Award-Winning Abstracts Focus on Diagnostic Criteria, Impact of Calcium Channel Blockers

[Editor's note: The following abstracts were chosen at the 7th International Pulmonary Hypertension Conference & Scientific Sessions for their outstanding contribution to the advancement of knowledge in pulmonary hypertension.]

Diagnostic Criteria for Idiopathic Pulmonary Arterial Hypertension (IPAH) Do Not Reflect Patients Treated for IPAH at a Referral Pulmonary Hypertension (PH) Clinic

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Background. Entry criteria for clinical studies of drug treatment in IPAH determine indications for treatment after drug approval We tested the hypothesis that study populations of IPAH are too narrowly focused to accurately represent clinical practice at a PH referral center.

Methods. The database registry of the Mayo Clinic Pulmonary Hypertension Clinic from 1996-2005 was reviewed. Patients (pts) with an invasively documented diagnosis of primary (or idiopathic) PAH were selected according to criteria at the time of their first visit which are commonly used as entry criteria for clinical studies of PAH. The characteristics of the selected population were observed as the inclusion criteria were altered or individually omitted.

Results. The size of the population expanded predictably as the inclusion criteria were loosened. The most strictly defined group (**A**) had only 30 pts as shown in **Table 1**. Group **B** (56 pts) represents the usual inclusion criteria of clinical drug studies. Groups **C-E** include pts in whom the clinical impression was that their diagnoses were IPAH despite some criteria either missing or falling outside usual limits. RVSP, PCWP and TLC remained quite similar among groups even as those criteria were omitted or altered, among those patients in whom measurements were made. SBP increased when a value <140 mm Hg was eliminated as a criterion. Medical treatment was examined in the most strictly and liberally defined groups (**A** and **E: Table 2**). The overall medical profile of each group was similar.

Table 1

	N	#Female(%)	Age	RVSP	MPAP	SBP	PCWP	TLC
A	30	21 (70)	47.8±13.2	90.7±22.5	54.6±9.4	119.3±12.4	9.3±3.1	91.4±11.3
B	56	37 (66)	48.7±13.6	91.4±23.6	54.7±10.0	132.7±20.8	9.4±3.1	95.8±14.1
C	61	40 (66)	48.1±13.4	89.2±26.5	53.9±10.5	133±20.6	9.3±3.0	95.6±13.9
D	167	130 (78)	47.9±15.1	91.2±22.0	54.5±11.2	132.8±22.2	9.5±3.3	93.8±15.3
E	193	151 (78)	49.6±15.3	90.9±22.0	54.1±11.1	134.2±22.9	10.6±4.2	93.7±15.2

A: Echo RVSP>40, mean PAP>25, SBP<140, PCWP≤15, TLC>70%
B. Mean PAP>25, PCWP≤15, TLC>70%, PVR>3
C: Mean PAP>25, PCWP≤15, TLC>70%
D: Mean PAP>25, PCWP≤15
E: Mean PAP>25, PCWP≤20

RVSP = echo-Doppler estimated right ventricular systolic pressure; MPAP = mean pulmonary arterial pressure; SBP = systolic arterial pressure; PCWP = pulmonary capillary wedge pressure; TLC = total lung capacity

Table 2

Group	None or CCB	Prostacyclin Analog	ET Receptor Antagonist	PDE-5 Inhibitor	Combination
A	7 (23%)	18 (60%)	3 (10%)	2 (7%)	5 (17%)
E	47 (24%)	110 (57%)	39 (20%)	7 (4%)	38 (21%)

CCB = calcium channel blocker; ET = endothelin; PDE-5 = phosphodiesterase-5
Percentages do not add up to 100 since some patients were on multiple drugs or combinations during follow-up

Comments and Conclusions. The population diagnosed with and treated for IPAH at this referral center is much larger than, but not dissimilar from, the population defined by conventional hemodynamic, pulmonary function and echocardiographic criteria. Many patients appear to be treated by extrapolation of data from a more narrowly defined population. It is untested whether these patients derive the same benefit from PH drug treatments. We suggest that future clinical drug studies of IPAH be expanded beyond the current narrow definition of IPAH.

Calcium Channel Blockers Impair Right Atrial Contractility and Cardiac Output in Non-Responders with Chronic Pulmonary Hypertension

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Background. The appropriate use of calcium channel blockers (CCB) in patients with chronic pulmonary hypertension (CPH) is controversial. Concern exists that CCB therapy in non-responders may further impair cardiac function, but their effects on right heart mechanics in responders versus non-responders remains unknown.

*P < .05 versus baseline	Baseline	CCB Non-Responder	CCB Responder
RV Systolic Pressure (mmHg)	60 ± 19	62 ± 20	39 ± 40*
Cardiac Output (L/min)	2.0 ± 0.8	1.6 ± 0.8*	1.6 ± 0.9*
RV ESPVR (mmHg/mL)	15.0 ± 11.3	13.3 ± 7.5	5.7 ± 3.0*
RV EDPVR (mmHg/mL)	1.5 ± 1.2	1.3 ± 0.7	1.0 ± 0.4
RA ESPVR (mmHg/mL)	1.8 ± 0.9	1.5 ± 0.6*	0.9 ± 0.4*
RA EDPVR (mmHg/mL)	1.3 ± 0.6	1.4 ± 0.7	1.3 ± 0.8
RA Reservoir Function	68 ± 21%	68 ± 13%	53 ± 18%*
RA Conduit Function	32 ± 27%	32 ± 13%	47 ± 18%*

Methods. In 16 dogs, right atrial (RA) and ventricular (RV) pressure and volume (conductance catheter) were simultaneously recorded after 3 months of progressive pulmonary artery (PA) banding. Diltiazem was given at 10 mg/h with the PA constricted (CCB non-responder). Responders were then created by releasing the PA band to unload the ventricle. RA and RV contractility and diastolic stiffness (slope of end-systolic and end-diastolic PV relations) were calculated and RA reservoir and conduit function were quantified as RA inflow with the tricuspid valve closed versus open, respectively.

Results. With CCB, RA contractility ($P < .03$) and cardiac output ($P < .004$) decreased in non-responders while RV pressure and contractility were unchanged (**Table**). After PA band release, the RA became less distensible, causing a shift from reservoir to conduit function ($P < .001$) and the contractility in both chambers decreased ($P < .007$). RA and RV diastolic function in non-responders and responders was not affected by CCB.

Conclusions. CCB did not impact RV function in non-responders, but significantly impaired RA contractility and cardiac output. In responders, afterload fell substantially to maintain cardiac output despite a decline in the normal RA and RV hyperdynamic contractile response to CPH. Thus, clinical use of CCB in CPH should be restricted to documented responders.

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