Meeting Report

The International Society for Heart and Lung Transplantation, 32nd Annual Meeting and Scientific Sessions
Prague, Czech Republic, 18–21 April 2012

Interest in pulmonary hypertension (PH) continues to grow within the International Society for Heart and Lung Transplantation (ISHLT). The PH program at the 32nd annual meeting held on 18–21 April 2012 in Prague, Czech Republic, was particularly strong, with 56 accepted abstracts and five symposia dealing with PH and right ventricular function. In this report, we will summarize selected oral abstract presentations dealing with a broad array of topics on PH and right ventricular function. These include original research on registries, prognosis, disease management, clinical trials, novel therapies, echocardiographic assessments and exercise hemodynamics.

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Registries, prognosis & disease management

In recent years multiple large patient registries have generated invaluable data on the clinical course and management of pulmonary arterial hypertension (PAH). Among the largest of these is the US-based REVEAL registry. Numerous publications have already been generated from this database of nearly 3000 patients [4]. Using a set of clinical variables routinely obtained at baseline, a simple risk calculator categorizes patients into five risk strata from low to very high, which are predictive of 1-year survival [5,6]. In abstract number 370, the ability of serial risk scores in 2547 PAH subjects surviving 1 year to predict mortality in the subsequent year was assessed [101]. Among 969 patients who had no change in their risk score, 1-year survival was 89.9%. In comparison, survival was 94% in 806 patients with a decrease and 84.8% in the group with an increase in risk score (p < 0.001). This study adds to other smaller reports [7] demonstrating the importance of serial assessments, in addition to baseline variables, in predicting outcomes in PAH.

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a correct prerereferral diagnosis was made in only 48%, and no PH was found in 21%. The absence of a right heart catheterization (RHC) was associated with incorrect referral diagnosis. Half did not have a V/Q scan, which is an essential diagnostic test in the evaluation of PH. This study highlights the frequent misdiagnoses and potential for inappropriate therapy for suspected PH in the nonexpert setting, particularly when the standard diagnostic algorithm is not adhered to \[8\].

In contrast to the remarkable advances in the treatment of PAH, there has been scant attention paid to quality of life and palliative care. Swetz and colleagues from the Mayo Clinic surveyed 76 PH clinicians and 276 patients to gauge their attitudes (abstract number 60). Several interesting findings were noted that will be extremely helpful in designing future intervention protocols. For example, fewer physicians (62%) reported high confidence in managing pain compared with PH-specific therapies (95%) and 43% felt that a palliative care referral represented ‘giving up’.

### Clinical trials/novel therapies

Several industry-sponsored clinical trial results were reported. In EPITOME-1 (abstract number 56), a new intravenous epoprostenol (Veletri\textsuperscript{6}, Actelion, Basel, Switzerland) with different excipients, which renders the compound more stable at room temperature and hence eliminates the need for ice packs, was compared with conventional Flolan\textsuperscript{6} (GlaxoSmithKline, Middlesex, UK) in the study of 30 PAH patients naive to injectable prostacyclin therapy. After 4 weeks, dosing and pharmacokinetics were similar, as were adverse effects and changes in 6-min walk distance (6MWD). Of note was the occurrence of three deaths (due to sepsis, right heart failure and cholecystitis) among the 20 patients in the Veletri group compared with zero out of ten in the Flolan group. None were attributed to epoprostenol. Veletri is US FDA approved. A new thermostable formulation is currently being developed (ClinicalTrials.gov identifier: NCT01462565 \[102\]).

ATHENA was an open-labelled single-arm study of ambisentan, an endothelin-receptor antagonist (ETA), added to therapy with a phosphodiesterase, type-5 inhibitor (PDE-5i) in 33 PAH subjects with functional class III limitations. After 24 weeks, pulmonary vascular resistance had fallen by 33%, 6MWD increased by 31%. Data after 48 weeks were presented (abstract number 57). Of note was the occurrence of three deaths (due to sepsis, right heart failure and cholecystitis) among the 20 patients in the Veletri group compared with zero out of ten in the Flolan group. None were attributed to epoprostenol. Veletri is US FDA approved. A new thermostable formulation is currently being developed (ClinicalTrials.gov identifier: NCT01462565 \[102\]).

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### Exercise hemodynamics

The relationship between exercise and pulmonary vascular disease was examined in several presentations. Three of these focused on the role of exercise in the diagnosis of PH in distinct patient populations. Armstrong and colleagues examined the predictive value of cardiopulmonary exercise testing parameters (specifically, the partial pressure of end-tidal CO\textsubscript{2} for the diagnosis of PH in patients with interstitial lung disease referred for lung transplantation \[101\]. When compared with other parameters, such as 6MWD and diffusing capacity for carbon monoxide, partial pressure of end-tidal CO\textsubscript{2} had 100% sensitivity and 89% specificity for the presence of PH by RHC. However, other parameters related to the 6MWD that have been shown to either predict the presence of PH or portend a poor prognosis in interstitial lung disease, such as heart rate recovery \[9\] or degree of desaturation \[10\], were not examined in this study.

A series of recent observations by Vonk-Noordegraaf’s group in Amsterdam, The Netherlands, has established that compliance (C) and resistance (R) follow a remarkably consistent inverse hyperbolic relationship, indicating that the distal pulmonary vasculature accounts for the majority of both \[11\]. At low R, fairly large reductions in C are associated with small increases in R. Girgis and colleagues (abstract number 178) thus hypothesized that restoring C, reflecting early pulmonary vascular disease, would be predictive of exercise-induced PH in SSC patients with normal resting mean pulmonary artery pressure \[101\]. Pulmonary
artery C, taken as stroke volume/pulse pressure, was 3.3 ± 1 ml/mmHg in eight SSc patients whose mean pulmonary artery pressure exceeded 35 mmHg during supine exercise compared with 5.2 ± 1.4 (p = 0.006) in nine patients without exercise-induced PH. By contrast, resting R was comparable. These preliminary findings support the idea that exercise-induced PH may indeed represent occult pulmonary vascular remodeling and that resting C may be a useful marker.

A group from the Slovak Republic, led by Lesny (abstract number 180), examined the utility of exercise during RHC to elicit occult left-sided heart disease in PH patients who demonstrated top-normal to mildly elevated pulmonary capillary wedge pressures at rest [101]. Using a bicycle ergometer-ramping protocol, they found seven out of 12 patients had increases in pulmonary capillary wedge pressure to greater than 18 mmHg, suggesting left heart disease as the etiology of abnormal resting hemodynamics. This work suggests that exercise RHC may be important to properly phenotype patients with resting PH, particularly to distinguish between WHO groups I and II disease.

Gerges and colleagues (abstract number 181) from Vienna examined a similar question in their large database of PH associated with congenital heart disease (CHD) to determine the prevalence of elevated left-sided filling pressures [101]. In this cohort of 116 patients with various types of CHD (pretricuspid, post-tricuspid and complex lesions), nearly half had elevated left-sided filling pressures, defined as a resting pulmonary capillary wedge pressure >15 mmHg. The authors concluded that the high prevalence of postcapillary PH in adults with CHD may influence response to PAH-specific therapy and, therefore, impact treatment decisions.

Summary

The 32nd Annual Meeting of the ISHLT included a broad array of topics on PH and RV function. Numerous scientifically provocative abstracts were presented, a sample of which is presented in this report. It is anticipated that this meeting will continue to be a prominent venue for the dissemination of original clinical and basic science research in the field of pulmonary vascular disease.

Financial & competing interests disclosure

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Websites

101 International Society for Heart and Lung Transplantation. www.abstract2view.com/isHLT
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