

Comorbid Burden and Survival Risk Metrics of Pulmonary Hypertension (PH) Patients in US-Clinical Care: Real-World Assessments from the TRIO Health PH Registry

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1. BACKGROUND AND AIM

The TRIO Health PH registry consists of patients in care in the modern era, differentiating it from existing registry populations (COMPERA/ASPIRE/REVEAL). We present descriptive assessments for the first 725 registry patients, enrolled July 2019 to October 2020, with evaluation of subsets of group 1 - pulmonary arterial hypertension (PAH) and group 4 - chronic thromboembolic pulmonary hypertension (CTEPH).

2. METHODS

TRIO Health PH registry is an observational, retrospective-prospective data collection, combining clinical and prescription data from eight US tertiary care centers. Patients enrolled were those that were prescribed PAH specific medications. Statistical analyses of the study population were via ANOVA and Tukey's studentized range procedure (continuous variables) or Chi-square or Fisher's exact test (categorical variables).

3. RESULTS

- Etiologic subgroups: idiopathic (IPAH, 34%, 243), associated with connective tissue disease (APAH-CTD, 29%, 210), Drugs & Toxins (11% 80), congenital heart disease (APAH-CHD, 6%, 46), and CTEPH (5%, 37). [Table 1]
- The highest proportion of overweight/ obese patients were in the CTEPH (81%, 30) and Drugs & Toxins (75%, 60) subgroups. [Table 1]
- At enrollment, hypertension was most common in Drugs & Toxins (51%, 41), CTEPH (49%, 18), IPAH (39%, 95), APAH-CTD (38%, 79). [Table 2]
- At enrollment, 88% of patients had NYHA functional Class II (46%, 253/554) or Class III (42%, 233/554) symptoms. At diagnosis, 78% of patients were Class II (23%, 72/312) or Class III (55%, 172/312); 18% (55/312) were Class IV. [Table 3]
- Mean 6-minute walking distance (6-MWD) was highest for Drugs & Toxins (381.3 m, n=73) and lowest for APAH-CTD (301.8 m, n=189). [Table 3]
- Mean pulmonary arterial pressure (mPAP) ranged from 38.6 mmHg (CTEPH, n=33) to 48.6 mmHg (APAH-CHD, n=41). [Table 3]
- Mean diffusing capacity for carbon monoxide (DL_{CO}), % predicted was lowest in CTD (40.6%, n=118) and IPAH (57.7%, n=155). [Table 3]
- Serum brain natriuretic peptide (BNP), heart rate and systolic blood pressure were not significantly different by subgroups. [Table 3]

4. CONCLUSION

- Overall cohort's baseline characteristics, including NYHA functional Class II/III, reduced 6MWD (less than 400m), and elevated BNP indicate a compromised group at intermediate risk for clinical progression.
- Continued evaluation of this contemporary real-world population will elucidate disease impact on quality of life, survival, current clinical practices, and place for precision medicine
- Limitations of the study include possible inaccurate entry of information at the source and under reporting of comorbidities.

Table 1 : Patient Demographics	Overall (n=725)	IPAH (n=243) [a]	CTD (n=210) [b]	Drugs & Toxins (n=80) [c]	CHD (n=46) [d]	CTEPH (n=37) [e]	p value < 0.05
Age (years) at enrollment, mean (SD)	58.7 (14.6)	59.0 (15.9)	60.6 (14.1)	54.8 (9.0)	49.5 (13.9)	62.8 (16.9)	a vs. d; b vs. c, d; d vs. e; c vs. e
Age (years) at diagnosis, mean (SD)	51.2 (15.6), (n=594)	51.1 (17.5), (n=208)	53.5 (14.5), (n=161)	47.5 (9.3), (n=77)	41.4 (14.7), (n=40)	58.6 (16.9), (n=29)	a vs. d; b vs. c, d; d vs. e; b vs. c
Gender, n (%)							
Female	545 (75%)	194 (80%)	184 (88%)	48 (60%)	36 (78%)	17 (46%)	a vs. c, e; b vs. c, d; c vs. d, e
Male	180 (25%)	49 (20%)	26 (12%)	32 (40%)	10 (22%)	20 (54%)	
Race, n (%)							
Caucasian	413 (57%)	161 (66%)	104 (50%)	59 (74%)	14 (30%)	21 (57%)	a vs. b, c, d, e; b vs. c, d; c vs. d, e; d vs. e
African American	131 (18%)	35 (14%)	51 (24%)	2 (3%)	0 (0%)	12 (32%)	
Hispanic	105 (14%)	36 (15%)	28 (13%)	13 (16%)	15 (33%)	2 (5%)	
Asian	45 (6%)	5 (2%)	15 (7%)	3 (4%)	13 (28%)	0 (0%)	
Other	18 (2%)	1 (0%)	9 (4%)	3 (4%)	3 (7%)	1 (3%)	
Unknown	13 (2%)	5 (2%)	3 (1%)	0 (0%)	1 (2%)	1 (3%)	
Body Mass Index, n (%)							
Underweight (BMI < 18.5)	21 (3%)	6 (2%)	11 (5%)	0 (0%)	1 (2%)	0 (0%)	a vs. b; b vs. c, e; c vs. d; d vs. e
Normal Weight (18.5 ≤ BMI < 25)	246 (34%)	67 (28%)	100 (48%)	18 (23%)	19 (41%)	7 (19%)	
Overweight (25 ≤ BMI < 30)	190 (26%)	65 (27%)	44 (21%)	20 (25%)	16 (35%)	12 (32%)	
Obesity (BMI ≥ 30)	257 (35%)	100 (41%)	51 (24%)	40 (50%)	10 (22%)	18 (49%)	
Unknown	11 (2%)	5 (2%)	4 (2%)	2 (3%)	0 (0%)	0 (0%)	
Behavioral History, n (%)							
Smoking (Current & Past)	310 (43%)	99 (41%)	67 (32%)	55 (69%)	15 (33%)	14 (38%)	a vs. c; c vs. b, d, e
Smoking (Never)	415 (57%)	144 (59%)	143 (68%)	25 (31%)	31 (67%)	23 (62%)	
Alcohol & Drug Use (Current & Past)	265 (37%)	70 (29%)	61 (29%)	70 (88%)	12 (26%)	15 (41%)	a vs. c; b vs. c; c vs. d, e
Alcohol & Drug Use (Never)	460 (63%)	173 (71%)	149 (71%)	10 (13%)	34 (74%)	22 (59%)	

Table 2: Patient Comorbidities, n (%)	Overall (n=725)	IPAH (n=243) [a]	CTD (n=210) [b]	Drugs & Toxins (n=80) [c]	CHD (n=46) [d]	CTEPH (n=37) [e]	p value < 0.05
Hypertension	280 (39%)	41 (39%)	79 (38%)	5 (11%)	18 (49%)	18 (49%)	a vs. d; b vs. c, d; c vs. d; d vs. e
Obstructive Sleep Apnea	216 (30%)	88 (36%)	47 (22%)	25 (31%)	8 (17%)	11 (30%)	a vs. b; a vs. c
Heart Failure	160 (22%)	45 (19%)	40 (19%)	25 (31%)	12 (26%)	8 (22%)	a vs. c; b vs. c
Thyroid Disease	159 (22%)	62 (26%)	55 (26%)	14 (18%)	6 (13%)	4 (11%)	
Hyperlipidemia	122 (17%)	45 (19%)	29 (14%)	29 (36%)	4 (9%)	8 (22%)	
Type II Diabetes mellitus	116 (16%)	52 (21%)	22 (10%)	13 (16%)	4 (9%)	6 (16%)	a vs. b
Chronic Obstructive Pulmonary Disease	100 (14%)	38 (16%)	21 (10%)	13 (16%)	6 (13%)	3 (8%)	
Coronary Artery Disease	79 (11%)	29 (12%)	20 (10%)	10 (13%)	4 (9%)	5 (14%)	
Pulmonary Embolism	74 (10%)	14 (6%)	10 (5%)	2 (3%)	3 (7%)	32 (86%)	a vs. e; b vs. e; c vs. e; d vs. e
Lung Fibrosis	66 (9%)	11 (5%)	44 (21%)	2 (3%)	1 (2%)	0 (0%)	a vs. b; b vs. c, d, e
Deep Vein Thrombosis	64 (9%)	16 (7%)	12 (6%)	4 (5%)	1 (2%)	18 (49%)	a vs. e; b vs. e; c vs. e; d vs. e
Valvular Heart Disease	37 (5%)	14 (6%)	13 (6%)	2 (3%)	3 (7%)	2 (5%)	
Renal Insufficiency	28 (4%)	5 (2%)	10 (5%)	2 (3%)	2 (4%)	2 (5%)	
Hepatitis C Virus	23 (3%)	5 (2%)	2 (1%)	7 (9%)	0 (0%)	0 (0%)	
HIV	12 (2%)	1 (< 1%)	0 (0%)	1 (1%)	0 (0%)	0 (0%)	
Type I Diabetes mellitus	6 (1%)	1 (< 1%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)	
Non-alcoholic Fatty Liver Disease	5 (1%)	2 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

Table 3: Patient Disease Characteristics	Overall (n=725)	IPAH (n=243) [a]	CTD (n=210) [b]	Drugs & Toxins (n=80) [c]	CHD (n=46) [d]	CTEPH (n=37) [e]	p value < 0.05
NYHA at diagnosis							
Class I	13/312 (4%)	4/132 (3%)	3/78 (4%)	2/35 (6%)	2/17 (12%)	1/15 (7%)	
Class II	72/312 (23%)	29/132 (22%)	20/78 (26%)	6/35 (17%)	4/17 (24%)	5/15 (33%)	
Class III	172/312 (55%)	75/132 (57%)	40/78 (51%)	23/35 (66%)	9/17 (53%)	7/15 (47%)	
Class IV	55/312 (18%)	24/132 (18%)	15/78 (19%)	4/35 (11%)	2/17 (12%)	2/15 (13%)	
NYHA at enrollment							
Class I	35/554 (6%)	9/203 (4%)	11/160 (7%)	3/48 (6%)	2/38 (5%)	4/25 (16%)	c vs. d
Class II	253/554 (46%)	99/203 (49%)	67/160 (42%)	15/48 (31%)	24/38 (63%)	11/25 (44%)	
Class III	233/554 (42%)	86/203 (42%)	69/160 (43%)	26/48 (54%)	10/38 (26%)	8/25 (32%)	
Class IV	33/554 (6%)	9/203 (4%)	13/160 (8%)	4/48 (8%)	2/38 (5%)	2/25 (8%)	
Risk Survival measures, mean (SD)							
6-MWD, meters	332.3 (134.1), n=658	345.5 (136.5), n=222	301.8 (132.5), n=189	381.3 (103.8), n=73	356.4 (126.5), n=43	338.6 (127.3), n=31	b vs. c
BNP, pg/ml	236.3 (510.0), n=669	194.8 (436.9), n=216	302.9 (675.6), n=195	186.7 (266.4), n=74	167.8 (201.1), n=45	354.3 (731.9), n=35	
Heart rate, beats per minute	82.9 (14.5), n=722	82.8 (14.4), n=242	82.8 (14.4), n=209	82.4 (14.9), n=79	82.0 (13.2), n=46	82.3 (14.9), n=37	
Systolic Blood Pressure, mmHg	118.0 (17.3), n=725	116.9 (16.4), n=243	118.3 (18.4), n=210	118.8 (17.9), n=80	114.8 (15.5), n=46	120.0 (15.5), n=37	
mPAP, mmHg	43.2 (14.3), n=682	43.5 (14.5), n=231	40.6 (13.3), n=196	47.9 (12.2), n=75	48.6 (20.4), n=41	38.6 (12.2), n=33	b vs. d; b vs. c; c vs. e; d vs. e
PCWP, mmHg	11.2 (5.3), n=672	11.8 (5.2), n=229	10.3 (4.6), n=196	10.8 (4.8), n=71	12.9 (7.9), n=38	12.4 (5.7), n=33	a vs. b; b vs. d
mRAP, mmHg	8.2 (5.6), n=663	8.7 (6.1), n=221	7.6 (4.8), n=192	9.4 (5.6), n=73	7.4 (4.5), n=40	9.6 (6.3), n=33	
DL _{CO} , % predicted	53.8 (21.7), n=417	57.7 (21.6), n=155	40.6 (16.2), n=118	72.6 (17.8), n=35	63.7 (23.1), n=24	62.6 (15.3), n=24	a vs. c; a vs. b; b vs. c, d, e