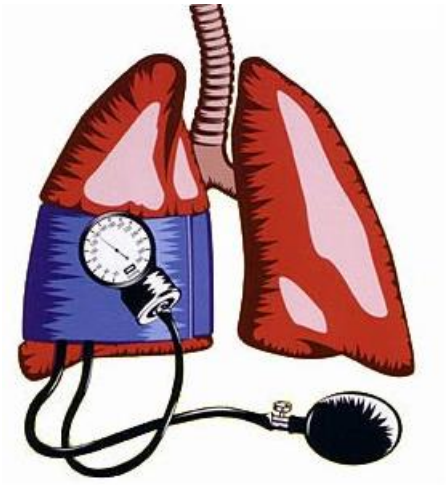
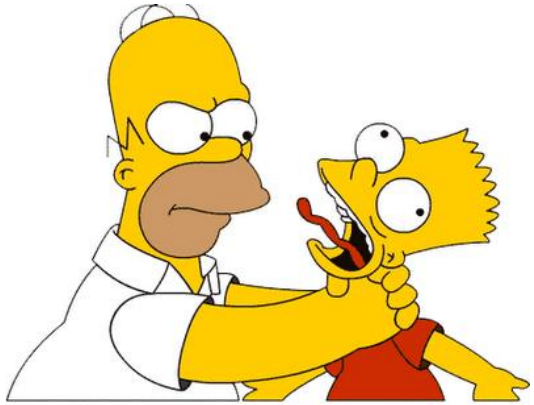




Diagnosis and assessment of Pulmonary Arterial Hypertension

한림대학교 강동성심병원
호흡기내과
박용범

Definition of PH

Mean pulmonary arterial pressure(mPAP)

Resting > 25 mmHg

Pulmonary arterial hypertension

adds the criterion of PCWP ≤ 15 mmHg and
a pulmonary vascular resistance >3 Wood units

Updated Clinical Classification of Pulmonary Hypertension (5th World Symposium, NICE 2013)

1. Pulmonary arterial hypertension
   - 1.1 Idiopathic PAH
   - 1.2 Heritable PAH
   - 1.2.1 BMPR2
   - 1.2.2 ALK-1, ENG, **SMAD9**, **CAV1**, **KCNK3**
   - 1.2.3 Unknown
   - 1.3 Drug and toxin induced
   - 1.4 Associated with:
   - 1.4.1 Connective tissue disease
   - 1.4.2 HIV infection
   - 1.4.3 Portal hypertension
   - 1.4.4 Congenital heart diseases
   - 1.4.5 Schistosomiasis

1′ Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

1″. Persistent pulmonary hypertension of the newborn (PPHN)

2. Pulmonary hypertension due to left heart disease
   - 2.1 Left ventricular systolic dysfunction
   - 2.2 Left ventricular diastolic dysfunction
   - 2.3 Valvular disease
   - **2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies**

3. Pulmonary hypertension due to lung diseases and/or hypoxia
   - 3.1 Chronic obstructive pulmonary disease
   - 3.2 Interstitial lung disease
   - 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
   - 3.4 Sleep-disordered breathing
   - 3.5 Alveolar hypoventilation disorders
   - 3.6 Chronic exposure to high altitude
   - 3.7 Developmental lung diseases

4. Chronic thromboembolic pulmonary hypertension (CTEPH)

5. Pulmonary hypertension with unclear multifactorial mechanisms
   - 5.1 Hematologic disorders: **chronic hemolytic anemia**, myeloproliferative disorders, splenectomy
   - 5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
   - 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   - 5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, **segmental PH**

Group 1 : PAH

1. Pulmonary arterial hypertension (PAH)

1.1. Idiopathic PAH

1.2. **Heritable**

1.2.1. **BMPR2**

1.2.2. **ALK1, endoglin (with or without hereditary hemorrhagic telangiectasia)**

1.2.3. **Unknown**

1.3. Drug- and toxin-induced

1.4. Associated with

1.4.1. Connective tissue diseases

1.4.2. HIV infection

1.4.3. Portal hypertension

1.4.4. Congenital heart diseases

1.4.5. **Schistosomiasis**

1.4.6. **Chronic hemolytic anemia** → **Group 5**

1.5 Persistent pulmonary hypertension of the newborn

1′. **Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)**

1. Pulmonary arterial hypertension

1.1 Idiopathic PAH

1.2 Heritable PAH

1.2.1 BMPR2

1.2.2 ALK-1, ENG, **SMAD9**, **CAV1**, **KCNK3**

1.2.3 Unknown

1.3 Drug and toxin induced

1.4 Associated with:

1.4.1 Connective tissue disease

1.4.2 HIV infection

1.4.3 Portal hypertension

1.4.4 Congenital heart diseases

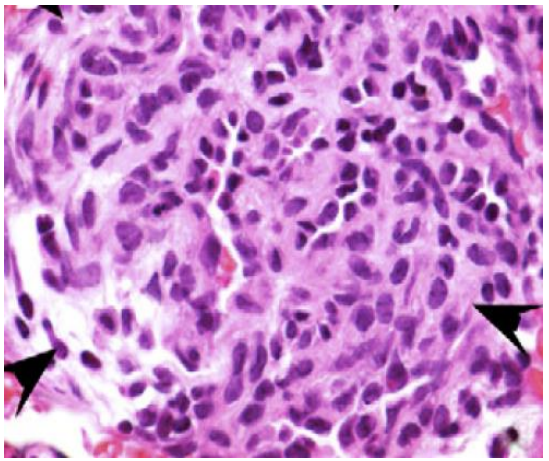
1.4.5 Schistosomiasis

1′ Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

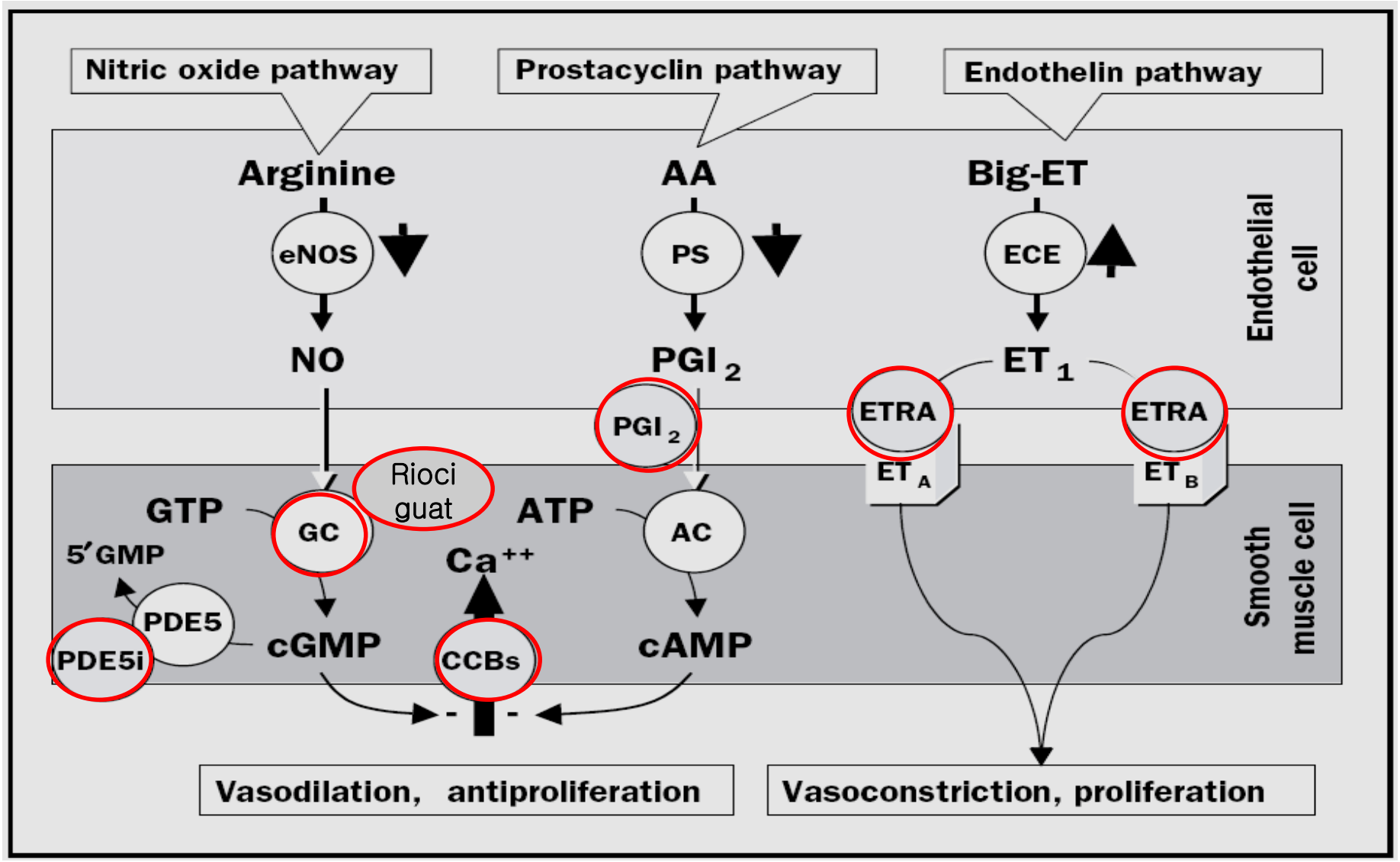
1″. **Persistent pulmonary hypertension of the newborn (PPHN)**

Pulmonary arterial hypertension (PAH)

- remodeling of the small pulmonary arteries
  → mechanism ; unknown
  → share morphological findings, clinical presentation, and clinical responsiveness to treatment with the continuous infusion of epoprostenol.
  → leading to a progressive increase in pulmonary vascular resistance and right ventricular failure

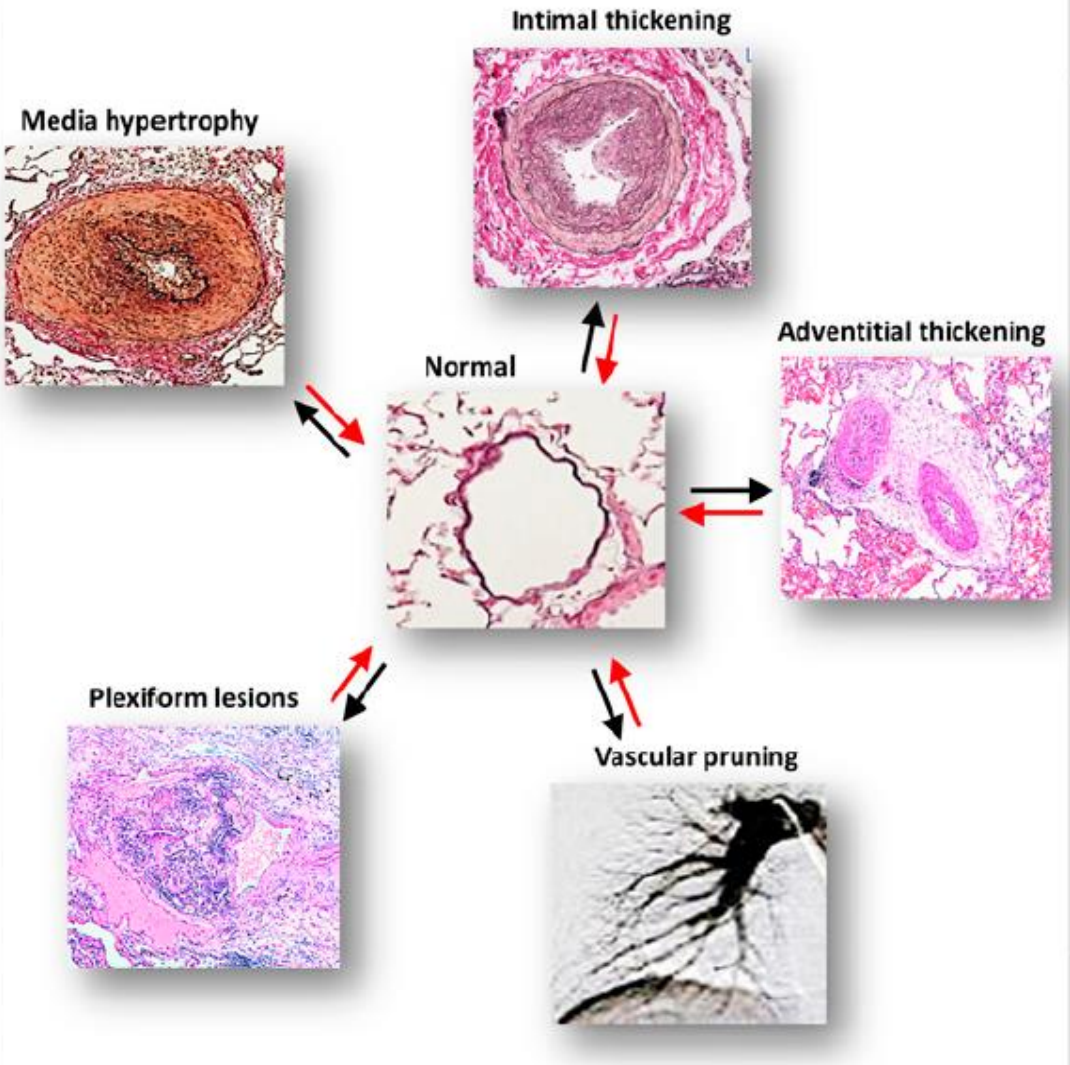


3 Mechanistic pathways known to the disturbed with PAH



McGoon MD et al. Mayo Clin Proc 2009;84:191-207

Reverse remodeling and regenerative strategies as future concepts for PAH treatment



Reverse remodeling and regenerative strategies – Class I PH

Anti-proliferative strategies
- Tyrosine kinase inhibitors

Transcription factor based therapies
- NFATc inhibitor
- PPARγ agonist
- Notch inhibitor

Anti – inflammatory strategies
- SDF1 blocker
- B cell antagonist

Epigenetic modulation based therapies
- microRNA mimics/ antagomirs
- HDAC inhibitors
- DNMT inhibitor

BMPR2 modulation strategies

Regenerative treatment strategies
- Genetically engineered EPCs
- Genetically engineered MSCs

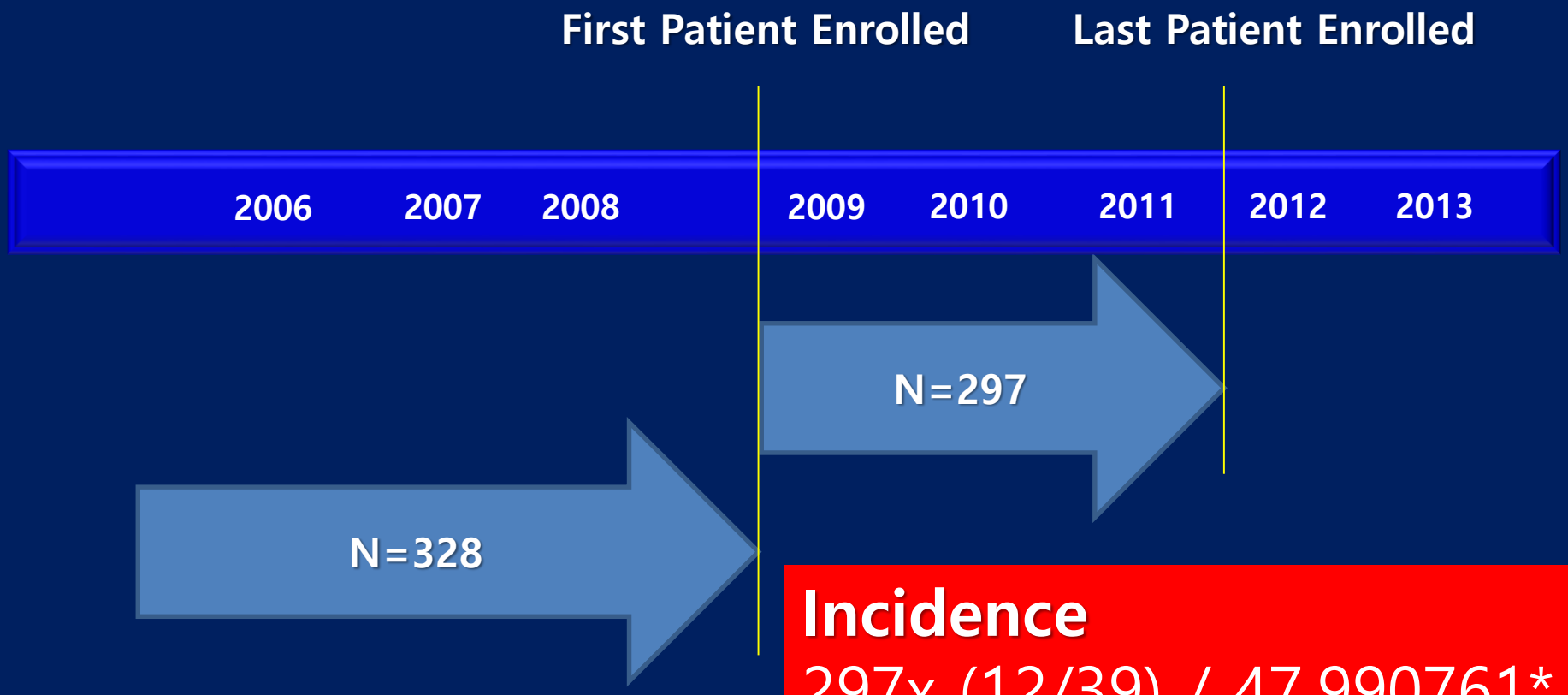
Diagnostic Criteria and WHO Categorization of PH

	All Groups	Group 1	Group 2	Group 3	Group 4	Group 5
Description	Elevated pulmonary artery pressure	Pulmonary arterial hypertension	Pulmonary venous hypertension	PH due to hypoxemia	Chronic thromboembolic PH	Miscellaneous or multifactorial PH
Estimated prevalence[b]	Up to 10%-20% of the general population	15 cases per million overall, 6 cases per million for idiopathic PAH[c]	>3-4 million in the United States	20% in COPD patients with a prior hospitalization for COPD exacerbation, >50% in advanced COPD; 32%-39% in interstitial lung disease	0.5%-2% (up to 3.8%) in survivors of acute pulmonary embolism	Unclear
Diagnostic criteria[d]						
Mean PA pressure, mm Hg	≥25	≥25	≥25	≥25	≥25	≥25
PCWP or LVEDP, mm Hg		≤15	>15	≤15	≤15	≤15
PVR, dynes/s/cm^5		>240		>240	>240	>240

JAMA. 2012;308(13):1366-1374

Korean PAH Registry (KorPAH)

Prevalent and Incident Cases



Incidence
297x (12/39) / 47,990761*
= **1.9/yr/million**

* Korean Statistical Information Service (2010)

Functional Assessment Classification of Patients with Pulmonary Hypertension

Class	*Description*
I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea, fatigue, chest pain, or near syncope.
II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest, but ordinary physical activity causes undue dyspnea, fatigue, chest pain, or near syncope.
III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest, but less than ordinary physical activity causes increased dyspnea, fatigue, chest pain, or near syncope.
IV	Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. They manifest signs of right-sided heart failure. Dyspnea and/or fatigue may be present at rest. Discomfort is increased by any physical activity.

Pulmonary Arterial Hypertension: Baseline Characteristics From the REVEAL Registry

David B. Badesch, MD, FCCP; Gary E. Raskob, PhD; C. Greg Elliott, MD, FCCP; Abby M. Krichman, BS, RRT; Harrison W. Farber, MD, FCCP; Adaani E. Frost, MD, FCCP; Robyn J. Barst, MD, FCCP; Raymond L. Benza, MD; Theodore G. Liou, MD, FCCP; Michelle Turner, MS; Scott Giles, BA; Kathy Feldkircher, PhD; Dave P. Miller, MS; and Michael D.McGoon, MD, FCCP

Chest 2010;137:376-87

Characteristic	All Patients[a]	IPAH	All Patients With APAH[b]	APAH Subgroup[c]			
				CHD	CVD/ CTD	Portal HT	Drugs/Toxins
Patients, No. (%)	2,525 (100)	1,166 (46.2)	1,280 (50.7)	250 (19.5)	639 (49.9)	136 (10.6)	134 (10.5)
Age at enrollment, mean ± SD, y	53.0 ± 14.0	53.1 ± 14.5	53.4 ± 13.4	45.5 ± 13.1	57.7 ± 13.0	53.3 ± 9.6	49.5 ± 10.6
Age at diagnosis, mean ± SD, y	50.1 ± 14.4	49.9 ± 14.8	50.7 ± 13.8	41.6 ± 13.3	55.5 ± 13.4	51.0 ± 9.5	46.0 ± 10.0
19-64, No. (%)	2,098 (83.1)	971 (83.3)	1,054 (82.3)	236 (94.4)	467 (73.1)	124 (91.2)	129 (96.3)
65-74, No. (%)	324 (12.8)	138 (11.8)	181 (14.1)	11 (4.4)	135 (21.1)	11 (8.1)	5 (3.7)
75 +, No. (%)	103 (4.1)	57 (4.9)	45 (3.5)	3 (1.2)	37 (5.8)	1 (0.7)	0 (0.0)
Female, No. (%)	2,007 (79.5)	936 (80.3)	1,014 (79.2)	184 (73.6)	576 (90.1)	68 (50.0)	113 (84.3)
Time from diagnosis to enrollment, mo							
Mean ± SD	35.6 ± 37.9	38.0 ± 40.4	32.7 ± 34.9	46.6 ± 50.3	26.9 ± 27.3	27.5 ± 31.1	42.6 ± 32.7
Functional class at enrollment,[d] No. (%)							
I	175 (7.6)	89 (8.3)	80 (6.9)	13 (5.7)	32 (5.7)	14 (11.4)	10 (7.8)
II	846 (36.7)	391 (36.4)	423 (36.6)	87 (38.3)	182 (32.2)	50 (40.7)	60 (46.5)
III	1,153 (50.0)	534 (49.7)	584 (50.5)	117 (51.5)	311 (54.9)	54 (43.9)	55 (42.6)
IV	130 (5.6)	60 (5.6)	69 (6.0)	10 (4.4)	41 (7.2)	5 (4.1)	4 (3.1)

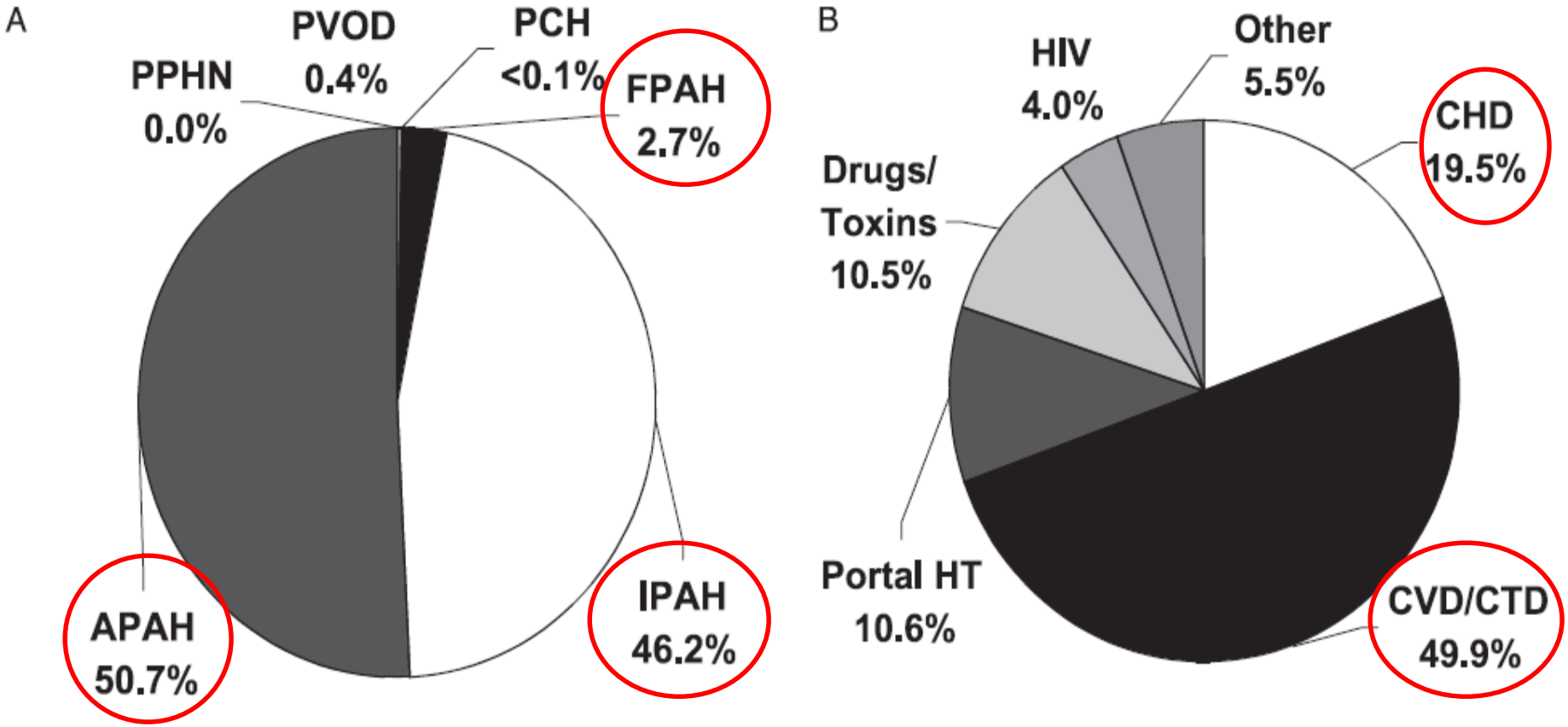
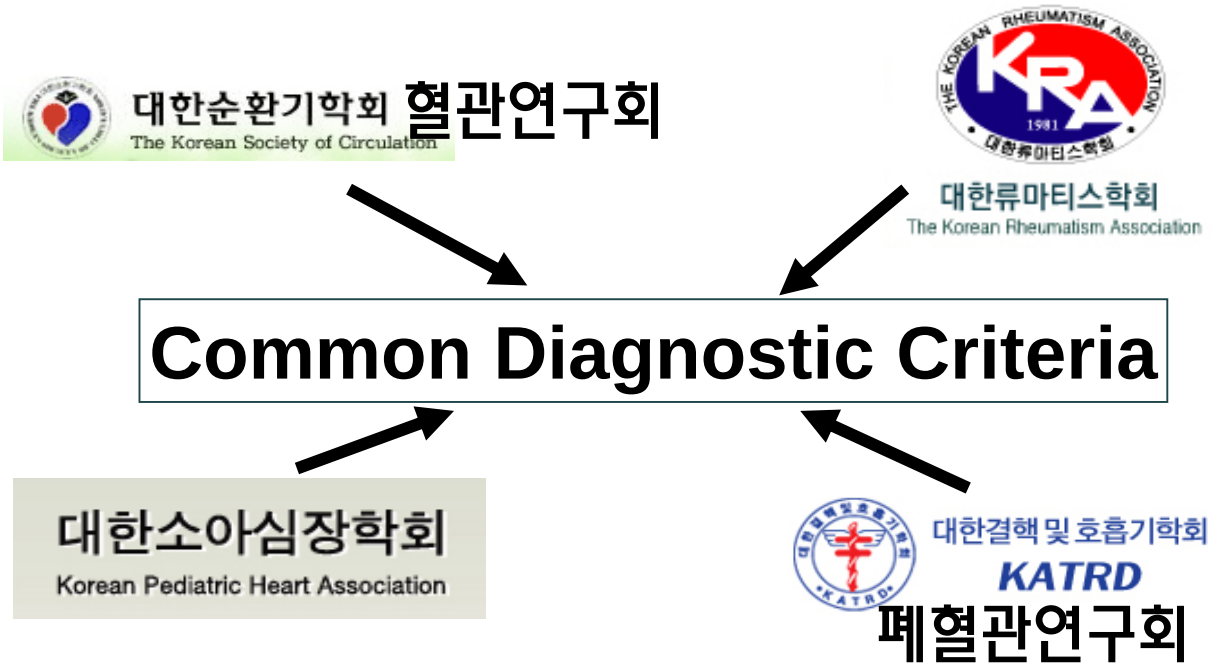


Figure 1. World Health Organization (WHO) Group I pulmonary arterial hypertension classification of REVEAL patients at enrollment. *(A)* WHO Group I PAH classification. *(B)* Breakdown of associated pulmonary arterial hypertension subgroup. APAH = associated PAH; CHD = congenital heart disease; CVD/CTD = collagen vascular disease/connective tissuedisease; FPAH = familial PAH; HT = hypertension; IPAH = idiopathic PAH; PAH = pulmonary arterial hypertension; PCH = pulmonary capillary hemangiomatosis; PPHN = pulmonary hypertension of the newborn; PVOD = pulmonary venoocclusive disease; REVEAL = Registry to EValuate Early And Long-term PAH disease management.

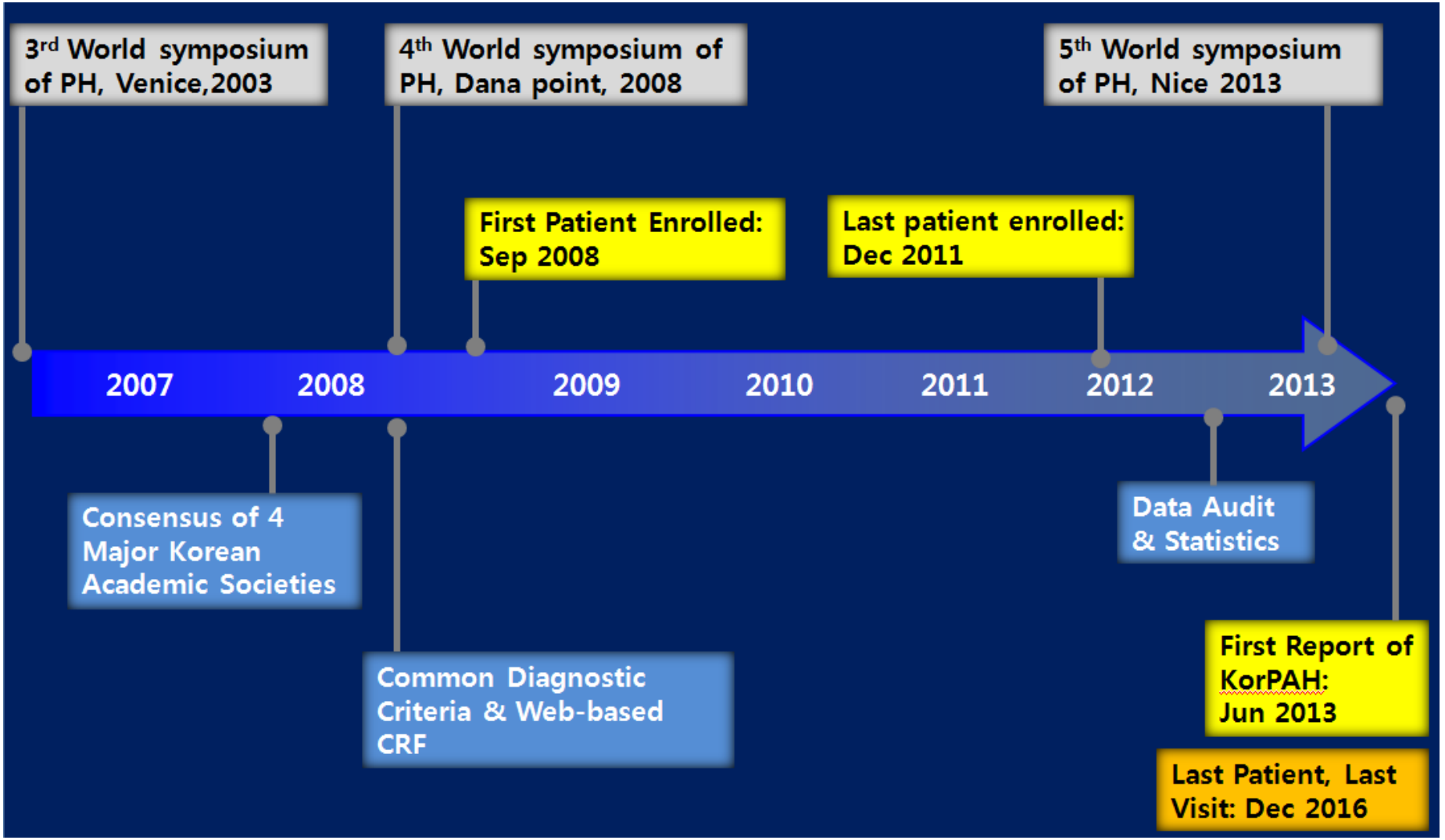
Korean PAH registry program



Objective : Clinical Characteristics of Korean PAH

Prevalence and Incidence
Gender, Age and Etiology
Clinical and Treatment status
Prognosis

Korean PAH registry Timeline



Korean PAH Registry (KorPAH)

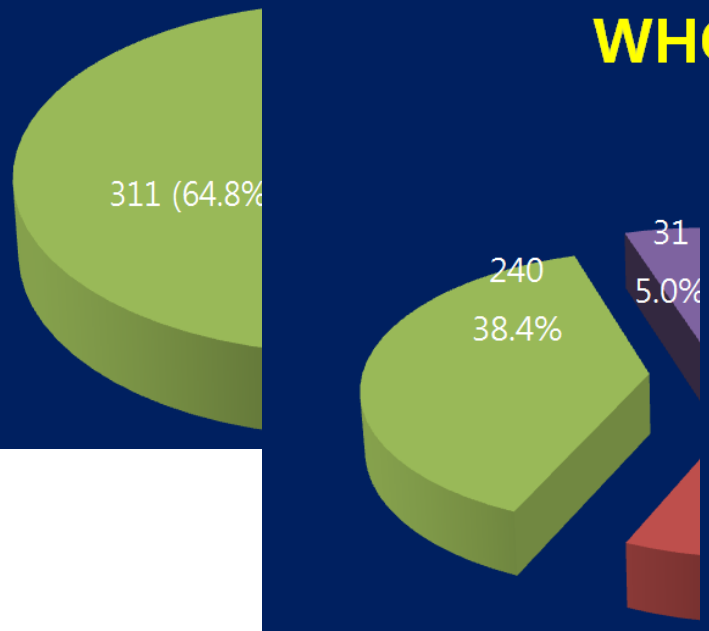
2008.9~2011.12

Etiology of PAH

Korean PAH Registry (KorPAH)

2008.9~2011.12
n=625

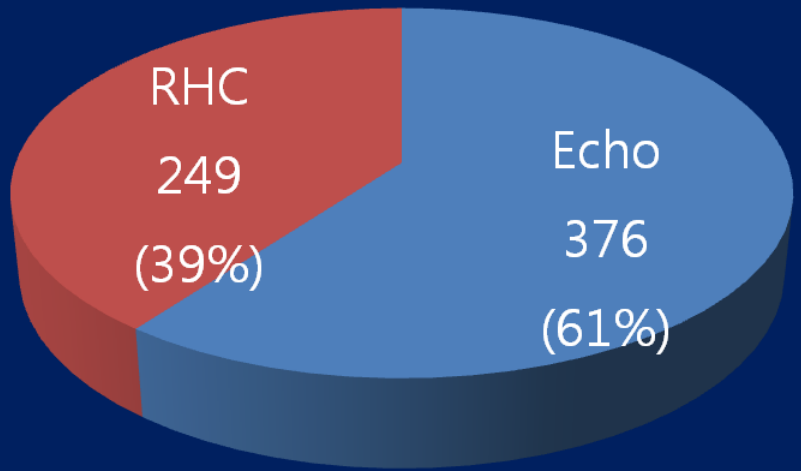
WHO-Fc Class



Korean PAH Registry (KorPAH)

2008.9~2011.12
n=625

Diagnostic Tools



IPAH vs. APAH

	All Patients	IPAH	All Patients with APAH	APAH subgroup		
				CHD	CTD	others
Patients, No. (%)	625 (100)	145 (23.2)	480 (76.8)	159 (33.1)	311 (64.8)	10 (2.1)
Age, mean ± SD, yrs	47.6 ± 15.7	45.1 ± 15.7	48.4 ± 15.7	41.1 ± 13.4	52.2 ± 15.6	47.7 ± 10.0
Female, No. (%)	503(80.5)	106(73.1)	397 (82.7)	116 (73.0)	274 (88.1)	7 (70.0)
Functional class, n (%)						
I	136 (21.8)	5 (3.5)	131 (27.3)	9 (5.7)	121 (38.9)	1 (10.0)
II	218 (34.9)	48 (33.1)	170 (35.4)	71 (44.7)	96 (30.9)	3 (30.0)
III	240 (38.4)	82 (56.6)	158 (32.9)	76 (47.8)	77 (24.8)	5 (50.0)
IV	31 (5.0)	10 (6.9)	21 (4.4)	3 (1.9)	17 (5.5)	1 (10.0)
Systolic BP, mean ± SD	114 ±16.8	116± 17.6	113±16.1	113± 14.8	111 ±18.3	118 ±21.3

	All Patients	IPAH	All Patients with APAH	APAH subgroup		
				CHD	CTD	others
6MWD (meter) mean ± SD	376 ± 124	398 ± 116	364 ± 127	382 ± 119	347 ± 133	277 ± 162
No.	203	72	131	72	55	4
		P value = 0.062				
BNP	516±1,093	465±1,001	562±1,176	645±1,423	362±444	871±662
	111	52	59	38	19	2
		P value = 0.644				
NT pro-BNP	2,798± 6,375	2,192± 3,244	2,876±6,673	1,900±5,047	3,234± 7,152	687±978
	263	30	233	51	176	6
		P value = 0.356				
DLCO	64.1 ±24.3	74.1± 20.7	59.3± 24.5	95.1 ± 34.5	56.3± 20.9	52.2±22.5
	279	92	187	15	167	5
		P value < 0.001				

RHC Data

	All Patients	IPAH	All patients with APAH	APAH subgroup		
				CHD	CTD	Others
Patients, No.	249	87	162	107	52	3
mPAP (mmHg)	55.3 ± 17.3	57.7 ± 18.2	50.4 ± 16.7	58.5 ± 16.1	44.4 ± 13.8	47.0 ± 17.0
No.	210	74	136	92	42	2
		P value = 0.135				
PCWP (mmHg)	8.18± 3.47	8.68 ± 3.18	7.66 ± 3.70	6.97 ± 3.64	8.67 ± 3.34	9.33 ± 6.03
No.	117	60	57	35	19	3
		P value=0.112				
Mean RAP (mmHg)	8.92 ± 5.64	9.74 ± 6.75	8.51 ± 5.00	7.80 ± 4.07	12.9 ± 8.10	10.0 ± 4.24
No.	129	43	86	73	11	2
		P value=0.296				
RVSP (mmHg)	74.2 ± 30.0	70.7 ± 26.9	77.1 ± 32.3	87.4 ± 30.2	49.9 ± 17.8	66.0 ± 50.9
No.	79	35	44	31	11	2
		P value=0.350				

Baseline Characteristics of Korean Registry, NIH Registry, and French Registry

Chracteristics	Korean Registry 2013 (Group I PAH)	REVEAL 2010 (Group I PAH)	French Registry 2006 (Group I PAH)
Cases, No	625	2525	674
Age, yr	48 ± 16	50 ± 14	50 ± 15
Female, No, (%)	503 (80.5)	2007(79.5)	440 (65.3)
WHO classification (%) I/II III/IV	 21.8/34.9 38.4/5.0	 7.6/36.7 50/5.6	 1/24 63/12
6 MWD (n= 203)	376 ± 124	366 ± 126	329 ± 109
Mean PAP, mmHg	55.3 ± 17.3	50.7± 13.6	55 ± 15

Should the term "borderline PH" be introduced for patients with a PAPm between 21 and 24 mm Hg?

Insufficient data to introduce the term "borderlinePH"
: because the prognostic and therapeutic implications remain unknown.

At risk for developing PAH

Patients with CTD (especially scleroderma)
Family members of patients with idiopathic PAH
Heritable pulmonary arterial hypertension [HPAH]

→ should be carefully followed

Should exercise-induced PH be reintroduced as part of the PH definition?

Because of the lack of a suitable definition, an exercise criterion for PH should not be reintroduced at the present time.

Further studies are needed to define which levels of exercise-induced elevations in PAPm and PVR have prognostic and therapeutic implications.

Should PVR be included in the definition of PH/PAH ?

Wood Unit

PVR should not become part of the general PH definition

PVR should be included in the hemodynamic characterization of patients with PAH as follows:
patients with PAH are characterized by pre-capillary PH
(i.e., PAPm ≥25 mm Hg, PAWP≤ 15 mm Hg, and PVR >3 WU)

Is PAWP of 15 mm Hg appropriate to distinguish between pre-capillary and post-capillary PH and how should PAWP be measured?

The cutoff for pre-capillary PH ; 15 mm Hg

✓All clinical trials generating evidence for the safety and efficacy of PAH-targeted therapies in patients fulfilling these criteria

✓ The current evidence does not support recommending left heart catheterization in all patients with PAH.

Should fluid or exercise challenge be used to distinguish patients with PAH from patients with PH due to LV dysfunction?

- ✓ Fluid challenge may be useful in identifying patients with occult HFpEF (heart failure with preserved ejection fraction)
  → meticulous evaluation and standardization before its use in clinical practice

- ✓ Administration of 500ml of fluid over 5 to 10 min ; safe and may help to distinguish patients with PAH from those with occult LV diastolic dysfunction

- ✓ The results of this test, however, must be interpreted with caution and should not be used alone to discard a diagnosis of PAH.

Additional Recommendations for RHC

- ✓ The zero level of the pressure transducer
  ; important impact on the hemodynamic results, especially on right atrium pressure and PAWP

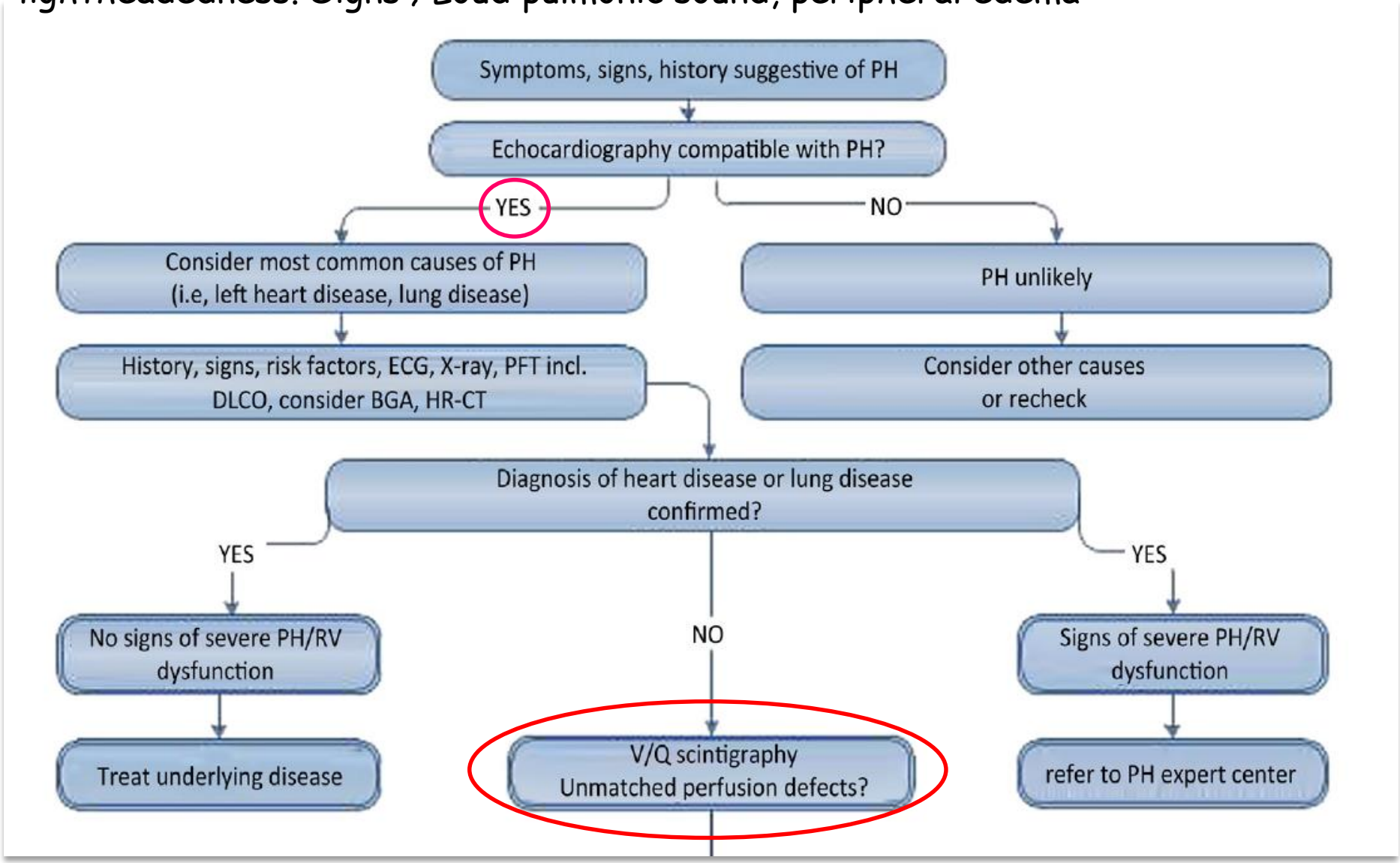
- ✓ Zeroing the pressure transducer at the midthoracic line in a supine patient halfway between the anterior sternum and the bed surface.
  → the level of the left atrium.

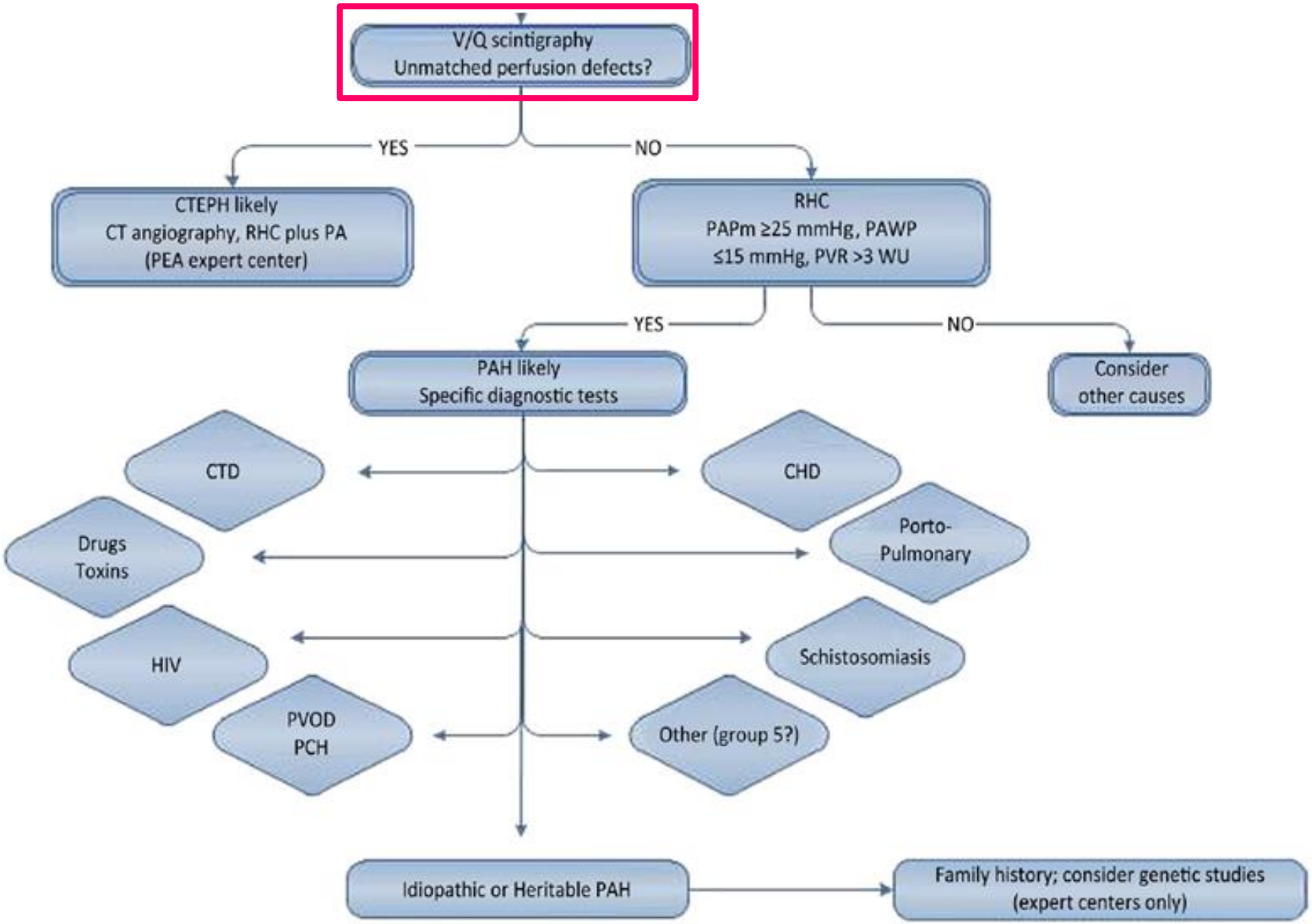
- ✓ PAWP ; the mean of 3 measurements at end-expiration

- ✓ Pulmonary vasoreactivity testing ; only IPAH

Diagnostic Approach in Patients With Clinical Suspicion of PH/PAH

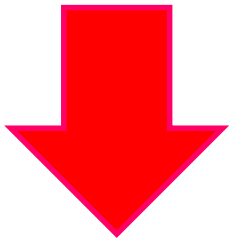
Symptoms ; DOE, fatigue, pre-syncope/syncope, chest pain, palpitation, dizziness, lightheadedness. Signs ; Loud pulmonic sound, peripheral edema



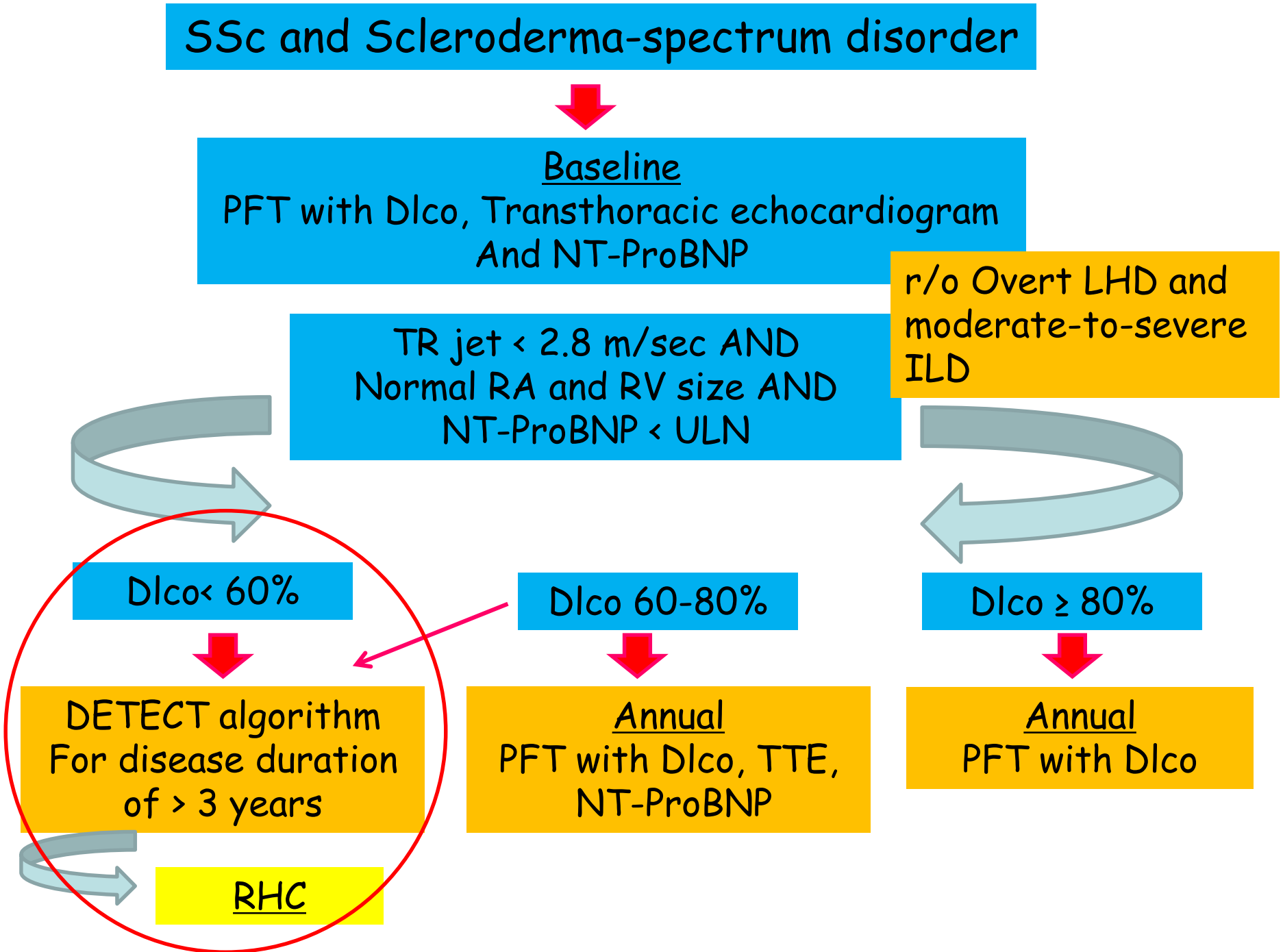

V/Q scintigraphy
Unmatched perfusion defects?
YES
NO
CTEPH likely
CT angiography, RHC plus PA
(PEA expert center)
RHC
PAPm ≥25 mmHg, PAWP
≤15 mmHg, PVR >3 WU
YES
NO
PAH likely
Specific diagnostic tests
Consider
other causes
CTD
CHD
Drugs
Toxins
Porto-
Pulmonary
HIV
Schistosomiasis
PVOD
PCH
Other (group 5?)
Idiopathic or Heritable PAH
Family history; consider genetic studies
(expert centers only)

Recommendations on screening of high-risk populations for PAH

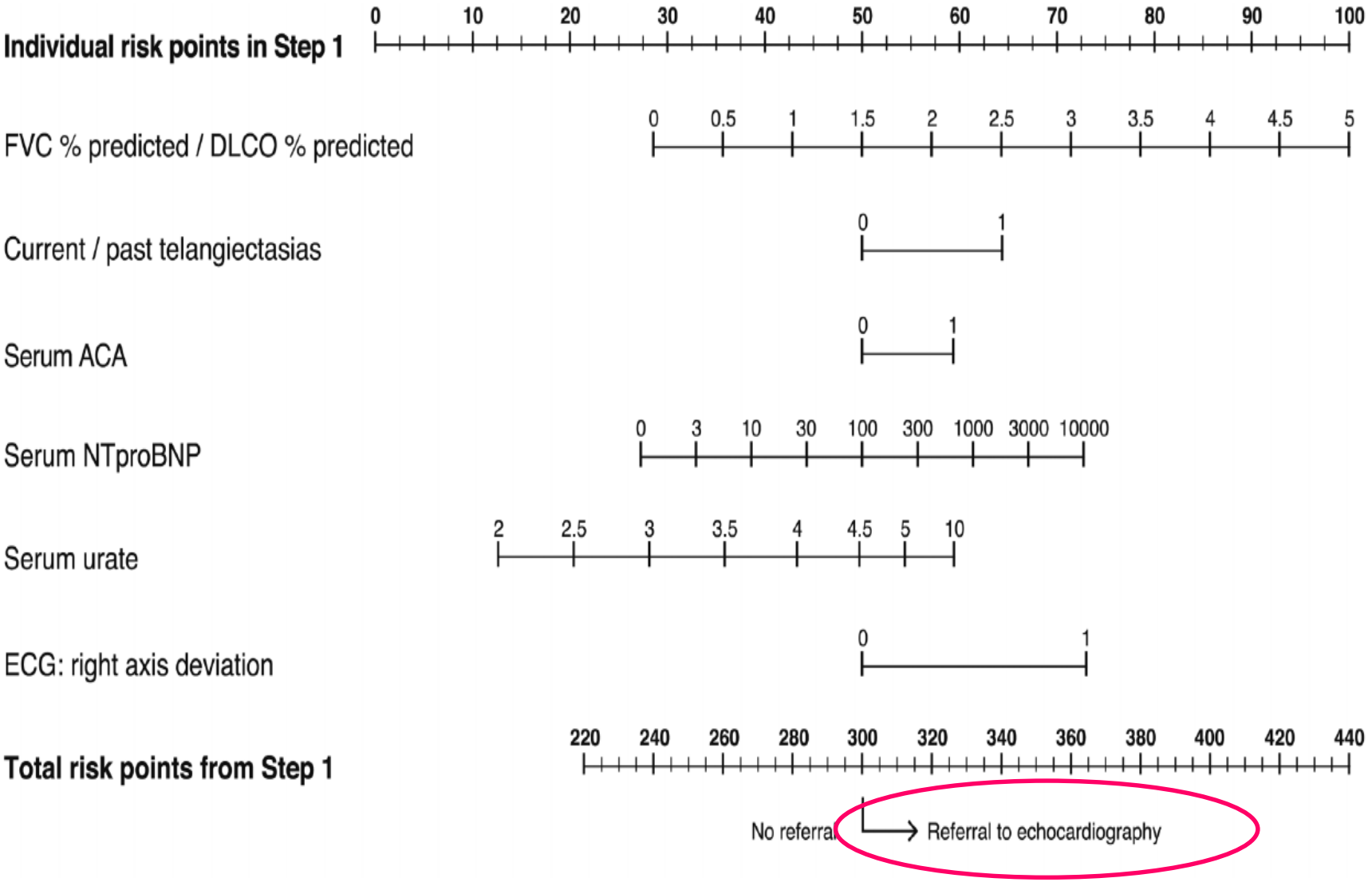
(cardiopulmonary) asymptomatic patients with the SSc spectrum of diseases, although there is a lack of evidence-based data.



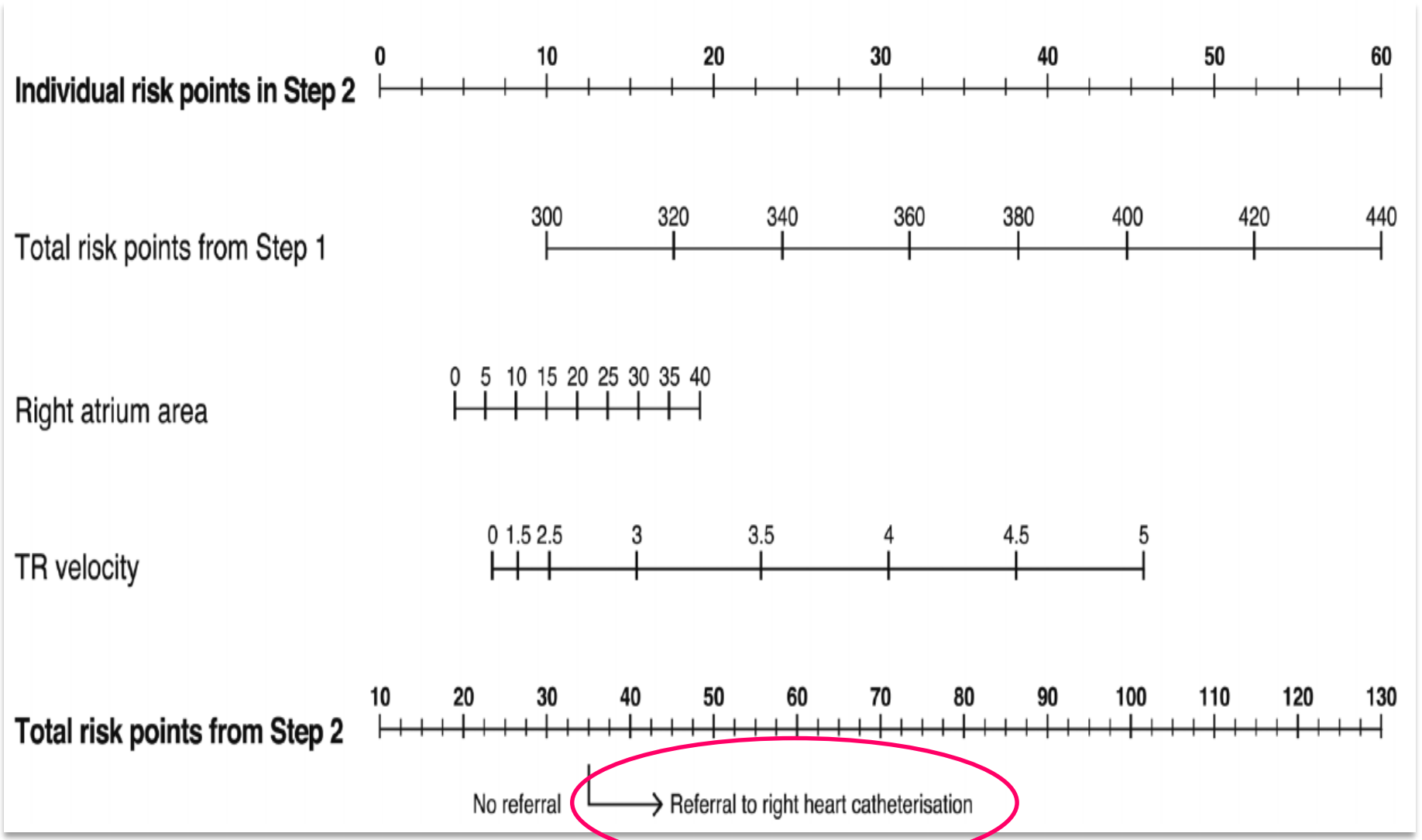
2-step approach


SSc and Scleroderma-spectrum disorder
Baseline
PFT with Dlco, Transthoracic echocardiogram
And NT-ProBNP
TR jet < 2.8 m/sec AND
Normal RA and RV size AND
NT-ProBNP < ULN
r/o Overt LHD and
moderate-to-severe
ILD
Dlco< 60%
Dlco 60-80%
Dlco ≥ 80%
DETECT algorithm
For disease duration
of > 3 years
Annual
PFT with Dlco, TTE,
NT-ProBNP
Annual
PFT with Dlco
RHC

Nomograms for practical application of the DETECT algorithm



Ann Rheum Dis. 2013 May 18. [Epub ahead of print]



Total risk points > 35

Ann Rheum Dis. 2013 May 18. [Epub ahead of print]

Model performance : Comparison of PAH detection approaches

Approach	RHC referral rate, % (positive detection assessments/all patients)	Overall missed PAH diagnoses, % (false negatives)	Overall sensitivity, %	Overall specificity, %	Overall PPV, %	Overall NPV, %
Primary analysis						
DETECT algorithm N=319	62	4	96	48	35	98
ESC/ERS guidelines*[1] N=371	40	29	71	69	40	89

*Evaluated on a subset of patients (N=371) with available data for the variables defined in the guideline, using the following criteria for RHC referral[1]: (a) Tricuspid regurgitant jet velocity >3.4 m/s; or (b) Tricuspid regurgitant jet velocity >2.8–≤3.4 m/s AND symptomatic (defined as at least one of the following DETECT parameters: current anginal pain, current syncope/near syncope, current dyspnoea, presence of peripheral oedema); or (c) Tricuspid regurgitant jet velocity ≤2.8 m/s AND symptomatic (defined as above) AND presence of additional echocardiography variables suggestive of pulmonary hypertension (defined as right atrium area >16 cm^2 and/or ratio of right ventricular diameter/left ventricular end diastolic diameter >0.8).

ESC/ERS, European Society of Cardiology/European Respiratory Society; NPV, negative predictive value; PAH, pulmonary arterial hypertension; PPV, positive predictive value (confirmed PAH out of all RHC referrals); RHC, right heart catheterisation.

Presence of Symptoms and Signs of PH

Symptoms ; DOE, fatigue, pre-syncope/syncope, chest pain, palpitation, dizziness, lightheadedness. Signs ; Loud pulmonic sound, peripheral edema

YES
1 abnormal result required

TR jet ≥ 2.8 m/sec
Or
RA and RV enlargement, irrespective of TR velocity
Or
NT-ProBNP > 2 times of ULN**
Or
FVC/Dlco ratio > 1.6**

No
2 of 3 abnormal result required

TR jet ≥ 2.8 m/sec
Or
NT-ProBNP > 2 times of ULN**
Or
FVC/Dlco ratio > 1.6**

**TTE without overt systolic dysfunction, greater than grade I diastolic dysfunction or greater than mild mitral or aortic valve disease or evidence of PH

Referral for RHC

ARTHRITIS & RHEUMATISM 2013;65:3194-3201

Survival data of PAH registries from Different Countries and Time Periods

Registry (Ref. #)	Study Cohort	1 yr, %		2 yrs, %		3 yrs, %	
		PAH	IPAH	PAH	IPAH	PAH	IPAH
U.S. NIH (17,18)	Inc	NA	68	NA	NA	NA	48
U.S. PHC (19)	Prev and Inc	84	NA	NA	NA	67	NA
French (9,21,22)	Prev and Inc	Ent 87	Ent 83	Ent 76	Ent 67	Ent 67	Ent 58
		Prev 88	Prev 89	Prev 79	Prev 77	Prev 71	Prev 69
		Inc 88	Inc 89	Inc 65	Inc 68	Inc 51	Inc 55
Chinese (23)	Inc	NA	68	NA	57	NA	39
U.S. REVEAL (8,24-33)†	Prev and Inc	85	91	NA	NA	68	74
Spanish (34)	Prev and Inc	NA	89	NA	NA	NA	77
UK (6,35)	Inc	79*	93	68*	84	57*	73
Mayo (38)	Prev and Inc	81	NA	NA	NA	61	NA
Compera (39)	Inc	NA	Ent 92	NA	Ent 83	NA	Ent 74
			≤65 yrs, 96		≤65 yrs, 91		≤65 yrs, 83
			>65 yrs, 90		>65 yrs, 79		>65 yrs, 68

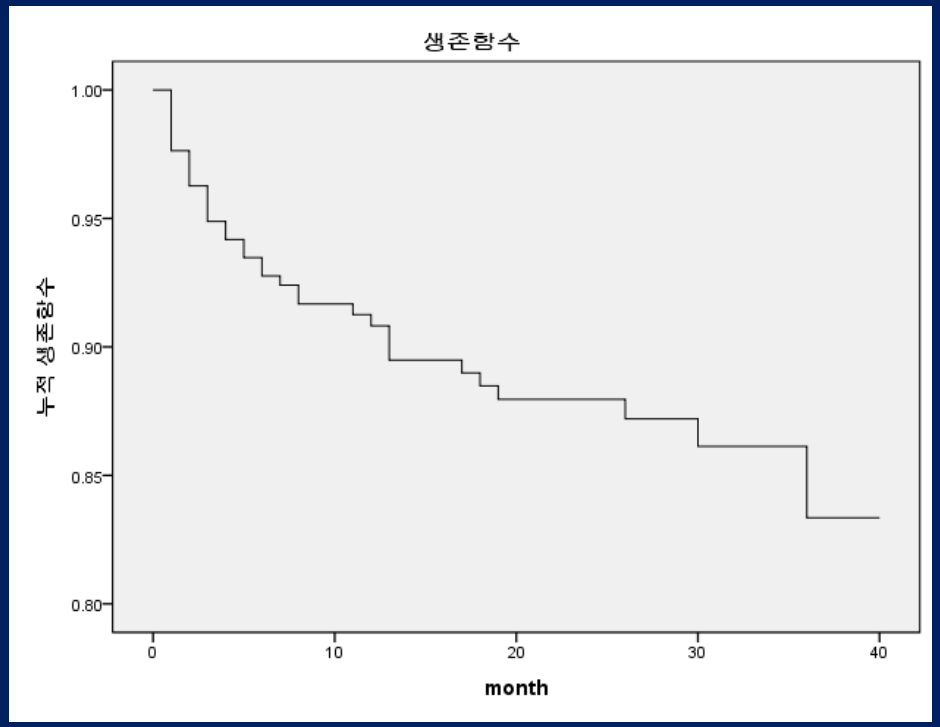
*Survival data calculated only from patients with IPAH and patients with CTD-PAH. †Data for U.S. REVEAL is from the time of diagnostic right heart catheterization.

Ent = entire study population; Inc = incident or newly diagnosed patients; Prev = prevalent or previously diagnosed patients; other abbreviations as in Table 1.

Korean PAH Registry (KorPAH)

Incident Case: Cumulative Survival Rate

2008.9~2011.12, n=297

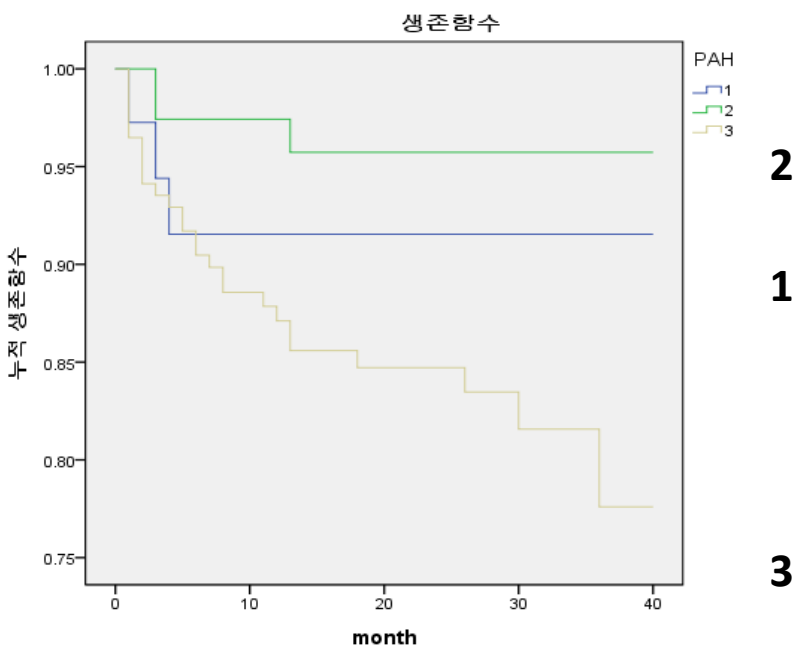


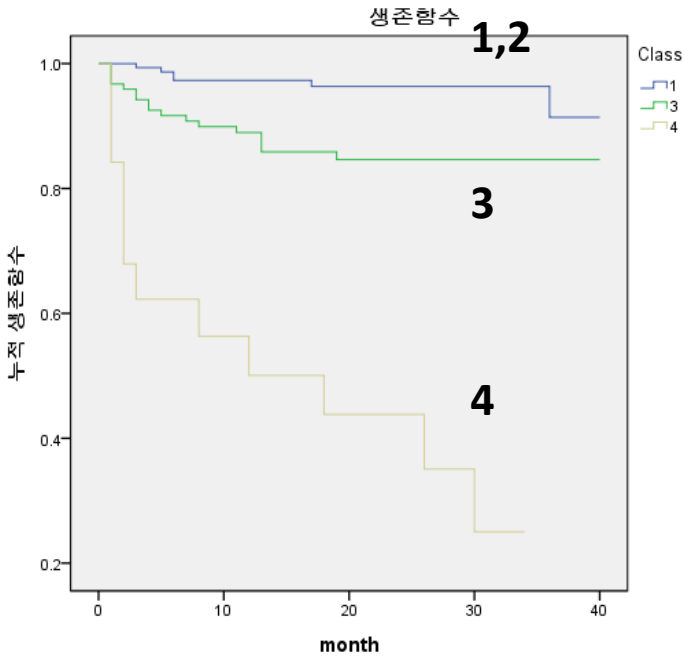
	Number At Risk	Cumulative Survival Rate
12 months	207	89%
24 months	126	88%
36 months	25	83%

Multivariate Predictors of Survival

Category	Increase Risk	Decrease Risk
Demographics	Sex (male) and age interaction (>65 yrs) (9,27,33,40) Age (6,19) Male (6,9,27,34) Etiology: CTD, (6,19,27,34,37,40) PoPH, (6,34,40); HPAH, (27,40); PVOD (6,34)	
Functional capacity	Higher NYHA/WHO class (23,40,19,27,34,37) Lower 6MWD (6,9,27,40)	Lower NYHA/WHO class (19,27) Higher 6MWD (6,9,27)
Laboratory and biomarkers	Higher BNP or NT-proBNP (27,40) Higher creatinine (27,40)	Lower BNP or NT-proBNP (27)
Imaging	Echo: pericardial effusion (27,37,40)	
Lung function studies	Lower predicted DLCO (27,37,40)	Higher predicted DLCO (27,40)
Hemodynamics	Higher mRAP (6,19,27,34,40) Lower CO or CI (6,9,34) Higher PVR or PVRI (27,40)	Higher CO or CI (19)

CTD showed worst outcome
Earlier Diagnosis Predicts Longer Survival
From KorPAH (Incident:297, 2008~2011)



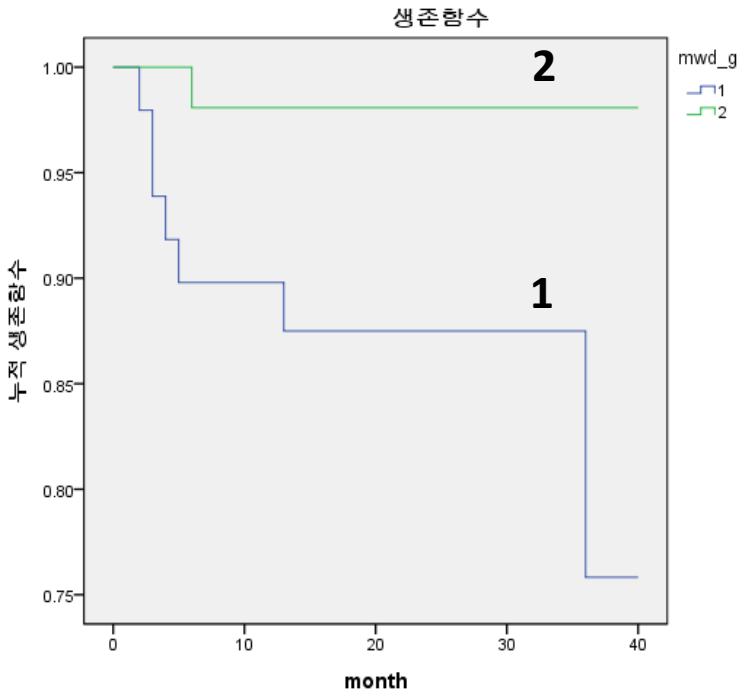


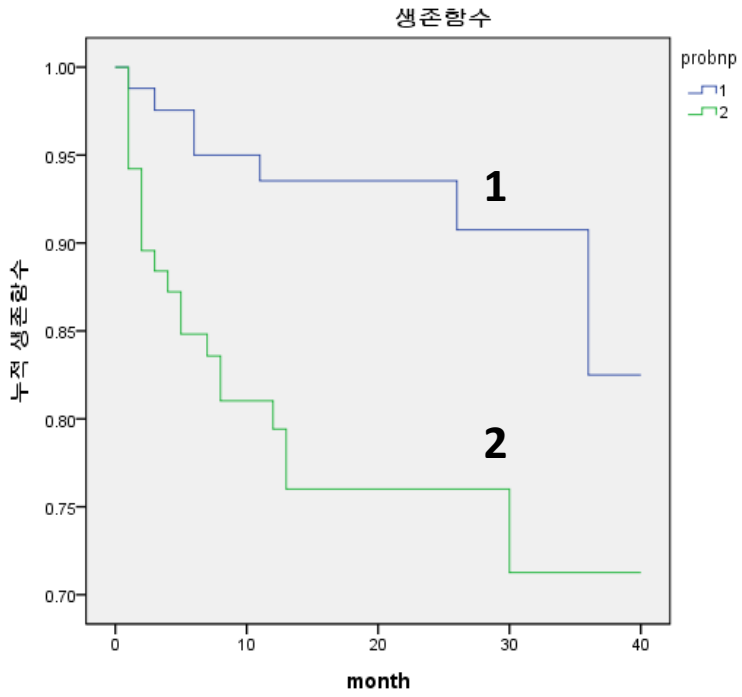
1: IPAH,
2: CHD,
3: CTD,
P value = 0.043

1: WHO-NYHA class 1 &2,
3: WHO-NYHA class 3,
4: WHO-NYHA class 4,
P value < 0.001

1: 380m ≥6MWD, 2: 380m < 6MWD, P value = 0.025

Earlier Diagnosis Predicts Longer Survival
From KorPAH (Incident Case:297, 2008~2011)

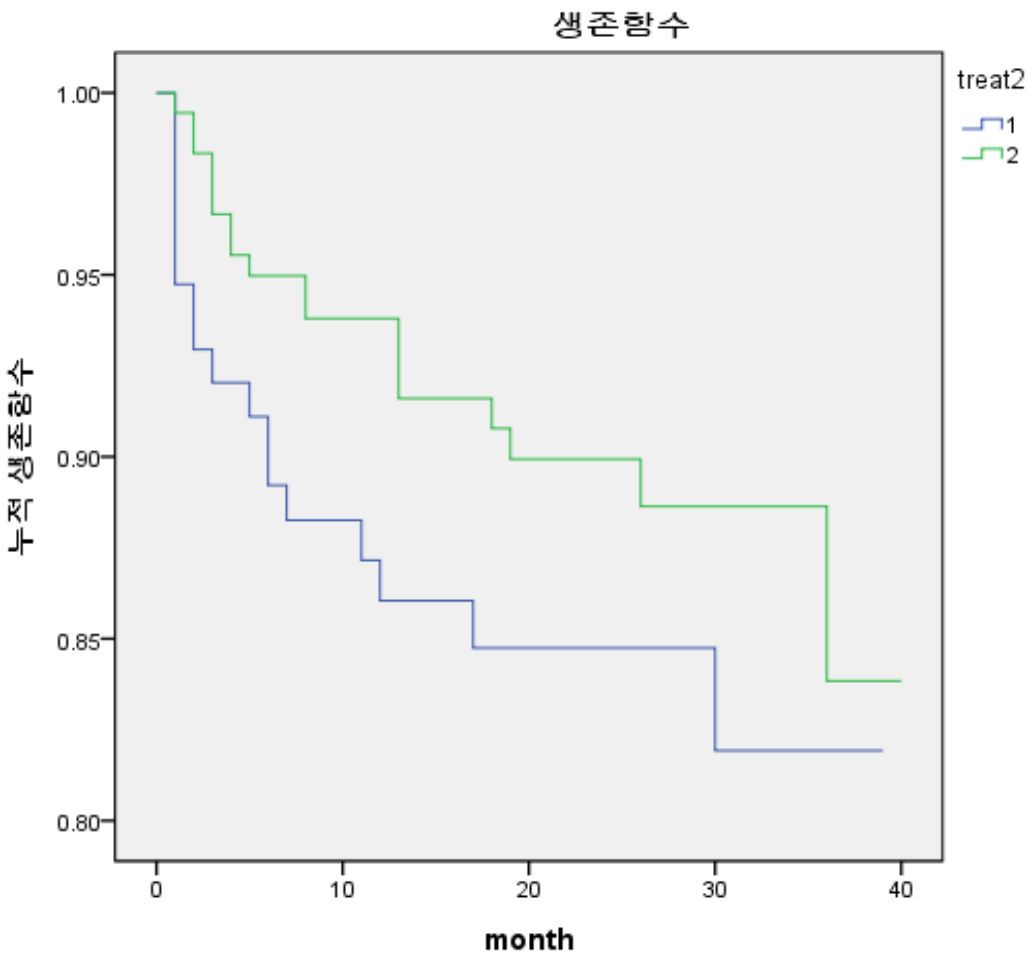




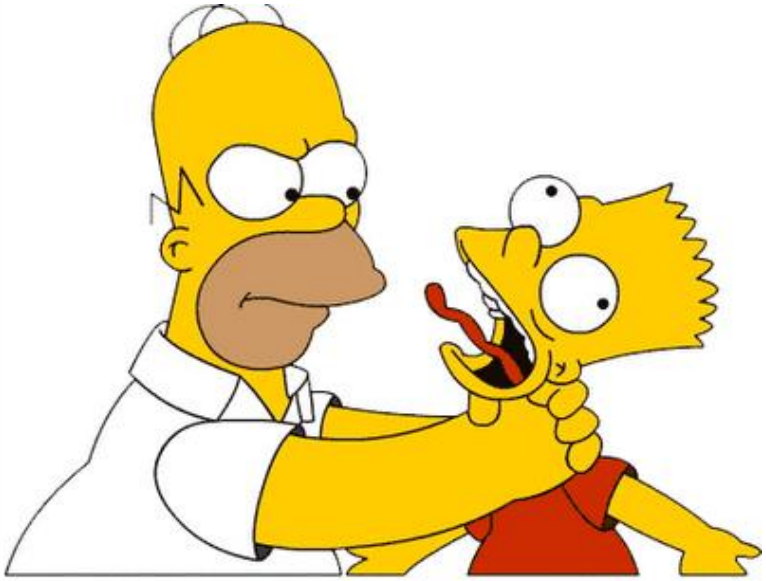
1: 6MWD < 380m,
2: 6MWD ≥ 380m,
P value = 0.025

1:NT-ProBNP < 797 ng/ml,
2:NT-pro-BNP ≥ 797 ng/ml,
P = 0.003

Targeted Therapy showed Longer Survival
From KorPAH(Incident Case:297, 2008~2011)



1: Conventional,
2: Targeted,
P = 0.09
-> But After correction of NYHA class and etc, 0.37 (0.19-0.76)



Thank you for your attention !!!