MONITORING OF CHANGED RIGHT VENTRICULAR SHAPE AND FUNCTION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (PAH)

4D RV-FUNCTION© - THE 4D ECHO SOLUTION

A WHITE PAPER OF TOMTEC IMAGING SYSTEMS
INTRODUCTION

The arteries that carry blood from the heart to the lungs become narrowed because of the lung disorder ‘pulmonary hypertension’. This makes it difficult for blood to flow through the vessels. Because of the increased workload, the blood pressure in these pulmonary arteries rises far above normal levels. This abnormally high pressure in the right ventricle causes an expanded size.

One impact of the disease severity is the existence of a RV failure. If a right ventricular failure exists, there is a significant higher morbidity and mortality risk. Right heart failure is the main cause of death in patients with PAH. Echocardiography and cardiac magnetic resonance imaging offer non-invasive evaluation of right ventricular function and shape.

Non-invasive and reproducible measures of right heart function can improve the management of PAH patients.

PAH AND THE RIGHT VENTRICLE

There are 15-50 subjects per million population PAH cases in Europe. For 740 million people in Europe, this would be up to 37,000 cases.

The World Health Organization (WHO) classifies pulmonary hypertension in 5 groups. Pulmonary arterial hypertension (PAH) represents group 1 (figure1). It combines diseases with similar pulmonary vascular characteristics.

PAH represents the type of PH in which the most important advances in the understanding and treatment have been achieved in the past decade. It is also the group in which PH is the ‘core’ of the clinical problems and may be treated by specific drug therapy. The inadequate adaptation of myocardial contractility seems to be one of the primary events in the progression of heart failure in a chronically overloaded right ventricle.

The consequent increase in PVR (pulmonary vascular resistance) leads to right ventricular (RV) overload, hypertrophy, dilatation, and eventually to RV failure and death.

In PAH patients RV size, shape and function measurements are clinically important. The right ventricular shape changes due to the high pressure. Compared to normal, RV function in PAH is reduced and the shape becomes more eccentric.

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Table 4 Updated clinical classification of pulmonary hypertension (Dana Point, 2000)

<table>
<thead>
<tr>
<th>1 Pulmonary arterial hypertension (PAH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Idiopathic</td>
</tr>
<tr>
<td>1.2 Heritable</td>
</tr>
<tr>
<td>1.2.1 BMPR2</td>
</tr>
<tr>
<td>1.2.2 ALK1, endothelin (with or without hereditary hemorrhagic telangectasia)</td>
</tr>
<tr>
<td>1.2.3 Unclassified</td>
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<tr>
<td>1.3 Drugs and toxins induced</td>
</tr>
<tr>
<td>1.4 Associated with (APAH)</td>
</tr>
<tr>
<td>1.4.1 Connective tissue diseases</td>
</tr>
<tr>
<td>1.4.2 HIV infection</td>
</tr>
<tr>
<td>1.4.3 Portal hypertension</td>
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<tr>
<td>1.4.4 Congenital heart disease</td>
</tr>
<tr>
<td>1.4.5 Scleroderma</td>
</tr>
<tr>
<td>1.5 Chronic thromboembolic pulmonary hypertension</td>
</tr>
</tbody>
</table>

2 Pulmonary hypertension due to left heart disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease

3 Pulmonary hypertension due to lung diseases and/or hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Acute hyperventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

4 Chronic thromboembolic pulmonary hypertension

5 PH with unclear and/or multifactorial mechanisms

5.1 Haematological disorders: myeloproliferative disorders, splenectomy.
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis.
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders.
5.4 Others tumoral obstruction, fibrosis mediastinitis, chronic renal failure on dialysis.

ALK-1 = activin receptor-like kinase 1 gene; APAH = associated pulmonary arterial hypertension; BMPR2 = bone morphogenic protein receptor, alpha 2; HIV = human immunodeficiency virus; PAH = pulmonary arterial hypertension.

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Figure 1 Classification of pulmonary hypertension2
HOW TO ANALYZE RV REMODELING?

There are several measurements for right ventricular function in 2D echocardiography, like FAC, TAPSE and RIMP. The limitations of the 2D measurements are well known. Foreshortening and geometric assumptions make 2D not well suitable for quantification.

This limitation can be solved by using 3D echocardiography. With the growing availability of 3D techniques such as magnetic-resonance imaging and 3D echocardiography, assessment of shape and functional changes in the right ventricle becomes feasible. Three-dimensional modalities offer superior accuracy and reproducibility in the assessment of RV shape and function.²

Although magnetic-resonance has excellent intra- and inter-observer variability it is expensive, not widely available and cannot be performed in patients with special conditions such as metallic implanted devices, claustrophobia and irregular heart rhythm.

Three-dimensional echocardiography is available and well validated against the gold standard MR. The latest guideline⁴ recommends 3D echocardiography measurements of RV when knowledge of RV volumes may be clinically important.

SPECIFIC RV SHAPE IN PAH PATIENTS

The beutel™ shape shows significant differences between a normal and a PAH patient. The PAH beutel shape is characterized by³

- Basal bulge (free wall lateral to tricuspid valve)
- Septal bowing into the LV
- Apical dilation
- Increased eccentricity (roundness) in all ventricular segments

Compared to the left ventricle (left image) the right ventricle shape (right image) is much more complex.
Figure 2 Remodeling of the right ventricle

**FUNCTIONAL MEASUREMENT IN PAH PATIENTS**

The values of PAH patients are also significantly increased compared to normals:

- EDV and ESV are higher in PAH patients.
- Stroke Volume, RV EF, TAPSE and FAC decrease compared to normal values.
Examples for normal values

<table>
<thead>
<tr>
<th>Global</th>
<th>2D</th>
<th>Manual Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV: 141.2 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESV: 59.6 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV: 81.7 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF: 57,82 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVLS (Septum): -23,52 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVLS (Freewall): -32,82 %</td>
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<td></td>
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</tbody>
</table>

Example for PAH results

<table>
<thead>
<tr>
<th>Global</th>
<th>2D</th>
<th>Manual Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV: 188,5 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESV: 117,5 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV: 71,0 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF: 37,66 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVLS (Septum): -25,65 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVLS (Freewall): -26,85 %</td>
<td></td>
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</table>

3D ECHO QUANTIFICATION OF THE RV BY 4D RV-FUNCTION

With 4D RV-FUNCTION² the 3D beutel and functional results are displayed in just a few steps.⁶

For people starting to use 3D echo for cardiac chamber quantification, the right ventricle is the most challenging. The new software developed by TomTec has managed to make this task seem much easier, by introducing more user-friendly controls and editing tools for endocardial contouring. In particular, the possibility to personalize the alignment workflow according to user’s preference and adopt it as a preset is very effective and time-saving.”

In end-diastole, the user sets a left and a right ventricular long axis to define a basic coordinate system. Based on that, a right ventricular-focused four-chamber view and a short axis view are derived by the system. Now the user has to define anterior and posterior junction of the right ventricular free wall with the interventricular septum and extend of the right ventricular cavity between septum and free wall in this short axis view.

Definition of the aortic diameter in an apical long axis view concludes the required manual input.

Dr. Denisa Muraru, University of Padova

[Images of echocardiograms]
The system analyzes ultrasound backscatter intensities within this user-defined coordinate framework and adapts a statistic right ventricular shape model to all available input data. This model is tracked over the entire cardiac cycle using speckle tracking technology. The resulting dynamic surface model can optionally be adjusted by the user in end-systole and end-diastole. Applied manual changes are propagated to all other frames of the cardiac cycle using the derived tracking information.

3D volumes over time are computed numerically from the dynamic surface model and used to calculate EDV, ESV, EF and SV. Additionally the surface model is intersected with the right ventricular-focused four chamber view to derive standard 2D measurements (RVLS, TAPSE, FAC and distances) from the same geometry. End-systole and end-diastole are identified as the frame with the lowest / largest ventricular volume.

CONCLUSION

An analysis of the right ventricle is indispensable in PAH patients. 3D Echocardiography offers all necessary information about the shape and function of the right ventricle for several therapeutic targets. Also the control of shape changes and values is an important support for the treatment and monitoring of PAH patients.

TOMTEC PROFILE

TOMTEC IMAGING SYSTEMS is leading the field of diagnostic medical imaging and ultrasound PACS applications. The product portfolio encompasses 2D and 3D/4D solutions to review and analyze multimodality imaging data. TOMTEC solutions are applicable in adult- and pediatric cardiology as well as women’s health, radiology and vascular imaging.

REFERENCES:

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