Survival of IPAH patients without PFO sub groups with mild vs moderate vs severe hypoxemia: Survival proportions

Abstract P138 Figure 1 Survival of IPAH patients without PFO based on severity of hypoxemia. Log rank comparisons

P139 SURVIVAL OF IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION BMPR2 MUTATION CARRIERS VS BMPR2 NON CARRIERS

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Introduction Idiopathic pulmonary arterial hypertension (IPAH) is a devastating condition characterised by the narrowing and obliteration of small pulmonary arteries, leading to elevated pulmonary arterial pressure and ultimately to right heart failure and death. Even with treatment, IPAH survival is poor with 3 year survival reported to be 63% on epoprostenol (McLaughlin, *Circulation* 2002). Pulmonary arterial hypertension (PAH) can be heritable, with mutations found in the bone morphogenetic protein type 2 receptor (BMPR2) gene found in > 70% of familial cases, (Lane, *Nat Genet* 2000). There are previous conflicting reports of worse survival in heritable PAH, but this has not previously been determined in the UK patient population.

Methods This study examined the retrospective database of 76 IPAH cases diagnosed between 2001–2006. 32 patients were screened for BMPR2 mutation. 13 were BMPR2+ve. Non-screened (NS) IPAH were included in the survival analysis (n=44). Survival time was taken from the time of initial diagnostic right heart catheterisation. Demographics, treatment, 6MWT, time to transplant and World Health Organization (WHO) classification were compared. Physicians were blinded to the BMPR2 status at time of treatment.

Results All three cohorts presented at baseline with no significant difference in functional class, 6MWT, hemodynamics except age, cardiac index (CI), right atrial pressure (RAP) and treatment modalities. Patients with BMPR2 mutation were significantly younger. Of the BMPR2+ve group, 6 patients were transplanted compared to zero in the BMPR2-ve group. The NS IPAH cohort had 2 patients transplanted and fewer patients were treated with prostanoids. Time to transplant was shorter in the BMPR2 mutation carriers, 2.65 years, vs. 3.1 years in the NS IPAH group.

Conclusion Survival for the first 5 years from diagnosis was similar in IPAH and heritable PAH. The BMPR2 +ve patients presented younger with severe disease and were treated more aggressively with 6 patients undergoing transplant in the 5 year period. BMPR2

mutation frequency was 41% from our cohort of 33 which is higher than previously reports of 20–30% (Morrell, *Proc Am Thorac Soc*, 2006). Survival for IPAH continues to be poor even with improvements in treatment. Patients with BMPR2 mutations present with severe disease earlier and time to lung transplant is shorter.

Abstract P139 Figure 1

P140 HIGH-DOSE OESTROGENS COMMENCED FOR GENDER REASSIGNMENT SURGERY MAY PREDISPOSE TO THE DEVELOPMENT OF CHRONIC THROMBOEMBOLIC PULMONARY VASCULAR DISEASE

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Background Chronic thromboembolic pulmonary hypertension (CTEPH) often occurs as a sequela of venous thromboembolism (VTE) however, there appears to be marked differences in laboratory risk-profiles between CTEPH and VTE. Clinically, exogenous oestrogens (EO) are known to increase the risk of acute DVT in a dose-dependent manner² but a pathological link with CTEPH is less clear. We describe a case-series of three patients with CTEPH and one with chronic thromboembolic disease without evidence of pulmonary hypertension diagnosed following administration of high-dose EO for gender re-assignment surgery (GRAS). This constitutes a long-term component of treatment, always commenced in males preoperatively.³

Methods Retrospective case note review from 2001–2012 of four patients evaluated for pulmonary arterial hypertension (PAH) at Papworth all receiving high-dose EO as part of GRAS.

Results Oestradiol (oral), Tibolone (transdermal) or privately prescribed unidentifiable “high-dose oestrogens” were received by two, one and one patients for 2, 4 and 1.5 years respectively. CTEPH was diagnosed (by accepted radiological and haemodynamic criteria) at 2, 4 and 2 years respectively after initiating oestrogens. All patients had negative thrombophilia screens and no other risk-factors for VTE or CTEPH. Three of the four patients discontinued oestrogen therapy, patient two continued with oestradiol whilst fully anti-coagulated. Table 1 outlines demographic and haemodynamic criteria.

Conclusions This series is the first to associate high-dose oestrogen therapy with chronic thromboembolic pulmonary vascular disease and should prompt suspicion of this disorder in patients undergoing GRAS with chronic effort breathlessness. Whilst the predisposition from EO in oral contraceptive or hormone replacement therapy is well recognised in acute VTE, we observe four patients who developed CTEPH following high-dose oestrogen therapy two of whom did not suffer prior VTE. Animal data suggesting a protective effect of oestrogen on pulmonary vasculature in PAH is discordant with our observations but the clinical mechanisms and interpretation of our findings are likely to be more complex.³

References

1. Holst A et al. Risk factors for venous thromboembolism - Results from the Copenhagen City Heart Study. *Circulation*. 121(17)2010:1896–1903.
2. Newfield et al. Female-to-male trans gender quality of life. *Quality of life research*, 2006 vol 15(9), 1447–1457.
3. Jesus Perez. Making Sense of the Estrogen Paradox in Pulmonary Arterial Hypertension. *AJRCCM* 2011; 184; 629.

Abstract P140 Table 1

	Patient 1	Patient 2	Patient 3	Patient 4
Age	47	41	75	48
Dose of oestrogens	“high dose”	Oestradiol 6mg/day	Tibolone 2.5mg/day	Oestradiol 6mg/day
Lead time to CTEPH diagnosis (yrs)	2	2	4	2
Antecedent VTE				
DVT	1996, 2000 & 2007	None	None	2008
PE	1995	None	None	2011
Smoking history	None	20 pack years	None	2.5 pack years
Haemodynamics at diagnosis				
Mean PAP (mmHg)	40	43	40	16
PVR (dynes)	595	592	777	110
Cardiac index (l/min/m ²)	2.2	2.1	1.6	2.8
Functional level at diagnosis				
WHO class	II	III	III	II
6min walk dist (m)	295	384	*30 (shuttle walk)	580
Spirometry				
FEV ₁	2.9 (95%)	4.2 (94%)	1.7 (59%)	3.4 (119%)
FVC	4.3 (122%)	5.1 (93%)	2.4 (62%)	4.6 (137%)
TLCO	79%	64%	45%	99%
Radiological distribution	Proximal	Distal (non-operable)	Proximal	Proximal
Outcome	Successfully operated. Still alive	Non-operable. Died 2009 of right heart failure	Declined surgery. Still alive	Awaiting surgery. Still alive

P141 OUTPATIENT MANAGEMENT OF SUSPECTED PULMONARY EMBOLISM AT A DISTRICT GENERAL HOSPITAL; A TWO MONTH REVIEW

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Background Studies have suggested that outpatient (OP) management of suspected pulmonary embolism (PE) is feasible.¹ At our DGH (popⁿ 289,400) the decision to manage a suspected PE as an OP is made clinically by the admitting physician. The aims of our study were

1. To ascertain the proportion of patients who underwent CTPA investigation that were managed as outpatients and subsequent nights saved.
2. To identify any further patients that could have been managed as OP and potential nights that could have been saved.
3. To determine if the outpatients met the current criteria for ambulatory management of PE.

Methods RADIS was used to collect all CTPA's performed between 1st September 2011 and 31st October 2011. Notes were requested.

Inclusion criteria Ambulatory, normal heart rate, respiratory rate, blood pressure and oxygen saturations (on air), any patient who was managed acutely as an OPPEI Score < 85.²

Exclusion criteria Any pre-existing in-patient that had a CTPA ordered where the primary admission (and reason for in-patient stay) was not for suspected PE, any patient who had their CTPA on the same day of discharge, OP CTPA where waiting time was > 2 weeks. PESI Score > 85.²

Results For the above period 105 CTPA's were performed. Average time from request to CTPA was 4.1 hours (1–21 hours.) Figure 1 shows the excluded patients. 15 patients were included; 7 were female, average age 47 years (18–78 years). All had a PESI score < 85. 11 were investigated as outpatients (1 PE +ve) and 4 were kept as inpatients (2 PE +ve). The 11 managed as outpatients resulted in 17 nights saved. The 4 inpatients (if managed as OP) could have saved an additional 6 nights.

Conclusion Over a 2 month period at our DGH most suspected PE patients (suitable for ambulatory care) are being identified resulting in significant (17 nights) bed savings.

1. Hogg K et al, *Emerg Med J* 2006; 23:123–127.
2. Aujesky D et al, *AJRCCM* 2005; 172(8):1041.

Abstract P141 Figure 1