

Research Article

Pulmonary Venous Index as Additional Diagnostic Criteria for Fontan Palliation

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Backgroud. The results of the Fontan operation, depending on the anatomy of the pulmonary arteries, have been studied quite well. Various indices have been proposed to assess the degree of hypoplasia of the pulmonary arterial bed (Nakata, Reddy, and McGoon indexes). At the same time, an obstruction of pulmonary venous blood return may be considered as a contraindication to Fontan operation. Aim of the Study. To present an optimal method for pulmonary venous index (PVI) calculation based on computed tomography angiography (CTA) enhancement of the heart data in patients with a functional single ventricle. Materials and Methods. 63 patients with a functional single ventricle (SV) underwent CTA (Philips, Brilliance iCT) before the Fontan operation. Axial sections were reconstructed to a thickness of 0.75-3 mm using soft tissue and lung filters, followed by postprocessing of the data (Horos and OsiriX software) and construction of multiplanar and 3D images. The diagnoses were presented by various types of SV of the heart. The age of the patients ranged from 3 to 30 years (median 7 years). Comparison of PVI was carried out in patients of two groups: those who survived the intervention (n = 55 patients) and those who died (n = 8). The evaluation of the pulmonary veins (PV) and the calculation of the pulmonary venous index (PVI) were carried out based on the measurement of each pulmonary vein at 2 levels (at the level of the orifices and bifurcation). The calculation of the PVI was carried out according to the formula: the sum of the cross-sectional area of the main pulmonary veins, related to the body surface area. 3 variants of PVI calculation were compared: taking into account the values of the PV areas at the level of the orifices, the bifurcation, and the sum of the minimum areas of each of the PVs. Results. In the group of survived patients, the median PVI at the level of the PV orifices was 292 mm/m^2 , and in the group of deceased, it was 242 mm/m^2 (p = 0.0326); at the level of PV bifurcation in the group of survivors, it was 299 mm/m², and in the group of dead patients, it was 281 mm/m² (p = 0.0776); the minimum PVI was 257 mm/m² in the survivor group and 218 mm/m² in the deceased group (p = 0.006). An ROC analysis performed to determine the critical value of the minimum PVI affecting survival after Fontan operation revealed that PVI measured taking into account the minimum dimensions of the areas of the PV is a significant risk factor for death after Fontan operation (p = 0.00015), with its value (cutoff) <233.5 mm²/m². Conclusion. The value of the minimum PVI can be an important morphological indicator of the state of PV blood return and serve as an additional criterion in determining indications for the Fontan operation.

1. Introduction

The progress in cardiac surgery and related facilities has provided a significant improvement in the results of complex congenital heart defect (CHD) surgical treatment. For the majority of them, anatomical corrections aimed at restoring disturbed structures of the heart has been developed and successfully applied. At the same time, some CHD characterized by univentricular hemodynamics radical repair is cumbered or cannot be performed. These patients are considered to undergo hemodynamic reconstruction using the right (venous) part of the heart bypass creation according to the Fontan method [1-5].

The success of hemodynamic palliation largely depends on compliance with the criteria proposed by Choussat et al. back in the late 70s of the last century [6]. Over time, most of the restrictions have been revised, but the size of the pulmonary arteries, the anatomy, pressure, and resistance of the pulmonary circulation, and the functional state of the systemic ventricle and the competence of the systemic atrioventricular valve are still relevant [7–9].

Various indices proposed to assess the state of the pulmonary arterial bed (Nakata pulmonary arterial index, Reddy lower lobe pulmonary index, and McGoon index), together with a number of other indicators, define the possibility of Fontan palliation. However, publications devoted to the study of the anatomy and functional conditions of pulmonary venous blood flow in patients with a functional single ventricle (SV) are few, and the problem is deemed to be misjudged, despite the fact that some authors point out that the presence of pulmonary vein stenosis may be a contraindication to the Fontan procedure [10].

The goal of the study paper is to present an optimal method of pulmonary venous index (PVI) calculation using computed tomography angiography (CTA) of patients with SV.

2. Materials and Methods

2.1. Patients. During 1983-2020 yrs, 550 Fontan palliations had been performed in the department of surgical treatment for the older children at the CHD Bakulev Center for CVS, 319 of them with extracardiac conduit modification. Our series included 63 patients who underwent computed tomography angiography (CTA) of the heart and great vessels before the Fontan procedure. Patients were divided into 2 groups: those who survived the intervention (n = 55 patients) and those who died (n=8 patients). In 1 case, Fontan takedown was performed due to acute heart failure with severe pleural, pericardial, and abdominal effusions, with an axillary arteriovenous fistula created on the 2nd day after the surgery. Patients' diagnoses were presented with various variants of functionally SV of the heart (Table 1). The age of the patients ranged from 3 to 30 years (median Me = 7, Q_1-Q_3 [6, 10], all patients underwent the extracardiac conduit modification with a Gore-Tex prosthesis. There were no significant differences between the groups in terms of the main clinical parameters of the patients presented in Table 2.

8 patients died early after the procedure due to multiple organ failure (MOF), accompanied by severe pleural and abdominal effusions, pulmonary artery or hepatic veins thrombosis, or broncho-pulmonary bleeding (Table 3). It is noteworthy that visceral heterotaxy syndrome (VHS) was diagnosed in 6 of 8 patients.

2.2. Computed Tomography Angiography Image and Analysis. A retrospective study was performed to calculate the pulmonary venous index (PVI). Patients underwent contrastenhanced ECG-gated cardiac CT imaging using 128-slice CT (Siemens, Somatom definition AS), 256-slice (Siemens, Somatom definition Flash), and 256-slice (Philips, Brilliance iCT). Scan parameters were a detector collimation of 128 4 0. 625 mm, a gantry rotation time of 270–280 ms, a tube voltage between 80 and 120 kV, and a tube current between 200 and 360 mAs, depending on the body habitus. The retrospective ECG-gated helical mode was performed to eliminate cardiac

TABLE 1: Anatomic diagnosis.

Diagnosis	N = 55 Survivors	N = 8 Dead
Tricuspid atresia	12	
Double inlet left ventricle	7	1
Double inlet right ventricle	4	
Unbalanced common atrioventricular canal	6	
Complex DORV	12	1
Complex CTGA	4	
Complex TGA	4	
Visceral heterotaxy syndrome	5	5
Other complex	1	1

DORV, double outlet right ventricle, CTGA, corrected transposition of great arteries, and TGA, transposition of great arteries.

motion artifacts. The ECG-controlled tube current modulation was used in the scan. The tube output was raised to the normal level within every cardiac cycle during a limited interval in the end-diastolic phase (60-80% of RR intervals) where data were most likely to be reconstructed. During the remaining part of the cardiac cycle, the tube output can be reduced by approximately 80% with a corresponding decrease in the tube current. The coverage of the scan was from the thoracic inlet to the diaphragm. After scanning, the data were reconstructed at 0.6–1 mm intervals, with a 512×512 matrix. An iodinated contrast medium was injected via peripheral veins with a volume of 2-3 ml/kg body weight followed by a saline chaser. Bolus tracking was used to determine an optimal scan beginning time. The CTA data were analyzed using the software "Horos" and "OsiriX." We used these workstations to create three-dimensional techniques (multiplanar reformation and volume rendering) (Figure 1(a)). All multiplanar reformations were doubleoblique reconstructions using perpendicular to each pulmonary vein (PV) (Figure 1(b)). The cross-sectional areas of the PV were obtained from the reformatted angiographic images by manually drawing the region of interest (Figure 1(c)). The cross-sectional areas of each PV were measured at two levels: at the level of the pulmonary vein ostium and bifurcation PV (Figure 2). The pulmonary vein index (PVI) was calculated by the following formula: the sum of the cross-sectional areas (S, mm²) of each pulmonary vein (right superior pulmonary vein (RSPV), right inferior pulmonary vein (RIPV), left inferior pulmonary vein (LSPV), left superior pulmonary vein (LSPV), and left inferior pulmonary vein (LIPV), correlated to the body surface area (BSA):

$$PVI = \frac{\left(S_{RSPV} + S_{RIPV} + S_{LSPV} + S_{LIPV}\right)}{BSA, \left(mm^2/m^2\right)}.$$
 (1)

We compared three variants of the pulmonary venous index: at the level of the pulmonary vein ostium (OstPVI), at the level of bifurcation PV (BifPVI), and the sum of the minimum cross-sectional areas of each pulmonary vein (minPVI).

The example of the pulmonary venous index calculation, included as a supplementary file, can be removed from the paper.

	Survivors $(n = 55)$	Dead $(n=8)$		
	M±SD	M±SD	p (Mann-Whitney t test)	
	Me $(Q_1 - Q_3)$	Me $(Q_1 - Q_3)$		
Age (vrs)	8.6 ± 4.4	9.6±7.3	p = 0.849	
	7.0 (6-10)	6.5 (5.5–13)	F	
$BSA (mm^2)$	0.93 ± 0.27	1.04 ± 0.53	p = 0.439	
Dorr (IIIII)	0.88(0.8-1)	0.8 (0.7 - 1.4)	<i>p</i> = 0.459	
SVEE (%)	61.7 ± 5.4	61.8 ± 5.5	p = 0.705	
SVEF (%)	60 (60-64)	62 (59–65)	p = 0.703	
	79.8 ± 5.6	71.8 ± 4.6	5 0.077	
SpO ₂ (%)	81 (78-84)	74 (71.5-81.25)	p = 0.077	
$Hb (\alpha l)$	173.3 ± 22.6	193.3 ± 29.7	p = 0.281	
HD (g/l)	156 (144–168)	162.5 (159.25–167.75)	p = 0.281	
$PAI(N_{1}, h_{2}, h_{3}, h_{3})$ (m m ² /m ²)	291.3 ± 117.8	277.5 ± 141.5		
PAI (INakata) (IIIII /III)	270 (206.3-345.6)	254 (183.2-396.3)	p = 0.398	
McGoon index	2.6 ± 0.7	2.5 ± 0.6		
	2.4 (2.0-3.1)	2.4 (2.0–2.9)	p = 0.203	
PAP (mmHg)	11.4 ± 2.5	13.1 ± 3.3		
	11 (10–13)	12.5 (9.5–14)	p = 0.177	
Severe AVVR	5	3	p = 0.061	
NYHA FC	III-IV	III-IV	p = 0.631	

TABLE 2: The main clinical parameters of patients.

SVEF, single ventricle ejection fraction, BSA, body surface area, PAI, pulmonary arterial index, PAP, pulmonary arterial pressure, and AVVR, atrioventricular valve regurgitation.

TABLE 3: Hospital mortality causes.

	Diagnosis	Complications	
1. pt.	VHS	MOF, severe pleural and abdominal effusions	
2. pt.	DILV. APA	APF, SVC and RPA thrombosis, PATE	
3. pt.	VHS	MOF, severe pleural and abdominal effusions, pulmonary bleeding	
4. pt.	VHS	MOF, hepatic veins and PA thrombosis	
5. pt.	VHS	MOF, pulmonary bleeding	
6. pt.	DORV, RVH	MOF, severe pleural and abdominal effusions, pulmonary bleeding	
7. pt.	VHS	CHF	
8. pt.	RVHS. APA	MOF, severe pleural and abdominal effusions, pulmonary bleeding	

MOF, multiorgan failure, SVC, superior vena cava, PA, pulmonary artery, DILV, double inlet left ventricle, RVHS, right ventricle hypoplasia syndrome, VHS, visceral heterotaxy syndrome, APA, atresia pulmonary artery, and APF acute pulmonary failure. RPA, right pulmonary artery, CHF, congestive heart failure, and PATE, pulmonary artery thromboembolism.



FIGURE 1: Chest MSCT AG, an example of the right inferior pulmonary vein (RIPV), the cross-sectional area at the orifice calculating. (a) 3D VRT image demonstrating the anatomy of the RIPV junction with the left atrium (red circle) at the site of the section calculated; (b) axial image at the IPVs level, the oblique-coronal plane (blue line) and the oblique-sagittal plane (yellow line) are displayed parallel to the orifice of the RIPV; (c) the plane of the RIPV orifice with a stroke around the perimeter of the vessel.



FIGURE 2: Scheme of the pulmonary veins' confluence into the atrium. RSPV, right superior pulmonary veins, RIPV, right inferior pulmonary veins, LSPV, left superior pulmonary veins, LIPV, left inferior pulmonary veins, LA, left atrium, green ovals, bifurcation of the pulmonary veins (level of segmental pulmonary veins confluence), and yellow ovals, the pulmonary vein orifices (level of confluence of the lobar pulmonary veins).

The patient was 3 yrs old patient (body surface area 0.56m²) with functionally single right ventricle, double outlet right ventricle, left ventricle hypoplasia, pulmonary artery atresia, and previous BCPC. CTA data were determined using the following indicators:

- (1) PVs cross-sectional areas at the level of the pulmonary vein ostium:
 RSPV = 32.4 mm², RIPV = 54.9 mm², LSPV = 24.8 mm², and LIPV = 23.5 mm²
- (2) Cross-sectional area of PVs at the bifurcation level:
 RSPV = 26.3 mm², RIPV = 54.9 mm², LSPV = 26.8 mm², and LIPV = 18.2 mm²

Using the obtained indicators and abovementioned formulas, PVIs were calculated:

- (1) OstPVI = $(32.4 \text{ mm}^2 + 54.9 \text{ mm}^2 + 24.8 \text{ mm}^2 + 23.5 \text{ mm}^2)/0.56 \text{ m}^2 = 242 \text{ mm}^2/\text{m}^2$
- (2) BifPVI = $(26.3 \text{ mm}^2 + 54.9 \text{ mm}^2 + 26.8 \text{ mm}^2 + 18.2 \text{ mm}^2)/0.56 \text{ m}^2 = 225 \text{ mm}^2/\text{m}^2$

The minimal values of each PV obtained from the measurements were used for minimal PVI (minPVI) calculating:

(3) minPVI = $(26.3 \text{ mm}^2 + 54.9 \text{ mm}^2 + 24.8 \text{ mm}^2 + 18.2 \text{ mm}^2)/0.56 \text{ m}^2 = 191 \text{ mm}^2/\text{m}^2$

3. Statistical Analysis

Statistical data were analyzed using IBM SPSS Statistics Version 22 and Statistica Version 10 software. The distribution of indicators was checked for normality using the Kolmogorov–Smirnov test. Quantitative indicators of different groups of patients with normal distribution of variables were evaluated by t Student's test. In the event that quantitative traits had an incorrect distribution, they were described using the median (Me is the value of the trait that divides the series into two equal parts) and the interquartile range [25%-75%], i.e., the interval between 25 and 75 percentiles. Comparison of two independent variables was carried out using the Mann–Whitney test. A comparative assessment of qualitative parameters in the same groups was carried out using the Fisher criterion. In order to determine the relationship between the indicators, Spearman (R) or Pearson (r) correlation analysis was used. Significant differences in *p* values (*p* value) were considered less than 0.05 when the result was obtained.

4. Results

In the group of survivors, the median OstPVI was 292 mm/m², in the "dead," it was 242 mm/m² (p = 0.0326); in the survivor group, BifPVI was 299 mm/m², and it was 281 mm/m² in the dead group (p = 0.0776); the minPVI was 257 mm/m² in the first group and 218 in the second group (p = 0.006). The median values of the PVIs variants are shown in Table 4.

As can be seen from Table 3, there was a valid difference between the OstPVI and minPVI when comparing data of the first and second groups, p = 0.03 and 0.006, respectively (Figure 3).

An ROC analysis with the construction of a prognostic model was performed to determine the critical value of the OstPVI and minPVI, affecting the survival after the Fontan procedure. It was revealed that the ostium PVI value (cutoff) $<264 \text{ mm}^2/\text{m}^2$ which is a significant risk factor for death after surgery (p = 0.0132). At the same time, the sensitivity and specificity of the indicator were 75% and 67.2% (Figure 4(a)). At the same time, the risk of death after the procedure increases with a value of minPVI (cutoff) $<233.5 \text{ mm}^2/\text{m}^2$ with a greater degree of reliability (p = 0.00025) compared with OstPVI. The sensitivity and specificity of this indicator are also higher than that of OstPVI and amounted to 87.5% and 70.9% (Figure 4(b)).

One patient with a minPVI of $209 \text{ mm}^2/\text{m}^2$ survived surgery but needed an urgent take-down Fontan procedure. Since this patient had a significantly lower minPVI than the rest of the survivors and most likely would have died without Fontan elimination, we considered it possible to recalculate the critical value of minPVI taking this patient into account. Thus, minPVI is also a significant risk factor for adverse outcomes after the Fontan procedure with an even higher degree of reliability (p = 0.00015), with its value (cutoff) <233.5 mm²/m², with sensitivity and specificity increasing to 88.9% and 72.2%, respectively (Figure 5).

5. Discussion

The priority of PV measurement and calculation in patients with functional SV belongs to Kawahira et al. [11]. The authors proposed to calculate the pulmonary venous index based on measuring the diameter of the PVs, which could be an indicator that reflects the capacity of the pulmonary vascular bed in patients with a univentricular heart and an important morphological indicator of the state of pulmonary

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TABLE 4: PV1 variant comparison.			
	OstPVI (mm/m ²)	BifPVI (mm/m ²)	minPVI (mm/m ²)
	Me $(Q_1 - Q_3)$	Me $(Q_1 - Q_3)$	Me $(Q_1 - Q_3)$
Survivors	292 (248.5-338.7)	299 (268.8-348.9)	257 (229.0-290.0)
Dead	242 (225.2-276.2)	281 (231.8-299.7)	218 (191.5-232.5)
p (Mann-Whitney test)	0.0326*	0.0776	0.006**

Variants of the pulmonary venous index: at the level of the pulmonary vein ostium (OstPVI), at the level of bifurcation PV (BifPVI), and the sum of the minimum cross-sectional areas of each pulmonary vein (minPVI) failure. *-compare to OstPVI between survivors and dead groups. **-compare to minPVI between survivors and dead groups.



FIGURE 3: Box plots of PVI variants median values. Red, Ostium PVI; green, bifurcation PVI; and blue, mPVI.

blood flow when selecting patients for univentricular palliation, especially in the presence of the heart isomerism [11, 12]. The PVI as a sum of the cross section of all 4 pulmonary veins proximal to their confluence with the atrium related to the surface area of the patient's body was measured using the late phase of pulmonary arteriography data.

The angiography PVI calculation method deems to have measurement fault as PV's cross-sectional surfaces are not circle. Thus, some measurement error typical for the angiocardiographic study is possible. Thus, some measurement errors typical for the angiocardiographic study are possible.

The author series aimed to define the effect of the PVI value on surgery outcomes included 30 patients with functional SV, aged from 3 to 81 months (mean 30 months). The studied pulmonary venous index in 16 of them underwent bidirectional cavopulmonary anastomosis/12 survived, and 4 cases were fatal. The PVI in survivors was 361 ± 153 and 275 ± 60 mm/m² in patients with a fatal outcome (p = 0.30). Of the 14 patients undergoing the Fontan procedure, 13 had a successful outcome and 1 had died. PVI in survivors was >285 and 137 mm/m^2 in case of death. The authors concluded that PVI is an important morphological indicator of pulmonary blood flow and may improve the decision-making strategy for patients with SV.

Unfortunately, the small number of clinical observations, a small age range, the lack of reliable data on the effect of the PVI on the result of the operation with the determination its boundary values, and the existing indirectness of measuring the cross-sectional area of the PVs based on an angiocardiographic study make the conclusions unclear.

Jia et al. reported a more accurate and less subjective method of PV cross-sectional area measuring and PVI calculation than angiocardiography [13]. The authors used CTA to assess the size of the pulmonary veins in patients. This method allows us to perform a three-dimensional reconstruction of the left atrium and PVs and more clearly visualize them throughout, from the segmental, lobar levels and their confluence with atrium [14]. The advantage of this method is the ability to determine the cross-sectional area of the pulmonary artery at any level as objectively as possible using multiplanar reconstructions. The authors proposed to calculate the PVI as the sum of the cross section of all lobar PVs proximal to 5 mm from their confluence with the atrium, related to the patient's body surface area. Their series of pulmonary artery atresia (PAA) with ventricular septal defect (VSD) and major aortopulmonary collateral (MAPCA)-staged surgical treatment shows that high values of PVI (>438 mm²/m²) accompanied with big-sized



FIGURE 4: ROC model for PVI. (a) Ostium PVI (6A) u. (b) mPVI. CI, confidence intervals, OR, odds ratio, and HR, hazard ratio.

pulmonary artery branches can be significant predictors of a good result. At the same time, the authors chose only 1 level of PV measurement for PVI calculation.

Yuan et al. presented the effect of PVI measured by the Qianjun Jia et al. method on the results of tetrology of Fallot complete repair and revealed that low PVI is a significant risk factor for early mortality [15].

Our method of assessing the PVs and calculating the PVI differs from others by the measurement of each pulmonary vein at several levels: from the confluence of the pulmonary veins at the segmental level to the lobar, bifurcation of the PVs, and the lobar at the level of the confluence of the PVs into the atrium, the mouth of the PVs. The PVI formula calculation should include the sizes of the PVs at the narrowest and hemodynamically significant areas. The anatomy of the pulmonary veins in each patient is variable, and the narrowing of the pulmonary veins can be located at different levels; thus, the PVI values obtained by the previously proposed methods may be overestimated and do not reflect the true conditions of the pulmonary venous blood flow.

The analysis of the data shows that the calculation of the PVI should be performed by summing up precisely the minimal cross-sectional of the PVs. The value of minPVI can be an important morphological indicator of the state of pulmonary venous blood return and an additional criterion in the determination of indications for Fontan palliation and at its value $<233.5 \text{ mm}^2/\text{m}^2$, a significant risk factor for death after surgery.

5.1. Limitations. The study had limitations with the absence of the initial date on total pulmonary resistance in a number of cases before the Fontan operation, which limits the intervariable relation between PVI and total pulmonary resistance.



	Confirmed		not confirmed		
Total	9	%	54	%	р
<233.5	8	88.9	15	22.8	0,00015
≥	1	11.1	39	72.2	

Wilson method for 95% CI		95% CI		
Sensitivity	88.89%	56.50%	98.01%	
Specificity	72.22%	59.11%	82.38%	
Positive predictive value	34.78%	18.81%	55.11%	
Negaitive predictive value	97.50%	87.12%	99.56%	
Accuracy	74.60%	60.64%	84.85%	
OR	20.8 (2.39-180.81)			
HR	3.2 (1.96-5.21)			

FIGURE 5: ROC model for mPVI with takedown included (8 dead +1 with takedown). CI, confidence intervals, OR, odds ratio, and HR, hazard ratio.

6. Conclusion

The minPVI could be considered as an important morphological indicator of the pulmonary venous blood return and serve as an additional criterion in estimating the indications for the Fontan operation.

Data Availability

All data used were included in the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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