Pulmonary Hypertension and the Battle for Best Predictors

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Pulmonary hypertension (PH) serves as an ongoing research field and with its pure precapillary manifestation pulmonary arterial hypertension (PAH) despite huge progress in therapy remains a severe clinical condition. Prostacyclin analogues and receptor agonists, endothelin receptor antagonists, phosphodiesterase type 5 inhibitors and guanyl cyclase activators are the cornerstones in treatment of PAH. This drugs dramatically changed prognosis of PAH patients in the last 15 years [1]. However, this progress is owing to early detection of the disease, strategies for combination therapy and systematic assessment of clinical response (goal directed therapy). A meta-analysis including 25 randomized controlled studies in naive PAH patients disclosed a relative risk reduction with monotherapy versus placebo of 44% (p = 0.016) [2].

An additional meta-analysis revealed a further reduction in clinical worsening with combination therapy in comparison to monotherapy (RR: -35%; p < 0.001) [3]. For risk assessment and goal setting clinicians and researchers struggle for best praxis variables and developed several risk models to predict outcome of PAH patients. In the evolution of this risk models different basal and follow up parameters deriving from clinical, functional and laboratory measures as well as variables from invasive -hemodynamic explorations of the right ventricle have been utilized in diverse calculators. The most well-known models are the REVEAL score and ESC/ERS PH guideline risk table [4]. Baseline variables and treatment response were used to stratify the one-year risk in low – intermediate and high-risk groups. These scores (or risk tables) were recently tested by diverse registries like the French Pulmonary Hypertension Network (FPNH) registry risk equation, the COMPERA registry and others more [1]. Great efforts were undertaken to simplify risk scores with less variables, especially to find good validated low risk criteria. Indeed NYHA FC- I-II, 6 minute walk distance (6MWD) > 440m, right atrial pressure (RAP) < 8 mmHg, cardiac index > 2.5 L/min/m$^2$, NT-pro-BNP < 300 pg/ml, venous oxygen saturation > 65% disclosed the highest yield in almost all risk calculations. Surprisingly, even a short cut of this panel using only three noninvasive variables: NYHA-FC, NT-pro-BNP and 6MWD are able to testimony an excellent long-term prognosis. Patients with all three low risk criteria came up with a 2-, 3- and 5-year survival of 100%, 99% and 98% respectively [5]. This gives hope, that follow up right heart catheterization could be avoided in patients inheriting this low risk criteria. But what, if there exist intermediate or high-risk criteria at baseline?

If the right heart is the “Holy Grail” in pulmonary hypertension and unquestionable it determines morbidity and mortality in PAH patients and PH patients generally, imaging functions and signs of the right ventricle or atrium could fulfill the hope of being robust measures of outcome with respect to baseline and or follow after treatment initiation.

D-shaping of the left ventricle means an uncoupled right ventricle to the pulmonary artery bed and is a clear sign of non-reversible right ventricle dysfunction finally deteriorating into right ventricle decompensation. Clearance of D-shaping after therapy means re-compensation of the right ventricle and is easily to detect by echocardiography [6]. Right ventricle reverse remodeling (RVRR) only happens when pulmonary vascular resistance is significantly reduced (at least by 40%) and then servers as an excellent prognostic marker. The respective event-free survival rates at 1, 3 and 5 years were 94%, 94%, and 94% in patients with RVRR and 75%, 55% and 24% in those without RVRR (p = 0.0001) [7]. Furthermore, patient phenotyping as by cluster analysis clearly demonstrates the importance of imaging

the right ventricle most easily performed by echocardiography. It helps physicians to identify patients especially at mediate risk which need a more aggressive therapeutic approach.

The next years we probably will see new risk scores which better utilize imaging measures and combine them with other noninvasive variables. Treatment response evaluation will include more parameters of right ventricle function of which right ventricle reversion will be one of the most promising. Especially in the face of a goal directed therapy right ventricle reverse reversioning might be the cornerstone in follow up decision making with respect for therapy escalation or not.

So, the battle is going on to search for even better risk calculator's or imaging criteria which secure prognosis and help to decide for best therapy.

Bibliography


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