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Assessment of Cardiorespiratory Fitness in Children who have Undergone Primary Arterial Switch Operation, in Long Term"- a Pilot Study

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Abstract

Background: *It is now known from a previous midterm study that, Primary ASO can be safely performed in children with regressed ventricle, irrespective of age with encouraging results1. Here we are reporting the long term cardiopulmonary fitness in children who have undergone primary ASO, for d-TGA with regressed ventricle and d-TGA with preserved ventricle between the year 2006-2014 and its comparison with that of an age matched control group.*

Materials and Methods: *Data of Children who underwent ASO between the year 2006-2014 by Dr. A.K Bisoi were collected and divided in to 2 groups of those who had regressed LV at the time of surgery and those who had preserved LV. Total 18 children were called for CPET and the results compared with that of 20 age matched control group children.*

Results: *In the present study no difference was found in rate of oxygen consumption (VO2 max) of post ASO children {group A + group B :34.23ml/kg/min} and control group children{group C:36.84ml/kg/min}.*

Conclusion: *Cardiopulmonary performance over long term after an ASO, irrespective of preserved or regressed LV at the time of ASO, is at par with normal children; rather it improves with age related catch up growth post operatively.*

Keywords: *(ASO-Arterial Switch operation, BMI-body mass index, CPET-cardiopulmonary exercise resting d-TGA- dextroposed Transposition of Great arteries, LV-left Ventricle.)*

Introduction

Primary arterial switch operation (ASO) in children older than 6 weeks with regressed ventricle has shown a good midterm result. It is now known from a previous midterm study that, primary ASO can be safely performed in children with regressed ventricle, irrespective of age with encouraging results[1]. Earlier, children of d-TGA with IVS more than 6 months of age, the concern that regression of LV myocardial mass renders the LV incapable of coping with the acutely increased work of systemic perfusion after an ASO, prevented surgeons to attempt ASO in older children [2].

Here we are reporting the long term cardiopulmonary fitness in children who have undergone primary ASO, for d-TGA with regressed ventricle and d-TGA with preserved ventricle between the year 2006-2014 and its comparison with that of the age, weight and BMI matched control group .

Methodology

In this comparative cross sectional study, the data of children from, "All India Institute of Medical Sciences" who underwent ASO by a single surgeon and received similar anaesthetic and post operative care between the year 2006-2014 were obtained from the operating theatre register and files which were retrieved from the hospital medical records section. Preoperative, Operative and Postoperative data were collected from the discharge summaries and they were called for cardiopulmonary exercise testing along with their routine follow up visit. After obtaining parental consent their height, weight, BMI (as per WHO reference charts and Z scores) were measured and calculated and echocardiography, Chest X-Ray, ECG and Cardiopulmonary exercise capacity testing (CPET)were done for them. Age, height, weight and BMI (as per WHO reference charts and Z scores) matched children with no history of any surgery or illness were called from local schools and trusts and after obtaining parental consents CPET was done. In CPET, peak oxygen consumption (VO_2 max.) and chronotropic index were assessed.

Three groups were formed-

Group A: children who underwent ASO with regressed ventricle i.e., d-TGA with IVS at the age of ≥ 2 months

Group B- children who underwent ASO with preserved ventricle

i.e., children who underwent ASO for:

B(i)-d-TGA with VSD at the age of ≤ 2 months.

B(ii)-d- TGA with IVS at the age of ≤ 3 weeks

Group C-The control group, children matched for age, gender, height, weight and BMI(kg/m^2) (as per WHO reference charts)with group A and B. Children were classified in the control group only after a complete normal check-up, including physical examination, chest X-Ray, electrocardiogram (ECG) and 2D-echocardiography (2D-ECHO).

Conduct of CPET:

Incremental exercise test performed on a treadmill (Cosmed®) adhering to a standardized modified Bruce protocol in a lab facility. Under the supervision of a certified trainer , trained in CPET, in a designated CPET lab. A 12-lead electrocardiogram was obtained during each minute of exercise and recovery. The heart rate and rhythm were monitored continuously, and blood pressure was measured manually at 2-minute interval. Gas exchange parameters were obtained throughout the exercise and during the first 2 minutes of recovery , on a breath-by-breath basis. The oxygen consumption and respiratory quotient were measured every 20 seconds. Serious cardiac arrythmias, fall in systolic blood pressure or progressive fall in oxygen saturation to ≤ 90% or termination request by the subject were kept as termination criteria.

Figure 1: One of the children who was involved in the study while doing the treadmill walk in CPET lab.

Exclusion criteria

(i) Children with any associated heart defects at present.

(ii) Children with absolute contraindications for CPET (fever, uncontrolled asthma, respiratory failure, acute myocarditis or pericarditis, uncontrolled arrhythmias causing symptoms or haemodynamic compromise, uncontrolled heart failure, acute pulmonary embolus or pulmonary infarction, and children with mental impairment leading to inability to cooperate.)

For control group:

Children with any chronic disease, medical condition (cardiac, neurological, respiratory, muscular or renal), or medical treatment and those requiring any further specialised medical consultation were not eligible.

Statistical analysis

Using statistical software DATAtab, the data were analysed.

(DATAtab Team (2023). DATAtab: Online Statistics Calculator. DATAtab e.U. Graz, Austria. URL https://datatab.net). Mean (Standard deviation)/ median (interquartile range) were used to describe the quantitative measurements. ANOVA (analysis of variance) is used to analyse the variants as and when applicable. Statistical significance was considered at $p<0.05$. Chi square test of significance was used to investigate association between Qualitative variables.

Results

Table (i)- Demographic details of the participants of the study.

Data with contact details retrieved		89	
could be contacted telephonically		38	
Turned to OPD and given consent for CPET		18	
Group	boys	girls	total
A	10	1	11
B	6	1	7
B(i)	2	1	3
B(ii)	4	0	4
C	14	6	20

For the sake of comparison of height, weight, BMI and parameters like VO_2 max participants were divided in to age groups of 7-8,9-10 and 11-13 years in each group.

Mean heart rate at rest for group C is 83 bpm while for group A,B(i) and B(ii)-it is 78,69 and 70 bpm respectively.

Mean SpO_2 at rest for every group was 98 % and at the peak of exercise it was 97% ,97%,98% and 98% for group C, A,B(i) and B (ii) respectively.

Mean waist/hip ratio for
group A-boys - 0.87±0.05 girls - 0.92
group B -boys 0.86 ± 0.05 girls - 0.86
group C- boys 0.83± 0.04 girls - 0.86 ± 0.08.

Chest X-Ray-was normal in all children.

Cardiac Findings

Screening of children with routine ECG and 2D-ECHO revealed
Moderate AR in 2 children [1 from Group A and 1 from Group B(i)]
RVOTO with mild gradients of 30 and 18 were found in 2 children [1 from group A and 1 from group B(ii)]
RBBB was found in two children of Group B(i), and one child of Group A.Type 1 block was found in one child of group B(ii) (same child having mild RV dysfunction) and left anterior hemiblock was found in one child of Group B(i).

Anthropometric Findings

Mean height of group C was 141.12 cm and Group A and B (i) and B (ii) were
136.58 cm ,134.83 cm and 140.20 cm respectively.

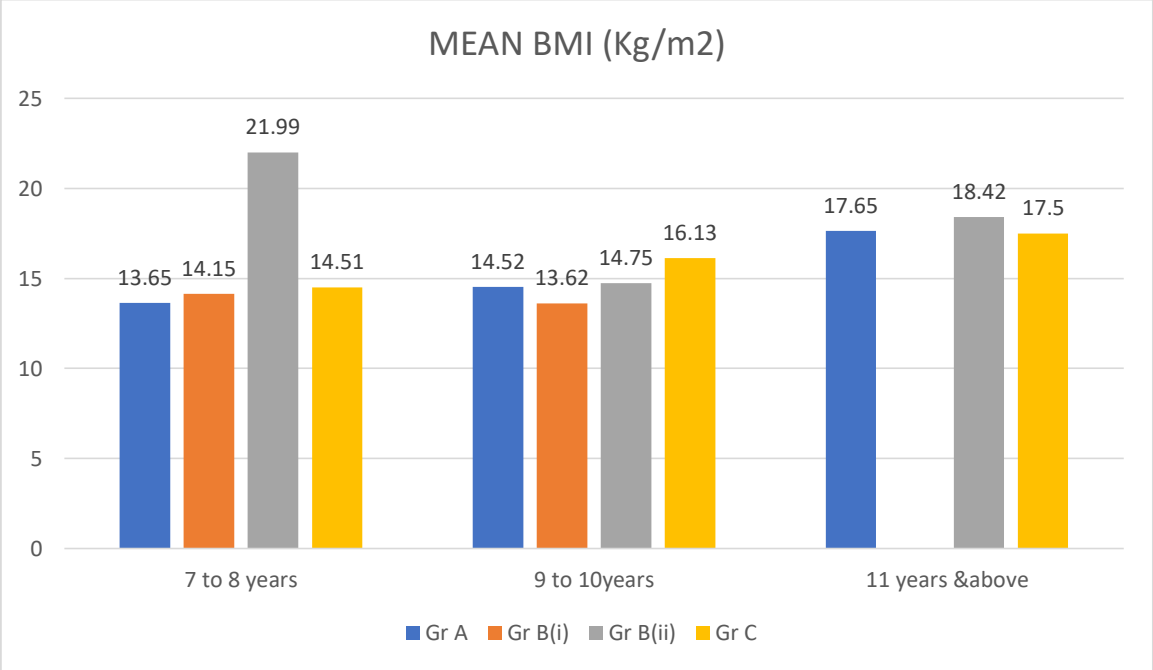

Figure 2-BMI group and age wise comparisons.

Mean BMI (kg/m2) for group C was 16.54, and for group A and B(i) and B (ii) were 15.42 , 13.79 and 17.48 respectively. The BMI of boys in the age group of 7-8 years who underwent ASO for D-TGA with regressed ventricle is less than the WHO reference range but is almost equal to group C, whereas for the children who underwent ASO for D-TGA with preserved ventricle is above the WHO reference range.

BMI of boys in the age group of 9-10 years in children who underwent ASO for d-TGA with regressed ventricle is lesser than the WHO reference range and is also lesser than group C. For the same age group boys and girls who underwent ASO for d-TGA with preserved ventricle the BMI is well within the reference range.

Whereas for the age group of 11-13 years (both boys and girls) BMI is well within the WHO reference range for both, the children who underwent ASO for d-TGA with regressed ventricle and for d-TGA with preserved ventricles.

It can be inferred that by the age of 11 years most of the post ASO children of both regressed and preserved ventricle groups are matching the normal control group children in terms of BMI.

CPET and observations:

Mean VO_2 max.(ml/kg/min)

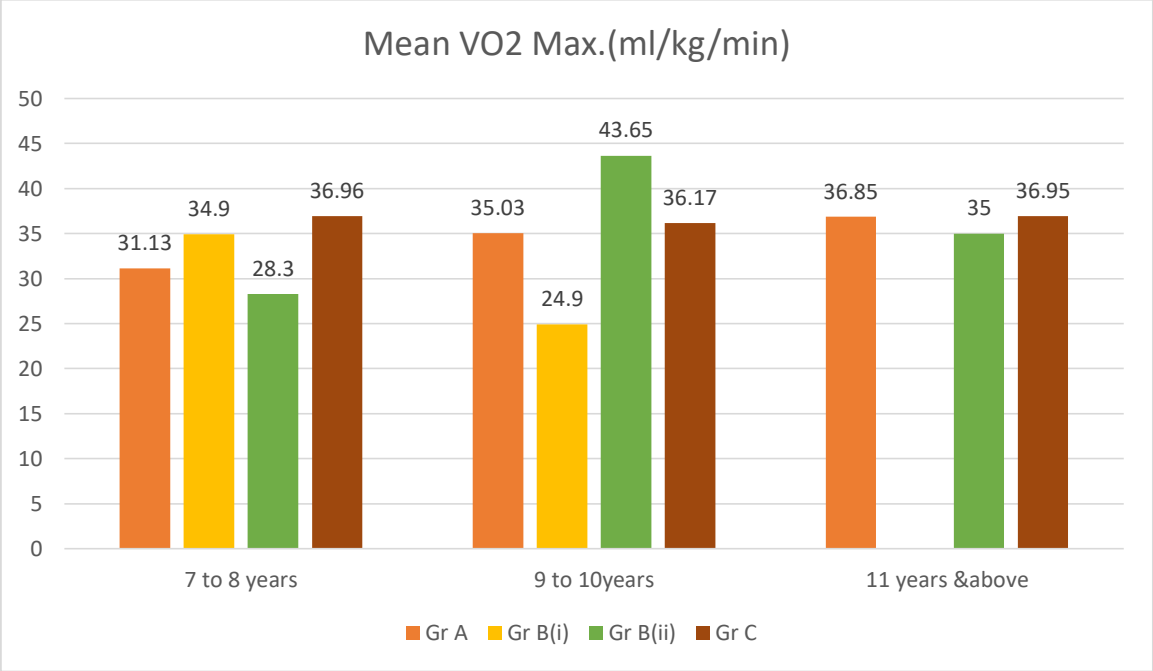

Figure 3- VO_2 max. Group and age wise comparisons

Table (ii)- $VO_{2\ max}$ mean and standard deviation

$VO_{2\ max}$(ml/kg/min)	**Group A**	**Group B**	**Group C**
Mean ± Std.	34.63 ± 4.44	33.61 ± 8.63	36.84 ± 8.5
95% Confidence interval of Mean	32.01; 37.25	27.22; 40.01	33.11; 40.56

For comparing group A,B{B(i)and B(ii)} and group C for $VO_{2\ max}$.(ml/kg/min) ANOVA (analysis of variance) was used .p value is 0.55.

$VO_{2\ Max}$.(ml/kg/min) statistical Analysis of Group (A+B)

Table (iii)- $VO_{2\ Max}$.-mean for children who underwent ASO vs.control group.

$VO_{2\ Max}$.(ml/kg/min)	A+B	C
Mean ± Std.	34.23 ± 6.17	36.84 ± 8.5
95% Confidence interval of Mean	31.38; 37.09	33.11; 40.56

The A+B group had lower values (M = 34.23, SD = 6.17) than the C group (M = 37.19, SD = 8.78).

A t-test showed that this difference was not statistically significant, with a p-value of 0.223 , which is above the specified significance level of 0.05.

There is no significant difference in maximum oxygen consumption ($VO_{2\ max}$, in ml/kg/min) in children who had undergone ASO with those of the control group and also the VO_{2max} for d-TGA with regressed ventricle and preserved ventricle is at par with the control group.

Mean Duration of exercise (min)

Table (iv)-group wise comparison of duration of exercise

Duration of exercise in minutes	Group A	Group B	Group C
Mean ± Std.	14.13 ± 1.98	12.96 ± 2.19	13.77 ± 1.8
95% Confidence interval of Mean	12.97; 15.3	11.34; 14.58	12.98; 14.56

For comparing group A,B{B(i) and B(ii)} and group C for exercise duration in minutes ANOVA (analysis of variance) was used, p value is 0.45.

There is no significant difference in the duration of exercise in minutes in children who had undergone ASO for d-TGA with regressed ventricle and ASO for the d-TGA with preserved ventricle and this is at par with group C.

Mean peak heart rate (bpm)

Mean peak heart rate for control group was 165 bpm and for group A,B(i) and B (ii) it was 160,140 and 181 respectively.

Mean peak heart rate % predicted:

mean peak HR % predicted for Group A was 78.64 ± 9.14,for group B was 77.43 ± 15.35 and for group C was 81.15 ± 9.78 with 95% Confidence interval of Mean 73.24; 84.04 , 66.06; 88.8 and 76.86; 85.44 respectively.

For comparing group A,B{B(i)and B(ii)} and group C for mean peak HR % predicted ANOVA (analysis of variance) was used. p value is 0.68.

There is no significant difference in the mean peak heart rate percentage predicted in children who had undergone ASO for d-TGA with regressed ventricle and ASO for the d-TGA with preserved ventricle and this is at par with group C.

Chronotropic index

It is given by formula

((max. heart rate-resting heart rate)/ [{220-age}-resting heart rate]) x 100

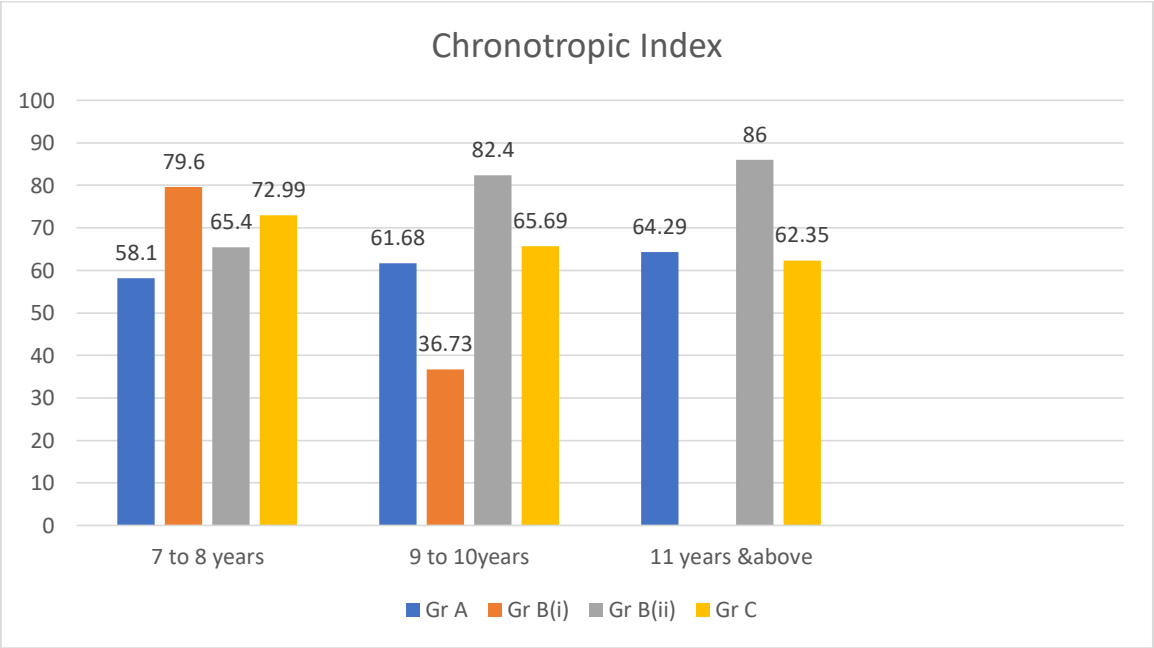

Figure 4- age wise and group wise comparison of chronotropic index.

Table (v)-group wise comparison of chronotropic index

Chronotropic index	Group A	Group B	Group C
Mean ± Std.	61.65 ± 18.54	67.04 ± 22.41	62.08 ± 21.98
95% Confidence interval of Mean	50.69; 72.61	50.43; 83.64	52.44; 71.71

Chronotropic index which is the standardized measure of heart rate increment during exercise that reflects the combined effects of age, resting HR and physical fitness. There is no significant difference in the chronotropic index of children who had undergone ASO for d-TGA with regressed ventricle and ASO for the d-TGA with the preserved ventricle and this is at par with the matched control group children.

For comparing group A,B{B(i)and B(ii)} and group C for chronotropic index,ANOVA (analysis of variance) was used . p value is 0.84.

Termination of exercise

Reason for termination of exercise for 28 children was fatigue, for 7 children it was leg cramp and for 2 it was breathlessness,1 child had asked to stop the treadmill voluntarily although he was not fatigued.

Discussion

A study was conducted by Amedro et al in the year 2018, to compare the cardiopulmonary fitness of children with congenital heart diseases (CHD) with that of age-adjusted and gender-adjusted controls and also intended to identify clinical characteristics associated with maximum oxygen uptake (VO_{2max}) in this population. It was a cross sectional multicentre study in which total of 798 children (496 CHD and 302 controls) underwent CPET. It was observed that VO_{2max} in children with CHD was weakly altered when expressed as a percentage of predicted values. However, VO_{2max} in this paediatric CHD cohort was significantly lower than in age-adjusted and gender-adjusted control children, and it was observed that a mean overall VO_{2max} decline of 0.84 mL/kg/min per year, more pronounced in the most complex types of CHD. This study suggested performing CPET in routine follow-up of children with CHD. This study also concluded that a study should be done to determine whether VO_{2max} change with age should be a main parameter to identify children with CHD eligible for cardiac rehabilitation[5].

In a study by Giardini et al published in 2009, 60 patients (44 males, age 13.3 ± 3.4 years) who had undergone a neonatal arterial switch operation were studied using the cardiopulmonary exercise test and transthoracic Echocardiography. The peak exercise oxygen uptake (VO_2), and heart rate were recorded and are expressed as the percentage of predicted values. The greatest velocity detected by echocardiography across the pulmonary valve, pulmonary trunk, or pulmonary branches was used in the analysis as an index of RVOT obstruction. The peak VO_2% was 84 ± 15%, and the peak heart rate percentage was 97 ± 8%. Of the 60 patients, 29 had an abnormal peak VO_2% (≤84%) and 3 (5%) had an abnormal peak heart rate percentage (≤85%). The maximal RVOT velocity was 2.3 ± 0.6 m/s, and it correlated with the peak VO_2% ($r = -0.392$, $p = 0.004$). On multivariate analysis, the presence of residual RVOT obstruction ($p = 0.0007$) was the only variable associated with a reduced peak VO_2%. Patients with a RVOT maximal velocity ≥2.5 m/s had a lower peak VO_2% than those with lower velocities ($p < 0.0001$). No relation was found between age at testing and the peak VO_2%. It was concluded that a reduced exercise capacity is relatively common in children and young adults who have undergone an arterial switch operation, but it does not decrease with age. The presence of residual RVOT obstruction seems to have an effect on exercise capacity[4].

In the present study PS was found in 3 children (1 in regressed ventricle group other 2 in preserved

ventricle group) but the PS in all these cases were trivial to mild, all the 3 children have ECG abnormalities in terms of RBBB, Type 1 block and left anterior hemiblock. The

$VO_{2\ max}$ was 32.8 ml/kg/min for the child with PS in group A , mean $VO_{2\ max}$(ml/kg/min)for the whole group was 34.63 ± 4.44, children in group B with PS had the $VO_{2\ max}$ of 35 ml/kg/min and 27.6 ml/kg/min respectively , mean of the whole group B was 33.61 ± 8.63, control group mean $VO_{2\ max}$(ml/kg/min) 36.84 ± 8.5.

Van Beek et al studied a total of 17 children with TGA (12 male and 5 female children; age 12.1 ± 2.0 years) treated with the arterial switch operation and compared them with 20 age-matched controls (13 male and 7 female children; age 12.8 ± 2.4 years) regarding their peak exercise capacity, peak workload, and peak heart rate, as assessed by cycle ergometry. The children's physical activity level was monitored for a 7-day period using a pedometer (a device that counts each step a person takes by detecting the motion of the person's hands or hips) and diary, and a questionnaire was used to assess physical activity participation and overprotection. The results demonstrated that TGA children showed a significantly reduced peak exercise capacity (47.4 ± 6.4 vs 41.1 ± 6.6 ml/kg/min; $p < 0.05$), maximal workload (3.7 ± 0.5 vs 3.1 ± 0.6 W/kg; $p < 0.01$), and maximal heart rate (189 ± 9 vs 180 ± 14 beats/min; $p < 0.05$) compared to the controls. No significant differences were found in the physical activity pattern or overprotection. It was concluded that, given the comparable physical activity level, but reduced exercise capacity in the TGA children, these children most likely fall short in their exercise performance because of restrictive hemodynamics rather than deconditioning from reduced daily life activity[5] .

In the present study , children who were physically active, were involved in sports activity have performed well in the cardiopulmonary exercise capacity assessment irrespective of their P-ASO status and regressed or preserved ventricle group, whereas control group children who were living a sedentary lifestyle had an average performance in this assessment. Current guidelines don't exclude any form of physical activity for ASO patients with no systolic dysfunction, normal pulmonary artery pressure, no aortic dilatation, no arrhythmias and no central cyanosis [6].

This underlines the importance of educating children with congenital or acquired heart disease and their families about a more active lifestyle

Study Limitations

Limitations of the study include that it is a nonrandomized, single-center comparative cross sectional study. The number of cases were limited.

Conclusions

In this study it has been observed that the cardiopulmonary performance during exercise in long term after an Arterial Switch operation is at par with the normal children who have no co-morbidities and the clinical status of regressed or preserved ventricle during surgery had no effect on the long term exercise capacity of the child rather it was seen improving with increasing age. In the children on follow-up after the ASO, it was seen to be improving with age and body habitus.

Declaration of Conflicting Interests

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