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TITLE:

The use of 3D echocardiography in surgical planning of the mitral valve in pediatric cardiology

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KEYWORDS:

Ultrasound, 3-dimensations, matrix probe, medical imaging, pediatrics, mitral valve, biomedical engineering

SUMMARY:

3D echocardiography of the mitral valve in pediatric cardiology produces full anatomic reconstructions that contribute to improved surgical management. Here, we outline a protocol for 3D acquisition and post-processing of the mitral valve in pediatric cardiology.

ABSTRACT:

Mitral valve disease in pediatric cardiology is complex and can involve a combination of annular, leaflet, chordae tendineae and papillary muscle abnormalities. Transthoracic two-dimensional echocardiography (2DE) remains the primary diagnostic imaging technique utilized in pediatric surgical planning. However, given that the mitral valve is a three-dimensional (3D) structure, the addition of 3D echocardiography (3DE) to better define the mechanisms of stenosis and/or regurgitation is advantageous. Transthoracic 3DE technology has improved with advances in probe technology and ultrasound scanners, producing images with good spatial resolution and adequate temporal resolution. Specifically, the addition of pediatric 3D transducers with higher frequencies and a smaller footprint provides better 3DE imaging in children. Improved efficiency of 3DE acquisition and analysis allow 3D assessment of the mitral valve to be more easily integrated by the sonographer, the cardiologist and the surgeon in mitral valve assessment. This improvement was also made possible by the postprocessing software optimization.

In this method paper, we aim to describe the transthoracic 3DE assessment of the mitral valve in children and its use in the surgical planning of pediatric mitral valve disease. Firstly, the 3DE assessment begins by selecting the correct probe and by obtaining a view of the mitral valve. Then, the appropriate data acquisition method should be selected based on the individual patient. Next, optimization of the data set is critical in order to properly balance spatial and temporal resolution. During live scanning or following acquisition, the data set can be cropped using innovative tools that allow the user to quickly obtain an infinite number of cut planes or

volumetric reconstructions. The cardiologist and surgeon can view the mitral valve en face; thus, accurately reconstructing its morphology in order to support medical or surgical planning. Finally, a review of some clinical applications is proposed, showing examples in pediatric mitral valve managements.

INTRODUCTION:

The mitral valve apparatus is a complex structure consisting of the mitral valve annulus, leaflets, chordae tendineae and left ventricular papillary muscles[1,2]. Pediatric mitral valve disease consists of an extensive range of morphologic abnormalities associated with congenital and acquired heart anomalies[3]. The description of the morphology of mitral valve disease and its underlying mechanisms are key parameters for the surgical planning[4]. This requires the use of accurate diagnostic imaging modalities. Echocardiography is established as one of the primary diagnostic techniques used in pediatric mitral valve disease[5]. Specifically, two-dimensional (2D) echocardiography in pediatric mitral valve disease remains the most widely used diagnostic method. However, due to the nature of 2D imaging, the sonographer, the cardiologist and the surgeon must mentally reconstruct this complex 3D structure to determine the pathological mechanisms.

With the ability to produce anatomically correct views and an infinite number of cut planes, three-dimensional (3D) echocardiography has the ability to enhance mitral valve imaging. The value of 3D echocardiography is shown in its ability to provide specific information about annular shape and dynamics, leaflet scallop prolapse and the zone of leaflet coaptation[6,7]. While 3D transesophageal echocardiography (TEE) has been shown to be the most accurate ultrasound modality in identifying adult mitral valve pathology[8], 3D transthoracic echocardiography (TTE) is more feasible in children due to a better acoustic window. 3D TTE has been proven to be highly accurate in discerning simple vs. complex mitral valve lesions and the need for surgical intervention[9]. Additionally, acquiring a 3D volumetric dataset allows surgeons and cardiologists to collaborate in post-processing, further enhancing surgical planning.

3D TTE technology has continued to improve with advancement in probe technology, ultrasound processing power, and post-processing efficiencies. The current 3D matrix probes can now acquire a full volume single-beat data set at a volume rate of approximately 25 volumes per second[10]. It is possible to further increase the volume rate of a single-beat data set above 25 volumes per second depending on the ultrasound vendor, probe technology and volume optimization. However, if the ECG gated (sub volumes) full volume method is used, this number can more than double, providing volumes rates that are needed in children. The higher heart rates in children compared to adults require higher temporal 3D resolution for diagnostic accuracy. Additionally, the development of specific pediatric 3D probe technology allowed for a higher scanning frequency, providing better spatial resolution that is crucial regarding the small size of the mitral valve and its apparatus[11]. Despite all these technological improvements, the vendors have managed to produce probes with footprints adapted to the anatomy of small children to maintain an optimal acoustic window. Lastly, new post-processing features, such as a quick cropping tools, allow for efficient post-processing.

In this paper, we describe the technique for 3D TTE assessment of the mitral valve in children, which can be applied to any ultrasound system with 3D TTE application. Additionally, post-processing of the 3D data will be reviewed and its benefit in the surgical planning. Finally, we will discuss some clinical applications of 3D imaging in children and include some examples.

PROTOCOL:

This protocol follows the guidelines of our institution's human research ethics committee.

NOTE: For the implementation of this protocol, a General Electric (GE) Vivid E95 or Philips Epiq 7C ultrasound system is used. On the GE Vivid E95 system, the user has a choice between the 4Vc-D (adult probe) or 6Vc-D (pediatric probe). On the Philips Epiq 7C, the user has a choice between the X5-1 (adult probe) or X7-2 (pediatric probe). See **Figure 1**.

1. Patient setup and probe selection

1.1. Position the patient in a left lateral decubitus position when possible. See **Figure 1, step A**.

1.2. Select the appropriate 3D matrix probe, pediatric or adult, based on the patient size and imaging window quality. In the majority of pediatric patients under the age of ten, a high frequency (pediatric) probe can be used when imaging from a parasternal imaging window due to the close proximity of the mitral valve. Over the age of ten, use of a pediatric probe can be attempted, however with excellent image quality on older children, the adult probe is more ideal. See **Figure 1, step B**.

NOTE: If the user only has access to an adult 3D matrix probe, for smaller pediatric patients, increase the scanning frequency for optimal spatial resolution.

2. Probe positioning and 2D image optimization

2.1. Apply a generous amount of gel to the selected 3D matrix probe.

NOTE: The optimal imaging window for 3D mitral assessment is a modified low parasternal long axis view. From this view, the mitral valve apparatus is in close proximity to the probe and the mitral valve leaflets to be relatively perpendicular to the ultrasound beam. In addition, a low parasternal long axis view provides full visualization of the entire mitral valve apparatus. See **Figure 1, step C**.

2.2. To obtain a modified low parasternal long axis view, position the probe on the chest in a standard parasternal long axis echocardiography view.

2.2.1. Slide the probe laterally on the chest until the mitral valve leaflets are more perpendicular to the ultrasound beam and the 2D imaging window is optimal (this position will be between the

standard parasternal window and standard apical window).

NOTE: If the patient does not have an optimal modified low parasternal view, a standard parasternal window and apical window in combination will allow full visualization of the mitral valve anatomy.

2.2.2. Center the mitral valve in the ultrasound sector by rocking the probe. Rocking the probe involves motion in the long axis of the probe along a fixed point while changing the angle of insonation away from 90 degrees. In 3D imaging, center the area of interest in the ultrasound sector to allow for a narrower volume and therefore better temporal resolution.

3. 3D Volume acquisition method

3.1. Begin by activating the **3D** button on the ultrasound console (may also be labelled 4D by some vendors) to enter a full volume display. The full volume display should begin as a real-time full volume.

NOTE: 3D Zoom can also be used to obtain a 3D data set of the mitral valve, however with its limited region of interest, would not be recommended because including surrounding structures can be important for surgical management.

3.2. If the patient is cooperative and able to hold their breath, use ECG gated full volume acquisition (see **Figure 1, step E**). Choose the number of sub volumes (heart beats) to use for the acquisition; on most ultrasound systems the number of sub volumes can be set between 2-6 (see **Figure 1, step H**). The higher number of sub volumes used during acquisition will result in a higher volume rate (increased temporal resolution) but can result in stitch artifacts related to breathing or motion as the sub volumes are put together.

3.3. If the patient is uncooperative or unable to hold their breath, real-time 3D full volume acquisition will eliminate the potential for “stitch” artifacts (see **Figure 1, step F**). However, the reduced temporal resolution is not ideal in children and will require the user to either sacrifice volume size (region of interest) or spatial resolution to compensate (both discussed in the next step).

4. 3D volume optimization (see Figure 1, step G)

4.1. Optimize the full volume size to include all the mitral valve annulus, chordae, papillary muscles and aortic valve where possible.

NOTE: With ECG gated acquisition, a larger volume of data can be acquired because of an increase in volume rate achieved via sub volumes.

4.1.1. A smaller volume of data will be required for real-time acquisition, in order to maintain a reasonable frame rate. Do this by narrowing the elevation plane and imaging in a parasternal

short axis to allow for full visualization of the mitral valve leaflets and annulus (see **Figure 2**).

4.2. Optimize 3D signal-to-noise ratio (quality of the images) by increasing the ultrasound line density when possible. An increase in ultrasound line density will result in a decrease in volume rate. Different vendors have variable terminology for this function. On the GE Vivid E95 ultrasound system, optimize the line density using the **Frame Rate** knob. On the Philips Epiq 7C ultrasound system, optimize the line density using the **Image Quality** touch screen button.

4.2.1. With ECG gated acquisition, increase the 3D volume line density because the use of sub volumes will maintain a good volume rate.

4.2.2. With real time acquisition, balance the 3D volume line density with an acceptable volume rate for the patient's heart rate.

4.3. Set the 3D gain settings higher than 2D gain settings to minimize drop-out in the mitral valve leaflets. Gain can be decreased during post-processing to further optimize the cropped image if needed.

5. Storing the 3D full volume acquisition (see Figure 1, step I)

5.1. If using ECG gated acquisition, ask the patient to hold their breath and remain still. Then activate the number of sub volumes (heart beats) selected. Wait at least the number of beats selected before pressing **Store** (the more sub volumes that are selected will result in a longer storing process)

5.1.1. Ensure there are no "stitch" artifacts present and the entire mitral valve is visible in the 3D volume before storing the final volume.

5.2. If using real time acquisition, store the final volume once all optimization is complete.

6. 3D color Doppler acquisition

6.1. Separately obtain a color Doppler 3D volume acquisition by adding color Doppler and following steps 3-5 of the protocol. Optimize the color Doppler box size as narrow as possible while including the entire mitral valve annulus. Set the color Doppler velocity scale between 60-80 cm/s.

6.2. Use ECG gated acquisition to maintain an adequate volume rate. Follow step 5.1 to store the 3D color Doppler volume.

NOTE: The addition of color Doppler to a 3D volume significantly reduces temporal resolution, making its feasibility in children difficult.

7. Post processing and cropping of the mitral valve

NOTE: Post processing and cropping of the mitral valve can be performed directly on the ultrasound system for immediate results. However, there is also dedicated GE software (EchoPAC) and Philips software (QLAB) that provide the same functions from a reviewing station. In addition, TomTec provides a universal software for post processing and cropping 3D datasets from both vendors.

7.1. Load the stored 3D volume of the mitral valve in a 3-panel multi-planar display (2D lateral plane, 2D elevation plane, and 3D reconstruction) and activate the quick cropping tool. The quick cropping tool requires two clicks and allows the user to crop in any plane.

NOTE: Different vendors will have variable terminology for the quick cropping tool. On the GE Vivid E95 ultrasound system, this cropping tool is labelled “2 Click Crop”. On the Philips Epiq 7C ultrasound system, this cropping tool is labelled “Quick Vue”.

7.2. To obtain an en face view of the mitral valve viewing from the left atrium (Surgeon’s view) follow the below steps (see **Figure 3, step E**).

7.2.1. Working from the 2D lateral plane (low parasternal long axis in this protocol), position the first curser within the left atrium, just above the mitral annulus. After the first position is set, drag the curser across the mitral valve towards the ventricular side and align the crop line parallel to the mitral valve annulus. Position the second curser within the left ventricle, ensuring the mitral valve leaflets are captured within your crop lines, and set this point (see **Figure 3 step B**).

7.2.2. The recommended display orientation for the mitral valve en face is anterior up[12]. Using the trackball, rotate the 3D mitral valve to position the aortic valve at the top of the screen.

7.3. To obtain an en face view of the mitral valve viewing from the left ventricle, simply flip the previous step cropped image 180 degrees (on some vendor systems there is a flip crop function that accomplishes this quickly) (see **Figure 3, step F**).

7.3.1. Crop the color Doppler 3D volume of the mitral valve in the same orientation as step 7.3.

7.4. Obtain a view of the mitral valve sub-valvar apparatus including the chordae tendineae and papillary muscles.

7.4.1. Working from the 2D lateral plane (low parasternal long axis in this protocol), position the first curser in the middle of the left ventricle. After the first position is set, drag the curser towards the posterior wall of the left ventricle and align the crop lines parallel with the long axis of the left ventricle. Position the second curser below the posterior wall and set this point (see **Figure 4**).

7.5. Optimize the 3D gain and compression settings.

7.5.1. Optimize the 3D gain settings to its lowest setting while maintaining minimal to no mitral valve leaflet drop-out.

7.5.2. Optimize 3D compression settings to include a wider or narrower range of color shades. 3D compression can improve 3D depth perception. On the Philips Epiq 7 system, adjusting the 3D compression is performed by rotating the **Compression** knob. On the GE Vivid E95 system, adjusting the 3D compression is performed by rotating the **Active Mode** gain knob.

7.6. Store the optimized, cropped 3D views of the mitral valve as separate cine loop clips.

REPRESENTATIVE RESULTS:

A good quality 3D data set of the mitral valve in pediatric echocardiography will have an optimal volume rate that is appropriate for assessing leaflet motion and excellent spatial resolution that utilizes superior axial resolution. To assess the success of the protocols 3D ECG gated acquisition, first determine whether any significant "stitch" artifact is present. In the presence of no artifact and if the acquisition was made using an excellent quality 2D low parasternal long-axis view, this 3D data set will provide diagnostic information about the entire mitral valve complex.

If ECG gated full volume cannot be used due to a significant "stitch" artifact caused by patient breathing and/or movement, real time 3D should be used. While this method will likely not provide one single volume of the entire mitral valve complex, utilizing a real time 3D acquisition with a narrow volume (in the elevation plane) will allow for better temporal resolution. With real time 3D acquisition, imaging of the mitral valve annulus and leaflets will be best visualized from a parasternal short axis window. While imaging of the mitral valve chordae tendineae and papillary muscles will be best visualized from an apical two chamber view **(see Figure 5, case 1C**).

Color Doppler, when added to a 3D full volume acquisition of the mitral valve, can enhance the assessment of mitral regurgitation. When viewed from the left ventricle, 3D color Doppler provides diagnostic information about mitral regurgitation location and vena contracta area (see **Figure 3**). However, it is worth noting that the addition of color Doppler significantly reduces temporal resolution, making its feasibility in children difficult.

Post-processing of 3D echocardiography data sets with the ability to obtain an infinite number of cut planes and anatomically accurate reconstructions provides one of the greatest benefits this method has in comparison to 2D echocardiography[13]. By producing en face 3D views of the mitral valve, the assessment of mitral regurgitation can be enhanced with true anatomic visualization of prolapsing/flail scallops, isolated clefts and zones of non-coaptation (see **Figure 3**). Additionally, there is available post-processing software that can quantify leaflet diameter, leaflet area, coaptation length and leaflet tenting height[14], all of which is not provided with standard 2D imaging. In the assessment of mitral stenosis, 3D echocardiography can provide direct planimetry of the mitral valve orifice area[13]. This method is more accurate than 2D echocardiography by allowing the user to obtain cut planes that identify the smallest orifice area. In addition, direct planimetry of a 3D data set is possible without the use of dedicated 3D software. Also, post-processing of the 3D data set in mitral valve stenosis, allows visualization of

the sub-valvar apparatus for accurate morphology and measurements of chordae tendineae length. With the continued evolution of efficient post-processing techniques, the ability to obtain accurate 3D reconstructions now requires a minimal time commitment.

Figure 1. 3D Mitral Valve acquisition protocol

(**A**) Patient positioned in left lateral decubitus position. (**B**) Select the correct probe and scan at the highest frequency possible. (**C**) Choose the best 2D echocardiography window, with the low parasternal long axis considered most ideal. (**D**) Determine whether the patient can hold their breath and remain still. (**E**) If yes, choose the ECG gated full volume acquisition. (**F**) If no, choose the real time 3D acquisition. (**G**) For both methods, adjust volume size, line density and gain to optimize temporal and spatial resolution. (**H**) For ECG gated acquisition, choose the number of sub volumes and ask patient to breath hold and remain still. (**I**) Acquire volume.

Figure 2. Real-time 3D acquisition parasternal short axis

Real-time 3D acquisition parasternal short axis. Beginning in a parasternal short-axis view of the mitral valve (**A**), activating real-time 3D will display the elevation plane (**B**) and the 3D rendered view (**C**). Narrowing the elevation plane (**D**) is important to achieve optimal resolution for a real-time acquisition.

Figure 3. Post-processing workflow

(**A**) Begin with a multiplanar display. (**B**) Activate quick crop function and position first point within the left atrium above the mitral annulus. Drag cursor across the mitral valve and align crop lines perpendicular to mitral annulus. Position second point within the left ventricle to set depth of reconstruction. (**C**) Orthogonal 2D plane showing mitral valve in short axis. (**D**) 3D reconstruction showing en face view of the mitral valve from the left atrial perspective. (**E**) Rotate image around the z axis to position anterior up (aorta at top of image). (**F**) Flip image 180 degrees around the y axis to visualize the mitral valve en face from the ventricular perspective. (**G**) Gain settings too low. (**H**) Gain settings too high. (**I**) Gain settings optimal.

Figure 4. Mitral valve sub-valvar apparatus workflow

Mitral valve sub-valvar apparatus workflow. Using a 3D volume acquisition of the mitral valve from a low parasternal imaging window, activate the quick cropping tool. Position the first curser in the center of the left ventricle (**A**), drag the cropping line towards the posterior wall (**B**) and set the second curser posterior to the left ventricle (**C**). The 3D rendered view on the right shows the postero-medial mitral attachments (**D**) and antero-lateral mitral attachments (**E**).

Figure 5. Mitral valve 3D cases

Mitral valve 3D Cases. Case 1 showing mitral valve anterior leaflet prolapse (A) with central mitral regurgitation (B) cropped from an ECG gated dataset acquired from a low parasternal long axis imaging window. (C) A real time 3D acquisition from an apical 2 chamber view showing short posterior leaflet chordae restricting motion. Case 2 showing three left ventricular papillary muscles (D) with the mitral valve chordae attachments (E) cropped from an ECG gated dataset acquired from a low parasternal long axis imaging window. Case 3 showing prolapse of the A3 and P3 scallops (F) and corresponding mitral regurgitation (G) cropped from an ECG gated dataset

acquired from a low parasternal long axis imaging window.

DISCUSSION:

For the operator/sonographer, 3D echocardiography is often met with several challenges. First, by nature there is significant variation in patient size, heart rate and cooperation during a pediatric echocardiography exam. These parameters make it difficult to have 3D specific protocols and therefore make the 3D acquisition operator dependent. Often training for sonographers is focused primarily on 2D imaging, leaving a gap in knowledge with regards to 3D image acquisition and interpretation. In addition, 3D temporal resolution is reduced when compared to 2D imaging, and the inability in some children to use ECG gated (sub volumes) acquisition, to increase volume rate, make this modality a challenge. In children with high heart rates, maintaining a high temporal resolution is critical to appreciate real time movement of the mitral valve leaflets. Another challenge associated with 3D imaging in children is access to a high frequency pediatric probe (for an optimal spatial resolution). While present adult 3D probes have a wide frequency bandwidth, their footprint and lower frequency is often not well suited for small children.

The use of one ultrasound probe for both the 2D and 3D assessment can add significant efficiencies to the 3D assessment process in children. New 3D ultrasound probes offer excellent 2D images, color Doppler and 3D volume quality. The ability to quickly capture a 3D volume at any point during the exam is particularly important in children. Secondly, for the operator, it is important to understand, through continuous training, what constitutes a good quality 3D acquisition. Additionally, to optimize the 3D assessment in children, before the acquisition the operator should determine what 3D information is important for the patient in order to guide the assessment process. For the reviewing cardiologist and surgeon, having direct access to post processing software will allow them to produce 3D reconstructions that will aid in surgical planning.

The quality of a 3D data set depends greatly on the quality of the 2D image. Thus, careful consideration should be paid to optimizing the 2D image of the mitral valve. Beginning in the most optimal 2D window available for each individual patient, parasternal or apical, will result in the best 3D image[14]. However, when possible, 3D TTE of the mitral valve from a parasternal long axis window will demonstrate most anomalies best[15]. As stated in the protocol, a small movement of the probe to a low parasternal long axis window will result in less leaflet drop out and consequently a better 3D image of the mitral valve. It is worth noting that when 2D image quality is technically difficult, the 3D acquisition will not produce clinically useful data.

Inherently, mitral valve assessment by 2D echocardiography requires multiple images and geometric conventions. Instead, 3D echocardiography provides any number of 2D slices and anatomically accurate 3D reconstructions of the mitral valve in one volumetric acquisition. Generally, the mitral valve by echocardiography is images with good acoustic quality, making this valve well suited for 3D assessment. Additionally, 3D imaging is no longer time consuming with improvements in acquisition methods and post-processing techniques. As mentioned in the protocol, an en face view of the mitral valve from the perspective of the left atrium (surgeon's

view) can be easily interpreted by surgeons. The addition of 3D echocardiography preoperatively allows for immediate review in the operating room with the surgeon. This provides an opportunity for the cardiologist and surgeon to agree on a clear mechanism and therefore improve surgical planning. Specifically in congenital heart disease, the ability to visualize the function of the mitral valve relative to its surrounding structures is a strong advantage of 3D echocardiography[16]. The need for 3D assessment of the mitral valve extends beyond the valve itself. This diagnostic modality has been shown to provide more accurate and reproducible left ventricular (LV) volumes[17] and left atrial (LA) volumes[18] that correlate better with cardiac magnetic resonance (CMR). Assessing LV and LA volumes accurately are important for mitral valve surgical planning as they are used in determining hemodynamic significance.

There remain many current limitations to 3D echocardiography, particularly 3D echocardiography in pediatric congenital heart disease. To apply 3D imaging in congenital mitral valve disease requires both a high level of anatomical understanding and 3D imaging proficiency. Furthermore with current technology, small children pose a significant challenge to 3D echocardiography with regards to their inability to cooperate with breath holding and their size. Also, there remain temporal resolution challenges with real time 3D imaging and children due to their higher heart rates. Continued improvements in real time 3D echocardiography technology will further emphasize its importance in pediatric cardiology.

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DISCLOSURES:
No conflict of interest

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Figure 1

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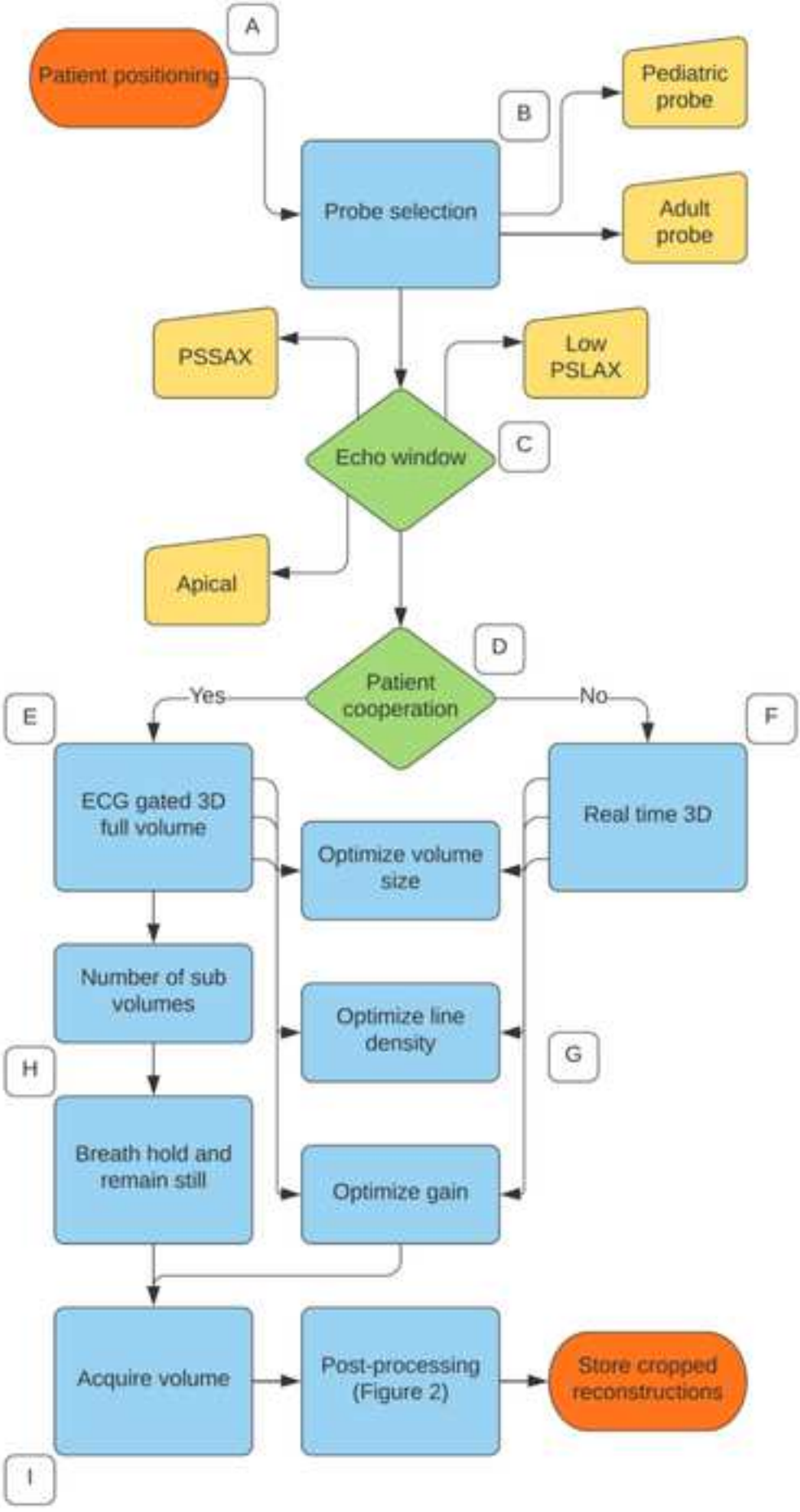

Figure 2

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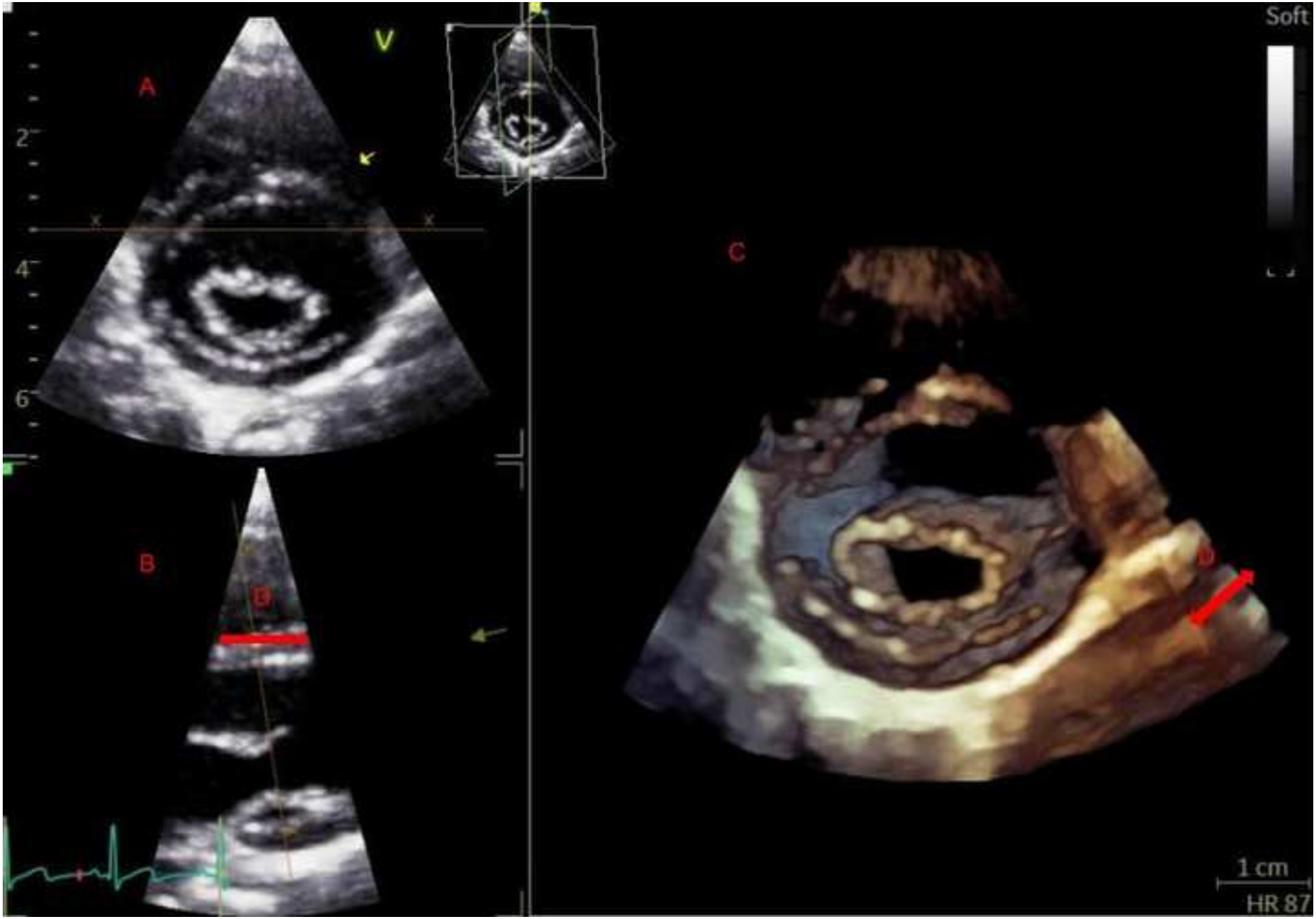

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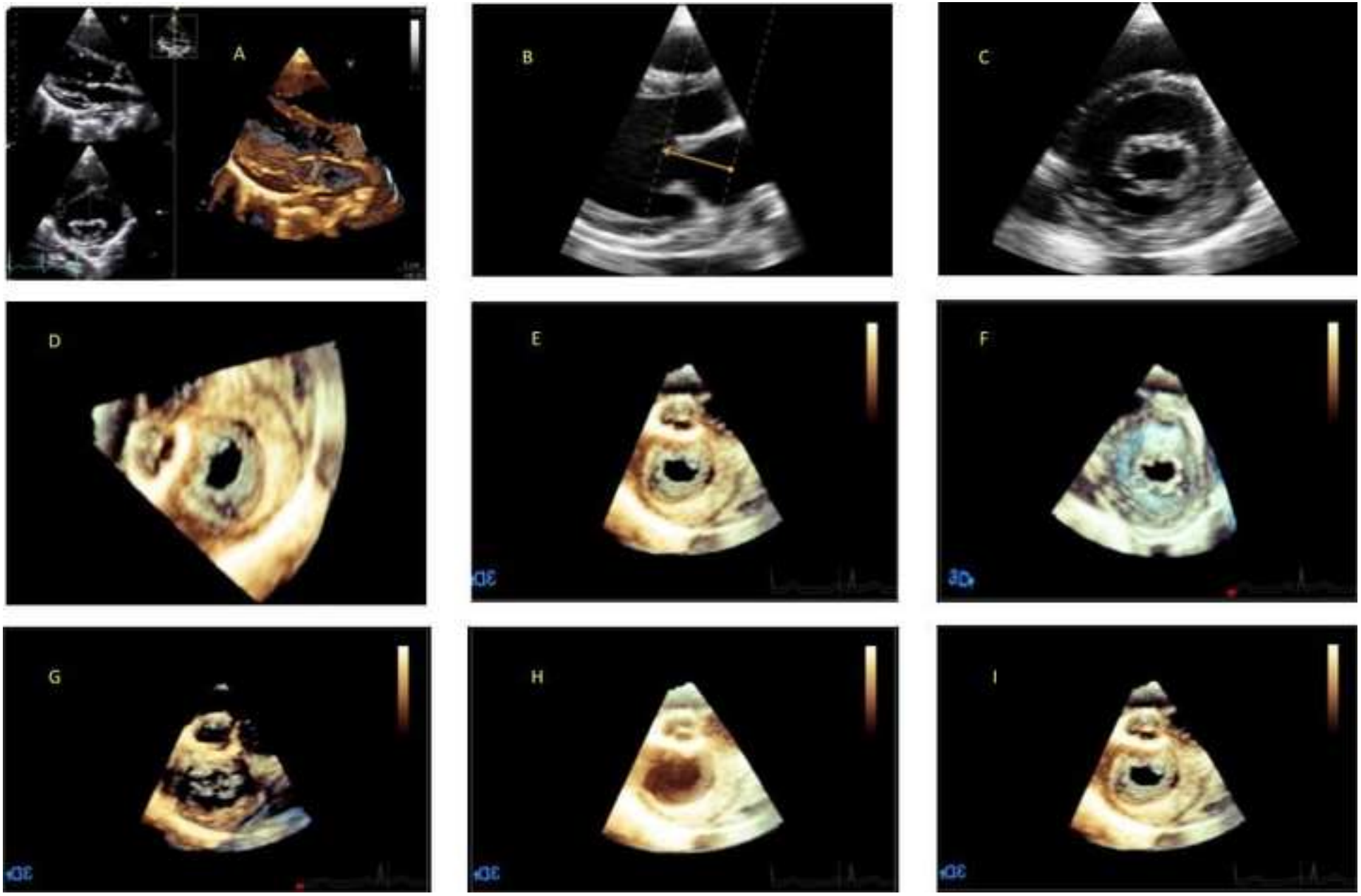

Figure 4

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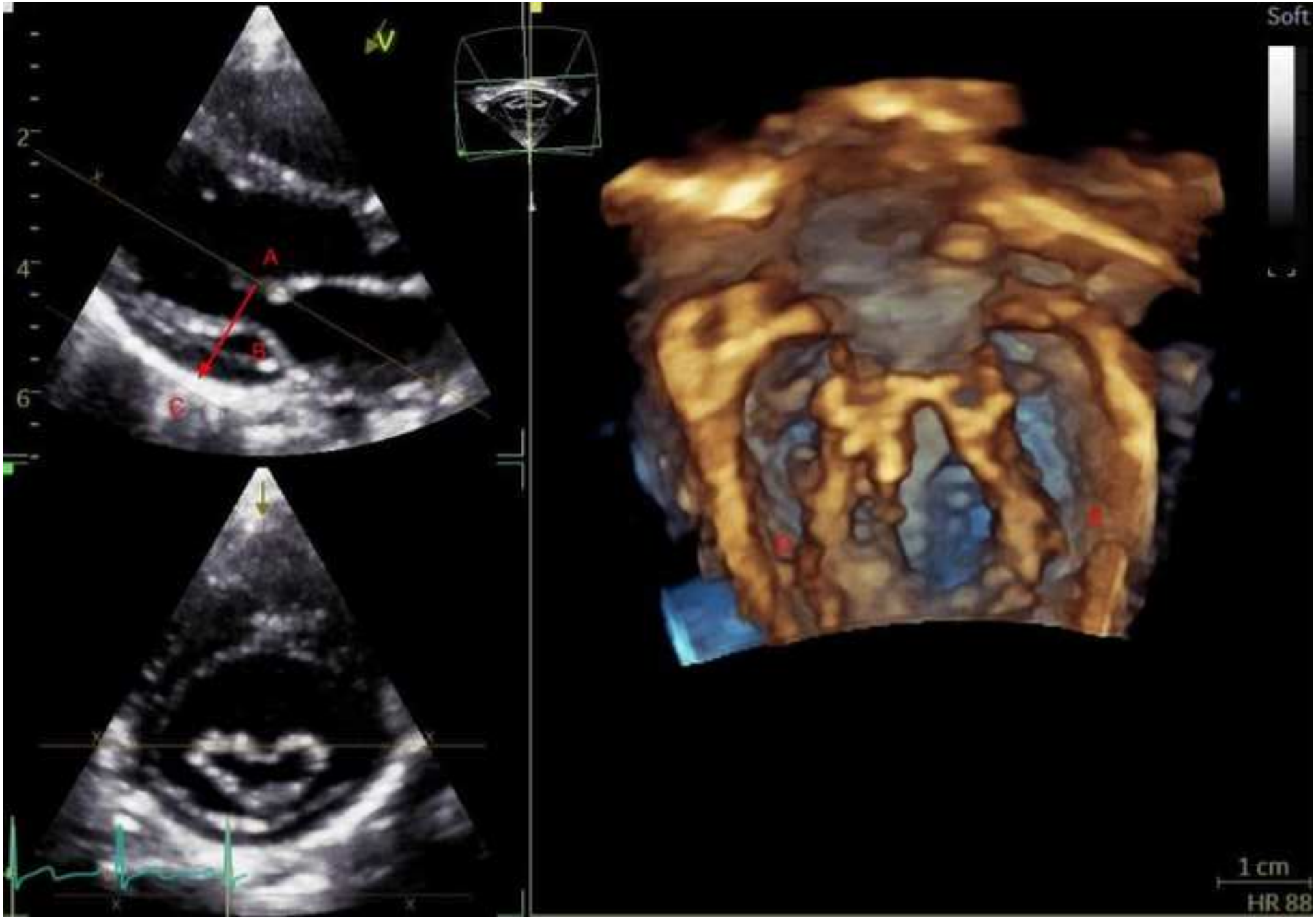

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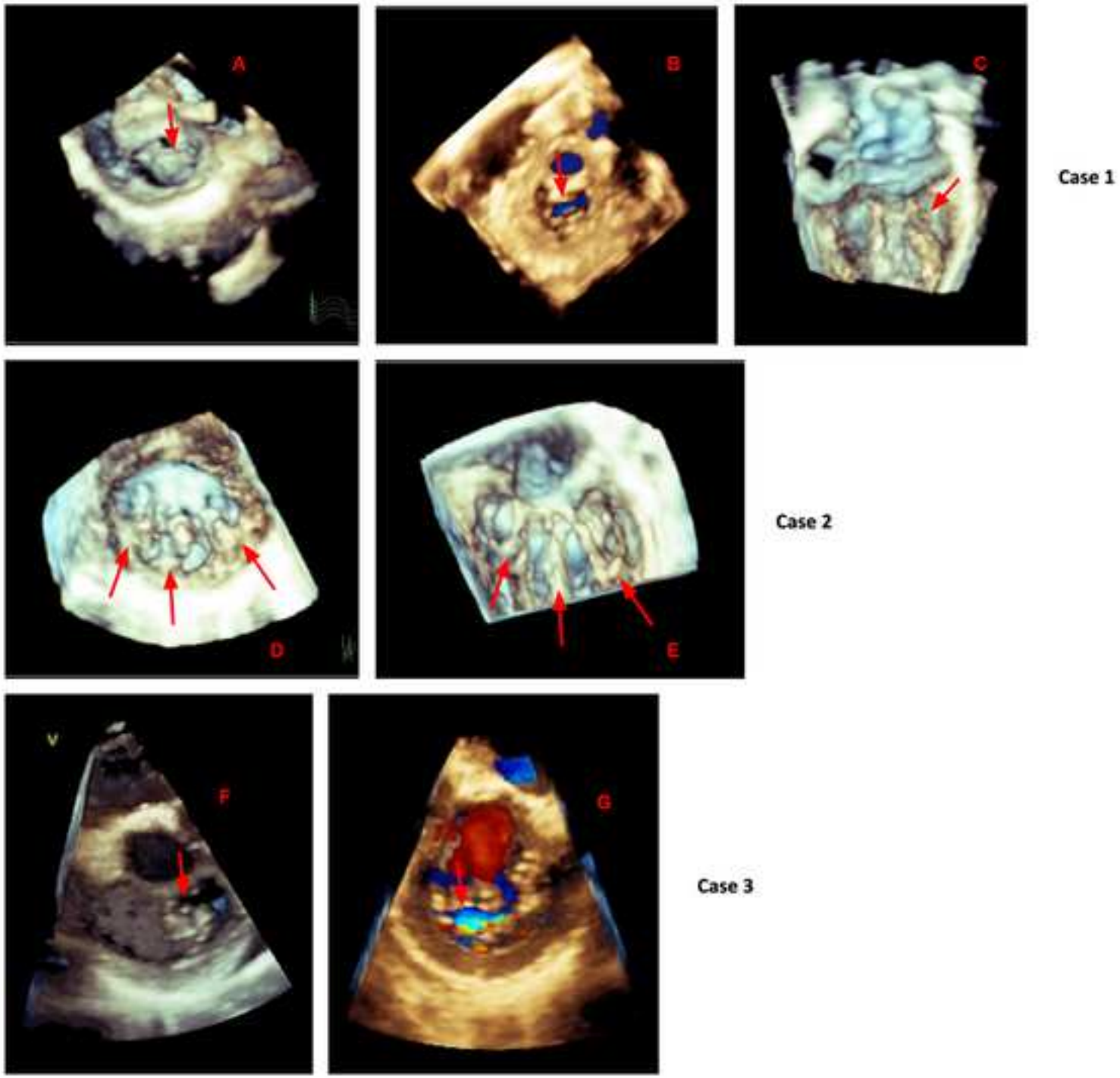

Name of Material/Equipment	Company	Catalog Number	Comments/Description
4Vc-D probe	General Electric		Ultraspound probe (GE)
6Vc-D probe	General Electric		Ultraspound probe (GE)
Epiq 7C	Philips		Ultrasound system
Vivid E95	General Electric		Ultrasound system
X5-1	Philips		Ultraspound probe (Philips)
X7-2	Philips		Ultraspound probe (Philips)

Answer to the reviewers:

Editorial and production comments:
Changes to be made by the Author(s) regarding the written manuscript:
1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.
Done.

2. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution's human research ethics committee.
Done. We added (line 104) :
This protocol follows the guidelines of our institution's human research ethics committee.

3. Please provide all experimental parameters and values used.
Done.

4. Are there any inclusion/exclusion criteria?
No.

5. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible.
Done.

6. For all computational steps, please provide all user input commands: button clicks or terminal commands, etc.
Not applicable.

7. Please remove the subheaders in the discussion.
Done

Reviewer #1:
I really enjoyed reading this article which described the rationale for, and provided a step-by-step approach to, imaging the pediatric mitral valve -- with a particular focus on features of interest for surgical repair. The manuscript is clear and well-written. It is of value to the community of pediatric imagers.
We thank the reviewer for these positive comments and we are glad he likes the manuscript.

A few comments:

1. Would it be possible to add a diagram or schematic describing the same techniques, applied to TEE view? That would be enormously helpful as it is just as common for the imager to obtain these views in the OR (if not moreso).
We are not doing 3D TEE in our centre. We are doing 2D TEE in pre-op to help the surgeon for the decision if needed. Therefore, we can't add a 3D TEE part in our article.

2. Could the authors be more specific about choice of pediatric 3d probe? Their assertion that the x7 probe can be used 'in the majority of pediatric patients' seems unlikely, given the excellent quality that the x5 can afford in the larger size child (Philips platform).

We have added the following statements to be more specific about probe selection with regards to age. However given that probe selection is patient dependent, being any more specific is not possible.
Part 1.2. (page 3) : In the majority of pediatric patients under the age of ten, […]. Over the age of ten, use of a pediatric probe can be attempted, however with excellent image quality on older children, the adult probe is more ideal (see figure 1, step B).

3. Do the authors recommend on-screen labeling of anatomic structures? If so, in what situations? In our laboratory we have found this helpful on occasion.
Yes we agree, sometimes labeling is used for complex non standard 3D image rederings such as in double out right ventricle. For the mitral valve, we do not do on-screen labelling.

4. For clarity of reading, It would be helpful if the protocol (beginning on line 133) referred directly to workflow described in Figure (1).
We added figure 1 references within the protocol to improve clarity of reading.

5. Minor point: in protocol section 7.3, should the word 'rotate' be replaced by 'flip'? Rotate makes one think of the Z axis.
We agree and have made the change.

6. 7.5.2 - please describe how to do this on the 2 platforms that are included.
We have added the following statements to 7.5.2.
On the Philips Epiq 7 system, adjusting the 3D compression is performed by rotating the "Compression" knob. On the GE Vivid E95 system, adjusting the 3D compression is performed by rotating the "Active Mode" gain knob.

Reviewer #2:
Thank you for submitting this intersting article to JoVE. I was pleased to receive it as a reviewer.

Manuscript Summary:
This method paper describes the techniques o for the acquisition, data processing and analysis of 3D data sets of the mitral valve with the aim of using these 3D data sets for the surgical planning of paediatric mitral valve disease. The article is well written and concise.

Major Concerns:
1. The aim of this method paper is to provide guidance for examiners who have not previously routinely performed mitral valve assessment by 3D echocardiography. While the aquisition of 3D data sets is very well and precise discribed, the part of the paper on data post-processing and data evaluation is too vague and not comprehensible even for a trained investigator. A more precise description of the post-processing and its illustration by correspondent figures is absolutely necessary here to provide sufficient information, so that a less experienced examiner can understand and independently perform the steps for data processing and imaging of the mitral valve.
We agreed and the figure 3 (former figure 2) has been re-adjusted to describe more clearly the post-processing worklow.
Details: The following technical details should be expanded and clarified to ensure that readers understand exactly the approach of the authors:
Line 213ff: please introduce the technical term "levation plane" and show an example. It would be nice to have an example which was aquired from the short axis view with data-postprocessing (cropping) and the resulting view of the MV.

We have added a new figure, Figure 2, which is acquired using a parasternal short axis image and displays the resulting 3D view of the mitral valve. At our center we use the term elevation plane which has also been included in the new figure.

Line 250: I am not sure if I am reading the sentence correctly - After storing the 3D data set, colour Doppler can be added .... I presume the authors want to do an additional colour Doppler 3D data set. Literally, however, this means to me that colour can be added retrospectively to the 3D dataset.
We agreee and have added the following statement to clarify this point.
A colour Doppler 3D volume aqusition can be separately obtained by adding colour Doppler and following steps 3-5 of the protocol.

Line 270: Please provide a multiplanar view or refer to a paper with multiplanar view.Please provide examples for the cropping.
We have added the multiplanar view to current Figure 3 (former Figure 2) to improve workflow as we agree this is the usual starting view.

Line 300/7.4.1. please provide corresponding figure a. typical figure for data aquisition, b. position of the cursors and setting of the points. This image is missing, in the text it is mentioned: SHOW A FIGURE FOR THIS.
We have included a new figure, Figure 4.

Line 329: please provide a typical image with a 3D dataset rendered from the parasternal short axis
We have included a new figure, Figure 2 which is a standard 3D dataset rendered from the parasternal short axis.

332: please refer to the images from the apical two chamber view. Regarding figure 3, was the aquisition of all images done frome the apical 2CV?
In figure 3 the aquisition window of the images and their orientation should be provided in the legend.
We agree and have added the imaging window and mode of acquisition to the legend in the current Figure 5 (former Figure 3).
Legend: Mitral valve 3D Cases. Case 1 showing mitral valve anterior leaflet prolapse (A) with central mitral regurgitation (B) cropped from an ECG gated dataset acquired from a low parasternal long axis imaging window. A real time 3D acquisition from an apical 2 chamber view showing short posterior leaflet chordae (C) restricting motion. Case 2 showing three left ventricular papillary muscles (D) with the mitral valve chordae attachments (E) cropped from an ECG gated dataset acquired from a low parasternal long axis imaging window. Case 3 showing prolapse of the A3 and P3 scallops (F) and corresponding mitral regurgitation (G) cropped from an ECG gated dataset acquired from a low parasternal long axis imaging window.

2. The figures are not self-explanatory, the legends are too short and not clear, the presentation of the images and the link within the text are not precise. It is difficult to follow the link between text and figures and vice versa.
See below our multiples comments and modifications. Legends have been adapted.

Figure 2: A: Obviously images 2A and 2B are images from the cropping view. This is difficult to understand for those who are not familiar with the cropping view. Propably a screenshot of the full cropping view including all planes will be helpful.
We have added the initial multiplanar view to current Figure 3 (former Figure 2)

Line 286 - please refer to the correct figure (2D)
We have added the proper figure reference

To obtain an en face view of the mitral valve viewing from the left atrium (Surgeons view) follow the below step. (see Figure 3, step E)

Line 292 please refer to the corresponding figure (2E)
We have added the proper figure reference
To obtain an en face view of the mitral valve viewing from the left ventricle, simply flip the previous step cropped image 180 degrees (on some vendor systems there is a flip crop function that accomplishes this quickly). (see Figure 3, step F)

Line 294 please refer to the corresponding figure
We have added the proper figure reference
Working from the 2D lateral plane (low parasternal long axis in this protocol), position the first curser in the middle of the left ventricle. After the first position is set, drag the curser towards the posterior wall of the left ventricle and align the crop lines parallel with the long axis of the left ventricle. Position the second curser below the posterior wall and set this point. (see Figure 4).

Line 337 please refer to the image of the corresponding figure (case 3 in figure 3)
We have added the reference image to the figure reference.
While imaging of the mitral valve chordae tendineae and papillary muscles will be best visualized from an apical two chamber view (see Figure 5, case 1C).

3. As a result, it may be difficult to reproduce the results of the study with the instructions given by the authors.
Thanks for the comments and we think the new presentation of data acquisitions and post-processing is clearer.

Minor Concerns:
The literature contains older papers which do not represent state of the art technology and current soft- and hardware used for data aquistion and data postprocessing. Using different software has a relevant impact on quantitative data. Results obtained from software used more than 10 years ago may not reflect the results obtained from up-to data equipment.
Line 263: please add to GE, Philips and TomTec the information about the version which allows to do the cropping etc. and where the head office is located.
Done. We added :
However, there is also dedicated GE software (EchoPAC, GE Healthcare, Milwaukee, WI, USA) and Philips software (QLAB, Philips Medical System, Bothell, Washington, USA) that provide the same functions from a reviewing station. In addition, TomTtec (TomTec Imaging Systems, Munich, Germany) provides a universal software for post processing and cropping 3D datasets from both vendors.

Line 116: The volume rate of full volume single-beat data sets can exceed the number of 25 volumes/s. I would suggest to use a range (from - to). This may depend on the probe and the vendor.
We agree that the volume rate of full volume single-beat data sets can vary and exceed 25 volumes/s. We are not aware of an acceptable volume/s range for this method. We have added a statement regarding impact vendor, probe and optimization can have on volume rate.
It is possible to further increase the volume rate of a single-beat data set above 25 volumes per second depending on the ultrasound vendor, probe technology and volume optimization.

Line 334: short comment about the pros and cons of this software in paediatric cardiology?

We would prefer not to add as « pros and cons » as we do not want to specify particular software. We prefer to remain neutral and present only the use of these softwares.
Line 348: I would suggest to add, that planimetry is possible without a dedicated software for AV-valves.
This is a very good point, a statement has been added, please see below.
In addition, direct planimetry of a 3D data set is possible without the use of dedicated 3D software.

Further suggestions:
The authors may discuss the added value of the 3D examination in comparison to the 2D examination and how it influenced the therapy planning using a concrete case.
We have already discussed this comparison between 2D/3D in our Discussion. However, we would prefer to stay on the technical comparaison than the application. This is the spirit of our Methodological paper.

Differences in the procedure for different patient sizes (newborns/infants, toddlers, schoolchildren, adolescents/adults) should be explained.
These differences are extremely « operator experience » related. In order to avoid confusion and inaccurate messages, we prefer to stay with the pure technical description of the 3D TTE.

Limitations: The article suggests that in any case, with a good 3D dataset, valve pathology can be completely visualised. In practice, however, it is often the case that the overview and localisation of the pathology can be taken from the 3D dataset, but the mechanism becomes much clearer in a very high-resolution 2D-loop (or even 2D-sweep). (e.g. mitral valve prolapse in infant/toddler -> 3D data set -> segmental assignment (e.g. segment A2) -> 2D-echo/colour Doppler -> visualisation of the elongated tendon filaments (would probably not be visible in this example in the 3D-dataset because the filaments are much too fine). Perhaps one or two sentences about the necessity to add 2D data for a complete evaluation mitral valve disease should be added.
As said above, we do think that it is very « operator dependant ». We do not think it is correct and reproducible to say that 2D is better than 3D for this or that situation. The use of both imaging techniques is recommended in the recent ACC/AHA guidelines. Each technique can be useful as long as the methodology of use is optimal. We hope that our paper serves this purpose.
We do not want to compare 2D and 3D for specific applications. This would be the topic of a separate article.

Thank you for this interesting paper and thanks again for submitting it.