3D printing and virtual reconstruction

in surgical planning of Double Outlet Right Ventricle repair

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Central message: Both 3DVVR and 3DPHM improved standard multimodal imaging in the definition of surgical strategy of complex DORV repair.

Perspective statement: Future prospective studies would be appropriate to assess the postoperative impact of 3DVVR and 3DPHM in surgical planning on patient short and long term outcomes.

Central Picture Legend: 3DVVR and 3DPHM used in the preoperative planning as supplementary modalities in the decision making of the surgical strategy.

Keywords: Double Outlet Right Ventricle; 3D virtual valvular reconstruction; 3D printed heart model; 3D modality in surgical planning; 3D printing
Abstract

Objectives

For more than a decade, 3D printing has been identified as an innovative tool for the surgical planning of Double Outlet Right Ventricle (DORV). Nevertheless, lack of evidence concerning its benefits exhorts to identify valuable criteria for future prospective trials.

Methods

We conducted a retrospective study involving 10 DORV patients operated between 2015 and 2019 in our center. During a preoperative multidisciplinary heart team, we harvested surgical decisions following a three incremental steps process: 1) multimodal imaging ; 2) 3D virtual valvular reconstruction (3DVVR); 3) 3D printed heart model (3DPHM). The primary outcome was the proportion of predicted surgical strategy following each of the three steps, compared to the institutional retrospective surgical strategy. The secondary outcome was the change of surgical strategy through 3D modalities compared to multimodal imaging. The incremental benefit of the 3DVVR and 3DPHM over multimodal imaging was then assessed.

Results

The operative strategy was predicted in 5 cases after multimodal imaging, in 9 cases after 3DVVR and the 10 cases after 3DPHM. Compared to multimodal imaging, 3DVVR modified the strategy for 4 cases. One case was correctly predicted only after 3DPHM inspection.

Conclusions

3DVVR and 3DPHM improved multimodal imaging in the surgical planning of DORV patients. 3DVVR allowed a better appreciation of the relationships between great vessels, valves and ventricular septal defect. 3DPHM offer a realistic pre-operative view at patient scale and enhance evaluation of the outflow tracts obstruction. Our retrospective study demonstrates benefits of preoperative 3D modalities and supports future prospective trials to assess their impact on postoperative outcomes.
List of abbreviations:

3DVVR: 3D virtual valvular annulus reconstruction
3DPHM: 3D printed heart model
ASD: atrial septal defect
CT: computed tomography
CTA: computed tomography angiography
DORV: double outlet right ventricle
MV: mitral valve
PA: pulmonary artery
PV: pulmonary valve
TGA: transposition of the great arteries
TTE: transthoracic echocardiography
TV: tricuspid valve
VSD: ventricular septal defect
INTRODUCTION

Congenital heart disease is a global concern in child and adult health. Without the ability to substantially reduce congenital heart disease prevalence, interventions and resources must be invested to improve mortality, operative outcomes, survival and quality of life (1).

Double outlet right ventricle (DORV) is a complex type of ventriculoarterial discordance accounting for 1-3% of all congenital heart diseases, with a reported incidence of 3-9 / 100'000 live births (2,3).

Due to its heterogeneity, each DORV case is unique, making surgical planning of its total repair one of the greatest challenges in the field of congenital heart disease (4). Numerous surgical techniques have been validated for the repair of DORV, including the intraventricular repair (5) and arterial switch operation (6), the Rastelli procedure (7), Réparation à l’Etage Ventriculaire (REV) (8), the Bex-Nikaidoh procedure (9-11) and the outflow tracts rotation, also known as half-turned truncal switch operation (12,13) or en-bloc rotation of the outflow tracts (14-17). The choice between these procedures is often difficult and dictated by the surgeon preferences as well as the heart anatomy and associated abnormalities. Imaging plays an important role in this assessment (4).

Imaging and 3D printing

Multimodal imaging, including transthoracic echocardiography (TTE), computed tomography (CT) and magnetic resonance imaging (MRI), is a key element in surgical planning using both 2D visualization and well-established 3D reconstruction techniques. Complex intracardiac
anatomy visualization can be improved with new 3D modalities (18). In particular, 3D virtual valvular reconstruction (3DVVR) and 3D printed heart model (3DPHM) have the potential to revolutionize the care of pediatric cardiac patients (19). However, its impact on surgical planning is still not well established. Although some studies have tried to demonstrate the utility of 3D printing in surgical planning for DORV patients (20-25), Batteux and al. mentioned the lack of evidence for such benefits due to heterogeneity of studied congenital heart disease and suggested that retrospective comparison of 3D models with standard multimodal imaging should be the first step to perform (25).

Therefore, this study aims to compare retrospectively the added value of 3DVVR and 3DPHM to standard multimodal imaging in the planning of DORV surgical repair.
MATERIAL AND METHODS

Study design

We conducted a retrospective study on 10 pediatric patients with DORV, who underwent surgical repair by a single surgeon in two tertiary hospitals between 2016 and 2019. The study was approved by the institutional review board (authorization 2017-00716, 31.01.2018). The inclusion criteria were DORV Transposition of Great Arteries (TGA)-type that could undergo surgical repair and availability of pre-operative echocardiogram as well as a cardiac MRI or CT. Patients’ data have been de-identified and uploaded in an institutional secured cloud server. Patients were discussed in a multidisciplinary pediatric heart team including two pediatric cardiologists, one cardiac surgeon and one cardiovascular radiologist. The incremental value of 3DVVR and 3DPHM was determined by a 3-steps evaluation process (Figure 1).

Step 1: multimodality imaging

All patients had a complete transthoracic echocardiogram, presented by a pediatric cardiologist (Supplementary Figure 1). 7 patients had MRI and 3 patients had CT, including a volume rendering of the blood pool, presented by the cardiovascular radiologist (Supplementary Figure 2). A first decision about the type of surgical repair was recorded at this point.

Step 2: 3D virtual valvular annuli reconstruction

3DVVR was carried out by segmentation of a model form either CT or MRI images using open-source software 3D Slicer (26). A semi-automated segmentation was completed by manual correction when needed. All four valvular annuli were manually depicted and kept opaque
whereas the blood pool was made semi-transparent. Chordal attachment aberrations and straddling were only analyzed on multimodal imaging (ETT, CT/MRI) and were not represented on 3DVVR nor 3DPHM. Each segment can be selectively faded or hidden, allowing user-defined visualization of the cavities and valves (Figure 2). A second decision about the type of surgical repair was recorded following 3DVVR visualization.

**Step 3: 3D printed heart model**

The process of 3D printing included image segmentation and exporting in STL file format using 3D Slicer, correction of the Standard Tessellation Language (STL) model by MeshMixer (Autodesk, Inc, San Rafael, CA, USA) and 3D printing with a Stratasys Object260 Connex 3 printer (version 29.11.0.19189). The resins used were VeroWhite Plus, VeroBlack and Veromagenta for the valves, and TangoPlus for the cardiac chambers and vessels. A 1:1 scale 3DPHM (Supplementary Figure 3) was presented in three parasagittal slices allowing complete visualization of cardiac chambers and great vessels. A third and final decision was then recorded.

At the end of the simulation, the previous original heart team decision as well as operative records with peroperative findings and performed surgical procedure were revealed. Based on these latter, an institutional retrospective surgical strategy, defined as a composite of the performed procedure and the final simulated heart team decision considering current available expertise, was finally defined as the gold standard and compared to each of the three steps decision.

**Primary and secondary outcomes**
The primary outcome was the proportion of correctly predicted surgical repair strategy following multimodal imaging, 3DVVR and 3DPHM. The secondary outcome was the change of surgical strategy between multimodal imaging step and the two 3D modalities steps (3DVVR and 3DPHM). The incremental benefit of 3DVVR and 3DPHM were then compared separately. We also reported patients outcomes, such as intensive care unit length of stay, hospitalization length of stay, in-hospital survival, reoperation rate, need of permanent pacemaker, and up-to-follow-up survival.

**RESULTS**

Ten patients with DORV operated in our institution between 2015 and 2019 were included in the study. All had DORV TGA-type with anteroposterior (n=7) and side-by-side aortopulmonary positions (n=3). Gender repartition was 6 males and 5 female patients. Mean age of pediatric patients was 4,4 years +- 4,1 years. Mean time between the surgical repair and the study was an average of 19 months. (see Supplementary Tables 1 and 2)

Surgical repair included 3 arterial switch operation, 3 Bex-Nikaidoh procedures, 1 intraventricular repair, 1 outflow tracts rotation, 1 postponed Bex-Nikaidoh after prior pulmonary artery (PA) banding and atroioseptotomy and 1 single ventricle palliation. The retrospective institutional surgical strategies following the 3 steps process resulted in 4 outflow tracts rotation, 3 Bex-Nikaidoh procedures, 2 arterial switch operation and 1 intraventricular repair. There were discrepancies between operative records and simulated heart team final decision for four patients due to temporal evolution of surgical expertise (for p01, single ventricle palliation changed for Bex-Nikaidoh ; for p03, Bex-Nikaidoh changed for outflow...
tracts rotation; for p05, PA banding and atrioseptotomy before Nikaidoh changed for PA banding and atrioseptotomy before outflow tracts rotation; for p10, arterial switch operation changed for outflow tracts rotation).

**Primary outcome: predictive value of multimodal imaging and 3D modalities**

Decisions for each case following the 3-steps simulation are summarized in Figure 6. According to retrospective institutional surgical strategies, the prediction after multimodal imaging concurred for 5 cases (p02, p04, p05, p06, p07 p09). The evaluation of 3DVVR confirmed the prediction of these 6 cases and brought 4 additional correct predictions (p01, p02, p03, p04, p05, p06, p07, p09, p10).

Finally, 3DPHM analysis confirmed those 9 cases and brought 1 additional correct prediction (p08), resulting in correct prediction for all 10 cases.

**Secondary outcomes: optimization of surgical strategy through 3D modalities and patient outcomes**

3D modalities contributed to optimization in surgical strategy for 5 cases. 3DVVR were involved in the modification of 4 cases (p01, p03, p04, p10), and 3DPHM in 1 case (p08).

Concerning 3DVVR modifications, two Bex-Nikaidoh were preferred to outflow tracts rotation (for p01 and p04) due to the better appreciation of pulmonary valve (PV) stenosis by the 3D rendering (Figure 3) (See p05 case description in Supplementary Table 3). In addition, two outflow tracts rotation were preferred to arterial switch operation, due to better evaluation of PV stenosis for p03 and PV dilation for p10 due to the high risk of neoaortic valve insufficiency.
in case of arterial switch operation (Figure 4) (See p10 case description in Supplementary Table 3).

3DPHM contributed to correct the prediction for one patient (p08) (Figure 5). This case was a complex anatomical DORV with a side-by-side aortopulmonary position, a non-committed VSD with inlet extension and an important straddling of the tricuspid valve with a chordal attachment on the left side of the septum. This makes intraventricular repair (LV-to-Ao baffles) impossible. Nikaidoh or outflow tracts rotation were compromised due to complex abnormal coronary pathway. The left coronary artery gave rise to the interventricular artery, the circumflex and the right coronary artery. An abnormal coronary artery with a suprasinusal ostium gave rise to conal and infundibular perforating arteries. This would have led to a high-risk root harvesting with potential coronary damage. Therefore, multimodal imaging advocated single ventricle palliation as the best surgical strategy. 3DVVR suggested a seemingly shorter distance between LV and PA but was not sufficiently convincing for a biventricular repair with arterial switch operation. 3DPHM with its 1:1 scale gave the best appreciation of the actual short LV-to-PA distance for resectability of subpulmonary conus, making arterial switch operation with LV-to-PA (neo-Aorta) baffling feasible. Retrospectively, the original heart team decision was a single ventricle palliation but peroperative findings changed the strategy for an arterial switch operation with LV to PA/neoartic valve baffling. In conclusion, 3DVVR was not convincing enough to support a biventricular repair. Only 3DPHM in this case allowed to foresee intraoperative findings and to correctly anticipate the applied surgical strategy.

The mean intensive care unit length of stay was 9.4 days (+- 7 days). Hospitalization length of stay was 19.8 days (+- 11.6 days). In-hospital survival was 100%. P01 went through a single
ventricle palliation, which means three operations at two years interval. P06 was reoperated at 5 days for a refection of the intraventricular tunnelisation due to residual left to right shunt. 3 days after the reoperation, complete atrioventricular block motivated a bicameral permanent pacemaker implantation. P07 needed a reoperation for tricuspid repair due to complete rupture of a tricuspid chordae at 4 days postop. Only one patient needed a permanent pacemaker after the reoperation. Up-to-follow-up survival could have been evaluated for two patients (p01 and p05), respectively 7 years and 2 years after their operations.
The main result of our study showed that surgical strategy was correctly predicted in 50% (5/10) by multimodal imaging, 90% (9/10) by 3DVVR and 100% by the 3DPHM. Both 3DVVR and 3DPHM improved the definitive surgical strategy prediction.

Our results concurred with current literature. Several studies demonstrate promising results concerning the use of 3D printing in preoperative planning. Valverde et al. (20) reported a multicentric prospective case-crossover study including 10 centers, 80 pediatric cardiologists and 22 surgeons using 3D models of various complex congenital heart disease, comparing the surgical indication using standard multimodality imaging alone, to the same process with 3DPHM, finally confronted to surgical findings. In this study, 3D models were considered helpful in optimizing surgical planning in 19/40 patients (48%). No data was provided on specific anatomical structures or key elements triggering modification of the decision with a wide heterogeneity of included heart defects.

Ryan et al. (21) retrospectively compared a pre-surgical 3DPHM group of 33 pediatric patients with DORV and D-TGA, with the routine imaging group of 113 cases, showing a reduction trend of mean operative time for the 3DPHM group. These results mirror findings from Zhao et al. (22), who compared 8 DORV cases in the 3DPHM group with 17 cases in the control group. 3DPHM group had shorter operative, cardiopulmonary bypass, aortic cross-clamping and mechanical ventilation time than control group. These findings implicitly indicate 3DPHM could play a critical role in enhancing pre-operative planning. However, Lau et al. (27) stressed that both studies did not achieve statistical significance, probably due small sample size, rather than unfavorable outcomes.
Our study entails multiple strengths. Firstly, the capacity of pluridisciplinary pediatric heart
team to orchestrate and manage pre-, per- and post-operative care of those complex cases
allowed 3DPHM evaluation for complex cases planning. Secondly, we focused on DORV
TGA-type exclusively, evaluating a homogenous group of patients. Thirdly, the free and open-
source 3D virtual reconstruction 3D Slicer software, represent a low-cost and effective
segmentation tool allowing easy deployment in clinical workflow.

Interestingly, 3DVVR was the most useful 3D modality for optimization of surgical strategy.
3DVVR incremental value resided in the evaluation of relative size of valvular annuli and their
relation to VSD. TTE offers non-invasive bedside valvulopathy assessment but may lacks
accuracy in measuring valvular dimensions in some patient categories, compared to MRI
(28,29). Nevertheless, MRI does not confer tridimensional intracardiac reconstruction. 3DVVR
conveys a pragmatic solution to this. This modality could also alleviate the cost, time and
availability of 3DPHM. Nevertheless, 3DPHM was particularly helpful to confront 3DVVR
findings at patients 1:1 scale, offering a realistic preoperating view and a better prediction of
postoperative potential outflow tracts obstruction. Hence, the surgeon could consider with more
confidence certain complex surgical strategies, such as outflow tracts rotation. Others 3DPHM
benefits, while not investigated in our study, are currently discussed in the literature (30):
clinical communication, patient’s family discussion and surgical rehearsal or training of
complex cases. New 3D tools are beginning to appear like virtual reality with the potential of
alleviating the need of printed models. Milan et al reported a retrospective study of 10 DORV
with complex VSD types undergoing 3DPHM and virtual reality in the surgical planning.
Multimodal imaging left 25 % of patients with an univentricular repair, which was then reduced
to 15% after 3DPHM evaluation, and only 5% after virtual reality. This latter helped to consider
biventricular repair, the arterial switch operation, for 95% of patients, in accordance with the actual surgical planning. (31)

Lau et al involved 29 practitioners to study the additional benefit of virtual reality and 3DPHM. The study demonstrated no significant differences between both technology but 72% of practitioners support both the additional benefits of virtual reality and 3DPHM compared to multimodal imaging visualization. (32)

Whether virtual reality is able to challenge the need for 3DPHM remains to be investigated in larger clinical trials.

Several limitations of our study were identified. Primary and secondary endpoints could be inherently biased due to the non-measurability of human factors that drive decision making. Important confounders such as evolving experience of the surgeon, the awareness of alternative strategies, personal/institutional bias, preferences of referring provider as well as risk aversion cannot be avoided. The retrospective virtual decision-making approach is not always correlated with real time decision secondary to potential clinical variables regarding a patient at the time of actual surgical planning. The same heart team took care of these cases several years ago, introducing a potential recognition bias in our study. We tried to minimize those biases with a multidisciplinary and consensual approach and a blinded analysis of the cases with an average surgery-to-study meantime of 19 months, but we acknowledge that they could still be present. Even if the choice of surgery strategy has inherently a subjective component, we believed that the present results are still valuable because they emphasized the objective part of our decision supported by imaging and that they could help other centers in their decision making.
Finally, we could not include all DORV patients of our institution due to absence of CT and MRI imaging for the patients operated on the basis of echocardiographic imaging only.

**Clinical studies and future evolution**

3DVVR and 3DPHM demonstrated a great potential to be routinely implemented for surgical planning of DORV patients. As the experience expands, demand for reconstructions and models will increase and its use will be integrated systematically. 3D rendering of the heart represent strong clarifying tools to assess the complexity of intracardiac architecture, to identify critical steps and anticipate anatomical pitfalls, thus bringing strategic and technical solutions for surgical planning of DORV patients. Future prospective studies are needed to quantitatively measure whether 3DPHM implementation reduces operative time, hospital length of stay, as well as morbidity and mortality rate. From there, cost-benefit analysis can be carried out to evaluate the efficiency of 3D modalities in DORV patients surgical planning.
CONCLUSION

Both 3DVVR and 3DPHM improved standard multimodal imaging for surgical strategy planning of complex DORV TGA-type patients according to our practice. 3D modalities contribute to strategy optimization of 5/10 cases. 3DVVR was involved in 4 optimizations and allowed to better appreciate 3D relationships between great vessels, their valves and VSD, which makes it the most useful 3D modality for surgical strategy planning. 3DPHM, contributing to optimize 1 case and correctly predicting all of them, was particularly helpful to assess 3DVVR findings at patient 1:1 scale, improve evaluation of any outflow tracts obstruction, offering a realistic preoperative view. This retrospective study confirmed the added value of 3DVVR and 3DPHM for surgical strategy planning and support future prospective studies to assess their postoperative impact on patient outcome.
REFERENCES


Figures:

Figure 1: Design of our study. 3DVR: 3D virtual reconstruction; 3DPHM: 3D printed heart model; DORV: Double Outlet Right Ventricle; CTA: CT angiogram; MRI: magnetic resonance imaging; TTE: transthoracic echocardiography.

Figure 2: A sequential 3D virtual reconstruction of anatomical segments A) post-segmentation 3D virtual reconstruction B) myocardium is hidden C) RA, LV and RV hidden, to appreciate intervalvular relationship with VSD. Aortic and mitral valves in red, pulmonary and tricuspid in blue, VSD in purple. D) Complete valvular visualization with VSD in purple.

Figure 3: 3D virtual valvular reconstruction and printed model of p04.

Figure 4: 3D virtual valvular reconstruction and printed model of p10.

Figure 5: 3D virtual valvular reconstruction and printed model of p08.

Figure 6: Sequential predicted surgical strategies, compared to original heart team decision, medical records to define retrospective institutional surgical strategy..

3DVR: changes due to 3D reconstruction; 3DPHM: change due to printed models;

ASO: arterial switch operation; IVR: intraventricular repair; OTR: outflow tracts rotation; SVP: single ventricular palliation.
**Supplementary Materials:**

Supplementary Table 1: Patients characteristics at admission

Supplementary Table 2: Description of DORV types and associated findings

Supplementary 3: Case description with 3DVVR and 3DPHM modified DORV cases

Supplementary Figure 1: TTE images: A) D-TGA B) Size discrepancy between aorta and pulmonary trunk C) Large subpulmonary VSD D) VSD with posterior extension E) Doppler of pulmonary trunk

Supplementary Figure 2: MRI acquisition: D-TGA with anteroposterior aortopulmonary position, subpulmonary VSD with posterior extension

Supplementary Figure 3: The model allowed a hands-on anatomical analysis with scale respecting dimensions. On the first image (right), a pseudo-sagital cut of the RV can be appreciated. The black delimited aortic annulus and magenta delimited TV. On the left, VSD is subpulmonary, and the pulmonary stenosis is denoted in black (arrow).
<table>
<thead>
<tr>
<th>Multimodal imaging</th>
<th>3DVR</th>
<th>3DPM</th>
<th>Original heart team decision</th>
<th>Recorded surgery</th>
<th>Institutional retrospective best surgical strategy</th>
<th>Optimization</th>
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<tr>
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11 DORV cases

Pediatric heart team
1 surgeon, 2 pediatric cardiologists, 1 radiologist

1st step
Multimodality imaging
TTE, CTA, MRI

2nd step
Multimodality imaging
+ 3DVR

3rd step
Multimodality imaging
+ 3DVR
+ 3DPHM

1st decision

2nd decision

3rd decision

Institutional retrospective
best surgical strategy
(= recorded surgery after 2018,
composite of recorded surgery
and institutional strategy)