhythm or need for defibrillation after aortic cross-clamp removal, intra and postoperative haemodilution parameters (CPB and postoperative minimum haematocrit levels and need for blood transfusion), intra and postoperative glucose levels and insulin requirements, intraoperative lactate levels, postoperative creatinine levels and dialysis requirements, and echocardiographic parameters related to myocardial injury at discharge: left ventricle end diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF). Operative mortality defined as death within 30 days post-surgery or discharge, was also analyzed.

Statistical analysis

Initially, the trial was designed to be a three-centre study and the sample size was calculated to detect differences of 30% or greater in CK. With an alpha risk of 0.05, a beta risk of 0.2 and accounting for a 10% participant loss, a total of 388 patients were required (194 patients in each group). At the end of 2021, recruitment process was slower than expected due to the very low number of patients operated during the COVID-19 pandemic, and because one of the centres refuse to participate. At the same time, new papers published after the beginning of our study comparing Del Nido with other cardioplegic solutions [5, 6] showed that postoperative biomarker levels were not as high as we expected when we calculated our initial sample size. That is why we recalculate our sample size to detect a 35% or greater difference in postoperative CK levels, with the same alpha and beta risks and the same 10% participant loss. Sample size changed from the initial 388 to 286 patients (143 patients in each group). That sample size change was approved on 2022 by the ethical committee and by the Spanish regulators (see the Supplementary Material for both approval documents).

Numerical variables were described as mean (standard deviation), or median (interquartile range). A Shapiro–Wilk normality test and a Levene's equality of variances test were performed. Univariate analysis was performed with the Student's *t*-test or Mann–Whitney *U*-test (if Shapiro–Wilk test rejected normal distribution or Levene test rejected homoscedasticity). Categorical variables were described as number (percentage). Univariate analysis was performed using chi-squared or Fisher's exact test (if cell frequency ≤ 5).

All data were analyzed using Stata/IC 14.2 for Mac (StataCorp College Station, TX).

RESULTS

Between July 2019 and August 2023, 311 patients were enrolled and randomized to receive either BS (159 patients) or DNS (152 patients) (Fig. 1). Table 1 shows preoperative characteristics. There were no statistically significant differences between groups. The mean age was 72.9 years in the BS group and 73.4 years in the DNS group, and the mean EuroSCORE-II was 1.25 and 1.35, respectively.

Table 2 presents intraoperative data. Total cardioplegia volume was significantly higher in DNS group (374.5 ml vs 1000 ml, $P < 0.001$, BS and DNS groups, respectively). The route of cardioplegia administration differed, with retrograde cardioplegia and direct coronary ostia cannulation more common in the BS group (51.7% vs 0.69% for retrograde, and 49.7% vs 15.3% for direct ostia cannulation). After cross-clamp removal, DNS group had higher rates of spontaneous rhythm (66.7% vs 43.1%, $P < 0.001$),

Table 1: Patients baseline characteristics

	Buckberg (n = 151)	Del Nido (n = 144)	*P* value
Male, n (%)	84 (55.6)	78 (54.1)	0.801
Age (y)	72.9 (66.0-77.8)	73.4 (68.4-77.9)	0.655
BMI	28.9 (26.0-31.9)	28.3 (25.7-31.2)	0.609
BSA (m^2)	1.92 (± 0.24)	1.88 (± 0.19)	0.135
Smoking, n (%)	16 (10.6)	21 (14.6)	0.301
Hypertension, n (%)	115 (77.2)	97 (67.4)	0.073
DM, n (%)	50 (33.1)	40 (27.8)	0.320
Dyslipidaemia, n (%)	103 (68.2)	83 (57.6)	0.060
COPD, n (%)	30 (19.9)	25 (17.4)	0.600
Peripheral vascular disease, n (%)	8 (5.3)	16 (11.1)	0.068
Creatinine (mmol/l)	76 (68-97)	77 (68-93)	0.857
Creatinine clearance (ml/min)			
≥ 90 ml/min, n (%)	46 (30.5)	37 (25.7)	0.632
60-89 ml/min, n (%)	59 (39.1)	67 (46.5)	
30-59 ml/min, n (%)	45 (29.8)	39 (27.1)	
<30 ml/min, n (%)	1 (0.7)	1 (0.7)	
Dialysis, n (%)	3 (1.99)	0	0.248
EUROSCORE II (%)	1.25 (0.85-1.88)	1.35 (0.97-1.89)	0.272
Atrial fibrillation, n (%)	21 (13.9)	19 (13.2)	0.258
NYHA Class, n (%)			
I	6 (4.0)	7 (4.9)	
II	111 (73.5)	89 (61.8)	0.105
III	34 (22.5)	47 (32.6)	
IV	0	1 (0.7)	
Hematocrit (%)	38.81 (± 4.66)	39.67 (± 3.84)	0.088
LVEF (%)	64 (58-68)	65 (58-70)	0.291
> 55, n (%)	130 (86.1)	125 (86.8)	0.388
45-55, n (%)	12 (7.9)	14 (9.7)	
30-45, n (%)	9 (6.0)	4 (2.8)	
< 30, n (%)	0	1 (0.7)	
LVEDD (mm)	48.12 (±7.65)	48.14 (± 7.76)	0.989
Aortic valve disease			0.945
Stenosis, n (%)	52 (34.4)	49 (34.0)	
Regurgitation, n (%)	13 (8.6)	11 (7.6)	
Combined disease, n (%)	86 (57.0)	84 (58.3)	
Predominantly AS, n (%)	79 (91.9)	80 (95.2)	
Predominantly AR, n (%)	5 (5.8)	3 (3.6)	
Both severe AS and AR, n (%)	2 (2.3)	1 (1.2)	

AS: aortic stenosis; AR: aortic regurgitation; BMI: body mass index; BSA: body surface area; COPD: chronical obstructive pulmonary disease; DM: diabetes mellitus; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

and less ventricular fibrillation requiring defibrillation (23.6% vs 49.7%, $P < 0.001$). No differences were observed in LVEF, inotropic use, or mechanical support for CPB weaning. Cell saver and hemofiltration use were similar. Although minimal intraoperative haematocrit was significantly lower in DNS group (27.2 vs 28.8%, $P < 0.005$), end-of-surgery haematocrit and intraoperative packed red blood cell transfusion did not differ. Peak intraoperative glucose levels were significantly lower in DNS group (median of 128 mg/dl vs 198 mg/dl, $P < 0.001$), as was intraoperative insulin administration according to local protocol (18.8% vs 51.0% of patients requiring insulin administration during surgery, $P < 0.001$).

Table 3 summarizes postoperative data. No differences were observed in peak CK and TnT levels (430 vs 414.5 U/l, and 284 vs 258 ng/l, for BS and DNS groups, respectively). Similarly, biomarker levels from postoperative days 1 to 5 showed no differences (Fig. 2). A linear correlation was found between peak CK level and cross-clamp time in both groups, while relation between TnT peak levels and cross-clamp was not linear (Fig. 3). There were no differences in postoperative inotropic or mechanical support, nor in renal function, with no differences in renal failure according to Acute Kidney Injury Network criteria (AKIN) [12] or dialysis requirements. Echocardiography at discharge revealed no differences in LVEF and LVEDD. Postoperative transfusion rates were similar (24.84% vs 21.38% for BS and DNS, respectively), and there were no differences in haematocrit at discharge. No differences were found in operative mortality, ICU, or in-hospital length of stay.

DISCUSSION

Interest in DNS for adult cardiac surgery has increased in recent years. Several retrospective observational studies suggest DNS may offer advantages over traditional blood cardioplegic solutions, and some randomized trials have compared both [5–7, 13]. This trial aimed to prospectively compare DNS with BS in a two-centre randomized study, involving a large population undergoing isolated AVR. Our findings indicate that DNS provides comparable myocardial protection to BS and can be used safely.

Some authors suggest that DNS could improve surgical workflow by shortening CPB and cross-clamp times, due to fewer redosing cardioplegia interruptions [14–16]. A randomized trial by Ucak and Uncu reached the same conclusion [13]. Nonetheless,

Table 2: Intraoperative characteristics

	Buckberg (n = 151)	Del Nido (n = 144)	*P* value
Total cardioplegia dose (ml)	374.5 (314-440)	1000 (1000-1000)	**<0.001**
Total cardioplegia volume including blood content (ml)	1872.5 (1570-2200)	1250 (1250-1250)	
Cardioplegia route administration			**<0.001**
Antegrade, n (%)	141 (93.38)	128 (88.89)	
Retrograde, n (%)	78 (51.66)	1 (0.69)	
Direct ostia cannulation, n (%)	75 (49.67)	22 (15.28)	
CPB time (min)	78 (64-97)	74 (61-92)	0.245
Cross clamp time (min)	58 (45-73)	57.5 (44-69)	0.524
Spontaneous rhythm after cross-clamp remove, n (%)	65 (43.05)	96 (66.67)	**<0.001**
Ventricular fibrillation requiring defibrillation, n (%)	75 (49.67)	34 (23.61)	**<0.001**
Defibrillation attempts (n)	2.34 (±1.85)	2.03 (±1.66)	0.293
Temporary pacemaker, n (%)	24 (15.89)	20 (13.89)	0.629
LVEF			0.790
>55%, n (%)	132 (87.41)	131 (90.97)	
45-55%, n (%)	11 (7.38)	8 (5.56)	
30-45%, n (%)	7 (4.70)	4 (2.78)	
<30%, n (%)	1 (0.67)	1 (0.69)	
Dobutamine at CPB weaning, n (%)	19 (12.58)	14 (9.72)	0.720
Low (<10 µg/kg/min), n (%)	16 (10.60)	12 (8.33)	
Moderate (10-15 µg/kg/min), n (%)	3 (1.99)	2 (1.39)	
High (>15 µg/kg/min), n (%)	0	0	
Norepinephrine at CBP weaning, n (%)	72 (47.68)	71 (49.31)	0.954
Low (<0.03 µg/kg/min), n (%)	60 (39.74)	61 (42.36)	
Moderate (0.03-0.05 µg/kg/min), n (%)	10 (6.62)	9 (6.25)	
High (>0.05 µg/kg/min), n (%)	2 (1.32)	1 (0.69)	
Epinephrine at CBP weaning, n (%)	1 (0.66)	1 (0.69)	0.739
Low (<0.05 µg/kg/min), n (%)	0 (0)	0 (0)	
Moderate (0.05-1µg/kg/min), n (%)	1 (0.66)	0 (0)	
High (>1 µg/kg/min), n (%)	0 (0)	1 (0.69)	
IABP at CPB weaning, n (%)	1 (0.67)	1 (0.69)	0.742
ECMO at CPB weaning, n (%)	2 (1.34)	0 (0)	0.498
Cell saver use, n (%)	144 (96.64)	140 (97.22)	1
Cell saver volume (ml)	322.5 (250-440)	347.5 (250-469)	0.229
Cell saver volume hematocrit (%)	45 (40-50)	45 (42.5-49)	0.259
Ultrafiltration, n (%)	4 (2.68)	11 (7.64)	0.066
Minimal intraoperative hematocrit (%)	28.8 (25.7-32.3)	27.2 (24.95-29.95)	**0.0045**
End of surgery hematocrit (%)	33.3 (30.4-36.6)	34 (31.1-37.6)	0.175
Peak intraoperative lactate level (mmol/l)	1.1 (0.8-1.4)	1.1 (0.9-1.4)	0.537
Peak intraoperative glucose level (mg/dl)	198 (176-228)	128 (111-156)	**<0.001**
Intraoperative insulin needed, n (%)	77 (50.99)	27 (18.75)	**<0.001**
Patients receiving red blood cells transfusion, n (%)	16 (10.6)	17 (11.81)	0.773
Surgical approach			0.611
Sternotomy, n (%)	113 (75.84)	104 (73.24)	
Upper mini-sternotomy, n (%)	36 (24.16)	38 (26.76)	

CPB: cardiopulmonary bypass; ECMO: extracorporeal membrane oxygenation; IABP: intraaortic balloon pump; LVEF: left ventricular ejection fraction.
Bold values in table 2 are values that reach statistical significance (in which *p* value is $p<0.05$).

we did not observe statistically significant differences in CPB and cross-clamp times. The typically short duration of AVR may reduce the need for multiple BS doses, diminishing group differences. However, we found significant differences in cardioplegia administration routes. DNS is generally administered as a single antegrade dose, with direct coronary ostia cannulation reserved for significant aortic regurgitation. In contrast, the BS group had higher rates of retrograde and direct ostia cannulation for cardioplegia administration [11]. This implies that DNS might simplify the surgical procedure, making it particularly appealing for minimally invasive strategies.

The trial by Ad *et al.* reported slightly lower troponin levels in the DNS group, though not statistically significant [5]. They suggested that the DNS group might experience an earlier peak in troponin levels, a finding also noted by García-Suárez *et al.* in their recent trial [7]. While we did not find statistically significant differences in myocardial injury biomarkers, slightly lower levels of both biomarkers were observed in the DNS group. Troponin T peaked on postoperative day 1 in both groups, whereas CK levels peaked later in the DNS group (postoperative day 2) compared to the BS group (postoperative day 1).

Ad *et al.* also found a trend towards reduced inotropic support in the DNS group [5], which could not be confirmed by other randomized trials. In our study, there were no differences in inotropic or mechanical support. The similar biomarker levels and lack of differences in inotropic or mechanical support suggest that DNS offers at least equivalent myocardial protection for patients undergoing AVR.

Spontaneous rhythm and ventricular fibrillation after cross-clamp removal are classically associated with myocardial protection [17]. Consistent with previous studies, we found that more patients in the DNS group returned to spontaneous rhythm, and fewer experienced ventricular fibrillation requiring defibrillation after cross-clamp removal.

Table 3: Postoperative data

	Buckberg (n = 153)	Del Nido (n = 145)	*P* value
CK postoperative peak level (U/l)	430 (280-665)	414.5 (296-667)	0.886
CK day 1 (U/l)	372 (249-550)	347 (241-520)	0.570
CK day 2 (U/l)	329 (234-620)	361.5 (246-520)	0.863
CK day 3 (U/l)	230 (144-482)	238 (149-394.5)	0.977
CK day 4 (U/l)	135 (81-210.5)	125 (82-215)	0.884
CK day 5 (U/l)	72 (49.5-117)	81 (49-133)	0.840
TnT postoperative peak level (ng/l)	284 (197-547)	258 (183-450)	0.255
TnT day 1 (ng/l)	257 (173-443)	237 (169-392)	0.266
TnT day 2 (ng/l)	240 (162.5-405)	202 (149-369)	0.151
TnT day 3 (ng/l)	201.5 (148-310)	176 (130.5-300)	0.081
TnT day 4 (ng/l)	178 (136-273)	165 (118-269)	0.319
TnT day 5 (ng/l)	167 (116-255)	139 (98.5-221.5)	0.085
Postoperative dobutamine needed, n (%)	17 (11.11)	15 (10.34)	0.217
Low (<10 μg/kg/min), n (%)	12 (7.84)	15 (10.34)	
Moderate (10-15μg/kg/min), n (%)	2 (1.31)	0 (0)	
High (>15 μg/kg/min), n (%)	3 (1.96)	0 (0)	
Postoperative norepinephrine needed, n (%)	50 (32.68)	57 (39.31)	.0.71
Low (<0.03 μg/kg/min), n (%)	42 (27.45)	52 (35.86)	
Moderate (0.03-0.05 μg/kg/min), n (%)	3 (1.96)	5 (3.45)	
High (>0.05 μg/kg/min), n (%)	5 (3.27)	0 (0)	
Postoperative epinephrine needed, n (%)	4 (2.61)	0 (0)	0.123
Low (<0.05 μg/kg/min), n (%)	0 (0)	0 (0)	
Moderate (0.05-1μg/kg/min), n (%)	4 (2.61)	0 (0)	
High (>1 μg/kg/min), n (%)	0 (0)	0 (0)	
Postoperative IABP, n (%)	4 (2.61)	0 (0)	0.123
Postoperative ECMO, n (%)	4 (3.27)	0 (0)	0.123
Re-exploration for bleeding, n (%)	5 (3.27)	6 (4.14)	0.767
Creatinine postoperative peak (mmol/l)	89.64 (74-134)	94 (73-125)	0.954
AKIN stage 1, n (%)	17 (11.11)	15 (10.34)	0.753
AKIN stage 2, n (%)	7 (4.56)	10 (6.90)	
AKIN stage 3, n (%)	11 (7.19)	5 (3.45)	
Renal replacement therapy, n (%)	5 (3.27)	0 (0)	.0.61
Patients receiving red blood cells transfusion, n (%)	38 (24.84)	31 (21.38)	0.343
Hematocrit at discharge (%)	29 (27-32)	29.85 (27-32)	0.494
LVEF (%)	59.5 (56-64)	60 (55-67)	0.333
> 55, n (%)	124 (82.12)	119 (83.22)	0.259
45-55, n (%)	22 (14.57)	14 (9.79)	
30-45, n (%)	7 (4.58)	12 (8.28)	
< 30, n (%)	0 (0)	0 (0)	
LVEDD (mm)	47.35 (±8.62)	46.86 (±7.78)	0.633
ICU length of stay (d)	3 (2-4)	2 (2-4)	0.075
In-hospital stay (d)	7 (6-9)	7 (6-9)	0.371
Operative mortality, n (%)	4 (2.65)	1 (0.69)	0.123

AKIN: Acute Kidney Injury Network; CK: creatine kinase; ECMO: extracorporeal membrane oxygenation; IABP: intraaortic balloon pump; ICU: intensive care unit; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; TnT: ultrasensitive Troponin T.

Glucose control is a frequently noted advantage of using DNS. As observed in other studies [7, 13], we found lower peak intraoperative glucose levels and reduced insulin administration rates in the DNS group. Intraoperative glycaemic control is not a minor issue, as it is linked to surgical site infection. 2017 Centers for Disease Control and Prevention guideline for prevention of surgical site infection recommended blood glucose target levels below 200 mg/dl in patients with or without diabetes (class IA recommendation) [18]. In our study, the median peak intraoperative glucose level was 128 mg/dl in the DNS group vs 198 mg/dl in the BS group. Only 18.8% of patients in DNS group required insulin to maintain target glucose levels, vs 51% in BS group. The improved glycaemic control with DNS is a benefit supported by various authors [3, 4, 7, 13, 19] though the correlation with reduced surgical site infection rates requires further investigation.

Haemodilution, resulting from the higher cardioplegia volume used with DNS, is a concern, particularly in shorter surgical procedures where fewer blood cardioplegic doses are needed, leading to a lower overall cardioplegia volume. Although we found a statistically significant difference in cardioplegia volume, we only observed a statistically significant difference in the minimum intraoperative haematocrit which favours the BS group (28.8% vs 27.2%). However, no differences were noted in end-of-surgery or discharge haematocrit levels, nor in intra- or postoperative red blood cell transfusion needs. Cell saver was widespread in both groups, and while there was slightly higher, but not statistically significant, use of ultrafiltration in the DNS group, this may account for the observed difference in intraoperative haematocrit recovery.

The impact of cardioplegia on renal function remains controversial. The trial conducted by Sanetra *et al.* in patients undergoing AVR [6] suggest a trend favouring DNS in postoperative creatinine levels, potentially due to the protective effects of lidocaine used in DNS [20, 21]. Contrarily, other clinical trials have not supported these findings. In our study, no significant differences were observed in peak postoperative creatinine levels.

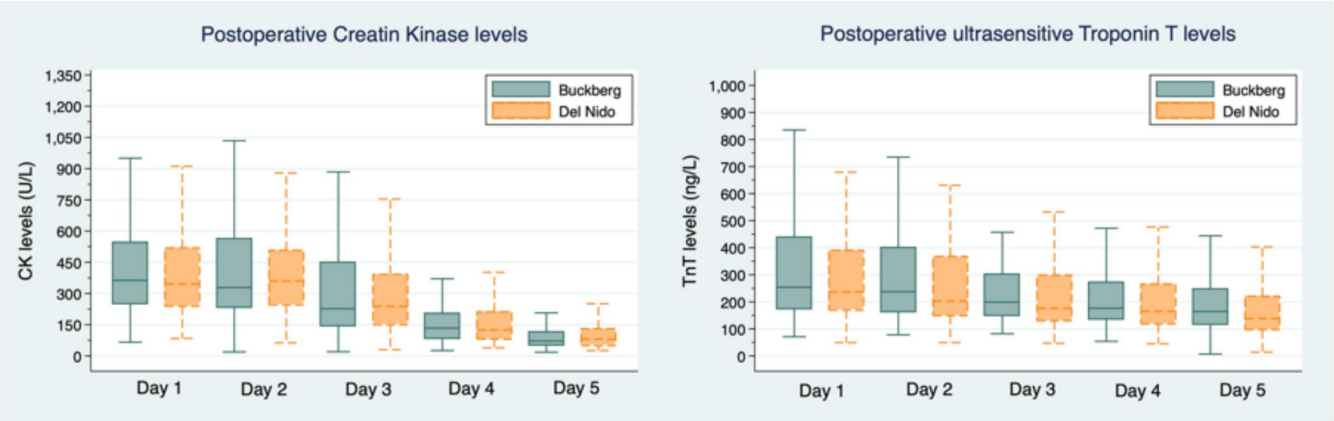


Figure 2: CK and TnT postoperative levels

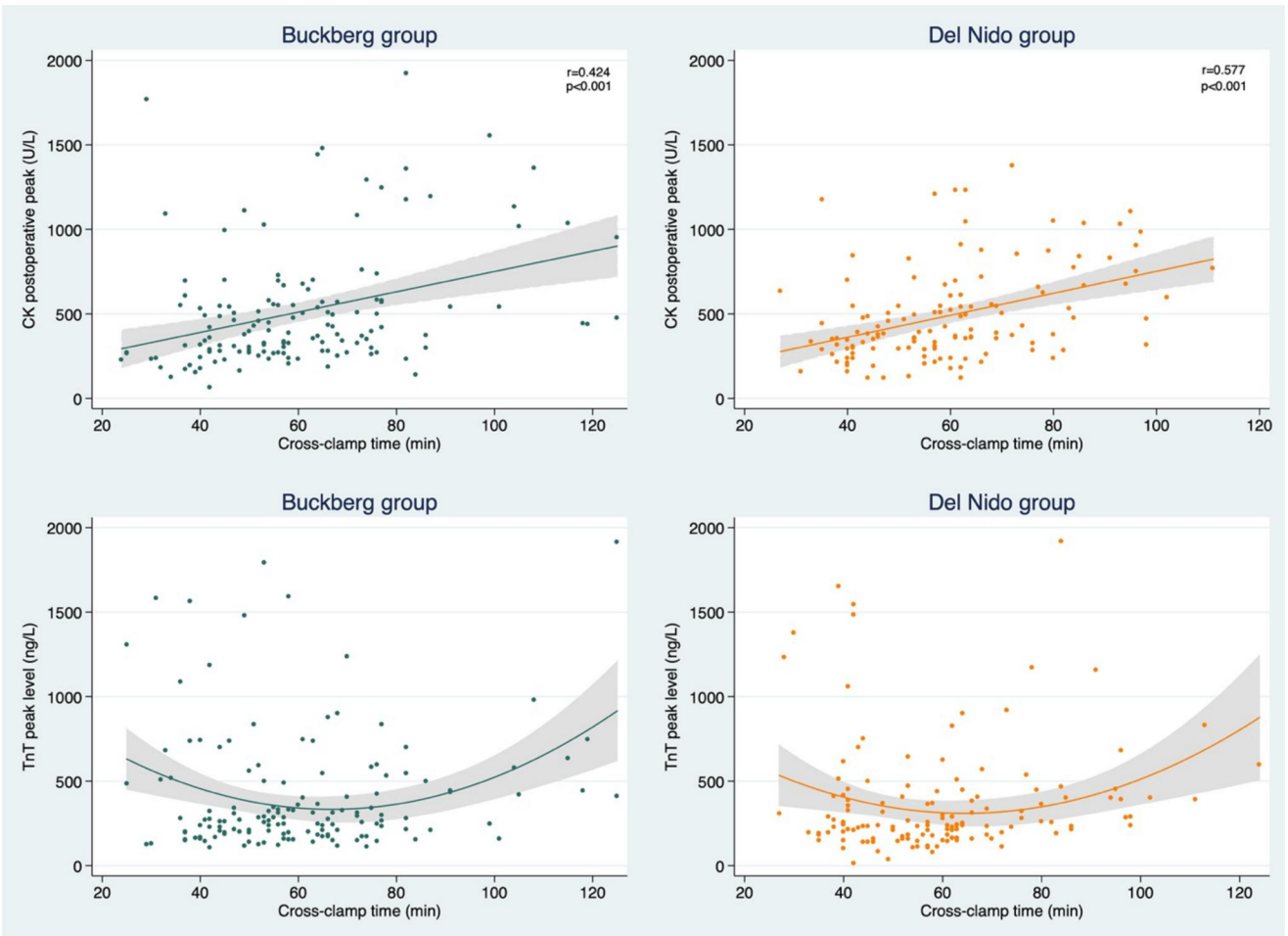


Figure 3: CK-TnT peak levels and cross-clamp time

Using AKIN criteria to classify postoperative renal injury, the DNS group showed lower rates of postoperative dialysis or AKIN 3 injury; nonetheless, that trend did not reach statistical significance. Recent trials involving DNS focus on myocardial protection parameters as the primary end-point. As suggested by Sanetra *et al.*, further research with renal function parameters as the primary end-point is needed to confirm or refute any potential protective effects of DNS against postoperative renal injury.

Study limitations

This study has several limitations. First, intraoperative personnel could not be blinded due to different cardioplegia administration protocols. Second, the analysis of multiple secondary outcomes increases the risk of type I errors, and therefore, conclusions regarding secondary end-points should be interpreted with caution. Third, the study lacked a unified treatment

protocol across the two participating centres with each following its usual clinical practice, potentially leading to variations in intraoperative and postoperative treatments.

CONCLUSION

No differences were detected when comparing DNS to BS in elective, isolated AVR. DNS may offer additional benefits, including better intraoperative glycaemic control, higher rates of spontaneous rhythm, reduced ventricular fibrillation requiring defibrillation after cross-clamp removal, and a more efficient surgical workflow with fewer interruptions for re-dosing. Although the total cardioplegia volume was higher with DNS, this did not correlate with an increased need for red blood cell transfusions or lower end-of-surgery or discharge haematocrit levels.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

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DATA AVAILABILITY

Data underlying this article will be shared upon request to the corresponding author.

Author contributions

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