3.1 Pulmonary arterial hypertension in patients with systemic sclerosis is independent of high-resolution computed tomography findings of interstitial lung disease

Tuppin M, Chambers D, Slaughter R, Mohammed O, and Kermeen F
School of Medicine, Queensland Center for Pulmonary Transplantation and Vascular Disease, Medical Imaging Department, The Prince Charles Hospital, University of Queensland, Brisbane, Queensland, Australia

Systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) may occur as an isolated arteriopathy or concurrently with systemic sclerosis associated interstitial lung disease. However, the extent to which the interstitial lung disease influences pulmonary arterial pressure (PAP) has not been well described in the literature. Therefore, this study aimed to determine how the high-resolution computed tomography (HRCT) features in patients with SSc-PAH correlate to measures of hemodynamics. A retrospective analysis of patients with a diagnosis of SSc-PAH treated at the Queensland Centre for Pulmonary Transplantation and Vascular Disease between 2002 and 2010 was conducted. Existing HRCT scans were scored for the presence and extent of interstitial lung disease features, and measurements taken of the main pulmonary arteries (MPA). These were then correlated to measures of hemodynamics attained by right heart catheterization. Fifty-seven patients with SSc-PAH (50 female), of mean (SD) age of 60.7 (9.6) years and mean (SD) PAP of 44.3 (14.3) mmHg were analyzed; 44/57 (77.2%) had an MPA greater than 30 mm, while only 14/57 (24.6%) had a pulmonary artery/ascending aorta ratio greater than 1.13. The MPA was most strongly correlated to the diastolic pulmonary artery pressure (r=0.545, P<0.01). There were no significant correlations between any of the other HRCT features and hemodynamics. These findings suggest that the development of pulmonary arterial hypertension is probably independent of the existence of interstitial lung disease in patients with systemic sclerosis. The MPA size should be regarded as the best marker of pulmonary hypertension on HRCT in this group of patients.

3.2 Imatinib for the treatment of pulmonary arterial hypertension and pulmonary capillary hemangiomatosis

Nayyar D, Muthiah K, Kumarasinghe G, Hettiarachchi R, Macdonald P, Kotlyar E, Hayward C, and Keogh A
St. Vincent’s Hospital, Darlinghurst, New South Wales, Australia

The effect of imatinib (a platelet-derived growth factor receptor antagonist) in two patients, one with pulmonary capillary hemangiomatosis (PCH) (Case 1), and the other with pulmonary arterial hypertension (PAH) (Case 2), was reviewed. Medical records and pulmonary hypertension database records were reviewed to obtain details of the clinical presentation, management regimen and clinical outcomes. Case 1 was a 62-year-old woman with PCH who deteriorated rapidly despite treatment with ambrisentan, doxycycline and epoprostenol. She was commenced on imatinib and within 2 days demonstrated significant symptomatic improvement (from functional Class IV to Class III). After 6 months of treatment with imatinib, there was a resolution in signs of right-sided heart failure, an improvement in exercise tolerance (increased 6-minute walking distance from 90 to 295 meters), and a reduction in pulmonary artery systolic pressure (83 to 45 mmHg). Case 2 was a 43-year-old woman with a 16-year history of severe idiopathic PAH with notable decline despite the use of combination therapy (iloprost, bosentan and sildenafil). In 2008, she was commenced on imatinib, which led to an improvement in her functional class (Class IV to Class III). These cases demonstrated a positive outcome of imatinib treatment in two different etiologies of pulmonary hypertension. Large clinical studies are necessary to mandate its wider use.

3.3 Abnormal pulmonary artery stiffness in pulmonary arterial hypertension: In vivo study with intravascular ultrasound

Lau EMT, Iyer N, Ilsar R, Bailey BP, Adams MR, and Celermajer DS
Department of Respiratory, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

There is increasing recognition that both resistance and compliance contribute to right ventricular (RV) afterload in pulmonary arterial hypertension (PAH). However, changes in the stiffness properties of the proximal elastic pulmonary arteries (PA) and the contribution of this to RV afterload have not been well studied. Furthermore, the effect of PAH-specific therapy on proximal PA stiffness is unknown. Using intravascular ultrasound (IVUS) and simultaneous right heart catheterization, 20 pulmonary segments in 8 PAH subjects and 12 pulmonary segments in 8 controls were studied to determine their compliance, distensibility, pressure-strain modulus and stiffness index β. PAH subjects underwent repeat IVUS examinations after 6 months of bosentan therapy. At baseline, PAH subjects demonstrated greater stiffness in all measured indices compared to controls: compliance (1.50±0.11×10⁻² mm²/mmHg versus 4.49±0.43×10⁻² mm²/mmHg, P<0.0001), distensibility (0.32±0.03 %/mmHg versus 1.18±0.13 %/mmHg, P<0.0001), pressure-strain modulus (720±64 mmHg versus 198±19 mmHg, P<0.001), and higher stiffness index β (15.0±1.4 versus 11.0±0.7, P=0.046). Strong inverse exponential relationships existed between mean pulmonary arterial pressure and compliance (r² =0.815, P<0.0001), and also between mean PAP and distensibility (r=0.790, P=0.002). Bosentan therapy for 6 months was not associated with significant changes in PA stiffness. Increased stiffness occurs in the proximal elastic PAs in patients with PAH, and may be an important contributor to the pathogenesis of RV failure in this condition.
3.4 An Australian tertiary referral centre experience of the management of CTEPH

Maliyasena VA, Hopkins PMA, Thomson BM, Dunning J, Wall DA, Ng BJH, McNeil KD, and Kermeen FD
Queensland Centre for Pulmonary Transplantation and Vascular Disease, the Prince Charles Hospital, Brisbane, Queensland, Australia

The intent was to report the outcome of pulmonary endarterectomy (PEA) surgery performed for chronic thromboembolic pulmonary hypertension (CTEPH) at a single tertiary centre. Design, setting, and participants: Prospective study of 35 patients with surgically amenable CTEPH undergoing PEA between September 2004 and September 2010. Functional data [New York Heart Association (NYHA) class, 6-minute walk test distance], hemodynamic data (echocardiography, right heart catheterization, and cardiac MRI), and outcome data (morbidity and mortality), were collected. Following PEA, there were significant improvements in NYHA class (pre 2.9±0.7 versus post 1.3±0.5, P<0.0001), right ventricular systolic pressure (pre 77.4±24.8 mmHg versus post 44.6±24.3 mmHg, P=0.0003), 6-minute walk distance (pre 438.0±97.9 meters versus post 520.2±81.4 meters, P=0.0005). Borg scores (pre 4.2±1.9 versus post 2.8±1.4, P=0.0123), mean pulmonary artery pressure (pre 42±15.1 mmHg versus post 24±8.8 mmHg, P=0.0001), and cardiac MRI indices (end diastolic volume pre 231.8±49.2 ml. versus post 148.1±45.5 ml, P<0.0001; end systolic volume pre 130.1±41.9 ml. versus post 78.8±25.6 ml, P<0.0001). Mean coronary bypass time was 258.7±26.16 minutes, with a mean clamp time of 110.9±35.26 minutes, a mean rewarming time of 81.76±27.02 minutes, and mean circulatory arrest time of 43.83±18.78 minutes. Mean ventilation time was 4.7±2.93 days (range 0.2-32.7), with a mean intensive care unit stay of 7.22±8.71 days (range 1.3-33.8). Complications included slow respiratory wean (25.7%), pericardial effusion (11.4%), persistent pulmonary hypertension (17.1%), reperfusion lung injury (20%) and cardiac tamponade (5.7%). One-year mortality post-procedure was 11.4%. Pulmonary endarterectomy can be performed safely with relatively low mortality.

3.5 N-Terminal pro-Brain Natriuretic Peptide (NT-proBNP) levels predict incident pulmonary arterial hypertension in systemic sclerosis (SSc) in the Australian Scleroderma Cohort Study (ASCs)

Thakkur V, Stevens W, Priorov D, Byron J, Patterson K, Hisarria P, Moore O, Roddy J, Zochling J, Sahhar J, Nash P, Tynmns K, Youssef P, Proudman S, and Nikpour M
St. Vincent’s Hospital Melbourne, Royal Adelaide Hospital, Royal Perth Hospital, The Menzies Institute, Monash Medical Centre, Sunshine Coast Rheumatology, Canberra Rheumatology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

To assess the use of NT-proBNP as a screening biomarker for SSc-PAH. NT-proBNP levels were assessed on patients with normal LV function and eGFR >30 ml/min enrolled in the ASCS, which currently includes over 1,150 patients across Australia. Group 1 (n=20) had definite PAH with pretreatment sera assessed. Group 2 (n=30) were considered “at risk” for PAH based on (i) sPAP on echo >36 mmHg, or (ii) FVC/DLCO% ≥1.6 and no significant ILD, or (iii) DLCO <50%, or (iv) resting mPAP of 20-25 mmHg at RHC. Group 3 (n=19) had ILD but no evidence of PAH on echo or RHC. Group 4 (n=31) were SSc controls. Group 1 (PAH) had significantly higher mean NT-proBNP levels than patients in Group 4 (SSc controls; P=0.0001). In addition, patients in Group 2 (“at risk”) had significantly higher NT-proBNP levels than those in Group 4 (SSc controls; P=0.008). NT-proBNP was positively correlated with echo parameters (P<0.0001). NT-proBNP was positively correlated with mPAP on RHC (adjusted estimate=0.048, 95% CI: 0.01-0.09, P=0.019), independently of corrected DLCO, FVC/DLCO% ratio and 6MWD. An NT-proBNP cut-point of >189.2 pg/ml had a likelihood ratio of 26.4 for presence of PAH (c-statistic=0.9; sensitivity 85%; specificity 97%). An NT-proBNP level <82.9 pg/ml had a likelihood ratio of 6.8 for exclusion of PAH (sensitivity 67.7%, specificity 90%). In the absence of LV dysfunction, NT-proBNP is a useful screening biomarker for PAH in SSc, with levels >189.2 pg/ml and <82.9 pg/ml defining patients with a high and low likelihood of PAH.

3.6 Survival and predictors of mortality in Australian patients with connective tissue disease-associated pulmonary arterial hypertension

Ngian GS, Stevens W, Byron J, Tran A, Roddy J, Minson R, Hill C, Chow K, Sahhar J, Proudman S, and Nikpour M
The University of Melbourne; St Vincent’s Hospital, Melbourne; Royal Perth Hospital, Perth; Flinders Medical Centre, Adelaide; The Queen Elizabeth Hospital, Adelaide; Royal Adelaide Hospital, Adelaide; Monash Medical Centre, Melbourne, Victoria, Australia

We sought to determine survival and factors predictive of mortality in connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH). This was a retrospective cohort study of patients with CTD-PAH recruited from 6 tertiary hospitals. Patients were identified from the Australian Scleroderma Cohort Study and registers of patients receiving pulmonary vasodilator therapy. Records were censored at 31/12/09. Survival was determined using Kaplan-Meier estimates. Univariate and multivariable predictors of survival were determined using log-rank/ Wilcoxon tests, and proportional hazards regression modeling. Among 117 patients (105 female) there were 32 deaths. Mean age at PAH diagnosis was 61.5±11.4 years. SSc was the most common underlying CTD, accounting for 104 patients (88.9%). Forty-eight patients (41.0%) had coexistent interstitial lung disease. Average duration of follow-up from PAH diagnosis was 2.6±1.8 years. Seventy patients (59.8%) received monotherapy, 12 (10.3%) sequential monotherapy, and 34 (29.0%) combination pulmonary vasodilator therapy. One-, 2- and 3-year survival was 94, 89 and 73%, respectively. On multiple regression analysis, higher baseline WHO functional class, higher baseline mRAP, lower baseline 6-minute walk distance, pericardial effusion and absence of warfarin or combination pulmonary vasodilator therapy were independent predictors of mortality. Among patients in this study, 3-year survival is 73%. Independent predictors of survival in our study included warfarin and combination pulmonary vasodilator therapy, neither of which has previously been shown to correlate with survival in CTD-PAH. Our findings suggest that earlier diagnosis, anticoagulation and combination pulmonary vasodilator therapy may improve survival in CTD-PAH.

3.7 Chronic thromboembolic pulmonary hypertension: MRI predictors of functional and haemodynamic outcomes with pulmonary endarterectomy

Ng BJH, Slaughter RE, Stragnell WE, Yerkovich ST, McNeil K, Dunning JJ, Hopkins PMA, and Kermeen FD
Queensland Centre for Pulmonary Transplantation and Vascular Disease, Centre of Excellence in Cardiovascular MRI, The Prince Charles Hospital, Brisbane, Queensland, Australia; UK Centre for Pulmonary Endarterectomy, Papworth Hospital, Cambridge, UK

The assessment of chronic thromboembolic pulmonary hypertension (CTEPH) with MRI before pulmonary endarterectomy (PEA) is well established. However, monitoring after PEA with the use of CMRI, MRA
and MR perfusion has not been studied together. Our objective was to identify the changes (Δ) in MRI parameters that predict functional and hemodynamic outcomes with PEA. Between 2004 and 2007, 19 subjects underwent MRI before and after PEA. CMRI, MRA and MR perfusion examined RV remodeling (RVEDV, RVESV, RVEF), pulmonary vasculature abnormalities at a segmental level and disease distribution respectively. During 24-month follow-ups, functional (WHO class, 6MWD) and hemodynamic outcomes (PVR, mPAP, cardiac index) were collected. In our cohort (mean±SE age 57±12 years, WHO class 2.8±0.7, 6MWD 41±103 meters and PVR 702±38 dynes/s/cm²), all but two subjects were in WHO class I/II post-PEA. PEA resulted in reduced PVR (262±133 dynes/s/cm²) that correlated with RVEDV Δ (r²=0.48, P=0.002) and RVESV Δ (r²=0.28, P=0.024). Multiple linear regression analysis demonstrated that RVEDV Δ and MR perfusion Δ were the strongest predictors of hemodynamic and functional outcomes, respectively. Based on MRA, disease clearance related to WHO class improvement at 6-12 months follow-up (P=0.041) on univariate analysis. MR perfusion Δ is a strong predictor of functional outcomes after PEA. RV remodeling, as demonstrated by CMRI Δ, is a significant predictor of hemodynamic outcomes. Based on MRA, disease clearance of at least four segments results in functional improvement. MRI is an invaluable non-invasive tool in assessing outcomes for patients undergoing PEA.

3.8 The demographics of pulmonary arterial hypertension associated with congenital heart disease: Results from a national registry

Strange G, Rose M, Kermeen F, King I, Vidmar S, Grigg L, Celermajer D, and Weintraub R (on behalf of the ANZ CHD-PAH Registry)
Royal Children’s Hospital, Melbourne; The Prince Charles Hospital, Brisbane; Royal Melbourne Hospital, Melbourne; Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

Pulmonary arterial hypertension (PAH) frequently accompanies childhood congenital heart disease (CHD) and may persist into adult life. The advent of specific PAH therapies for PAH prompted formation of a national ANZ registry in 2010 to document the incidence, demographics, presentation and outcomes for these patients. This multicenter, prospective, web-based registry enrolls patients with CHD-associated PAH being followed in a tertiary center. The inclusion criteria stipulated patient age >16 years, a measured mPAP >25mmHg at rest or echocardiographic evidence of PAH or a diagnosis of Eisenmenger syndrome, and followed since 1/1/2000. A single observer collected standardized data during a series of site visits. So far, 137 patients (61.3% females) have been enrolled. The mean age (SD) at the time of PAH diagnosis or confirmation in an adult center was 28.3 (6.7) years and 41 (29.9%) patients were aged >30 years at this time. The mean duration of follow-up was 8.0 (4.4) years. Thirty-eight (27.7%) patients were in WHO functional Class II and 96 (70.1%) in Class III at the time of diagnosis; 134 of 137 (97.8%) had congenital systemic-pulmonary shunts, and 97 (70.8%) never underwent intervention; 43 (31.4%) had Down syndrome. Confirmation of PAH by recent cardiac catheterization was available in 90 (65.7%) subjects. During follow-up a total of 19 (13.9%) patients died or underwent transplantation. CHD associated with PAH in adult life has resulted in a new population with unique needs. This registry will allow documentation of clinical course and long-term outcomes for these patients.

3.9 Lung disease, particularly pulmonary arterial hypertension, is the major cause of death in the Australian Systemic Sclerosis Cohort Study

Stevens W, Thakkar V, Moore O, Byron J, Proudman S, Zochling J, Rody J, Sahbar J, Nash P, Youssef P, Major G, Tynns K, Hill C, Burgess A, Schrieber A and Nikpour M
The University of Melbourne; St Vincent’s Hospital, Melbourne; Royal Perth Hospital, Perth; Flinders Medical Centre, Adelaide; The Queen Elizabeth Hospital, Adelaide; Royal Adelaide Hospital, Adelaide; Monash Medical Centre, Melbourne, Victoria, Australia

The objectives of this study were to determine the cause of death among a cohort of patients with systemic sclerosis (SSc). The Australian Systemic Sclerosis Cohort Study is a national multicenter prospective study of patients with SSc. Comprehensive disease data are captured at least annually on all patients. Deaths and details on the cause of death and other comorbidities are recorded. Since 2007, 1,136 patients have been enrolled. Mean±SD follow up was 2.1±0.88 years. Sixty-nine deaths had been reported. Mean±SD age at death was 67.3±10.1 years. Disease duration at time of death was significantly shorter in patients with diffuse SSc than in patients with limited SSc (mean 12.0±13.0 versus 20.0±14.1 years, P=0.006). Cause of death was determined to be SSc-related in 39 (57%), unrelated to SSc in 29 (42%). The leading cause of SSc-related death was lung disease, accounting for 43% of total deaths and 76% of SSc-related deaths. Among the 30 lung-related deaths, 20 patients had isolated PAH, 3 ILD and 7 had both ILD and pulmonary arterial hypertension (PAH). Other SSc-related deaths were classified as multiorgan in 3, sepsis related to SSc in 2, GIT involvement in 2, renal crisis 1, and SSc myocardial disease 1. The second most common cause of death was cancer, accounting for 14 deaths (20% of total deaths). Cardiovascular events were responsible for 8 deaths (11.6% of total deaths). Despite the advent of new therapies, PAH remains a major cause of death in our patients. Earlier detection and treatment of this complication through screening may improve survival.

3.10 Evolution of a pulmonary hypertension clinic

Cicovic A, McWilliams T, Coverdale HA, Whyke K, Stewart C, and Wasyswich CA
Green Lane Cardiovascular Service, New Zealand Heart and Lung Transplant Service, Auckland City Hospital, Auckland, New Zealand

Pulmonary arterial hypertension (PAH) is associated with a high morbidity and mortality. Since the 1990s PAH-specific therapy has been shown to be effective in improving symptoms and survival. Access to therapy has been tightly controlled in New Zealand due to the high cost of therapy. In June 2009, PAH-specific drug therapy was funded through Special Authority, and all patients were required to commence sildenafil as first-line therapy. This study describes the population of adult patients followed in the Auckland City Hospital PAH clinic. All patients followed long term at the PAH clinic are entered into a database allowing longitudinal evaluation. Patients within this cohort included those treated before the availability of funded therapy and those treated in the current era. Ninety-seven patients (74 female; 76%) were followed. Mean age at the time of diagnosis was 49 (SD 17) years. Most had PAH due to connective tissue disease (42, 43%) and idiopathic PAH (36, 38%). At diagnosis mean PVR was 9.1 WU (SD 5.5WU), median WHO functional class was 3, and mean 6-minute walk distance 335 m. (SD 131 m.). Patients had been treated with a variety of medications (particularly sildenafil (78%), bosentan (28%) and iloprost (24%)), 1/4 were treated with combination drug therapy, 25%. Of patients seen since 2000, 21 of 92 have died (data censored 1/3/2011). This study describes a unique group of PAH patients who were commenced on sildenafil as first-line therapy. Escalation to combination therapy is common (due to disease progression/failure of monotherapy).
We did not find an association between serum IL-6, IL-13, FGF-2, VEGF levels and fractalkine (P=0.12) in SSc patients with and without PAH. VEGF was 39.5±12.4 mmHg. There were no significant differences seen in 1) versus 26.3±2.6 mmHg (Group 2). The mean PAP in Group 1 at RHC was 65.3±27.8 mmHg (Group 3) versus 50.4±16.9 mmHg (Group 1) with idiopathic pulmonary arterial hypertension (IPAH) has not been well described in the literature. A retrospective analysis of patients with a diagnosis of IPAH treated at the Queensland Centre for Pulmonary Transplantation and Vascular Disease between 2002 and 2010 was conducted. Existing CT scans were reviewed for the presence of neovascularity, and correlations were made to measures of hemodynamics attained by right heart catheter and transathoracic echocardiography. Forty-five patients with IPAH (25 female), of mean (SD) age of 53.5 (16.9) years and mean (SD) PAP of 50.4 (2.2) mmHg were included in the analysis. Neovascularity was present in 8/45 (17.8%) patients, with half of these patients having this feature in more than 50% of their lungs. Neovascularity was generally distributed throughout the entirety of the lung parenchyma, with no predominance for either the left/right lungs or upper/lower zones. There was a moderate positive correlation to all measures of hemodynamics that was strongest for the diastolic pulmonary arterial pressure (r=0.415, P<0.01), and a positive correlation to the six-minute walk distance (r=0.305, P<0.05). This is the first study to demonstrate a correlation between neovascularity and both pulmonary arterial pressures and six-minute walk distance in patients with IPAH. The presence of this feature may be evidence of severe and longstanding pulmonary arterial hypertension leading to the development of pulmonary plexogenic arteriopathy.

### 3.12 Novel biomarkers of dysregulated angiogenesis are not specific to pulmonary arterial hypertension in systemic sclerosis

**Thakkar V, Patterson K, Stevens W, Byron J, Moore O, Roddy J, Zochling J, Sahhar J, Nash P, Tymms K, Youssef P, Proudman S, Nikpour M, and Hisarria P**

St. Vincent’s Hospital Melbourne, Royal Adelaide Hospital, Royal Perth Hospital, The Menzies Institute, Monash Medical Centre, Sunshine Coast Rheumatology, Canberra Rheumatology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

Dysregulated angiogenesis mediated by cytokines, chemokinies and growth factors has been postulated to underlie the pathogenesis of systemic sclerosis (SSc)-related pulmonary arterial hypertension (PAH). We undertook an exploratory study of these factors evaluating whether a single serum measurement could be used as a biomarker in SSC-PAH. Two main clinical groups were selected from the Australian Scleroderma Cohort Study (ASCs): Group 1 (n=20) had definite PAH defined by Dana Point criteria on RHC; Group 2 (n=26) were SSC controls with no evidence of cardiopulmonary disease. Serum IL-6, IL-13, FGF-2, VEGF and fractalkine levels were measured with the commercially available Millipore Milliplex MAP Human cytokine/chemokine panel. Patients in Group 1 (PAH) were older at the time of study (62±10.3 versus 48±10.1 yrs) and had a longer disease duration (20.4±2.9 versus 7.6±1.3 yrs.) than patients in Group 2 (controls). The mean echocardiography defined systolic pulmonary artery pressure (PAP) was 65.3±27.8 mmHg (Group 1) versus 26.3±26 mmHg (Group 2). The mean PAP in Group 1 at RHC was 39.5±12.4 mmHg. There were no significant differences seen in levels of IL-6 (P=0.23), IL-13 (P=0.97), VEGF (P=0.14), FGF-2 (P=0.34) and fractalkine (P=0.12) in SSC patients with and without PAH. VEGF levels (P=0.05) appear to be higher in diffuse subtype of the disease. We did not find an association between serum IL-6, IL-13, FGF-2, VEGF, fractalkine and SSC-PAH. While these factors may play a role in the pathogenesis of SSC and SSC-PAH, their serum levels do not appear to correlate with clinical PAH.

### 3.13 Treatment for pulmonary arterial hypertension complicating congenital heart disease in adults: Results from a national registry

**Rose M, Strange G, Kermeen F, King J, Vidmar S, Grigg L, Weintraub R, and Celermajer D (on behalf of the ANZ CHD-PAH Registry)**

The Royal Children’s Hospital, Melbourne; The Prince Charles Hospital, Brisbane; Royal Melbourne Hospital, Melbourne; Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

Pulmonary arterial hypertension (PAH) complicates 5-10% of adult congenital heart disease (CHD). Improving survival in CHD patients has resulted in a new cohort of adults for whom PAH-specific therapy has recently become available. We established a nationwide registry for adults with PAH complicating CHD, documenting lesions, treatment patterns and outcomes. This multicenter prospective, web-based registry enrolls patients with CHD-related PAH being followed in a tertiary center, since 1/1/2000. The inclusion criteria include age >16 years, a measured mPAP >25 mmHg at rest, echocardiographic evidence of PAH, or a diagnosis of Eisenmenger syndrome. Standardized data were collected by a single observer during site visits. There are 137 patients enrolled with 134 (97.8%) being in WHO functional Class II or III at their first eligible visit. The current mean (SD) age was 38±12.7 years. Of the patients, 134 of 137 (97.8%) had congenital systemic-pulmonary shunts and 97 (70.8%) patients had never undergone intervention. At latest follow-up, a total 89 of 137 (65.0%) patients were receiving a PAH-specific therapy, including an endothelin receptor antagonist in 77 (56.2%), a PDE5 inhibitor in 20 (14.6%), a prostanoid in 2 (1.5%) and a calcium channel blocker in 4 (2.9%). Anticoagulants (warfarin or antiplatelet agent) were being used in 31 (22.6%) and diuretics in 30 (21.9%). PAH complicating often complex CHD is an increasing clinical problem. Of symptomatic adults with CHD associated PAH, 35% were not receiving PAH-specific therapy. The proportion of untreated patients may well be higher outside tertiary centers.

### 3.14 Serum ICAM-1 levels are related to the presence of interstitial lung disease in systemic sclerosis

**Thakkar V, Patterson K, Stevens W, Byron J, Moore O, Roddy J, Zochling J, Sahhar J, Nash P, Tymms K, Youssef P, Proudman S, Hisarria P, and Nikpour M**

St. Vincent’s Hospital Melbourne, Royal Adelaide Hospital, Royal Perth Hospital, The Menzies Institute, Monash Medical Centre, Sunshine Coast Rheumatology, Canberra Rheumatology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

Recent studies have suggested elevated ICAM-1 (intercellular adhesion molecule-1) and VCAM-1 (vascular cell adhesion molecule-1) levels may be markers of pulmonary arterial hypertension in systemic sclerosis (SSc-PAH). Four clinical groups were selected from the Australian Scleroderma Cohort Study (ASCs): Group 1 (n=20) had definite PAH; Group 2 (n=19) had ILD; Group 3 (n=23) were SSC controls; Group 4 (n=34) were normal healthy controls. Patients with LV dysfunction were excluded. Serum VCAM-1 and ICAM-1 levels were measured using the Millipore Milliplex MAP Human 2-Plex Panel (Millipore Corporation, Billerica, MA, USA). Mean ICAM-1 levels were significantly higher in the ILD group compared to the PAH (380.4±168.3 versus 266.4±88.4 ng/ml, P=0.035), SSC control (380.4±168.3 versus 257.3±97.8 ng/ml, P=0.006) levels.
and healthy control (380.4±168.3 versus 201.8±57.2 ng/ml, P=0.0001) groups. Notably there was no significant difference between the PAH group and SSC or healthy normal controls. Among those with I LD there were no significant differences in ICAM-1 levels between those who did or did not have previous cyclophosphamide treatment for SSC-ILD (P=0.36). VCAM-1 levels were shown to be significantly higher in SSC patients than normal healthy controls (1420.0±53.4 versus 1125.6±46.9 ng/ml, P=0.0005) but were not specific for PAH. ICAM-1 levels are associated with the presence of significant SSC-ILD. However, ICAM-1 level does not appear to be a specific marker for the presence of PAH. VCAM-1 levels are raised in SSC patients but are not specific for PAH.

3.15 Predictors of six-minute walk distance in patients with systemic sclerosis associated pulmonary hypertension

Tippin M, Chambers D, Slaughter R, Mohammed O, and Kermeen F
School of Medicine, Queensland Centre for Pulmonary Transplantation and Vascular Disease, Department of Medical Imaging, The Prince Charles Hospital, The University of Queensland, Brisbane, Queensland, Australia

The six-minute walk distance (6-MWD) is frequently used as a measure of exercise capacity in patients with systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH). However, multiple patient factors may have an influence on the distance achieved. Therefore, this study aimed to evaluate 6-MWD predictors in patients with SSc-PAH. A retrospective analysis of patients with a diagnosis of SSc-PAH treated at the Queensland Centre for Pulmonary Transplantation and Vascular Disease between 2002 and 2010 was conducted. A regression analysis (automatic linear modeling, forward stepwise, information criterion) for 6-MWD using measures of hemodynamics and respiratory function, as well as interstitial lung disease features evident on HRCT, was conducted. Fifty-seven patients with SSc-PAH (50 female), of mean (SD) age of 60.7 (9.6) years and mean (SD) PAP of 44.3 (14.3) mmHg were included in the analysis. The most predictive model had 45.0% accuracy, with a mean (SD) residual of 0.000 (1.011). It retained only the forced vital capacity (B=118.520), diffusing capacity for carbon monoxide (B=19.760), alveolar volume (B=-90.036), interlobular septal thickening (B=-12.879) diastolic pulmonary arterial pressure (B=-2.730) and ground-glass opacification (B=-4.225) as significant covariates, with an intercept (B=303.581). These findings suggest that the HRCT features of ground-glass opacification and interlobular septal thickening, in addition to respiratory function and hemodynamics, are also important predictors for the 6-MWD. This may be a function of the underlying pathology that is not captured satisfactorily through measures of respiratory and hemodynamics, and should be taken into account when evaluating the 6-MWD in patients with SSc-PAH.

3.16 Stretching the boundaries: The effectiveness of Tai chi in PAH

Harris JE, Scale HE, McKinnon K, Cornwall PL, Morris N, and Kermeen FD
Johns Hopkins Medical Institutions, Baltimore, MD, USA

Psychological and cardiopulmonary benefits of Tai chi (TC) have been reported for healthy populations, and in a wide range of patient groups, including hypertension and heart failure. The effectiveness of TC has never been studied in pulmonary arterial hypertension (PAH). The aim of this study was to assess the benefits of TC in relation to psychosocial and cardiopulmonary outcomes, in idiopathic PAH (iPAH) and PAH related to connective tissue disorders (CTD-PAH). Twelve patients with iPAH or CTD-PAH (NYHA Class II–III) underwent a crossover study involving a 12-week period of "usual activity" followed by a 12-week TC intervention program. Primary outcome measures of 6-MWD, resting and exercise SpO2, BORG scale, heart rate response, Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR), Depression and Anxiety Stress Scale (DASS), and the Spirituality Index of Well-Being (SIWB) were performed at baseline, 12 weeks and 24 weeks. The cohort consisted of 10 females with a mean age of 54 years (SD=13.76). Comparisons between baseline and 12-week data revealed no significant differences in 6-MWD (t=0.44, P=0.42), resting SpO2 (t=-0.971, P=0.36), BORG (t=0.31, P=0.76) and heart rate response (t=-1.35, P=0.21), and exercise SpO2 (t=-1.514, P=0.16) and BORG (t=-0.87, P=0.40). Comparison of psychosocial outcomes between baseline and 12-week data revealed no significant differences in total scores on the CAMPHOR (t=-0.25, P=0.81), DASS (t=-0.27, P=0.80) and SIWB (t=1.59, P=0.14). Initial results have suggested that the study cohort had stable physical and psychosocial status, with outcomes following TC intervention to be analyzed and presented.

3.17 The hidden risk of a 6-minute walk test in pulmonary arterial hypertension

Scale H, Harris J, Hall K, and Kermeen F
School of Public Health and Community Medicine, University of New South Wales, Sydney, New South Wales, Australia

The 6-minute walk test (6-MWT) is a standard clinical estimate of functional capacity and is routinely used to evaluate response to specific pulmonary arterial hypertension (PAH) therapies. While malignant ventricular arrhythmias are reported to be rare in PAH patients, atrial fibrillation and atrial flutter are equally common and invariably associated with deterioration and right ventricular failure which may potentially increase the risk of performing a 6-MWT. Electrocardiographic monitoring is not routinely recorded during a 6-MWT. Case report of ventricular fibrillation (VF) arrest following a 6-MWT: A 25-year-old female with surgically repaired congenital heart disease with associated pulmonary hypertension on combination PAH therapy; Electrocardiography: Severe RV dilatation, moderate RA dilatation, RVSFP 61 mmHg, moderate LV dysfunction with LV EF 43%, RHC: mean PAP 37 mmHg, CI 2.1 L/min/m2; PVR 10 WU, WHO class ll. 6-MWT: 610 m, SpO2 nadir 85%. One minute post 6-MWT, a patient suffered VF cardiac arrest. Coronary angiogram and IVUS (intravascular ultrasound) with exercise excluded compression of left main coronary artery from a dilated pulmonary artery as possible cause. Review of defibrillator and pacemaker rhythm suggestive of polymorphic VT secondary to LV dysfunction as probable cause. Implantable defibrillator inserted. This case highlights the need for identification of patients at risk of cardiac arrhythmias associated with PAH and the need for ECG monitoring while undertaking simple tests of functional capacity.

3.18 Symptoms to definitive diagnosis of pulmonary arterial hypertension

Strange G, Keogh A, Stewart S, Carrington M, Kermeen F, Williams T, and Gabbay E
Monash University, Melbourne; St Vincent’s Hospital, Sydney; Royal Perth Hospital, Perth; Lung Institute of Western Australia; University of Notre Dame; Baker IDI, Melbourne; The Prince Charles Hospital Melbourne; The Alfred Hospital, Melbourne; and University of Western Australia, Australia

Diagnosis of pulmonary arterial hypertension (PAH) has historically been delayed. We examined time to diagnosis (TTD) and factors potentially...
contributing to any delay. We retrospectively enrolled consecutively diagnosed patients with idiopathic PAH (iPAH) from four pulmonary hypertension (PHT) centers (total n=32) throughout Australia (January 2007 and December 2008). All patients underwent right heart catheterization (RHC); other forms of PHT were excluded. Patients were interviewed by an examiner blinded to history prior to review of medical records. Multivariate regression analysis was performed to determine factors correlated with TTD. On RHC, mPAP (43.9±13.6 mmHg), PVR (8.8±5.7 wood units), CI (2.74±0.92) and PCWP (11.74±3.76 mmHg) were consistent with PAH. Mean TTD from symptom onset was 47.1±34.2 months. Functional class (FC) at symptom onset was FC II (95%) FC III (5%), compared to FC II (5%), FC III (90%) and FC IV (5%) at diagnosis. Patients were reviewed 5.0 (IQR 1-10) times by their general practitioner (GP) and consulted an average of three specialists prior to diagnosis of iPAH. TTD in iPAH patients was 3.9 years, suggesting significant delays persist. Patients experienced a FC deterioration during this time of delay. Factors significantly associated with a delay in diagnosis include older age, number of GP visits, higher systolic BP, and lower HR.

3.19
Pulmonary hypertension is a common disease: The Armadale echo study

Strange G, Playford D, Stewart S, Kent A, Deague J, and Gabbay E
Monash University, Melbourne, Australia; Royal Perth Hospital, Western Australia; University of Notre Dame Western Australia; Lung Institute of Western Australia, The Baker IDI, Melbourne, Australia

There have been few studies describing the epidemiological of pulmonary hypertension (PHT). We examined the prevalence of all forms of PHT in a population found to have elevated right ventricular systolic pressures (RVSP) at echocardiography (echo). Armadale is a town of 165,450 people 40 kilometers from Perth, Western Australia. We extracted the estimated RVSP (eRVSP) from 10,314 patients (15,633 studies) in our laboratory between 2003 and 2009. We included all patients with a PASP >40 mmHg or with insufficient tricuspid regurgitation for eRVSP. Between 2003 and 2009, 936 patients were found to have PASP >40 mmHg (9%), and 3,321 patients had insufficient TR to accurately estimate RVSP (32%). We calculated a minimum cumulative prevalence of 3,257 patients/million of the population for all forms of PHT. In an unselected population of patients in a general echo laboratory, PHT is common (9% of patients) with a cumulative prevalence of all forms of PHT at least 3,257 patients/million of the population. In our population, a significant proportion of patients had no obvious cause for their PHT (15%).