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Correlation between three-dimensional echocardiography and cardiopulmonary fitness in patients with univentricular heart: A cross-sectional multicentre prospective study *

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Keywords:

Single ventricle Three-dimensional echocardiography Aerobic fitness Maximum oxygen uptake Congenital heart disease

*Tweet: 3D echocardiography measures univentricular in heart correlate with cardiopulmonary fitness, as determined by VE/VCO2slope. 3D VO2maxand echocardiographymay be of value in single ventricle follow-up, provided that the technique and analysis software are improved.

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1. Abbreviations

CPET cardiopulmonary exercise test EDVi indexed end-diastolic volume ESVi indexed end-systolic volumeSF-36 36-item Short Form Health Survey SV single ventricle VE/VCO2slope ventilatory efficiencyVO2max maximum oxygen uptake.

abstract

Background:

The prognosis of patients with a functional single ventricle has improved, with better cardiopulmonary fitness, health-related quality of life and survival. Conventional echocardiography remains the first-line technique in single ventricle follow-up. Three-dimensional (3D) echocardiography has shown recent value in congenital cardiology, but its ability to predict functional status in patients with a single ventricle remains unknown.

Aim:

To evaluate, in patients with a single ventricle, the association between 3D echocardiography variables and functional status determined by cardiopulmonary fitness.

Methods:

Children and adults with a functional single ventricle were prospectively enrolled in this multicentre study. Cardiopulmonary fitness was assessed by cardiopulmonary exercise test, with measures of maximum oxygen uptake (VO2max) and ventilatory efficiency (VE/VCO₂ slope). 3D echocardiography was performed with off-line reproducibility analyses, using Tom Tec Arena TM software. Health-related quality of life was assessed using the SF-**36 questionnaire.**

Results:

A total of 33 patients were screened, and 3D echocardiography analyses were feasible in 22 sub-jects (mean age 28 ± 9 years). 3D echocardiography ejection fraction correlated with percent-predictedVO_{2max} (r = 0.64, P < 0.01), VE/VCO₂ slope (r = -0.41, P = 0.05), two-dimensional echocardiography ejection fraction (r = 0.55, P < 0.01) and health-related quality of life physical functioning dimension (r = 0.56, P = 0.04). 3D echocardiography indexed end-systolic volume correlated with percent-predicted VO2max(r = -0.45, P = 0.03) and VE/VCO₂ slope (r = 0.65, P < 0.01). 3D echocardiography reproducibility was good.

Conclusions:

Single ventricle ejection fraction and volumes measured by 3D echocardiography correlated with cardiopulmonary fitness, as determined by two main prognostic cardiopulmonary exercise test variables: VO2maxand VE/VCO₂ slope. Despite good reproducibility, 3D echocardiography feasibility remained limited. 3D echocardiography may be of value in single ventricle follow-up, provided that the technique and analysis software are improved.

2. Background

Significant advances in prenatal diagnosis, surgical techniques and postoperative care have led to increasing survival rates among patients with single ventricle (SV) physiology [1]. However, these patients still have high morbidity and mortality, requiring lifelong follow-up, as well as repeated invasive procedures and prolonged hospitalizations [2].

Among the different non-invasive examinations used during follow-up of patients with SV physiology, the prognostic role of the cardiopulmonary exercise test (CPET) has been demonstrate [3–5]. Indeed, two main CPET variables – maximum oxygen uptake(VO_{2max}) and ventilatory efficiency (VE/VCO₂ slope) – correlated with functional status, quality of life and mortality in SV [6–9]. The VE/VCO2slope has been validated more recently as a surrogate marker for morbidity and mortality in adult heart failure [8,9], and in patients with congenital heart disease [6,7]. This variable is of particular interest in patients with complex congenital heart disease, especially SV, as it does not require maximal exercise.

Cardiac imaging is the main diagnostic tool for evaluating cardiac function. However, the accurate evaluation of SV functional status using conventional two-dimensional (2D) echocardiography remains limited, and multimodality cardiac imaging, involving echocardiography, cardiac magnetic resonance imaging and cardiac computed tomography, is recommended [3,10]. Nevertheless, the identification of non-invasive cardiac imaging variables with prognostic value, such as ventricular volume and function, remains challenging, given the physiological and anatomical heterogeneity in SV [11].

Three-dimensional (3D) echocardiography has shown recent potential in patients with congenital heart disease [12, 13], as it can provide fast and reproducible assessment of SV volumes and ejection fraction, with acquisition of full-volume data sets within a few seconds [14], and fair-to-good accuracy compared with cardiac magnetic resonance imaging [15–18]. Therefore, volume assessment by 3D echocardiography could become a valuable technique for serial routine follow-up in patients with SV [15, 17, 19]. Nevertheless, 3D echocardiography remains controversial in SV, and its prognostic value has not yet been established.

In this study, we aimed to evaluate, in patients with SV, the association between 3D echocardiography variables and functional status determined by cardiopulmonary fitness

.3. Methods

3.1. Study design and population

This prospective multicentre cross-sectional study was carried out from November 2021 to June 2022 in three tertiary care congenital heart disease centres in France: Bordeaux University Hospital; Saint-Pierre Institute; and Montpellier University Hospital.

All paediatric and adult patients with an SV, as defined by the American College of Cardiology congenital heart disease classification [20], and aged \geq 7 years, were consecutively recruited during their routine follow-up.

3.2. Clinical and paraclinical variables

All patients enrolled in the study underwent the following examinations: physical examination; electrocardiogram; transthoracic echocardiography; biological sample test (N-terminal prohormone of brain natriuretic peptide, haemoglobinaemia, haematocrit, creatinine, bilirubin, albuminaemia); and CPET. Adult patients were also asked to complete the 36-item Short Form Health Survey (SF-36) questionnaire, a validated generic instrument evaluating the main dimensions of health-related quality of life (physical functioning, energy, emotional well-being, social functioning and general health) [21].

The following clinical variables were collected: sex; age; weight; height; New York Heart Association (NYHA) functional class; and SV anatomy. Depending on the ventricle's predominant morphology, subjects were classified as functional left or right SV.

3.3. Echocardiography variables

To determine feasibility and reproduce real-life practice, all eligible patients were consecutively enrolled, regardless of echogenicity; no contrast agent was used, and an ultrasound examination was performed by the patient's usual congenital cardiologist. Echocardiography examinations were performed on different ultrasound systems: EPIQ CVx (Philips, Andover, MA, USA); Affiniti 70 (Philips, Andover, MA, USA); and Vivid E95(General Electric, New York, NY, USA). Image acquisitions were performed using the following matrix transducers: X5-1 and X7-2 probes for Philips systems; and the M5S probe for General Electric systems. According to the international recommendations, electrocardiogram-gated 3D full volume sweeps were acquired from the apical view, with breath-holding during the four-beat acquisition phase [22].



Fig. 1. A–B. Three-dimensional (3D) echocardiography tracking for single ventricle (SV); the green lines represent endocardial tracking for morphological right SV (A) and left SV (B). 2Ch: two-chamber view; 3Ch: three-chamber view; 4Ch: four-chamber view; bpm: beats per minute; EF: ejection fraction; EDV: end-diastolic volume; EDVi: indexed end-diastolic volume; EV: end-systolic volume; ESVi: indexed end-systolic volume; LV: left ventricle; SAX: short-axis view.

Echocardiography recordings were prospectively stored in DICOM format, and offline analyses were performed by a single investigator (V.F., congenital cardiology fellow) who was blinded to clinical and CPET data. A second analysis was performed on all recordings, by the same investigator (V.F., congenital cardiology fellow), to assess intra observer reproducibility, and by a second investigator (V.P., congenital cardiology resident), to assess inter-observer reproducibility, with no access to the results of the first analysis. Echocardiography analyses were performed using Tom Tec Arena TM software, version 40 (Tom Tec Imaging Systems GmbH, Unterschleissheim, Germany), a vendor-independent program that can measure all echocardiographic images stored in DICOM format.

Conventional 2D echocardiographic variables for the SV were collected: ejection fraction and volumes using the biplane Simpson method; 2D global longitudinal strain; atrioventricular valve Doppler variables; annular plane systolic excursion; and valve stenosis or regurgitation [23]. As adult and paediatric patients were eligible for the study, all volume variables were indexed to body surface area. Left and right SV volumes were analysed using, respectively, 4D left ventricle and 4D right ventricle dedicated Tom Tec Arena TM software. Postprocessing included the setting of the position of the tricuspid valve, the mitral valve and the cardiac apex, to determine the orientation of the heart. The best possible views containing a full volume set were chosen for the analysis. The "four"-chamber, coronal and sagittal sections of the ventricle were semi-automatically bordered at end-diastole and end-systole (Fig. 1). A manual correction was performed when necessary. The endocardial tracking included papillary muscles, whereas trabeculae were mostly excluded from the volume because of poor differentiation between trabeculae and myocardium [24]. Then, the software generated a 3D volume of the SV throughout the cardiac cycle, with calculation of volumes and ejection fraction. In case there were two functional ventricles with a large septal defect (as in atrioventricular septal defect), the endocardial tracking included both ventricles, using the software adapted to the predominant ventricle.

3.4. CPET variables

The main prognosis outcome selected in this study was cardiopulmonary fitness, evaluated by CPET, and represented by two major variables: VO_{2max} and VE/VCO_2 slope [6, 25, 26].

As in our previous studies using CPET procedures, all centres used a similar cycle ergometer triangular protocol to obtain a homogeneous incremental overall duration of between 10 and15 minutes: a 1-minute rest; a 3-minute warm-up (10 to 20 Watts)in increments of 10, 15 or 20 Watts each minute; a pedalling rate of 60 to 80 revolutions per minute; a 3-minute active recovery (20Watts); and a 2-minute rest [27, 28]. The exercise test was considered as maximal when three out of the four following criteria were reached: respiratory exchange ratio (VCO₂/VO₂) \geq 1.1; maximum heart rate > 85% of maximal age-predicted heart rate; limit of the patient's tolerance despite verbal encouragement; plateau of VO₂(VO_{2max}) despite increasing exercise intensity. When oxygen uptake did not reach a plateau, which is very common in patients with SV, the peak VO₂ was recorded. VO_{2max} values were normalized as a percentage of the predicted VO_{2max}, using reference values for cycle ergometer test in the general population (named as percent-predicted VO2max) [29,30].

The VE/VCO₂ slope corresponds to the ventilation increase in response to CO₂ production, and thus reflects increased ventilatory drive (increased values corresponding to impaired ventilatory efficiency) [31]. The VE/VCO₂ slope was calculated from breath-by-breath data and determined using linear regression of minute ventilation (VE) and CO₂ production (VCO2) obtained during incremental exercise. The VE/VCO2slope value was measured from the beginning of incremental exercise (after the warm-up period) to maximum exercise [6, 9].

Other CPET variables were collected, as previously detailed [27, 28]: maximum workload; maximum heart rate; heart rate reserve; oxygen pulse increase during exercise; and ventilatory anaerobic threshold.

3.5. Formal aspects

The study was conducted in compliance with the Good Clinical Practices protocol and Declaration of Helsinki principles. Our institutional review board approved the study protocol, and the study was registered on ClinicalTrials.gov (NCT05118152). Informed consent to participate in the study was obtained from all patients, including parents or legal guardians of children.

3.6. Statistical analysis

The study population was described with means \pm standard deviations or medians (interquartile ranges) for quantitative variables, and with frequencies for qualitative variables. Continuous variables distributions were tested using the Shapiro–Wilk test.

Correlations between echocardiography results and other variables were evaluated with Pearson or Spearman correlation coefficients.

Inter- and intra-observer reproducibilities of 3D echocardiography readings were assessed by calculating intraclass correlation coefficients (ICCs) of type (2, 1). As defined by Koo et al., values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9 and greater than 0.90 were indicative of poor, moderate, good and excellent reliability, respectively [32].

Statistical significance was set at 0.05, and analyses were per-formed using Statistical Analysis Systems Enterprise Guide, version4.3 (SAS Institute, Cary, NC, USA).

4. Results

4.1. Patients' characteristics

During the study period, a total of 33 patients with SV were screened and were eligible for the study, but only 22 of them (13male subjects) were finally analysed, including three children and 19 adults aged 10 to 43 years (mean age 28 ± 9 years) (Table 1). The SV morphology was left for 15 subjects, and 20 patients had undergone total cavopulmonary anastomosis surgical repair at the time of the study (two patients with SV and pulmonary stenosis had undergone Glenn surgery). Most patients were in NYHA functional class I or II (n = 21).

Overall, the SV systolic function assessed by echocardiography was preserved, with median ejection fraction values of 55.8% (interquartile range 50.0–60.0%) using 2D measures, and 59.2%(interquartile range 43.9–63.2%) using 3D measures.

However, cardiopulmonary fitness was impaired, with a meanVO2maxraw value of $21.1 \pm 8.8 \text{ mL/kg/min}$, and a mean percent-predicted VO2maxvalue of $56.8 \pm 18.8\%$. Ventilatory efficiency was altered overall, with a median VE/VCO₂ slope increase to 37.7(interquartile range 32.9-42.6).

4.2. Correlation between 3D echocardiography and cardiopulmonary fitness

The SV ejection fraction measured by 3D echocardiography correlated with both CPET variables: the percent-predicted VO2max(r = 0.64, P < 0.01) and the VE/VCO₂ slope (r = -0.41, P = 0.05) (Fig. 2).

The SV volumes measured by 3D echocardiography correlated with percent-predicted VO2max(r = -0.45, P = 0.03 for indexed end-systolic volume [ESVi]) and VE/VCO₂ slope (r = 0.52, P = 0.01 for indexed end-diastolic volume [EDVi]; r = 0.65, P < 0.01 for ESVi).

4.3. Correlations between **3D** echocardiography and secondary outcomes

The ejection fraction measured by 3D echocardiography correlated with 2D biplane Simpson measures (r = 0.55, P < 0.01), 2D global longitudinal strain (r = -0.58, P < 0.01) and the SF-36 physical functioning dimension of health-related quality of life (r = 0.56, P = 0.04).No significant association was found between 3D echocardiography variables and biological markers, or between SV 3D volumes and any of the secondary outcomes (Fig. 2, Table 2).The ejection fraction measured by 3D echocardiography correlated with 2D global longitudinal

strain (r = -0.58, P < 0.01)(Fig. 2). 2D global longitudinal strain also correlated with percentpredicted VO2max(r = -0.57, P < 0.01) (Table 3).

4.4. Feasibility and reproducibility

Assessment of SV function using 3D echocardiography was not possible in one third of the eligible population (n = 11 out of the 33screened patients), as the Tom Tec Arena TM software was unable to analyse 3D data because of image acquisition artefacts. Indeed, in some cases, insufficient resolution occurred because of a poor acoustic window (n = 5) or insufficient breath-holding capacity (n = 1). Also, in extremely dilated SV (n = 5), a portion of the ventricle protruded from the acoustic window, so we missed volume in the data set and endocardial tracking was incomplete.

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Clinical variables	78.0
Age (years)	28±9
Eamala	0/411
Penale	12(50)
Male	13(39)
weight (kg)	00.5±10.4
BMI (kg/m*)	20.3 (18.5-23.9)
SV morphology	
Left SV	15 (68)
Right SV	7 (31)
SV anatomy	eo los inte
Tricuspid atresia	10 (45)
Double-outlet right ventricle	4(18)
Mitral atresia	3(14)
Double-inlet left ventricle	2 (9)
Atrioventricular septal defect	2(9)
Pulmonary atresia	1(5)
Number of previous surgeries	2.9 ± 1.0
Negative chronotropic arrhythmic drugs	8(36)
Renin-angiotensin system inhibitors	11 (50)
Diuretic drugs	3(14)
Implantable device (pacemaker or defibrillator)	2(9)
NYHA functional class	
	13 (59)
I	8(36)
m	1(5)
IV	0(0)
Opportunition at part (91)	075+67
COUT warishing	36.3 2 9.6
Why (and the family)	211.00
Descent predicted V() (9)	50 Q ± 10 Q
VEVCO alare	30.0 1 10.0
Vestilators according threshold (and the facing)	157:55
Ventilatory anaerooic mresnoid (mt/kg/min/	13.3 ± 0.0
Heart rate reserve (beats min)	02.0±28.7
Maximum workload (Watts)	90.5±30.8
Oxygen pulse increase during exercise (multiplier	2.4±0.8
factor)	
Exercise-induced armythmia	U
Echocardiography variables	
2D biplane Simpson ejection traction (%)	55.8 (50.0-60.0)
2D EDV (mL)	122.3 (101.1-175.0)
2D EDVI (mL/m ²)	79.7 (59.8-109.0)
2D ESV (ml.)	54.6 (42.0-68.9)
2D ESVi (mL/m ²)	33.0 (25.3-50.9)
2D global longitudinal strain (%)	-20.3 ± 8.4
TDI left lateral wall peak early diastolic velocity (e')	12.1 ± 4
(cm/s)	
E/e' ratio	4.9 (3.7-8.5)
TDI left lateral peak systolic annular velocity (cm/s)	8.1±2.7
TDI right lateral peak systolic annular velocity (cm/s)	6.4 ± 2.1
Left annular plane systolic excursion (mm)	13.5 ± 2.8
Right annular plane systolic excursion (mm)	11 ± 4.1
3D ejection fraction (%)	59.2 (43.9-63.2)
3D EDV (mL)	118.3 (79.0-203.0)
3D EDVi (mL/m ²)	68.7 (51.6-103.5)
3D ESV (mL)	45.8 (38.6-112.6)
20 535 (-1)(-2)	27.9 (23.0.60.4)

Data are expressed as mean \pm standard deviation, number (3) or median (interquartile range). 2D: two-dimensional; 3D: three-dimensional; BMI: body mass index; CPET: cardiopulmonary exercise test; EDV: end-diastolic volume; EDV: indexed end-diastolic volume; ESV: end-systolic volume; NVHA: New York Heart Association; SV: single ventricle; TDI: tissue Doppler imaging; VE/VCO₂ slope: ventilatory efficiency; VO_{2max}: maximum oxygen uptake.

In patients for whom SV function assessment using 3Dechocardiography was possible (n = 22 out of the 33 screened patients), intra observer reproducibility was good for ejection fraction (ICC = 0.78, 95% confidence interval [CI]: 0.56–0.90) and volumes (ICC = 0.74, 95% CI: 0.49–0.88 for EDVi; ICC = 0.69, 95% CI:0.39–0.85 for ESVi). Inter observer reproducibility was excellent for volumes (ICC = 0.82, 95% CI: 0.62–0.92 for EDVi; ICC = 0.86, 95% CI:0.71–0.94 for ESVi), and moderate for ejection fraction (ICC = 0.62,95% CI: 0.29–0.82) (Table 4).



Fig. 2. Correlation matrix between three-dimensional (3D) ecbocardiography variables (single ventricle ejection fraction and volumes) and primary (cardiopulmonary exercise test) or secondary outcomes. Shades of blue indicate increasing negative correlation coefficient; shades of red indicate increasing positive correlation coefficient. 2D: two-dimensional; EDV: end-diastolic volume; EDV: indexed end-diastolic volume; EF: ejection fraction; EDV: end-diastolic volume; EDV: indexed end-diastolic volume; EV: end-systolic volume; EDV: indexed end-diastolic volume; NT pro BNP: N-terminal prohormone of brain natriuretic peptide; VE/VCO₂ slope: ventilatory efficiency; VO_{2max}: maximum oxygen uptake. * P<0.05; ** P<0.01.

Table 2

Correlation between three-dimensional echocardiography ejection fraction and secondary outcomes (conventional echocardiography and quality of life).

	3D echocardiography ejection fraction	
	Coefficient (7)	р
2D echocardiography variables		
Biplane Simpson ejection fraction	0.55	< 0.01
Atrioventricular valve peak early diastolic velocity (E)	0.04	0.86
Atrioventricular valve peak early diastolic velocity (A)	0.35	0.12
E/A ratio	-0.35	0.12
TDI left lateral wall peak early diastolic velocity (e')	0.54	< 0.01
E/e' ratio	-0.37	0.09
TDI left lateral peak systolic annular velocity	0.54	0.01
TDI right lateral peak systolic annular velocity	0.32	0.16
Left annular plane systolic excursion	0.32	0.17
Right annular plane systolic excursion	0.07	0.78
SF-36 dimensions		
Physical functioning	0.56	0.04
Role limitations because of physical health	0.06	0.84
Role limitations because of emotional problems	0.35	0.22
Energy	0.44	0.12
Emotional well-being	0.37	0.19
Social functioning	0.28	0.33
Pain	0.42	0.14
General health	0.19	0.51
Health change	0.05	0.78

2D: two-dimensional; SF-36: 36-item Short Form Health Survey; TDI: tissue Doppler imaging.

Table 3

Correlation between two-dimensional global longitudinal strain and cardiopulmonary exercise test variables.

CPET variables	Coefficient (r)	P
Percent-predicted VO2mat (%)	-0.57	< 0.01
VO _{2mas} (mL/kg/min)	-0.63	< 0.01
VE/VCO ₂ slope	0.21	0.35
Anaerobic threshold (mL/g/min)	-0.64	< 0.01
Heart rate reserve (beats/min)	-0.21	0.36
Maximal workload (Watts)	-0.18	0.43

CPET: cardiopulmonary exercise test; VE/VCO2 slope: ventilatory efficiency; VO2mas: maximum oxygen uptake.

Table 4

Interobserver and intraobserver reproducibility for three-dimensional echocardiography (n=22).

3D echocardiography variables	Intraobserver reproducibility	Interobserver reproducibility
Ejection fraction (%)	0.78 (0.56-0.90)	0.62 (0.29-0.82)
EDV (mL)	0.76 (0.52-0.89)	0.83 (0.64-0.92)
EDVi (ml/m ²)	0.74 (0.49-0.88)	0.82 (0.62-0.92)
ESV (mL)	0.70 (0.41-0.86)	0.87 (0.72-0.94)
ESVi (mL/m ²)	0.69 (0.39-0.85)	0.86 (0.71-0.94)

Data are expressed as intraclass correlation coefficient (95% confidence interval). 3D: three-dimensional; EDV: end-diastolic volume; EDVi: indexed end-diastolic volume; ESV: end-systolic volume; ESVi: indexed end-systolic volume.

5. Discussion

In this prospective multicentre study, we found that SV ejection fraction and volumes measured by 3D echocardiography were significantly associated with cardiopulmonary fitness and health-related quality of life, with good reproducibility, but limited feasibility.

The correlation found in this study between SV ejection fraction and volumes, using 3D echocardiography and the two main cardiopulmonary fitness variables, is of clinical interest, as VO_{2max} and VE/VCO_2 slope are two major prognostic predictors in SV [6,25,26].Indeed, a decline in percent-predicted VO2maxabove 3% per year has been found to be an independent risk factor for morbidity and mortality in adults with SV [33]. Moreover, impaired ventilatory efficiency, marked by an increased VE/VCO_2 slope above 31.5,has been reported to be an independent risk factor for morbidity and mortality in children and adult patients with SV [25]. Similar results were reported by one paediatric cardiac magnetic resonance imaging study, where systolic SV function correlated with cardiopulmonary fitness [34]. However, cardiac magnetic resonance imaging is not widely available, may be time consuming and expen-sive, and usually requires sedation in the paediatric population [35].Hence, the application of 3D echocardiography is attractive because of its availability, non-invasive

nature, favourable costs and absence of sedation. The value of 3D echocardiography has been discussed in patients with heart failure, as well as in other types of congenital heart disease [36–38], but it is essential to know how robust this technique is, and how it can help to assess functional status and morbidity in patients with complex congenital heart disease, such as SV.

Indeed, the wide spectrum of SV includes various complex anatomical features, multiple surgical procedures and different haemodynamic conditions [20], which, altogether, make 3Dechocardiography analysis difficult. In fact, in our study, 3D echocardiography analysis was not feasible in one third of the eligible population. This may reflect real-life routine practice, but there is surely room for technical and medical improvements. A better overall gain adaptation could result in better endocardial border visualization, and specific training is advisable for physicians and sonographers dedicated to cardiac imaging in congenital heart dis-ease. Therefore, cardiac magnetic resonance imaging should be used as a priority in patients with SV for whom 3D echocardiography analysis is not possible.

Nevertheless, good-to-moderate intra observer and inter observer reproducibilities for the assessment of SV volumes and function using 3D echocardiography were found in this study. Data analyses with Tom Tec Arena TM vendor-independent software seems appropriate in close-to-real-life use, as echocardiograms are usually performed on different ultrasound machines by different sonographers. Moreover, we observed a good correlation between3D and 2D echocardiography assessment of ejection fraction, suggesting potential value for 3D echocardiography in the followup of patients with SV physiologies. Indeed, analyses of SV volumes and function using 2D echocardiography are based on geometrical assumptions [39]. Furthermore, in this study, ejection fraction measured by 3D echocardiography correlated with 2D strain (a marker of global systolic ventricular function). Similar results have been reported in adult patients with heart failure [40]. Zaidi et al. found a correlation between 2D strain and some biomarkers in patients with SV [41]. However, the prognostic value of 2D strain in patients with SV remains undetermined.

Interestingly, ejection fraction measured by 3D echocardiography was associated with the physical functioning dimension of health-related quality of life, which further reinforces the relevance of using 3D echocardiography in the follow-up of patients with SV. Indeed, patient-reported outcomes have been increasingly used in clinical research in congenital cardiology [42], and the physical dimension of health-related quality of life is classically associated with the major prognostic factors in congenital heart disease, such as NYHA functional class [43], VO_{2max} [28] or ventricle ejection fraction [44]. Unsurprisingly, impaired exercise performance alters the quality of life of patients with SV [45]; therefore, the use of 3Dechocardiography could be of interest in future research on cardiac rehabilitation using patient-reported outcomes in patients with SV [27].

5.1. Study limitations

In this pilot study, data from cardiac magnetic resonance imaging were not prospectively available for all patients. In the rare studies evaluating 3D echocardiography in patients with SV, SV volumes were systematically compared with cardiac magnetic resonance imaging, with controversial results [15–18].

The number of subjects analysed in the study was limited, basing our results on univariate analyses, but was roughly equivalent to similar studies [15,19]. Finally, the Tom Tec Arena TM software used in this study for right and left SV analyses was only validated for structurally normal right or left ventricles, respectively, and normal systemic and pulmonary outflow tracts. Therefore, the abnormal morphology and atypical location of the outflow tracts in SV required several manual tracking corrections. Technical refinements in the current version of the software are clearly necessary to make it more robust for univentricular anatomy

.6. Conclusions

In this multicentre study, SV ejection fraction and volumes measured by 3D echocardiography correlated with cardiopulmonary fitness, as determined by two major prognostic CPET variables: VO_{2max} and VE/VCO_2 slope. Moreover, 3D echocardiography variables were associated with conventional 2D echocardiography variables, as well as with the physical dimension of health-related quality of life. Despite good reproducibility, the feasibility of 3D echocardiography in patients with SV remained limited, as the software was unable to perform the analysis in one third of the eligible population. These results suggest a potential value of 3Dechocardiography in the follow-up of patients with SV physiologies, provided that the technique and analysis software are improved.

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Disclosure of interest

The authors declare that they have no competing interest.



Central illustration, Correlation between three-dimensional (3D) echocardiography and cardiopulmonary fitness in patients with univentricular heart: a cross-sectional multicentre prospective study, CPET; cardiopulmonary exercise test; VE/VCO2 slope; ventilatory efficiency; VO2max: maximum oxygen uptake.

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