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Morphological and functional assessment of the right ventricle using 3D echocardiography

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TITLE:

Morphological and Functional Assessment of the Right Ventricle Using 3D Echocardiography

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KEYWORDS:
3D echocardiography, right ventricle, echocardiography, ultrasound, cardiology, imaging, cardiovascular

SUMMARY:
Here, we provide a step-by-step acquisition and analysis protocol for the 3D volumetric assessment of the right ventricle, mainly focusing on the practical aspects that maximize the feasibility of this technique.

ABSTRACT:
Traditionally, it was believed that the right side of the heart has a minor role in circulation; however, more and more data suggest that right ventricular (RV) function has strong diagnostic and prognostic power in various cardiovascular disorders. Due to its complex morphology and function, assessment of the RV by conventional two-dimensional echocardiography is limited: the everyday clinical practice usually relies on simple linear dimensions and functional measures. Three-dimensional (3D) echocardiography overcame these limitations by providing volumetric quantification of the RV free of geometrical assumptions. Here, we offer a step-by-step guide to obtain and analyze 3D echocardiographic data of the RV using the leading commercially available software. We will quantify 3D RV volumes and ejection fraction. Several technical aspects may help to improve the quality of RV acquisition and analysis as well, which we present in a practical manner. We review the current opportunities and the limiting factors of this method and also highlight the potential applications of 3D RV assessment in current clinical practice.

INTRODUCTION:

Echocardiography came a long way from its first clinical applications in the 1950s[1]. The first one-dimensional ultrasound probes were designed to provide simple linear diameters of the chamber walls and lumens; however, they undoubtedly represent a milestone in cardiovascular imaging. The development of two-dimensional (2D) ultrasound imaging was another major step by providing much more precise quantification of morphology and function and is still considered to be the standard method in everyday clinical practice. Nevertheless, 2D echocardiography-based assessment still carries a major limitation of the technique: imaging of a given chamber from a few tomographic planes does not adequately characterize the morphology and function of a three-dimensional (3D) structure. This problem is even more pronounced in the case of the right ventricle (RV): compared to the relatively simple bullet-shaped left ventricle (LV), the RV has a complex geometry[2] that cannot be adequately quantified using linear diameters or areas[3]. Despite these widely known facts, RV morphology and function are usually measured by such simple parameters in the clinical practice.

For many decades, the RV was considered to have a much less important role in circulation compared to its left counterpart. Several landmark papers defeated this standpoint showing the strong prognostic role of RV geometry and function in a wide variety of diseases[4-7]. Numerous studies demonstrated the incremental value of RV measurement even by using relatively simple conventional parameters, which highlights the importance and need for more precise quantification of the chamber with potentially meaningful clinical value.

3D echocardiography overcomes several limitations of the 2D assessment of the cardiac chambers. While the measurement of volumes and also functional parameters free of geometrical assumptions may be of high interest in the case of the LV as well, it may gain particular importance in the assessment of the RV[8]. 3D-derived RV volumes and ejection fraction (EF) are shown to have significant prognostic value in various cardiovascular conditions[9,10].

Nowadays, several vendors provide semi-automated solutions for 3D RV assessment with validated results against gold standard cardiac magnetic resonance (MR) measurements[11,12]. The technical requirements of 3D assessment are essential parts of a state-of-the-art cardiovascular imaging department nowadays, and it is expected that it will soon be part of the general equipment in every echocardiography lab. With proper expertise in 3D acquisition and post-processing, 3D RV analysis can be easily implemented into the standard examination protocol.

PROTOCOL:

The protocol follows the guidelines of the institution’s human research ethics committee and the patients of the clinical cases gave their written informed consent to the study.

1. Technical requirements

1.1. For 3D acquisition and analysis, use appropriate software and hardware. Use ECG cables of the echocardiography device; moreover, it is mandatory for the complete 3D acquisition protocol described below.

1.2. For 3D acquisition, use a 3D echocardiographic probe and 3D-compatible ultrasound machine. For 3D RV volumetric analysis, use dedicated software.

2. Acquisition

2.1. In the vast majority of cases, perform 3D acquisition of the RV using apical views. In opposed to the LV-focused views, a different patient positioning is recommended. If substantially better image quality can be achieved by switching to one intercostal space over the correct apical view, this foreshortened view may enable better 3D image quality. The foreshortening can be corrected during 3D analysis.

2.1.1. Compared to the standard apical echocardiographic acquisition, where the left lateral decubitus position (patient lying on the left side with the left arm stretched above the head) is recommended, have the patient lean back slightly more to enable a more lateral position of the transducer.

2.1.2. Choose an image depth that only includes the RV. Unnecessarily large depth may lower the acquisition frame rate with the lack of beneficial effects regarding RV volumetric analysis.

2.2. Confirm the correct RV-focused view from 2D echocardiography images. If the free wall of the RV is poorly visualized even from this view, the expected 3D image quality will not be optimal for further analysis.

2.3. Switch to the live 3D imaging using the **4D** button, where further correction of the RV view can be performed.

2.4. While the **3D live** mode may be quite pleasing aesthetically, use the **12 Slice** mode for the 3D view, which shows a triplane image of the region of interest as well as 9 cross-sectional planes that can be freely modified. By rotation and correct positioning of the cut planes, confirm the visibility of the entire RV free wall (including the outflow tract and apical segments).

2.5. Further adjust the image by using the left tilting of the sector (second page on the touch screen) to improve RV visualization.

2.6. Use two 3D acquisition modes for RV volumetric analysis: the **multi beat** and the **single beat** mode. Use both of these approaches in every patient however, in some cases (e.g., certain arrhythmias, severe dyspnea of the patient), only the latter one may be feasible.

2.7. Using **single beat** mode, achieve a tradeoff between image quality and frame rate. Choose an optimal image depth, width, and frame rate (lower panel of the touch screen) and obtain 3D loops of the RV without any further action. This method is feasible in the majority of patients; however, it yields generally lower image quality and frame rate compared to the **multi beat** approach.

2.7.1. In case of an average (60-70/min) heart rate, keep a lower frame rate limit of 16 frames/s for adequate RV analysis; however, if tachycardia is present even higher frame rates are recommended.

2.8. Using the **multi beat** mode, reconstruct the acquired 3D loop from a given number of heart cycles that can be selected on the touch screen (2,3,4 and 6 beat modes can be used). In contrast with the single beat acquisition, generally better image quality and frame rate are expected; however, it requires relatively constant heart cycle lengths and also patient compliance due to the mandatory breath-hold maneuver. The maneuver is essential to avoid the so-called stitching artefacts: when the acquired 3D volume is stitched together, unequal cardiac cycle lengths and/or motion due to breathing may result in this phenomenon.

2.8.1. After correct positioning of the probe and setting of the machine (similarly to “single beat” mode), ask the patient to take a deep breath and hold it. In this case, the expanding lungs usually cover the entire image.

2.8.2. Ask the patient to exhale slowly, strictly with guidance. In parallel with the deflation of the lungs, the RV becomes visible again.

2.8.3. When the entire RV (free wall and septum) reappears, ask the patient to hold breath in this state.

2.8.4. By clicking to **multi beat** on the screen, begin the acquisition, and the 3D loop builds up during the given amount of heart cycles.

2.8.5. When the acquisition is ready (the entire RV is visualized), ask the patient to breathe freely again.

2.8.6. Check the obtained loop to ensure if there are no stitching or drop-out artifacts.

3. 4D RV analysis

3.1. Using dedicated software, perform 3D volumetric analysis of the RV. After choosing the RV-focused 3D loop from the patient library, open the software from the **Measurement** window found in the **Volume** folder.

3.2. After opening the software, orient the RV on four predefined cut planes.

3.2.1. Put two markers (TV Center) to the center of the tricuspid valve in the upper and lower left long-axis planes. Adjust the long-axis of the image to the actual long axis of the RV by using the rotation tool. Reference images on the upper right edges show how the correct orientation should appear.

3.2.2. On the upper and lower right panels, align the short-axis images into the correct position by rotation. Similarly to the previous step, reference images help in this process as well.

3.3. After finishing, click **Set landmarks** to the next step of the analysis. Set landmarks in two images.

3.3.1. On the left side, mark the tricuspid annulus at the free wall (TV free wall) and septum (TV septum) and the RV apex on the previously oriented apical four-chamber view.

3.3.2. On the right side, set the RV posterior (LV/RV posterior) and anterior insertion points (LV/RV anterior) and the RV free wall (RV free wall). Similarly to the previous window, reference images in the upper right corner help regarding the correct setup. After setting all landmarks, the software automatically jumps to the next window (**Review**).

3.4. In this window (**Review**), review and manually correct the automatic endocardial border detection throughout the entire cardiac cycle, if necessary. By default, 9 panels can be seen: on the left side, 3 moving loops (1 long-axis and 2 short-axis), on the middle the end-diastolic frames of the same images, and on the right side the end-systolic ones.

3.4.1. In the case of false tracking, freely correct the endocardial borders (green lines), the tracked border by clicking on them. Using the rotation tool on the short axis, review images tracking along the entire circumference of the RV. Adjust the magnitude of correction by choosing **Pen size** on the right side panel. If the tracking is considered to be correct, click on the **Results** in the same panel.

3.5. In the last section, review the final 3D volumetric data and other calculated parameters on the upper right side (**Worksheet** panel). Beyond RV volumes and ejection fraction, the software also displays 2D parameters, such as linear (mid, basal, and long-axis) diameters, as well as FAC and TAPSE values derived from the predefined apical four-chamber view. The software also shows a long- and short axis of the RV (left side), a 3D live model of the RV (upper middle), and a volume-time curve of the chamber (lower right).

3.5.1. In case of the need for further adjustments in the tracking, every previous steps are available for correction by clicking on them on the right panel. If the tracking and the 3D parameters are considered to be valid, save the results by clicking on “Approve and exit” on the same panel.

REPRESENTATIVE RESULTS:

3D analysis of the RV is feasible in a wide variety of cardiovascular diseases. Case 1 is a healthy volunteer with normal ventricular volumes and function (**Figure 1**). Case 2 is a post-mitral valve repair patient who is a typical example for the conflicting results of conventional 2D assessment: while TAPSE is markedly reduced, the patient does not show any signs of RV dysfunction and a maintained RV global systolic function was confirmed by normal 3D RV EF (**Figure 2**). Both patients had excellent echocardiography window with consequential great tracking quality. Case 3 is a semi-professional athlete with dilated cardiomyopathy (**Figure 3**). Only moderate image quality was achievable (the outflow tract is poorly visualized); however, 3D RV analysis was successful, showing good agreement with cardiac MR results.

FIGURE AND TABLE LEGENDS:

Figure 1: 3D RV analysis of a healthy volunteer. On the left panels, a long axis (upper panel) and a short axis (lower panel) image of the RV can be seen. The green line represents the endocardial border. The central upper image is a 3D model of the RV based on the current analysis. Beyond RV volumes and ejection fraction, the software displays 2D parameters, such as linear (mid, basal and long-axis) diameters, as well as FAC and TAPSE values derived from the predefined apical four-chamber view (right upper panel) and a volume-time curve is also generated (right lower panel).

Figure 2: 3D RV analysis of a post-mitral valve repair patient. While 3D RV volumes and EF are in the normal range, TAPSE is markedly lower. Reduced longitudinal shortening of the RV is a common phenomenon following cardiac surgery however, the majority of these patients do not show signs of RV failure. 3D EF assessment confirms maintained global systolic function despite markedly reduced TAPSE values.

Figure 3: Case of an athlete with dilated cardiomyopathy. 3D RV volumes are increased, while 3D RV EF is mildly reduced. Note the suboptimal image quality with a poorly visualized RV outflow tract. Despite the poor echocardiographic window, RV analysis shows good agreement with cardiac MR-derived measurements considering the known systematic volume underestimation of 3D echocardiographic RV analysis compared to the gold-standard cardiac MR (RVEDV: 168 mL; RVESV: 99 mL; RVEF: 41%).

DISCUSSION:

3D analysis of the RV represents an important step in everyday cardiology practice. In parallel with the growing interest of the morphology and function of the previously neglected cardiac chamber, these novel solutions provide clinically meaningful information about the right side of the heart. While 3D acquisition has several aspects that markedly differ from 2D echocardiographic imaging, by keeping special attention to the critical points and by using a thorough protocol, 3D RV analysis may progress from a scientific tool to an essential step of echocardiographic examination. With optimal image quality and proper expertise, RV volumetric analysis using echocardiography may take only a few minutes from acquisition to results with high feasibility[13]. The significantly lower costs and shorter procedure time make it an appealing alternative to the gold standard cardiac MR examination in several cases.

Nevertheless, 3D analysis may not be feasible in every scenario. The most important limitation factor is echocardiographic image quality: in patients with a poor 2D echocardiographic window, acceptable 3D image quality is rarely achievable. Still, it is important to mention that various maneuvers (lateral positioning of the probe, foreshortening, proper presets) may improve 3D image quality. Suboptimal visualization of the RV outflow tract is not uncommon, however it is usually well tolerated by the RV analysis solutions providing reliable results. Using 3D loops with stitching, drop-out artifacts are strongly discouraged, therefore, recording of multiple loops and post-acquisition control are highly recommended.

3D examination of the RV opens the possibility of 3D RV deformation analysis and regional assessment of the chamber as well[14]. It is well known that maintained EF does not preclude significant changes in RV mechanics[4]. Evaluation of RV deformation reveals distinct changes of RV contraction pattern in a wide variety of populations, such as post-cardiac surgery patients[15-17], congenital heart disease[18], pulmonary arterial hypertension[19-21], and elite athletes[22]. Moreover, measurement of segmental morphology and function may be of high interest in diseases where regional remodeling of the RV is expected, such as arrhythmogenic cardiomyopathy[23] or congenital heart disease patients[24]. In conclusion, post-processing of 3D RV data may provide novel parameters of the chamber with incremental diagnostic and prognostic value.

ACKNOWLEDGMENTS:
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Figure_1

Click here to access/download;Figure;Case_1.tif

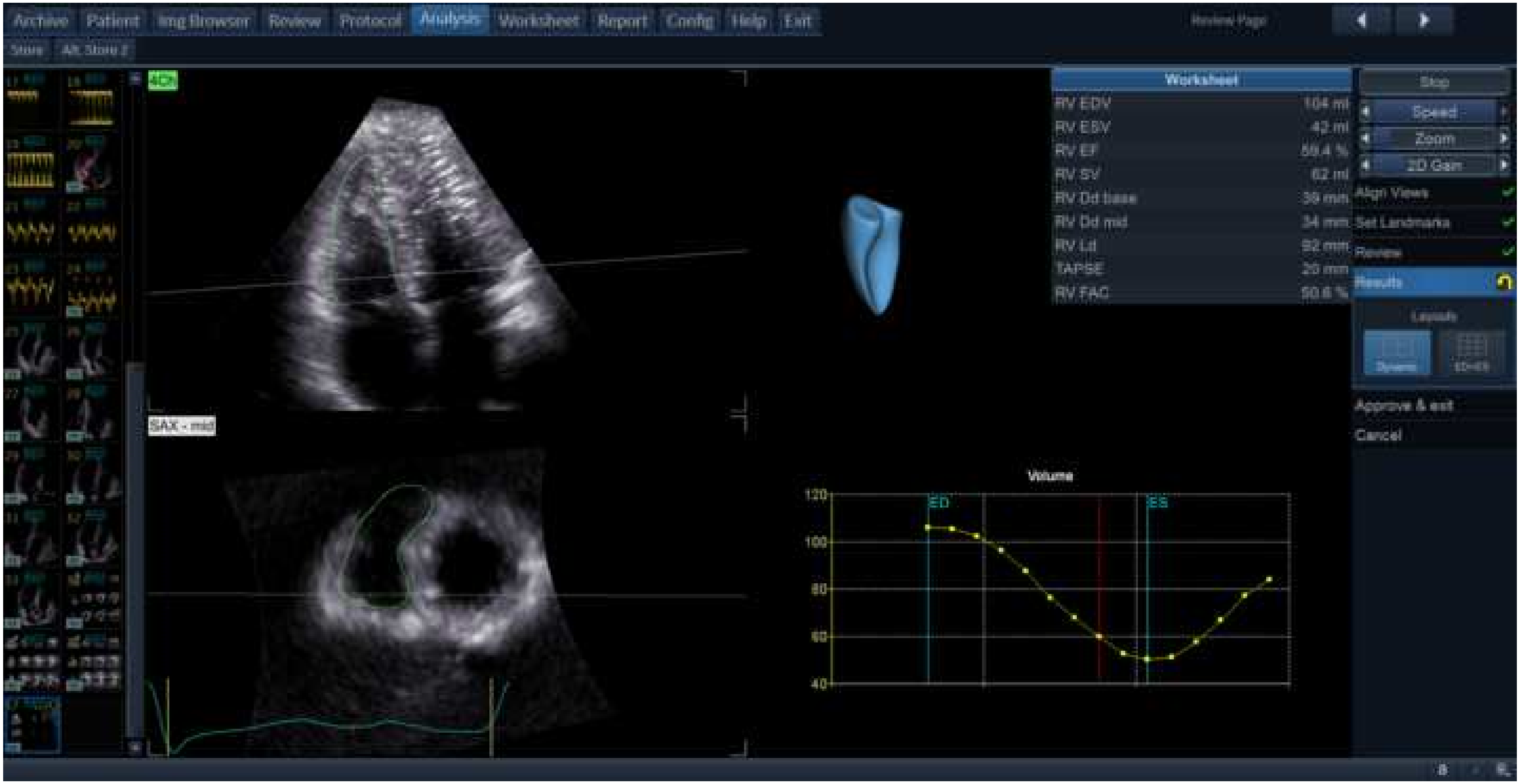
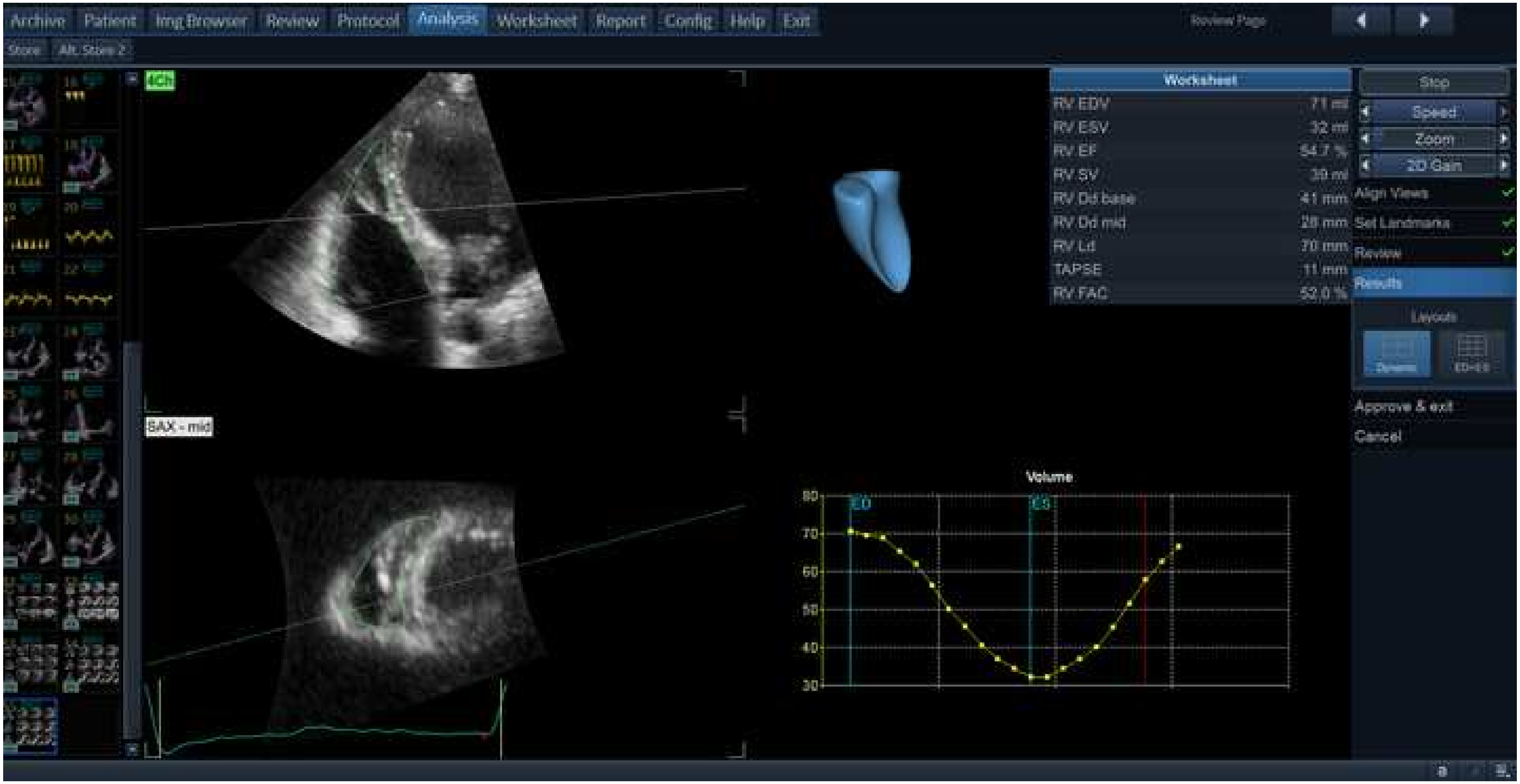
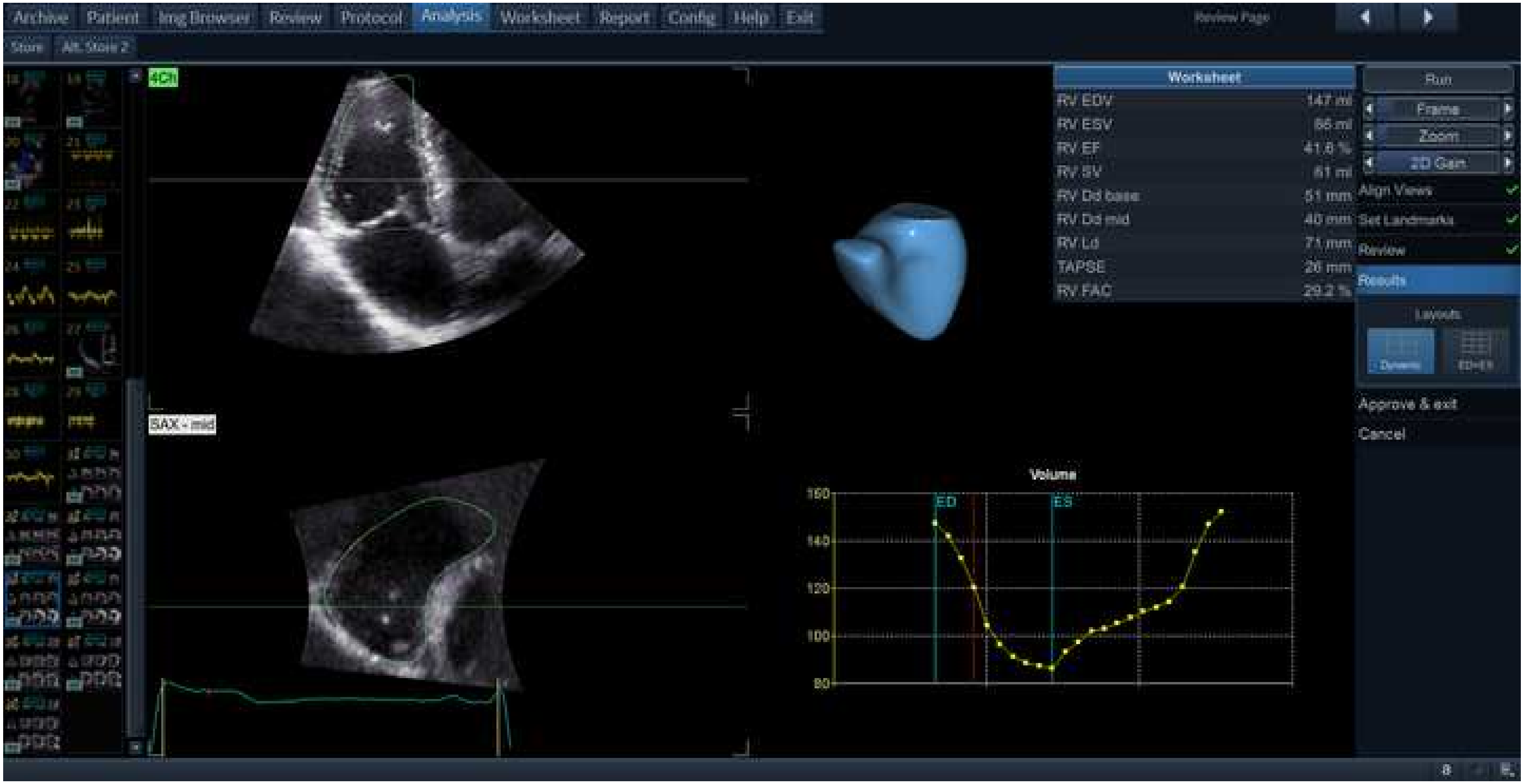


Figure_2

Click here to access/download;Figure;Case_2.tif



Click here to access/download;Figure;Case_3_revised.tif



Name of Material/ Equipment	Company
3V-D/4V-D/4Vc-D	General Electric
4D Auto RVQ	General Electric
E9/E95	General Electric
EchoPac v203	General Electric

Catalog Number	Comments/Description
n.a.	ultrasound probe
n.a.	software for analysis
n.a.	ultrasound machine
n.a.	software for analysis

Response to Reviewers

We would like to thank Ronald Myers Ph.D. Senior Science Editor of Journal of Visualized Experiments and the two expert Reviewers for the careful and constructive evaluation of our manuscript entitled: "Morphological and functional assessment of the right ventricle using 3D echocardiography". We understand that the Reviewers and the Editor found merit in our study. We also understand that a number of issues were raised, and the manuscript was not found suitable for publication. We are confident that the raised issues can be resolved through careful revision. Thus, we have heeded all of the Reviewers' and Editor's helpful propositions and prepared a revised version of the manuscript, which includes several extensive alterations in the text, as suggested. Please find our point-by-point responses to the comments below. We think that our work has the potential to make a fine contribution and hope to publish our paper in the Journal of Visualized Experiments.

Editor

Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

Thank you for your comment! We have thorougly proofread the manuscript and also reviewed it with a native english speaker grammar editor.

Please provide at least 6 keywords or phrases.

Thank you for your comment! We have provided 7 keywords.

Please ensure that the Abstract is between 150-300 words.

Thank you for your comment! We have modified the Abstract which is currently 175 words.

JoVE cannot publish manuscripts containing commercial language. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.

Thank you for your comment! We have removed all the commercial product names from the manuscript.

5. Please revise the Introduction to include all of the following:

a) A clear statement of the overall goal of this method

b) The rationale behind the development and/or use of this technique

c) The advantages over alternative techniques with applicable references to previous studies

d) A description of the context of the technique in the wider body of literature

e) Information to help readers to determine whether the method is appropriate for their application

Thank you for your comment! We have extended the Introduction (mostly to also fulfill the last section of Your guideline) as follows: *„The technical requirements of 3D assessment are essential parts of a state-of-the-art cardiovascular imaging department nowadays, and it is expected that soon it will be part of the general equipment in every echocardiography lab".*

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.

Thank you for your comment! We have extended the protocol as follows: *„The protocol follows the guidelines of our Institution's human research ethics committee and the patients of our clinical cases gave their written informed consent to the study."*

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. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note."

Please organize the sections as if you are describing how you performed your experiment. Patient, patient preparation, echochardiogram acquisition, RV analysis, data analysis, etc.

The Protocol should contain only action items that direct the reader to do something.

Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Please include all the button clicks, knob turns etc.

The Protocol should be made up almost entirely of discrete steps without large paragraphs of text between sections. Please simplify the Protocol so that individual steps contain only 2-3 actions per step

There is a 10-page limit for the Protocol, but there is a 2.75-page limit for filmable content. Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

Please describe the result with respect to your experiment, you performed an experiment, how did it help you to conclude what you wanted to and how is it in line with the title. e.g., how do these results show the technique, suggestions about how to analyze the outcome, comparison with existing techniques

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As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations.

Please include a Disclosures section, providing information regarding the authors' competing financial interests or other conflicts of interest. If authors have no competing financial interests, then a statement indicating no competing financial interests must be included.

Please revise the table of the essential supplies, reagents, and equipment. The table should include the name, company, and catalog number of all relevant materials in separate columns.

Thank you four your suggestions! We have modified the Protocol with a more imperative tense. We have also highlighted the most important part which should be filmed.

Reviewer #1

The technique described is specific for one single echo vendor. As 3D echo capability is now widely available in multiple echo vendors, a more generic approach of 3D RV echo imaging instead of user manual-like approach for a single vendor should be discussed.

Thank you for your important comment! We are aware that 3D RV assessment varies between vendors, and unfortunately, distinct steps of the analysis may be substantially different between the softwares. Especially in case of the image acquisition, we tried to give a general approach which may be applicable to every 3D-capable echocardiography machine, and also focused on several aspects of 3D RV analysis which aids generalizability of our protocol. However, description of every vendor's approach exceeds the aims and possibilities of our manuscript.

Reviewer #2

Abstract line 44: the analysis of "deformation patterns" based on 3D echo is an advanved technique in most cases only available to research groups. In the protocol described in the manuscript there is no analysis of deformation patterns described, therefore this should be deleted in the abstract.

Thank you for your comment! As there is definitely no RV myocardial deformation analysis described in the manuscript, we have removed this part of the Abstract.

P4 L74/75: studies reporting accuracy compared to cardiac MRI should be referenced; please also provide reference for CMRI validation of the software "4D auto RVQ"; it would also be interesting for the reader how accurate 3D echo compared to CMRI is with regard to the systematic bias by 3D echo

Thank you for your comment! We have added references regarding the validation of 3D echocardiographic RV analysis.

P6 L125: the manuscript reports a framerate of 16fps as a miniumum for 3D volume acquisition. The required frame rate always depends on the heart rate of the patient. In my opinion 16fps is the minimum in patients with heart frequencies around 60-70bpm. Please include the range of heart rate for the frame rate given and discuss why a high frame rate is important. The issue of frame rates should also be added to the discussion section. This would fit in the 2nd paragraph of the discussion.

Thank your for your comment! We have modified this section of the protocol as follows: *„In case of an average (60-70/min) heart rate, lower frame rate limit of 16 frames/sec has to be kept for adequate RV analysis, however, if tachycardia is present even higher frame rates are recommended."*

P6 L132: what is the reason for the breath-hold maneuver (e.g. stitching artifacts)

Thank you for your comment! We have extended this part of the protocol as follows: *„The maneuver is essential to avoid the so-called stitching artefacts: when the acquired 3D volume is stitched together, unequal cardiac cycle lengths and/or motion due to breathing may result in this phenomenon."*

P9 L203-206: good agreement with CMRI is reported. The CMRI data for volumes and EF would be interesting for the reader.

Thank your for your question! To comply with this and your next suggestion, we have extended this part of the cases as follows: *„Despite the poor echocardiographic window, RV analysis shows good agreement with cardiac MR-derived measurements considering the known systematic volume underestimation of 3D echocardiographic RV analysis compared to the gold-standard cardiac MR (RVEDV: 168 mL; RVESV: 99 mL; RVEF: 41%)."*

P10 L227: please provide EDV and ESV of the CMRI measurements

Thank your for your question! We have extended this part of the cases as follows: *„Despite the poor echocardiographic window, RV analysis shows good agreement with cardiac MR-derived measurements considering the known systematic volume underestimation of 3D echocardiographic RV analysis compared to the gold-standard cardiac MR (RVEDV: 168 mL; RVESV: 99 mL; RVEF: 41%)."*

P11 L253 "pulmonary hypertension". Reference DOI: 10.1093/ehjci/jev171 could be added.

Thank you for your suggestion! We have added this article as a reference.

P11 L253-256: the studies cited report on CMRI measurements and not on 3D echo data. There are a few published techniques for RVOT assessment based on mesh datasets (for example DOI: 10.1016/j.echo.2017.12.009 and DOI: 10.1053/j.jvca.2019.02.011). These articles should be referenced as this might be an upcoming application of 3D RV echocardiography.

Thank you for your suggestion! We have added these references to relevant parts of the Discussion.

Protocol: paragraph 1.1 and 1.2 should be switched

Thank your for your comment! We have switched these parts of the protocol.

Figures: Figures should be numbered correctly

Thank you for your comment! We have corrected the numbering of the Figures.

Figure 3: posterior wall in the short axis is not tracked correctly

Thank you for your comment! We have corrected the RV analysis of Case #3.

Once again, we would like to thank the Editors and Reviewers for the meaningful comments and suggestions. We really hope that our manuscript is improved and our revised paper will be acceptable for publication in Journal of Visualized Experiments.

On behalf of all authors,

Bálint Károly Lakatos M.D.