Reference values and the Z-score values of tricuspid annular plane systolic excursion in Chinese children

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Abstract
To establish age-specific and body surface area (BSA)-specific reference values of Tricuspid Annular Plane Systolic Excursion (TAPSE) for children under 15 years old in China. A retrospective study was conducted in Children’s Hospital Attached to the Capital Institute of Pediatrics. A total of 702 cases were included in this research to establish reference values of TAPSE in Chinese children. SPSS 25.0 (IBM) was used for data analysis. Lambda-mu-sigma method was used to calculate and construct the age-specific and BSA-specific percentiles and Z-score curves of TAPSE. The mean value of TAPSE increased with age and BSA from 0 to 15 years in a nonlinear way and reached the adult threshold (17 mm) until 1 year old. There was no difference between genders. TAPSE values increased with age and BSA in Chinese children aged between 0 and 15 years and there was no difference between boys and girls. A prospective, multicenter cohort study from different parts of China is supposed to be conducted in the future to reflect the whole spectrum of TAPSE in Chinese children.

Keywords TAPSE · Reference values · Right ventricular systolic function · Children

Introduction
The assessment of right ventricle (RV) systolic function is important in patients with congenital heart disease, especially during the perioperative period. However, in comparison to left ventricle, the structure of RV is more complex [1], which hampering the development of non-invasive techniques evaluating RV function. More recently, researches on RV have been significantly improved both in quantity and quality with new techniques approach [2–4]. Cardiac magnetic resonance (CMR) is known to be a gold standard for measurement of the ejection fraction (EF) as well as volume and the cardiac mass, especially for RV. Whereas, CMR is inferior to echocardiography no matter in facility, portability, costs or time consumption [5, 6]. Among different parameters evaluating RV systolic function, TAPSE, which mainly represents the longitudinal RV contraction has been recommended for routinely clinical use in adults by the American Society of Echocardiography (ASE) since 2010 [7]. The guideline pointed out that TAPSE less than 16 mm indicates decreased RV function. However, for children, it is improper to use one single cutoff value to evaluate RV function for children at different ages because of their developmental characteristics. Therefore, growth-related reference values of TAPSE are required for clinical use in children.

Over the past 10 years, several centers from different countries have reported their reference values of TAPSE in children [8–13]. To date, there are still no available reference values of TAPSE for Chinese children, so we conducted this study to determinate reference values of TAPSE in Chinese children aged 0–15 years.
Methods

Population

Of 877 medical records we screened, a total of 702 children were finally selected for this study, including 393 males (56.0%) and 309 females (44.0%) respectively. We included children aged 0–15 years old because of the scarcity of 16–18 years old adolescent in children’s hospital. All subjects were selected from those who had accepted echocardiography examinations in outpatient department from September 2020 to July 2021. Subjects were included if they were aged between 0 and 15 years and their echocardiography index except for TAPSE were normal. Premature and low birth weight infants and patients who had hypertension, pulmonary hypertension, arrhythmia, Kawasaki disease as well as those who were diagnosed with growth retardation, chromosomal disease or receiving cardiac medication were excluded.

Echocardiographic techniques

Patients were examined in a resting state with Philips IE 33 Doppler ultrasonocardiograph with a transducer of S5-1 and frequency of 1–5 MHz. Uncooperative subjects aged between 3 months and 3 years old were allowed to use Chlорal hydrate under the consent of the guardian. TAPSE was measured according to the 2010 ASE Guideline: placing sampling point at the junction of the anterior tricuspid annulus and the RV free wall in the standard apical four-chamber view, the amount of longitudinal motion of the annulus at peak systole is the value of TAPSE [7] (Fig. 1).

Statistical analysis

SPSS 25.0 (IBM) was used for statistical analysis. Quantitative data were shown as median and IQR (25th and 75th percentile) or mean ± SD (Standard Deviation) as appropriate, categorical data were shown as counts and

Fig. 1 Measurement of TAPSE in M-mode echocardiography. a TAPSE in apical four-chamber view, the M-mode sampling line was placed at the junction of anterior tricuspid annulus and RV free wall at the end of RV diastole. b M-mode tracing curve, the white arrow represents the upper and lower measure points. TAPSE, tricuspid annular plane systolic excursion; RV right ventricle; LV left ventricle; RA right atrium; LA left atrium
percentages. BSA was calculated using the Stevenson formula \([\text{BSA} \, \text{m}^2] = 0.0128 \times \text{weight[kg]} + 0.0016 \times \text{height[cm]} - 0.1529\). For continuous variables, the Unpaired t-test or Wilcoxon rank-sum test was used to test significance of differences. \(P < 0.05\) was considered to be significant. Lambda-mu-sigma (LMS) method (LMS Chart Maker Pro Version 2.3, Medical Research Council, London, UK) was used to establish growth-related curves of TAPSE, mainly by converting the skewed distribution to normal using the maximum penalized likelihood method and smoothing the growth curves of TAPSE through cubic natural smoothing spline functions. We optimized the curves of median (M), coefficient of variation (S) and Box-Cox transformation power (L) \([15]\) orderly by increasing and/or decreasing the equivalent degrees of freedom (edf) by 1 unit until the change in deviance is modest. Once a growth-related model has been fitted, the original data were presented as numerous spots in a Z Scores Graph, which could be used for excluding outliers. TAPSE that greater than +3SD or less than −3SD will be eliminated and rest of the data were used to conduct a new fitted model. Z values of TAPSE \((y)\) were calculated from the L, M and S curves, using values appropriate for age or BSA, as the following two formulae layout.

\[
Z = \frac{(y/M)^L - 1}{L \times S}, \text{ if } L \neq 0
\]

\[
Z = \log \left(\frac{y/M}{S}\right), \text{ if } L = 0
\]

Origin Pro 2019b was used to plot reference values curves of TAPSE across the age and BSA ranges.

### Results

Subjects were separated into sixteen groups according to BSA and nineteen groups according to age. The age of the children was 62(23,96) months, with average height of 112(86,133) cm, weight of 19(12,30) kg, TAPSE of 19.3 ± 3.9 mm, LVEDD of 33.6 ± 7.2 mm, LVESD of 20.5 ± 4.4 mm, LVEF of 69.4% ± 4.4%, LVFS of 38.1% ± 3.7%. There were no statistically significant differences between genders in these characteristics \((P > 0.05)\), seen in Table 1. We also found no significant differences on TAPSE values between boys and girls in different subgroups, seen in Table 2.

Data from 702 children were analyzed to draw age-related reference percentile as well as Z-score values and BSA-related reference percentile as well as Z-score values. Through four rounds of screening and LMS model fitting, we finally chose 0, 4, 4 and 1, 4, 4 as the best set of the edf of L, M and S for BSA and age in model fitting. The deviance in BSA was smaller than that in age (3282.8 vs. 3305.6), which means the fit goodness in BSA is better than that in age. Tables 3 and 4 respectively presented the Z-score and percentile reference values of TAPSE according to age and BSA. Overall, the mean value of TAPSE showed an increasing trend with both age and BSA. As was shown in Table 3, TAPSE increased from a mean value of 10.1 mm in neonates to 22.7 mm in 15 years old children. Similarly, the mean value of TAPSE increased from 9.1 mm (BSA ≤ 0.2 m²) to 23.3 mm (BSA > 1.6 m²), as was shown in Table 4. Figure 2 respectively presents the smoothed LMS curves for mean, mean ± 1SD, mean ± 2SD, mean ± 3SD and the 3th percentile, 10th percentile, 25th percentile, 50th percentile, 75th percentile, 90th percentile, 97th percentile for TAPSE in different age and BSA groups. As was shown in Fig. 2, TAPSE increased rapidly with age in a nonlinear way and reached the adult level (17 mm) until 1 year old, then

### Table 1 Anthropometric Characteristics of Population

|                  | Total | Male         | Female        | \(P\)  |
|------------------|-------|--------------|---------------|--------|
| Age, month, median (IQR) | 62(23,96) | 58(21.96) | 67(31.97) | 0.263  |
| Height, cm, median (IQR) | 112(86,133) | 110(86,134) | 113 (85,133) | 0.799  |
| Weight, kg, median (IQR) | 19(12,30) | 19(12,31) | 19(12,29) | 0.612  |
| BSA, m², median (IQR) | 0.77(0.54,1.04) | 0.76(0.52,1.06) | 0.80(0.60,1.02) | 0.719  |
| TAPSE, mm, mean ± SD | 19.3 ± 3.9 | 19.4 ± 4.0 | 19.2 ± 3.9 | 0.478  |
| LVEDD, mm, mean ± SD | 33.6 ± 7.2 | 33.8 ± 7.6 | 33.2 ± 6.8 | 0.271  |
| LVESD, mm, mean ± SD | 20.5 ± 4.4 | 20.7 ± 4.6 | 20.3 ± 4.1 | 0.224  |
| LVEF, %, mean ± SD | 69.4 ± 4.4 | 69.3 ± 4.2 | 69.4 ± 4.5 | 0.750  |
| LVFS, %, mean ± SD | 38.1 ± 3.7 | 38.0 ± 3.5 | 38.1 ± 3.9 | 0.727  |

BSA body surface area; TAPSE tricuspid annular plane systolic excursion; LVEDD left ventricular end-diastolic dimension; LVESD left ventricular end-systolic dimension; LVEF left ventricular ejection fraction; LVFS left ventricular fractional shortening
increased slightly until 15 years old, both in Z-score curves as well as percentile curves. BSA-based growth curves of TAPSE showed similar trend both in Z-score curves and percentile curves. Figure 3 shows the comparison of the 50th percentile curves of TAPSE among different studies [8, 11–13], as was shown in Fig. 3, the 50th percentile of TAPSE in Chinese children were close to Japanese children and approximately 1–4 mm higher than those reported by Koestenberger et al. before 7 years old, however, its growth curve became more flat after 7 years old in compared with other countries. Besides, the 50th percentile of TAPSE in Turkish children obtained in 2020 were 1–2 mm higher than that obtained in 2015.

**Discussion**

A deep understanding of RV function is helpful for improving the prognosis of patients with cardiovascular disease [16–19]. Unfortunately, non-invasive techniques evaluating RV function remain hampered because of RV’s complex

| Table 2 | Classification table for TAPSE values between genders |
|---------|-----------------------------------------------------|
|         | Male | Female |          |          |
|         | N    | Mean  | SD      | N    | Mean  | SD      | P    |
| BSA (m²) |      |       |         |      |       |         |      |
| ≤ 0.20   | 10   | 9.4   | 1.8     | 8    | 8.9   | 1.6     | 0.529|
| 0.20–0.30| 17   | 11.4  | 1.9     | 14   | 11.3  | 1.7     | 0.914|
| 0.30–0.40| 21   | 15.6  | 1.7     | 20   | 15.7  | 1.9     | 0.926|
| 0.40–0.50| 46   | 17.0  | 1.8     | 23   | 16.7  | 1.7     | 0.504|
| 0.50–0.60| 36   | 17.6  | 2.3     | 14   | 17.8  | 2.3     | 0.812|
| 0.60–0.70| 40   | 19.8  | 2.2     | 39   | 18.8  | 2.1     | 0.047|
| 0.70–0.80| 48   | 20.3  | 1.9     | 39   | 19.9  | 1.9     | 0.339|
| 0.80–0.90| 31   | 21.1  | 2.5     | 34   | 20.6  | 2.4     | 0.346|
| 0.90–1.00| 27   | 20.8  | 2.3     | 31   | 21.2  | 2.7     | 0.563|
| 1.00–1.10| 31   | 21.6  | 2.2     | 34   | 21.5  | 2.9     | 0.826|
| 1.10–1.20| 22   | 21.7  | 2.1     | 17   | 22.1  | 2.7     | 0.612|
| 1.20–1.30| 10   | 21.7  | 2.8     | 10   | 20.8  | 2.2     | 0.430|
| 1.30–1.40| 9    | 23.6  | 3.2     | 11   | 22.0  | 2.8     | 0.261|
| 1.40–1.50| 19   | 23.1  | 3.9     | 5    | 22.5  | 2.4     | 0.760|
| 1.50–1.60| 9    | 21.9  | 2.6     | 6    | 22.7  | 5.1     | 0.700|
| >1.60    | 17   | 24.2  | 2.9     | 4    | 23.5  | 3.9     | 0.666|

**TAPSE** tricuspid annular plane systolic excursion; **BSA** body surface area; **SD** standard deviation
structure. Unlike LV, RV consists of two layers of fibres that contribute to contraction. The superficial myocardial fibres which arranged in a circumferential direction and paralleled to the atrioventricular groove were thinner and mainly participate in the transverse contraction of RV. While the deep myocardial fibres which was longitudinally aligned from the apex to base was relatively thick and mainly engaged in the longitudinal contraction of RV [20].
In general, RV longitudinal contraction accounts for 80% of RV systolic function [21, 22].

Assessment of RV systolic function is of great importance in clinical. The current methods for the assessment of RV contraction include CMR, 2-dimensional and 3-dimensional echocardiography. Typically, CMR is regarded as a gold standard to evaluate RV geometry and function, whereas the use of CMR is limited due to its high cost as well as time consumption and for patients who had implantable devices cannot be used, too [5, 6]. New technique such as 3-dimension echocardiography allows comprehensive and quantitative assessment of RV geometry and function, but this method requires special echocardiography training and is also time-consuming [23].

TAPSE, which is a simple and reusable indicator to assess RV systolic function by longitudinal displacement of the anterior tricuspid annulus, was first validated by Kaul in 1984 [24] and has been considered to represent RV contraction for years [25]. It was recommended to be used routinely to estimate RV systolic function in adults with a lower limit (16 mm) of reference values for impaired RV function by ASE 2010 Guideline [7]. In 2015, ASE changed the cutoff value from 16 to 17 mm, which means the TAPSE values less than 17 mm represents impaired RV function.

**Fig. 2** Reference values curves of TAPSE based on age and BSA cohort. a Z-scores of TAPSE based on age. Red area, mean to mean− 1SD or mean to mean + 1SD; Yellow area, mean− 1SD to mean− 2SD or mean + 1SD to mean + 2SD; Green area, mean− 2SD to mean− 3SD or mean + 2SD to mean + 3SD. b Z-scores of TAPSE based on BSA. Red area, mean to mean− 1SD or mean to mean − 1SD; Yellow area, mean− SD to mean− 12SD or mean + SD to mean + 2SD; Green area, mean− 2SD to mean− 3SD or mean + 2SD to mean + 3SD. c Percentiles of TAPSE based on age. Red area, 25th–50th or 50th–75th; Yellow area, 10th–25th or 75th–90th; Green area, 3th–10th or 90th–97th. d Percentiles of TAPSE based on BSA. Red area, 25th–50th or 50th–75th; Yellow area, 10th–25th or 75th–90th; Green area, 3th–10th or 90th–97th. TAPSE tricuspid annular plane systolic excursion; BSA body surface area; SD standard deviation.
systolic function [26]. Both these two guidelines are recommendations for adults, whereas there is no guideline or expert consensus that recommends TAPSE reference values for children.

Koestenberger from Austria first reported reference values and Z-score values of TAPSE in children in 2009 [11], then several studies from other countries such as Spain, Turkey, Japan and sub-Saharan Africa determined reference values of TAPSE in children after that [8, 11–13, 27]. As has been reported by Fahrettin Uysal [8], the mean TAPSE value of Turkish children in 6–12 months age group is only 13.46 mm while it is 15.17 mm in Spanish children at the same age group [13]; in Japan, the mean TAPSE value of the 6–12 months children is 16.9 mm [12], which is much higher than both of the former two countries. Up to now, reference values of TAPSE in Chinese children has not been reported yet. Therefore, our study was undertaken to attain growth-related reference values of TAPSE in Chinese Children. We found that TAPSE increased with age and BSA in Chinese children under 15 years old, which is consistent in current literatures. However, our results also suggest that differences do exist in specific subgroups among different racial groups. For example, the trend of TAPSE value in Asian such as Chinese and Japanese children increased rapidly and reached the adult level (17.0 mm) until 1 year old, which grew faster than that of the Caucasian children. Besides, we found that in the same country, such as in Turkey, the 50th percentile of TAPSE in children in 2020 was about 1–2 mm higher than that in 2015, which means TAPSE might increase by years. All of these differences might be explained by genetic diversity, economic status and diet habits [8, 12]. Accordingly, we highlight the importance of applying racial-specific reference values of TAPSE in clinical practice. Apart from that, we hold the opinion that clinicians need to refresh the reference values of TAPSE in children every few years in order to correctly evaluate RV systolic function in children.

This finding is meaningful for Chinese children, especially for those with cardiopulmonary diseases, as RV function could be affected by different disease states such as acute respiratory distress syndrome (ARDS) as well as post-operation period in congenital heart diseases and different treatment. For instance, RV systolic function influences strategies to adjust positive end-expiratory pressure (PEEP) in patients with ARDS [28]; procedures involving tricuspid valvuloplasty [29] and cardiopulmonary bypass (CPB) with pericardial incision [20] were shown to have adverse effects on RV systolic function. Therefore, applying improper reference values of TAPSE can lead to the misjudgment of RV systolic function, which may interfere the decision-making in treatment.

In conclusion, we established the growth-related normal ranges of TAPSE for children aged between 0 and 15 years in China. We found that TAPSE values in Chinese children increase with age and BSA, which is consistent with the previous studies. Notably, the mean value of TAPSE is still below the adult threshold (17 mm) recommended
by ASE until 1 year old in China. We hope these reference values could be used for the correct interpretation of RV systolic function for Chinese children. However, there are two limitations in our present study. First, we only recruited a relatively small number of children for this study and the retrospective design of the present study prevented us from assessing the effects of feeding method on the development of TAPSE in children, especially in neonates. Second, this was a single-center study and we think a prospective, large sample size and multicenter cohort study from different areas of China is supposed to be performed in the future to reflect the whole spectrum of TAPSE in Chinese children.

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Declarations

Conflict of interest The authors have no relevant financial interest to disclose.

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