HELLENIC PULMONARY HYPERTENSION REGISTRY (HOPE) CURRENT DATA 2019

Maria Boutsikou[1], Alexandra Arvanitaki[2], Anastasia Anthi[3], Sotiria Apostolopoulou[4], Aikaterini Avgeropoulou[5] , Eftychia Demerouti[4], Christos Feloukidis[2], George Giannakoulas[2], Dimitrios Farmakis[2], Charalambos Karvounis[2], Panagiotis Karyofyllis[4], Ioanna Mitrouska[6], Sophia Mouratoglou[2], Katerina K. Naka[7], Stylianos Orfanos[3], Evangelia Panagiotidou[8], Georgia Pitsiou[8], Spyridon Rammos[4], Ioannis Stanopoulos[8], Adina Thomaidi[9], Dimitrios Konstantonis[3], Christos Pappas[3], Apostolos Armaganidis[3], Iraklis Tsangaris[3], Dimitrios Tsiapras[4], Vassilios Voudris[4], George Anastasiadis[10], Athanasios Manginas[1]

Outline

- Baseline and follow up data of patients with CTEPH
- Baseline and follow up data of patients with haematological disorders
- Current data regarding patients with left heart disease
- Current data regarding patients with pulmonary disorders

Pulmonary Hypertension: Classification

Table 4 Comprehensive clinical classification of pulmonary hypertension (updated from Simonneau et al.[5])

1. Pulmonary arterial hypertension
1.1 Idiopathic 1.2 Heritable 1.2.1 BMPR2 mutation 1.2.2 Other mutations 1.3 Drugs and toxins induced 1.4 Associated with: 1.4.1 Connective tissue disease 1.4.2 Human immunodeficiency virus (HIV) infection 1.4.3 Portal hypertension 1.4.4 Congenital heart disease (Table 6) 1.4.5 Schistosomiasis
1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
1'.1 Idiopathic 1'.2 Heritable 1'.2.1 EIF2AK4 mutation 1'.2.2 Other mutations 1'.3 Drugs, toxins and radiation induced 1'.4 Associated with: 1'.4.1 Connective tissue disease 1'.4.2 HIV infection
1''. Persistent pulmonary hypertension of the newborn
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 2.5 Congenital /acquired pulmonary veins stenosis
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 (Web Table III)
4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions
4.1 Chronic thromboembolic pulmonary hypertension 4.2 Other pulmonary artery obstructions 4.2.1 Angiosarcoma 4.2.2 Other intravascular tumors 4.2.3 Arteritis 4.2.4 Congenital pulmonary arteries stenoses 4.2.5 Parasites (hydatidosis)
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms
5.1 Haematological disorders: chronic haemolytic anaemia, 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: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

BMPR2 = bone morphogenetic protein receptor, type 2; EIF2AK4 = eukaryotic translation initiation factor 2 alpha kinase 4; HIV = human immunodeficiency virus.

European Heart Journal
doi:10.1093/eurheartj/ehv317
ESC/ERS GUIDELINES

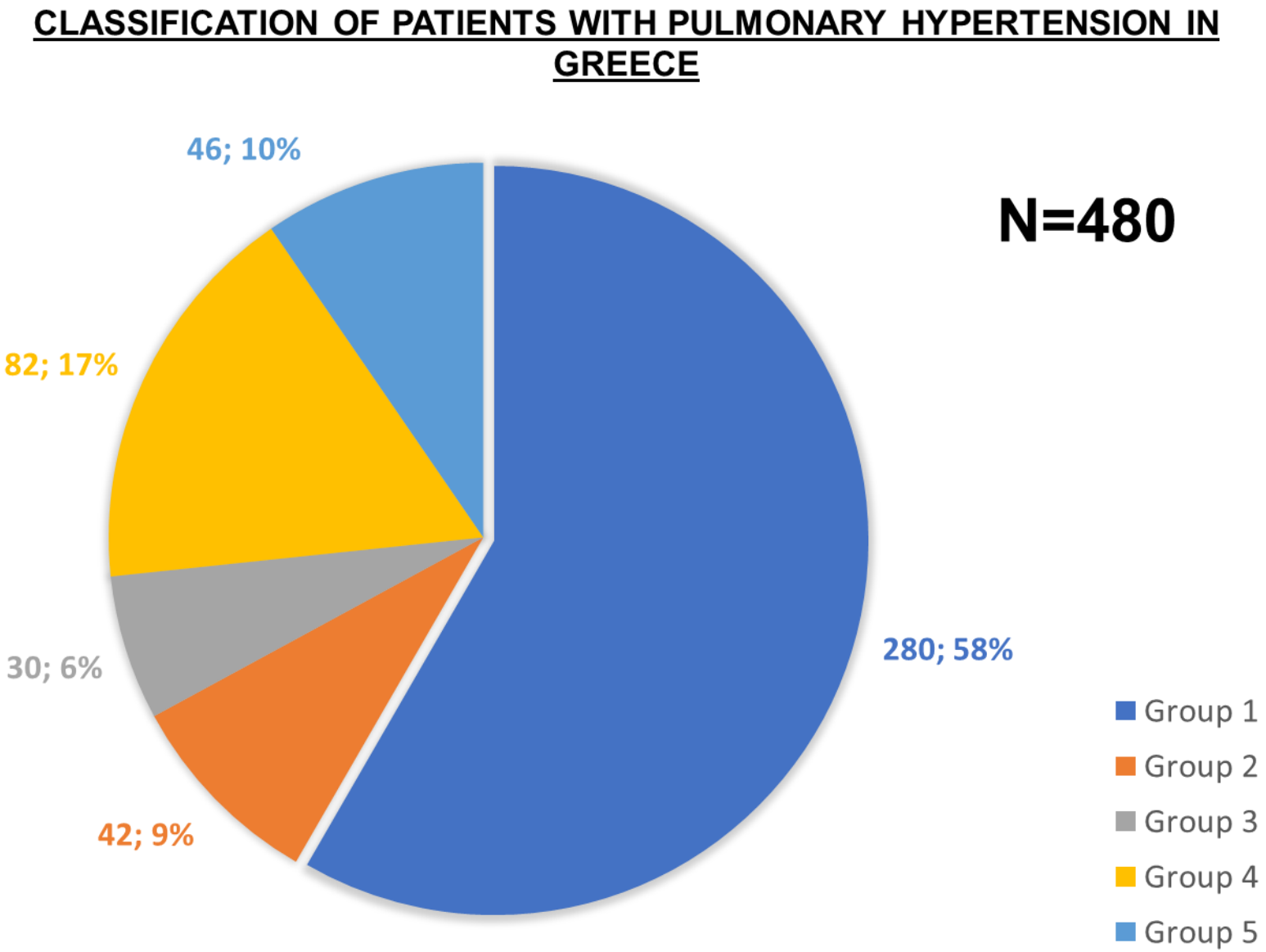
2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Greek Pulmonary Hypertension Registry
3.PH Classification

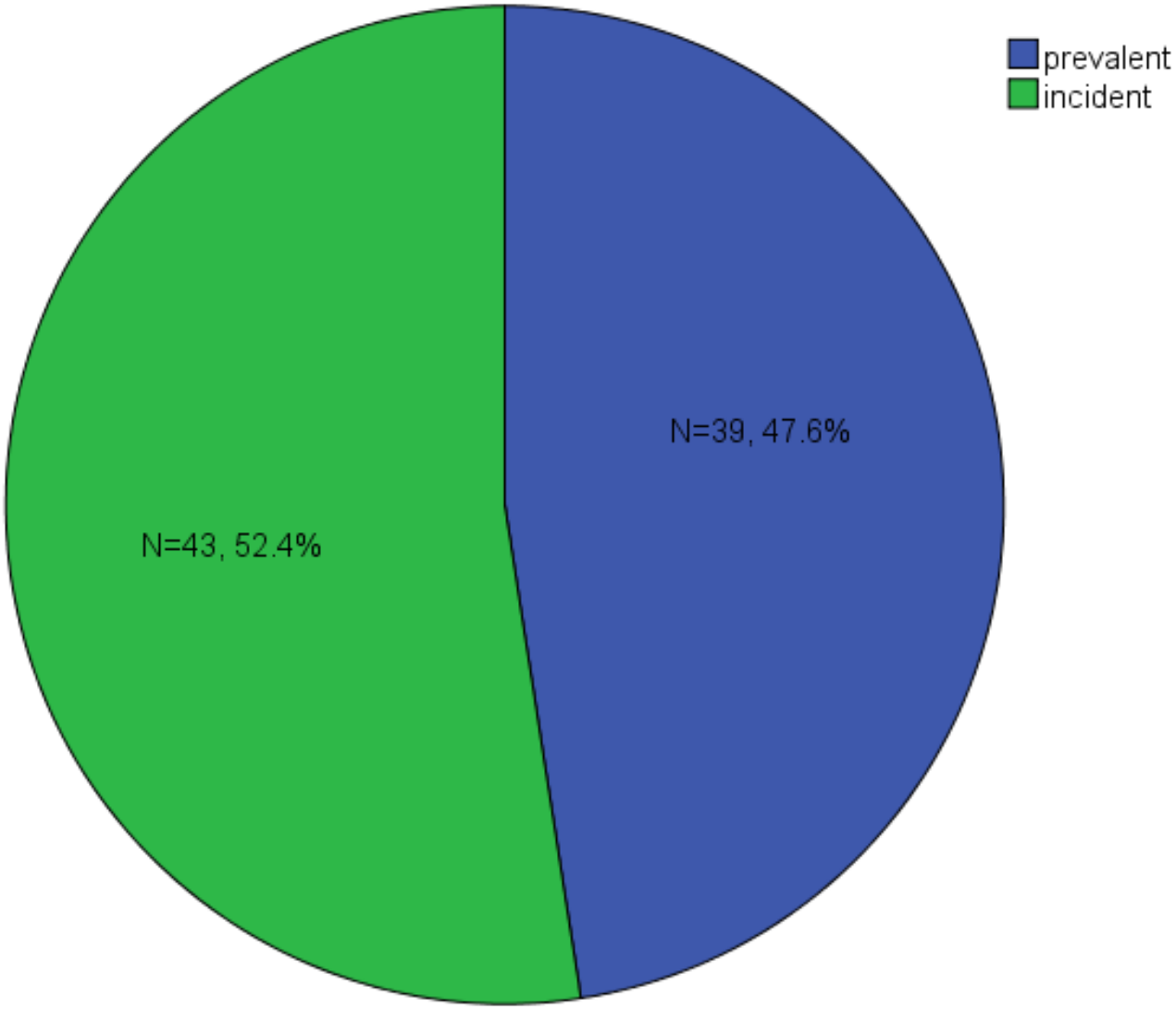
Greek PAHTool Registry



Chronic thromboembolic pulmonary hypertension (GROUP4)
Purpose and Methods

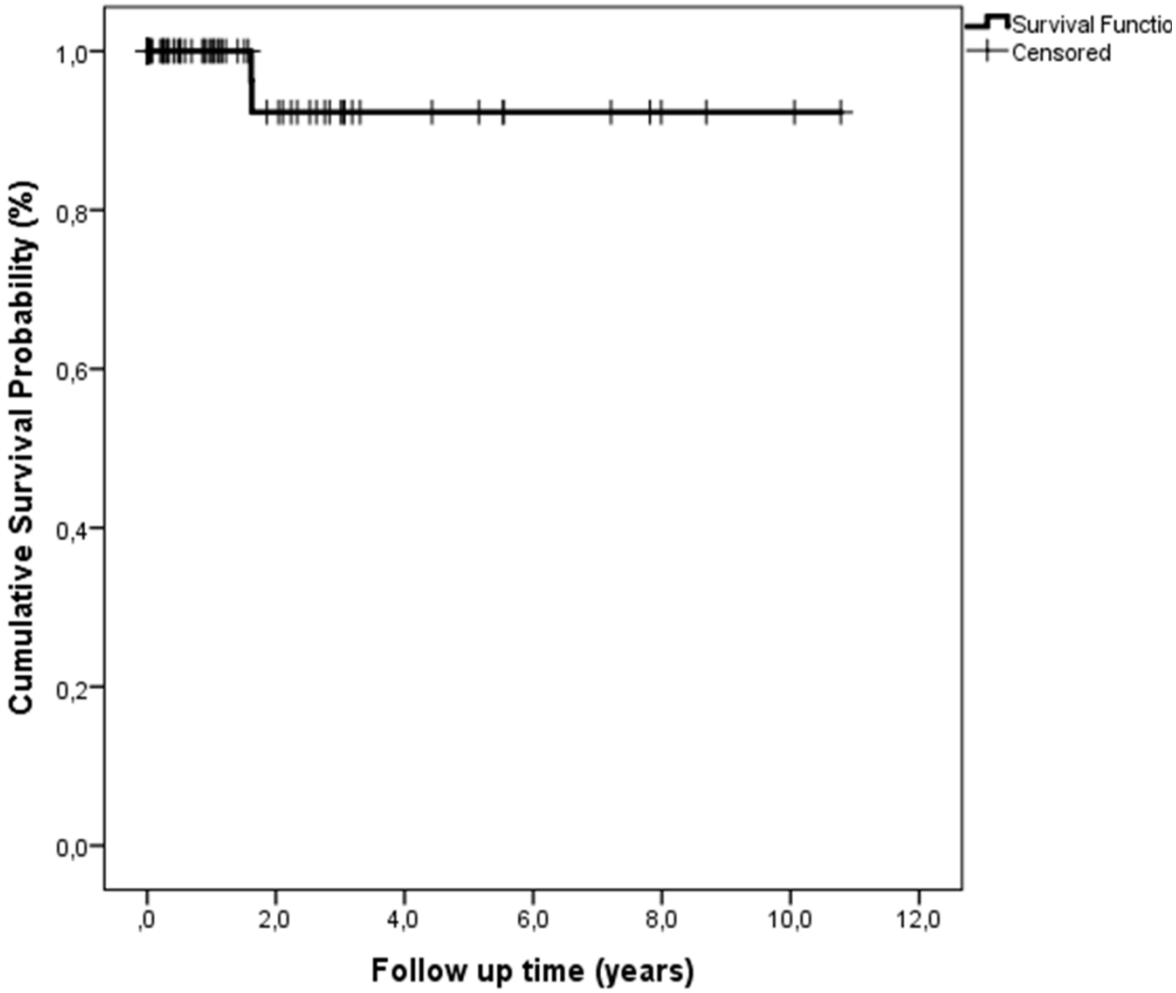
We conducted a prospective, observational study from 2015 to 2019 with a joint collaboration from ten pulmonary hypertension expert centers in Greece and described the demographics, management and follow up of patients with CTEPH

Chronic thromboembolic pulmonary hypertension



Results
Survival (GROUP 4)

- Follow up data N=55
- Median (IQR)FU period 1.5(2.5)y
- 2 deaths
  - RHF
  - SCD
- mortality rate 1.5 deaths per 100 patients-years)

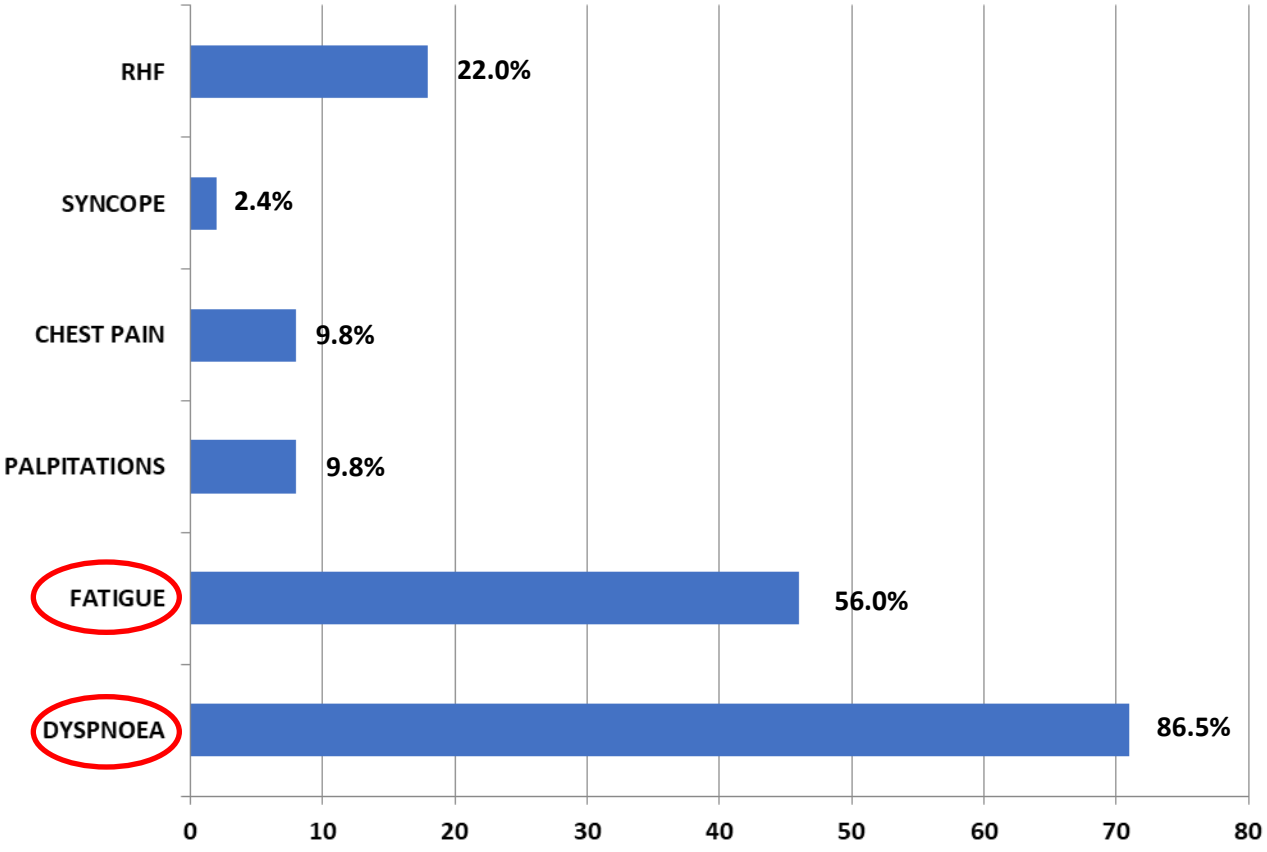


Results
Demographics (GROUP 4)

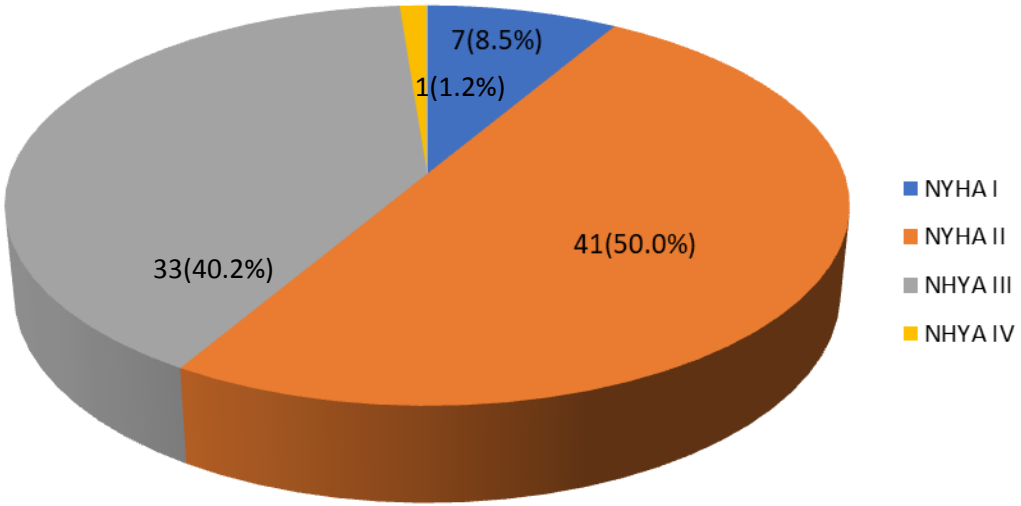
Demographics of patients with CTEPH	
	N=82
Age, (years)	59.2 ± 16.3
Female sex, n (%)	48(58.5)
BMI, (Kg/m²)	27.6± 6.4
Incident patient, n (%)	43(52.4)

Comorbidities of patients with CTEPH	
	N (%)
Atrial fibrillation	4(4.9)
Arterial hypertension	29 (35.4)
Diabetes mellitus	7 (8.5)
Dyslipidemia	7(8.5)
CAD	4(4.9)
Dialysis	1 (1.2)
Liver disease	1(1.2)
Previous PE	44 (53.7)
Previous DVT	7 (8.5)
Splenectomy	7 (8.5)
Hematological disease	16 (19.5)
Thyroid disease	12(14.6)
Obesity (BMI≥30kg/m²)	21 (25.6)
COPD	10(12.2)
Smoking	24 (29.3)
Depression	6(7.3)

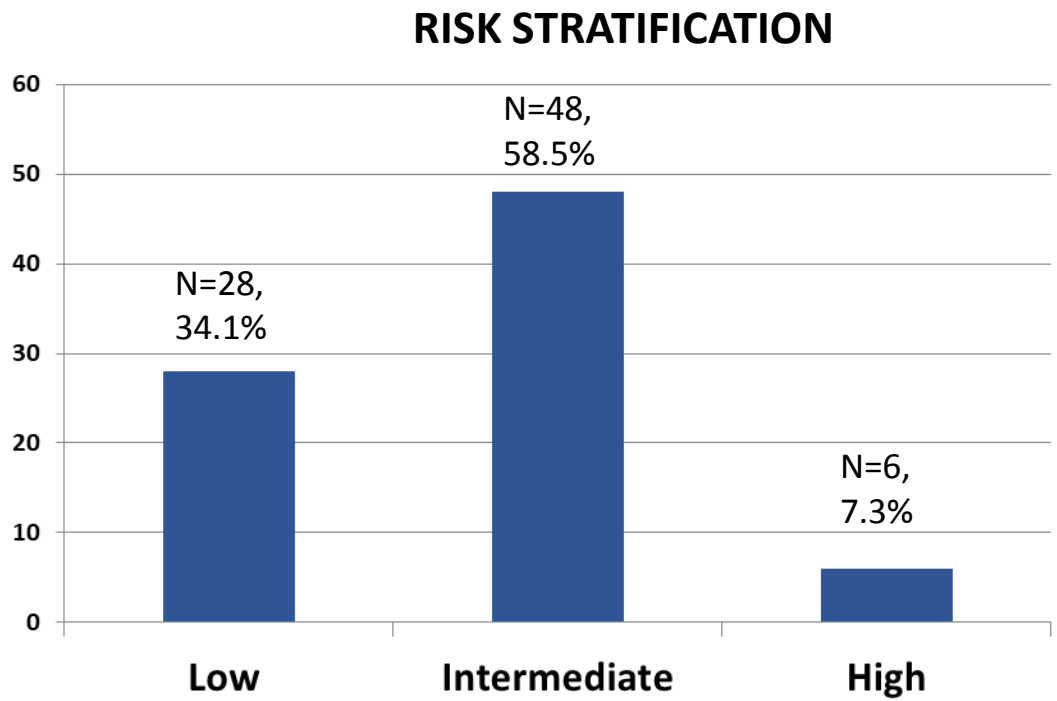
Results
Symptoms (GROUP 4)



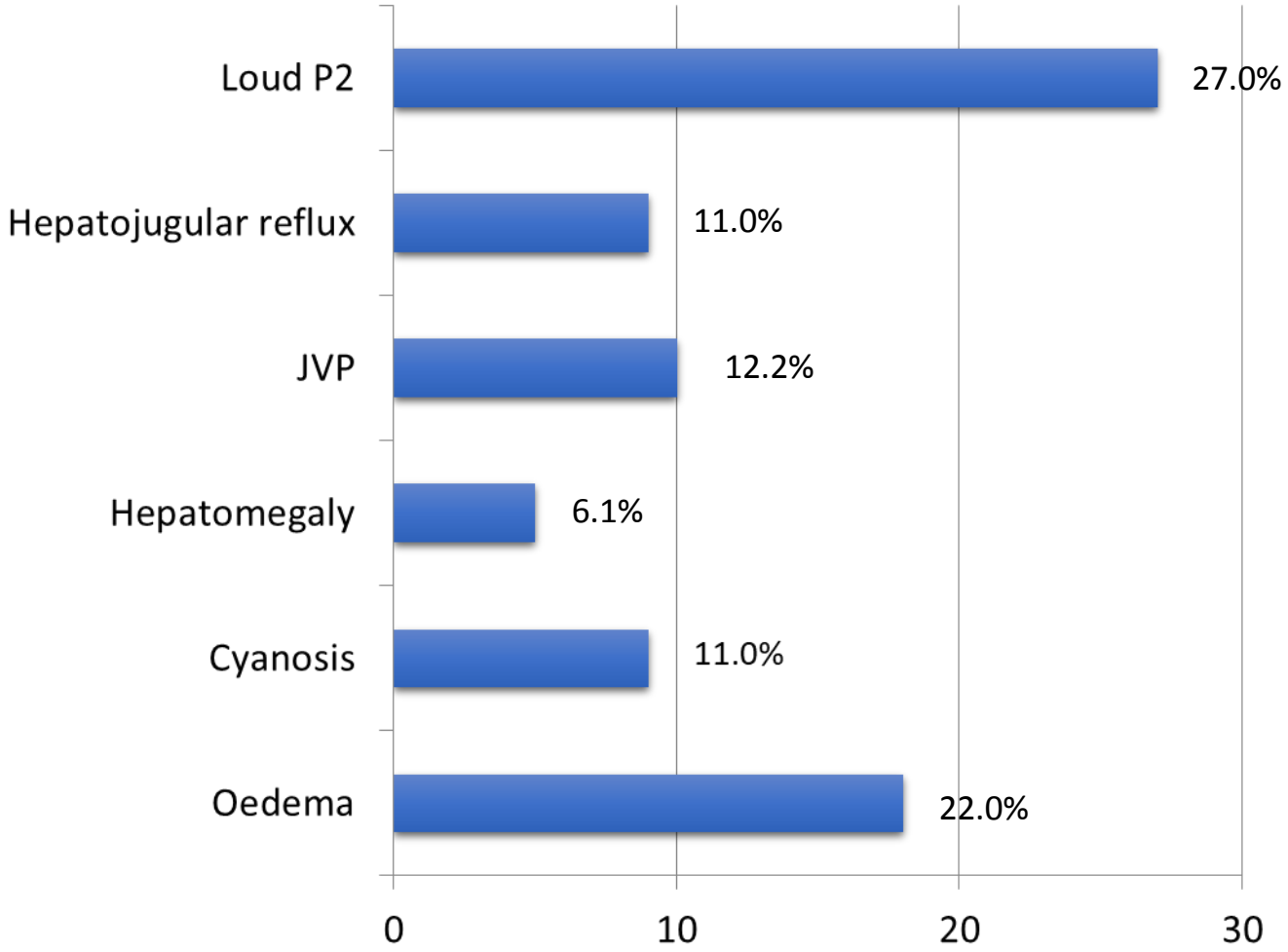
Results
Functional and neurohormonal characteristics(GROUP4)



	Baseline (N=82)	Follow up (N=55)
6-MWD (m) (mean±SD)	325±167	428±166.1
NT-proBNP (pg/mL) Median (IQR)	498(1064)	107(261)



Results
Clinical Signs (GROUP 4)



Results
Diagnostic parameters (GROUP 4)

Echocardiography

	Baseline	Follow up	P value
RVEDD (mm)	33.4±12.3	40.1±27.7	0.542
TAPSE, mm	18.5±4.7	16.9±5.9	0.049
TR Vmax, m/s	3.9 ± 0.7	3.7±0.8	0.210
RVSP, mmHg	73.2 ± 21.4	65.0±24.6	0.234

Hemodynamics

	Baseline	Follow up	P value
mRAP, (mmHg)	7.9±4.4	8.3±4.5	0.045
sPAP, (mmHg)	76.9±19.3	60.2±22.6	<0.001
dPAP, (mmHg)	26.7 ± 7.5	22.0±7.0	0.001
mPAP, (mmHg)	44.9±10.9	37.0±11.3	<0.001
PAWP, (mmHg)	10.7±3.9	11.2±2.3	0.163
CO, (L/min)	4.5±1.4	5.0±1.3	0.004
CI, (L/min/m^2)	2.4±0.7	2.7±0.7	0.032
PVR, (WU)	8.2±4.0	10.8±6.3	0.924
SVO_2, (%)	65.8±9.3	68.6±9.2	0.003
HR, (bpm)	78.0 ± 10	75±15	0.670

Results
Diagnostic parameters (GROUP 4) (baseline)

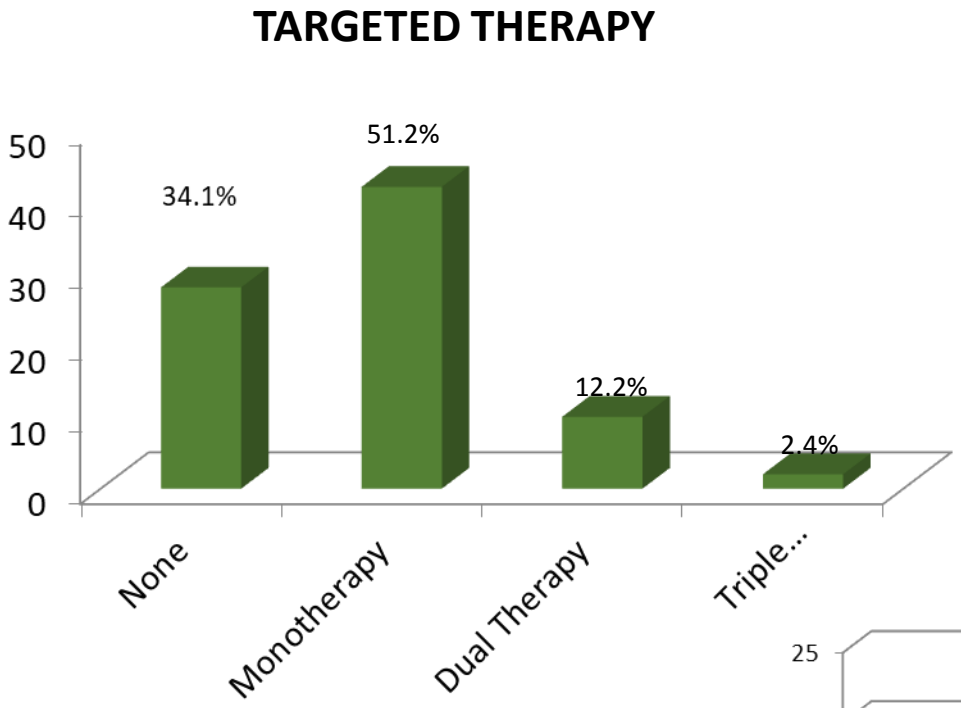
Lung function test

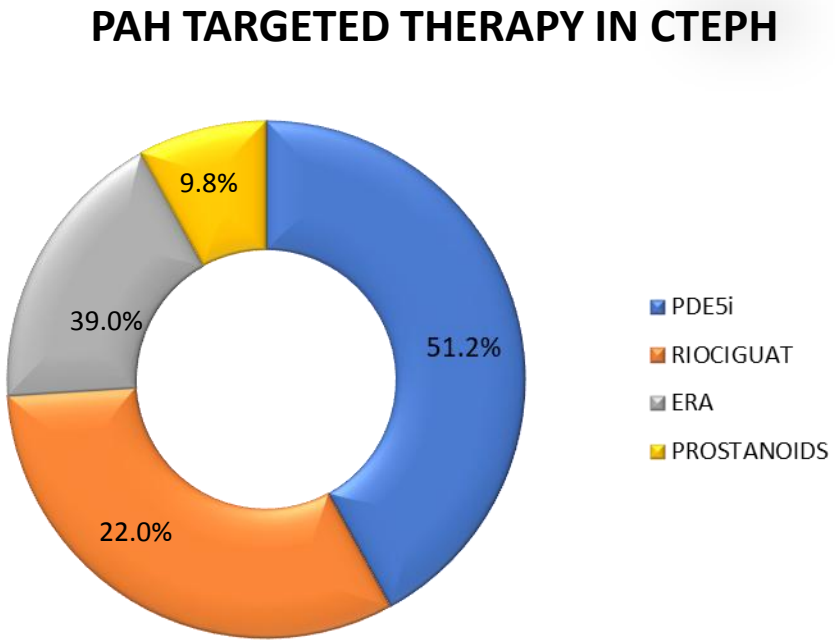
FEV1, (% pred)	83.6±15.1
FVC, (% pred)	87.9± 14.6
FEV1/FVC	77.8 ± 10.4
TLC, (%pred)	81.3±11.7
DLCO/SB, (%pred)	69.07 ± 21.3

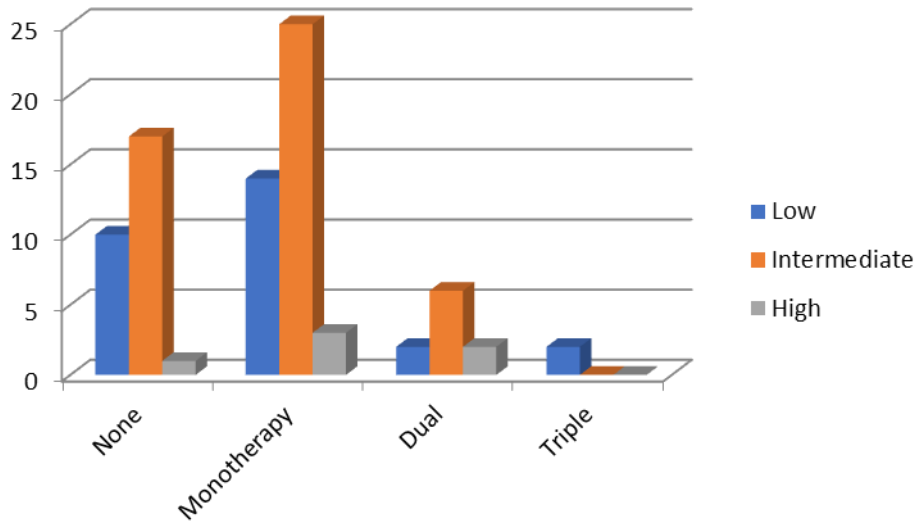
Other diagnostic procedures

V/Q scintigraphy	50 (61.0)
Abnormal V/Q scan	39 (47.6)
Chest CT	42 (51.2)
Central thrombi	16 (19.5)
Peripheral thrombi	22 (26.8)
Mural thrombi	9 (11.0)
Pulmonary Angiography	19 (23.2)

Results
Medical therapy (GROUP 4) (baseline)

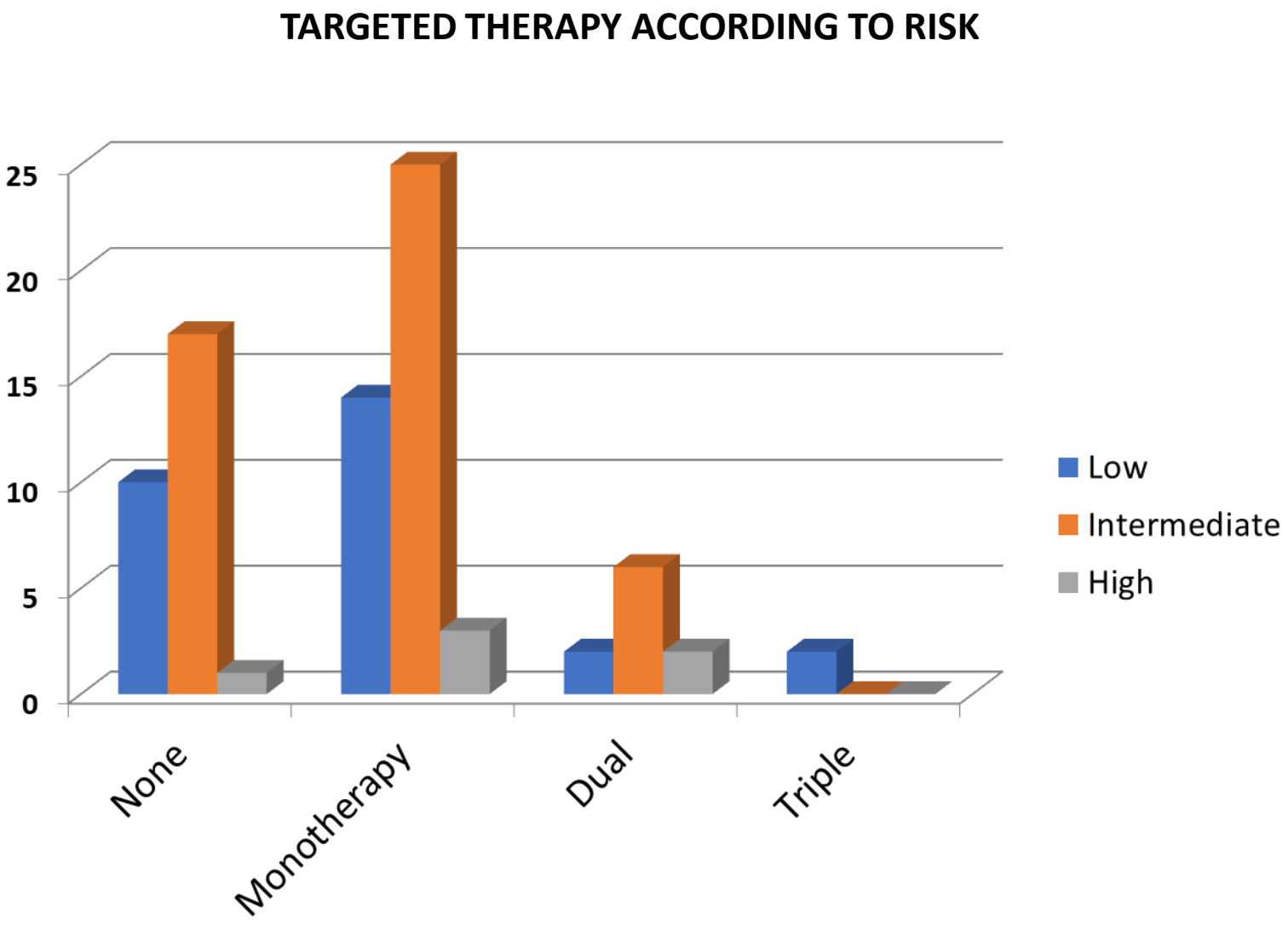




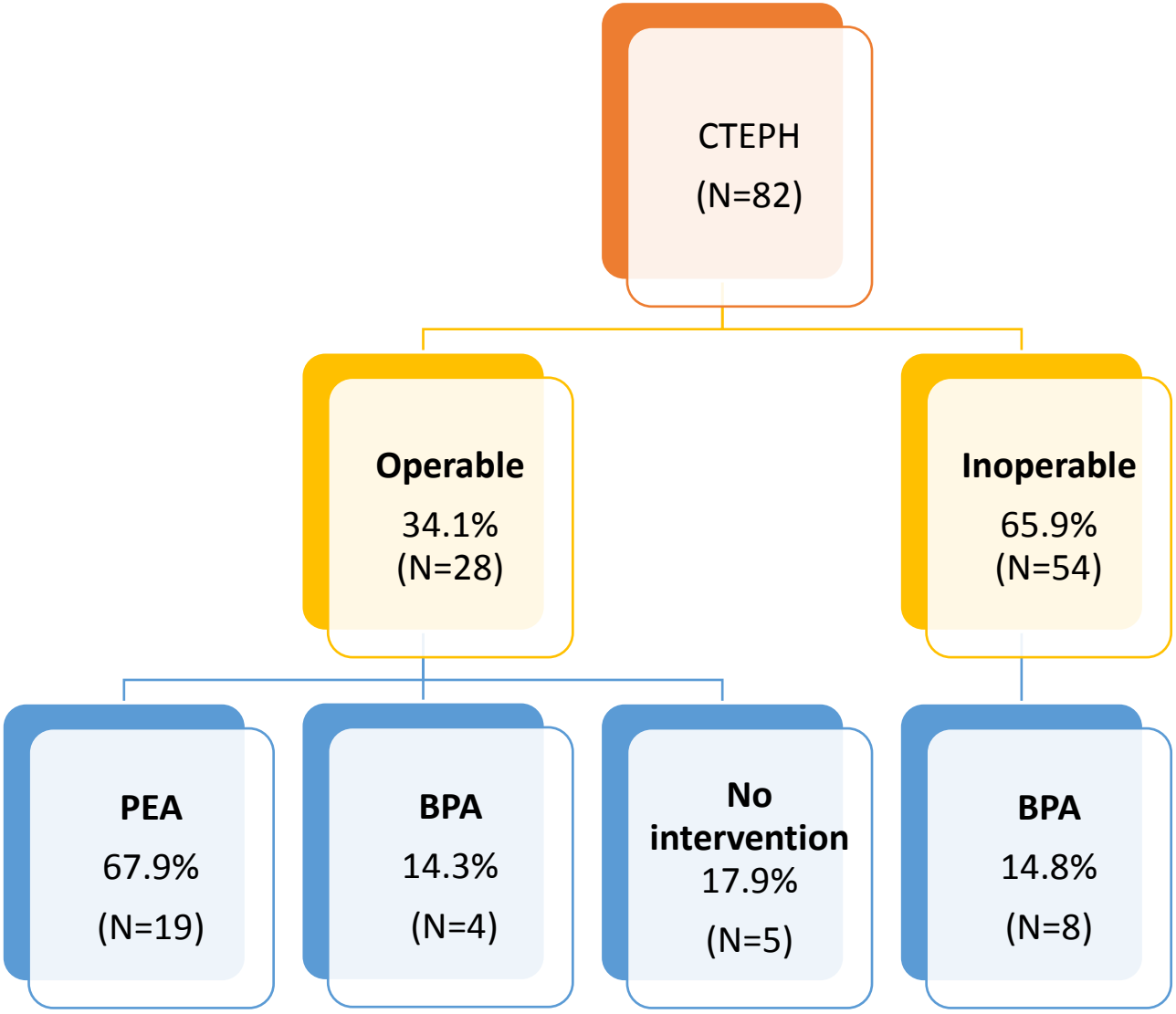


Non specific treatment, n (%)	
Oxygen therapy	24 (29.3)
OAC therapy	62 (72.6)
Diuretics	44 (53.6)

Results
Medical therapy (GROUP 4) (baseline)



Results
Interventional therapy



Group 5: PH with unclear and/or multifactorial mechanisms

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

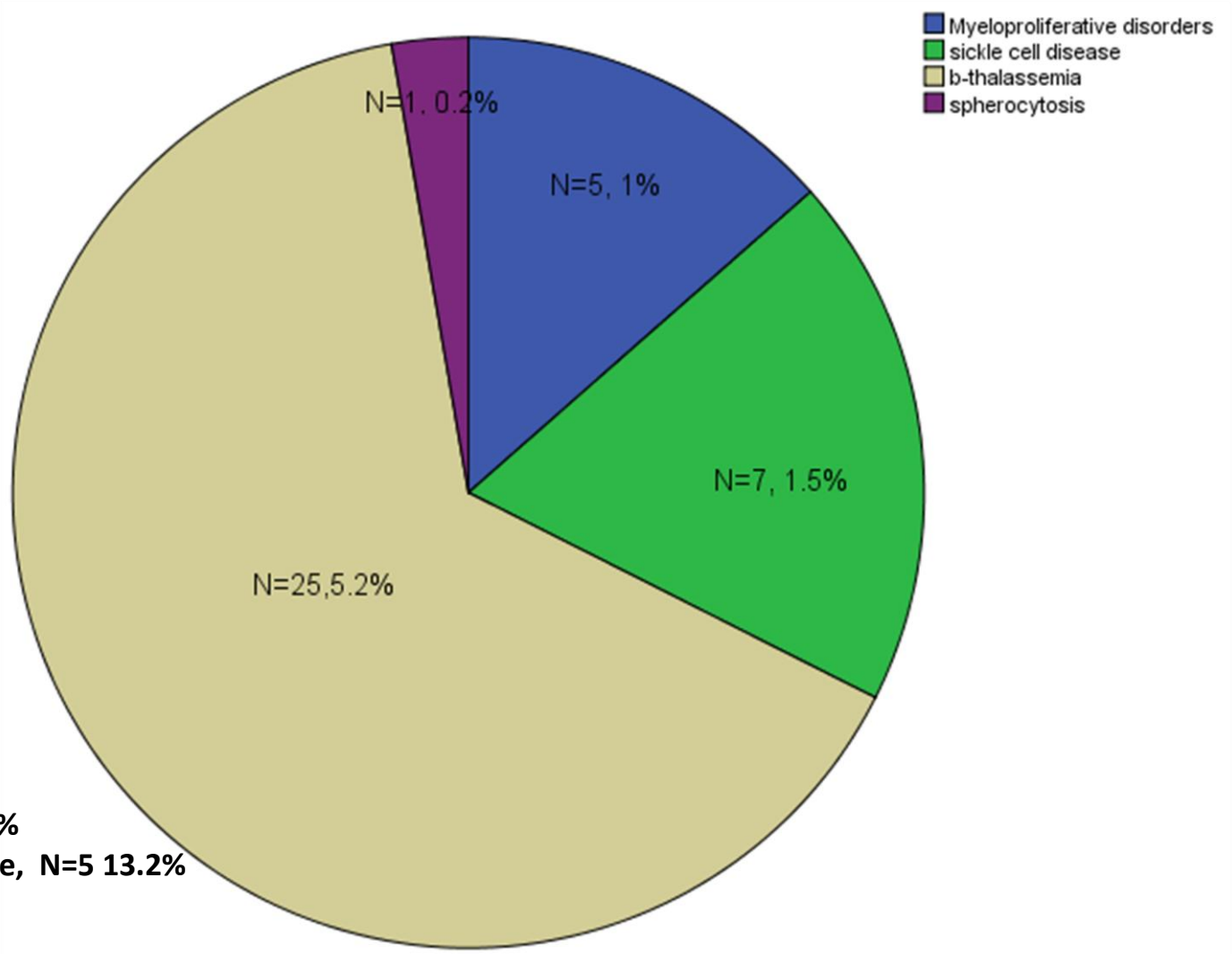
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, 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: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

BMPR2 = bone morphogenetic protein receptor, type 2; EIF2AK4 = eukaryotic translation initiation factor 2 alpha kinase 4; HIV = human immunodeficiency virus.

Patients with haematological disorders (Group 5)

N=46 patients in Group 5 out of 480 PH patients
N=38 patients (28, 73.7% incident) with haematological disorders

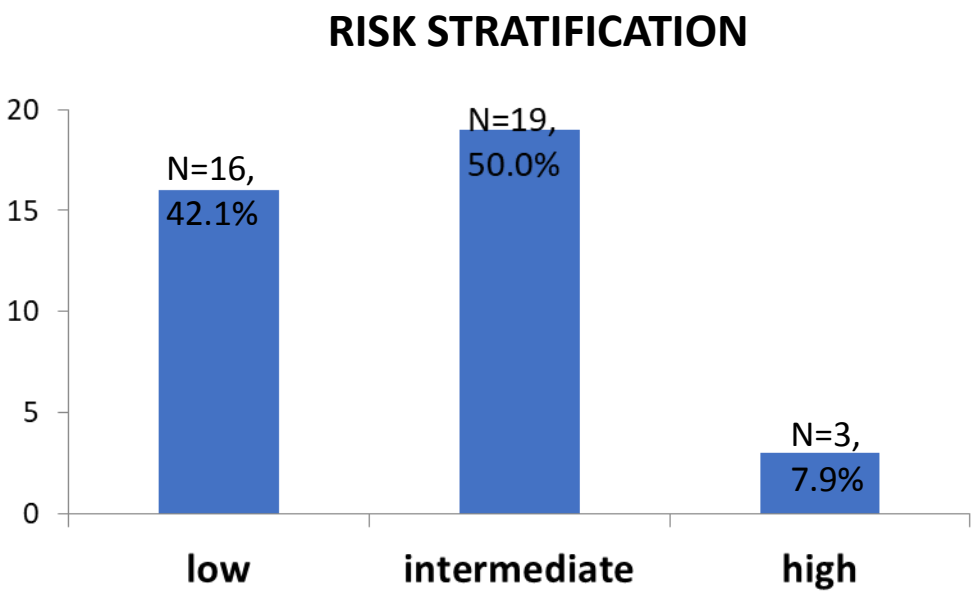


B thalassemia N=25, 65.8%
Sickle cell disease, N=7, 18.4%
Promyeloproliferative disease, N=5 13.2%
Scpherocytosis , N=1, 2.6%

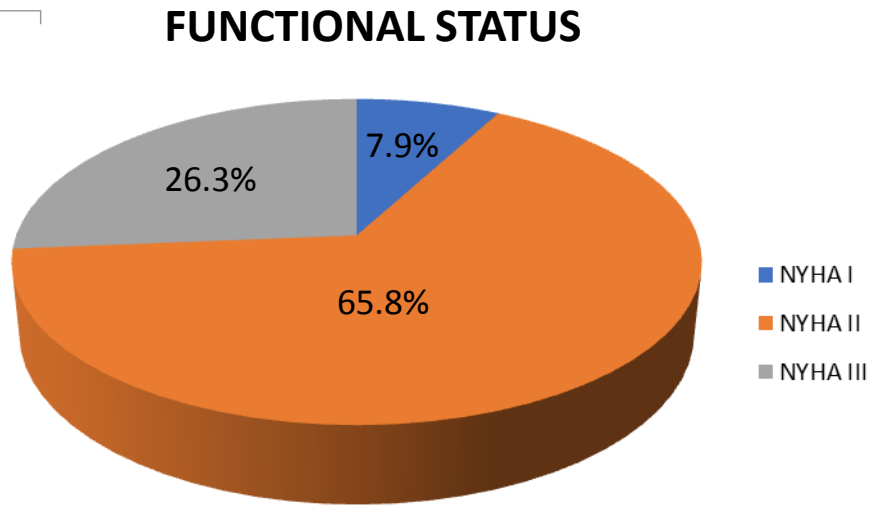
Group 5. Patients with haematological disorders

- Mean age of patients was (mean±SD) 52.8±10.6 years,
- More than half of them were females (N=20, 52.6%).
- Thirteen patients underwent splenectomy (34.2%, 5.6% of total), due to
  - thalassemia (N=10, 26.3%, 2.1%),
  - myeloproliferative disorders (N=2, 0.4%)
  - scherocytosis (N=1, 0.2%).
- Median (IQR) Follow up period: 1.3(1.0)years
- Among 16 patients with available follow up data, 1 death was reported over 26,5 patient-years of follow up (mortality rate 3,8 deaths per 100 patients-years). The cause of death in this case was heart failure.

Group 5. Patients with haematological disorders
Functional and neurohormonal characteristics

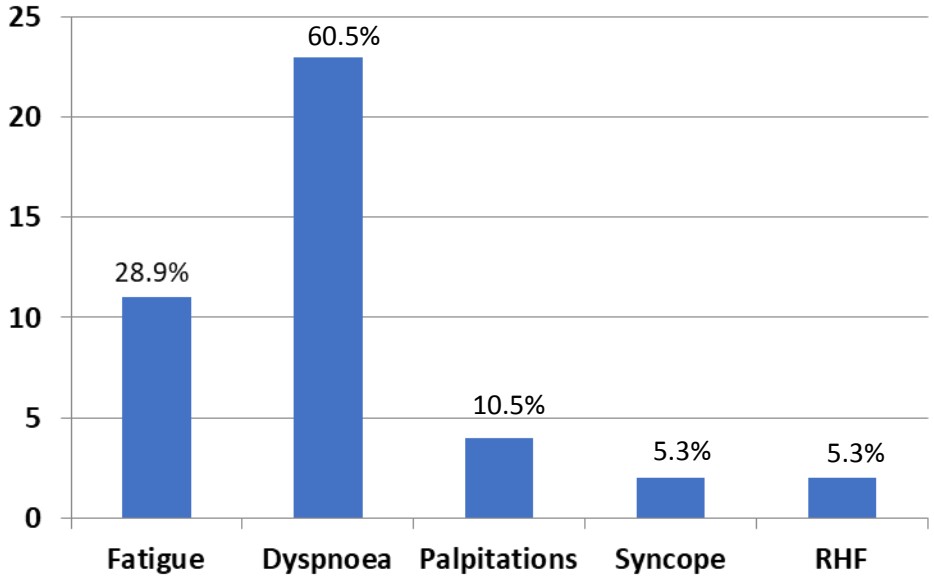


	Baseline (N=38)	Follow up (N=16)
6-MWD (m) (mean±SD)	350.8±189.7	487.0±91.3
NT-proBNP (pg/mL) Median (IQR)	343(1933)	244(1977)

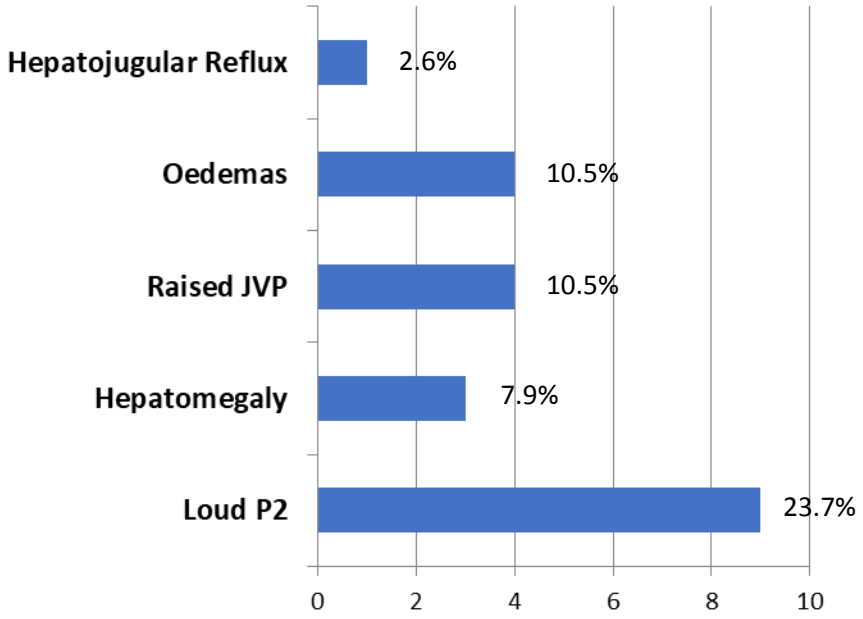


Group 5. Patients with haematological disorders Symptoms and clinical presentation

Symptoms



Clinical signs



Results
Diagnostic parameters (GROUP 5)

Echocardiography

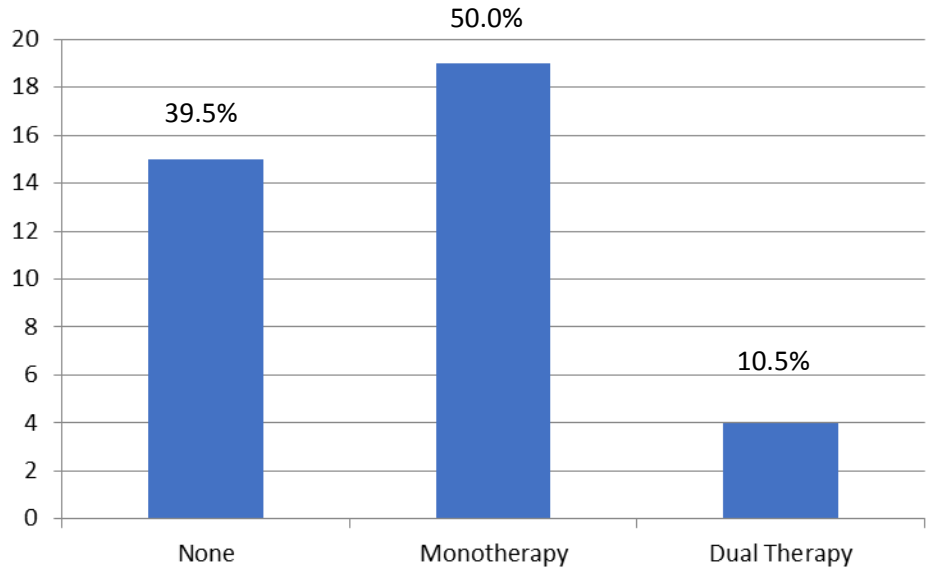
	Baseline	Follow up	P value
RVEDD (mm)	46.0±10.1	36.5±6.4	-
TAPSE, mm	20.8±4.7	18.0±2.8	-
TR Vmax, m/s	3.9 ± 0.7	3.2±0.8	0.743
RVSP, mmHg	73.4 ± 29.7	51.0±22.9	0.870

Hemodynamics

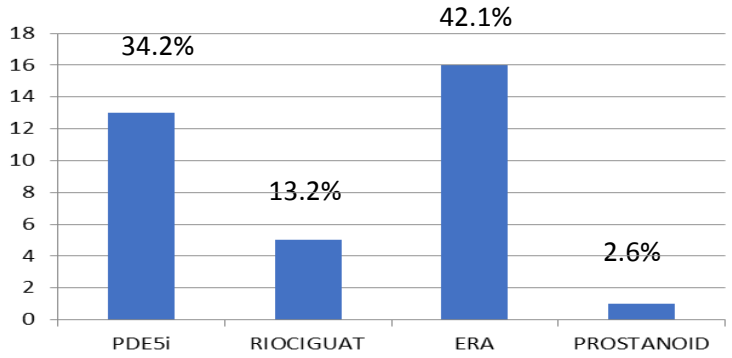
	Baseline	Follow up	P value
mRAP, (mmHg)	9.3±3.9	7.6±2.6	0.270
sPAP, (mmHg)	61.1±14.2	53.4±15.9	0.104
dPAP, (mmHg)	22.4 ± 6.3	16.8±4.4	0.196
mPAP, (mmHg)	37.9±8.0	32.2±8.0	0.116
PAWP, (mmHg)	12.2±3.2	13.2±4.0	0.255
CO, (L/min)	4.9±1.5	5.9±1.5	0.191
CI, (L/min/m^2)	2.4±0.7	2.7±0.7	0.032
PVR, (WU)	5.7±2.6	6.2±3.3	-
SVO_2, (%)	60.8±11.6	65.3±9.8	0.037
HR, (bpm)	77±10	77±11	0.270

Results
Medical therapy (GROUP 5) (baseline)

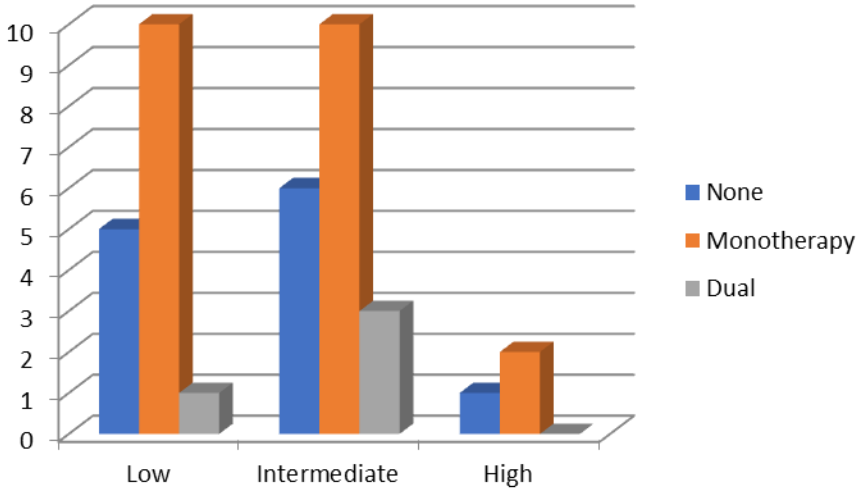
TARGETED THERAPY



PAH TARGETED THERAPY



TARGETED THERAPY ACCORDING TO RISK



Non specific treatment, n (%)	
Oxygen therapy	15(39.5)
OAC therapy	62 (72.6)
Diuretics	19 (50.0)

Results
Demographics Group 2

Demographics of patients with LHD

	N=42
Age, (years)	60.7 ± 19.5
Female sex, n (%)	21(50.0)
BMI, (Kg/m²)	26.8±5.5
Incident patient, n (%)	32(76.2)

RISK STRATIFICATION

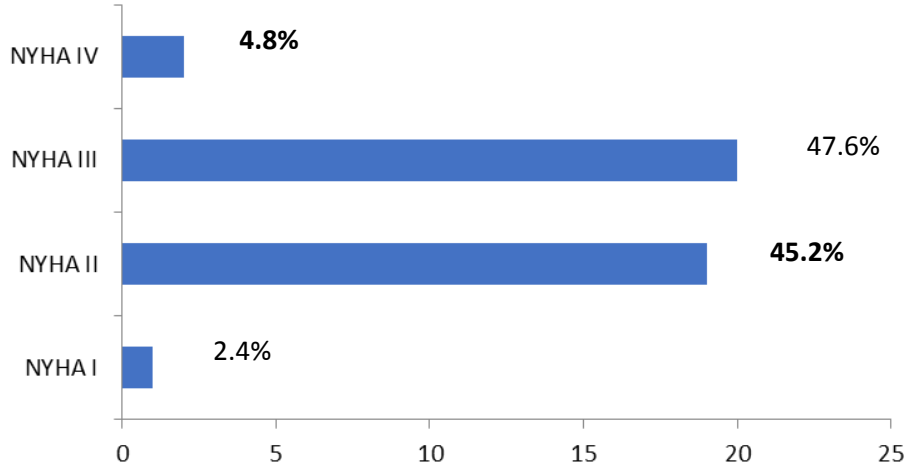
	N(%)
Low	4(9.5)
Intermediate	28(66.7)
High	10(23.8)

Comorbidities of patients with LHD

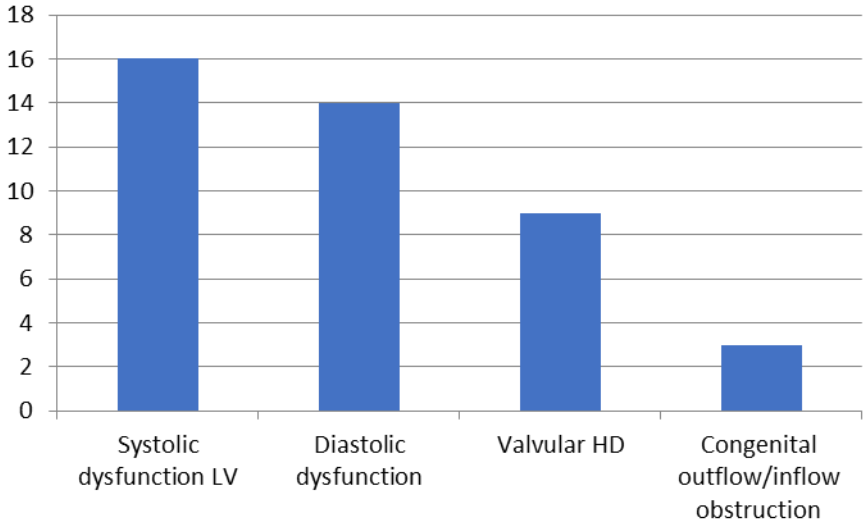
	N (%)
Atrial fibrillation	15(35.7)
Arterial hypertension	12 (28.6)
Diabetes mellitus	7(16.7)
Dyslipidemia	6(14.3)
CAD	13(31.0)
Renal insufficiency	4 (9.5)
Hematological disease	3 (7.1)
Thyroid disease	4(9.5)
Obesity (BMI≥30kg/m²)	9(21.4)
COPD	7(16.7)
Smoking	4 (9.5)

Results
Functional and neurohormonal characteristics(GROUP 2)

FUNCTIONAL STATUS



GROUP 2: SUBGROUPS



	Baseline (N=42)
6-MWD (m) (mean±SD)	316.6±148.1
NT-proBNP (pg/mL) Median (IQR)	1006.5(2940)

Results (IV)
Clinical Signs (baseline) (GROUP 2)

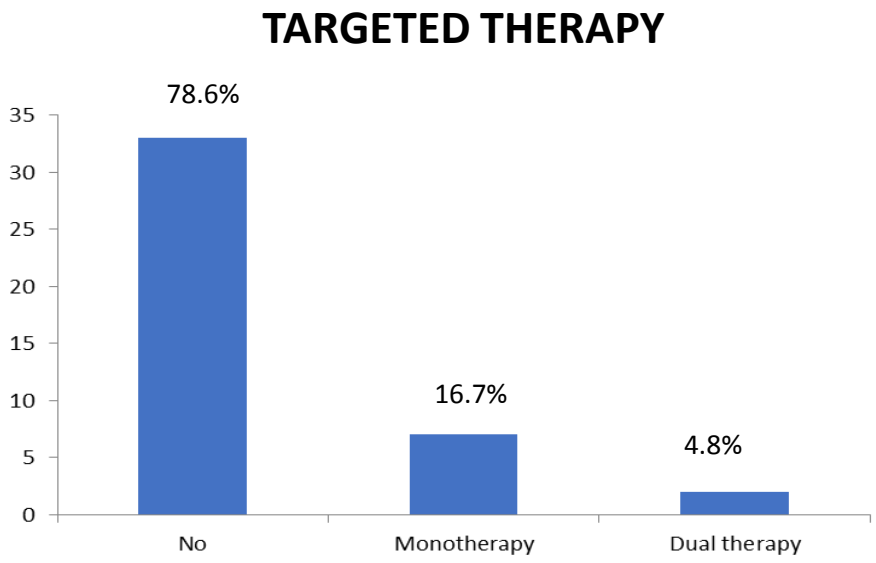
Clinical signs	N(%)
Cyanosis	2(4.8)
LoudP2	5(11.9)
Hepatomegaly	3(7.1)
Raised JVP	8(19.0)
Oedema	9(21.4)
Hepatojugular reflux	7(16.7)

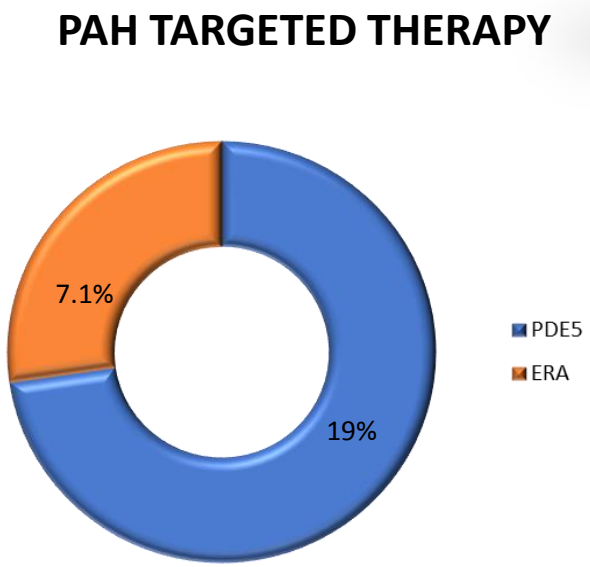
Results
Diagnostic parameters (GROUP 2)

Echocardiography	
	Baseline
RVEDD (mm)	33.4±17.7
TAPSE, mm	18.3±5.5
TR Vmax, m/s	3.8 ± 0.8
RVSP, mmHg	68.8 ± 24.0

Hemodynamics	
	Baseline
mRAP, (mmHg)	13.5±5.8
sPAP, (mmHg)	67.5±20.2
dPAP, (mmHg)	26.5 ± 10.0
mPAP, (mmHg)	44.1±11.1
PAWP, (mmHg)	25.9±8.1
CO, (L/min)	4.3±1.8
CI, (L/min/m^2)	2.6±1.4
DPG, (mmHg)	2.5±2.1
PVR, (WU)	4,29±2,3
SVO$_2$, (%)	63.5±11.2
HR, (bpm)	77.0 ± 12

Results
Medical therapy (baseline) (GROUP 2)





Non specific treatment, n (%)	
Oxygen therapy	10 (23.8)
OAC therapy	13 (31.0)
Diuretics	41 (97.6)

Results
Demographics (GROUP 3)

Greek PAHTool Registry

Demographics of patients

	N=30
Age, (years)	68.2 ± 12.5
Female sex, n (%)	12(40.0)
BMI, (Kg/m²)	28.5±5.0
Incident patient, n (%)	20(66.7)

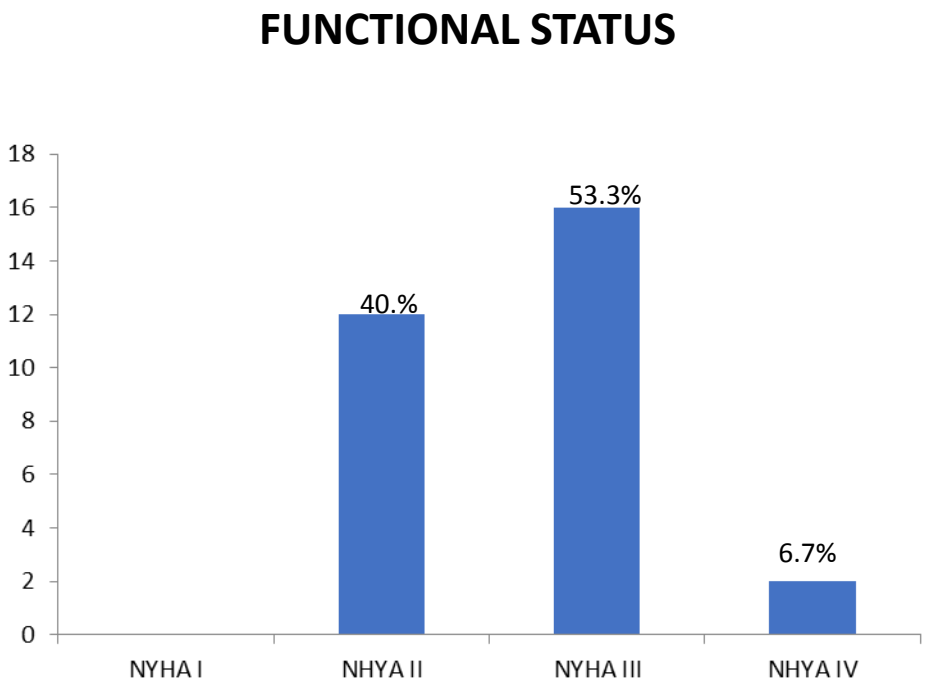
Comorbidities of patients

	N (%)
Atrial fibrillation	2(6.7)
Arterial hypertension	13 (43.3)
Diabetes mellitus	8(26.7)
Dyslipidemia	6(20.0)
CAD	7(23.3)
Renal insufficiency	2(6.7)
Hematological disease	3 (7.1)
Thyroid disease	5(16.7)
Obesity (BMI≥30kg/m²)	13(43.3)
COPD	17(56.7)
Smoking	17(56.7)

RISK STRATIFICATION

	N(%)
Low	8(26.7)
Intermediate	19(63.3)
High	3(10.0)

Results
Functional and neurohormonal characteristics (GROUP3)

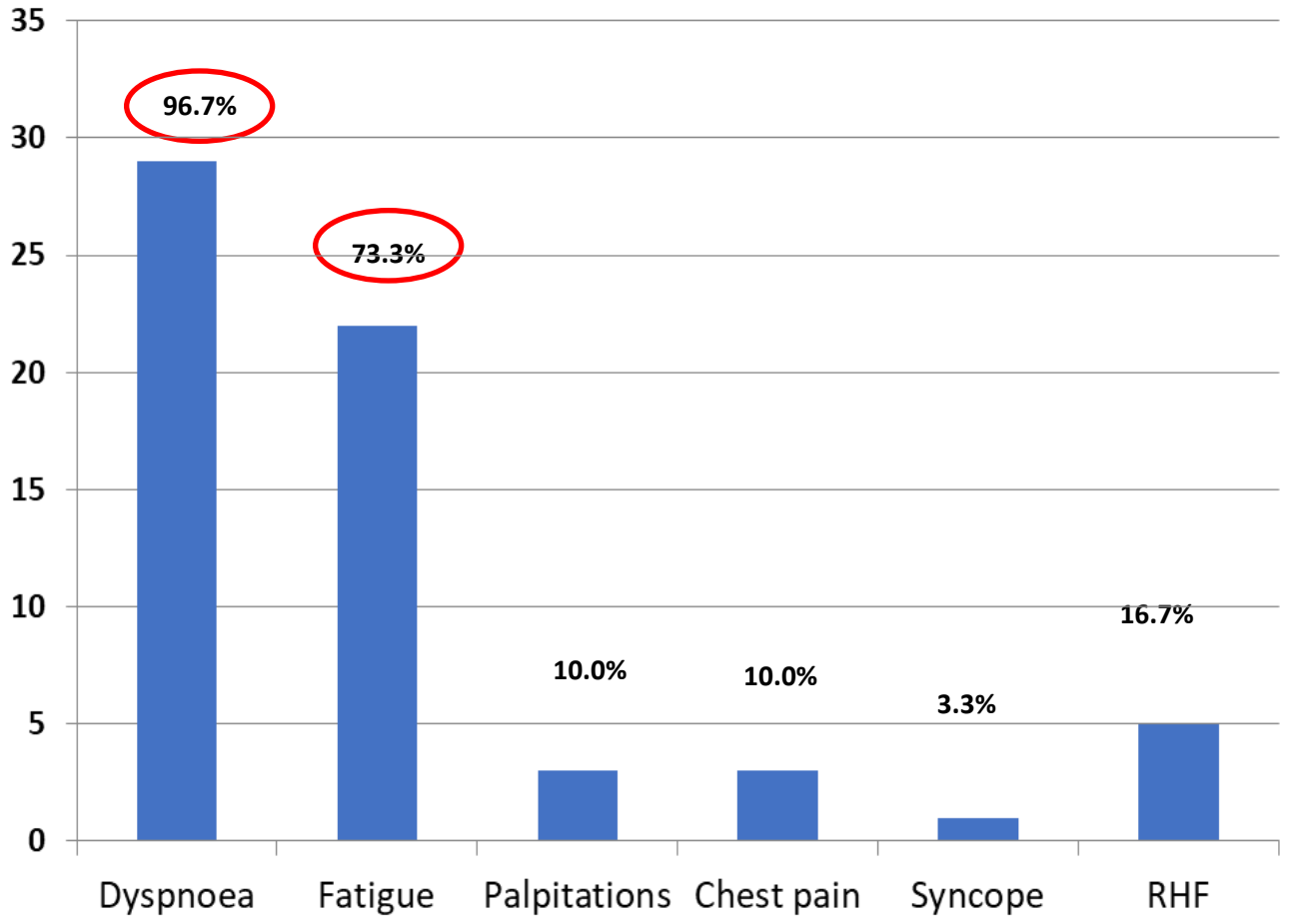


	Baseline (N=30)
6-MWD (m) (mean±SD)	193.4±202.3
NT-proBNP (pg/mL) Median (IQR)	761.0(3227)

Results
Clinical Signs (baseline) (GROUP3)

Clinical signs	N(%)
Cyanosis	2(4.8)
LoudP2	5(11.9)
Hepatomegaly	3(7.1)
Raised JVP	8(19.0)
Oedema	9(21.4)
Hepatojugular reflux	7(16.7)

Results
Symptoms (BASELINE) (GROUP 3)

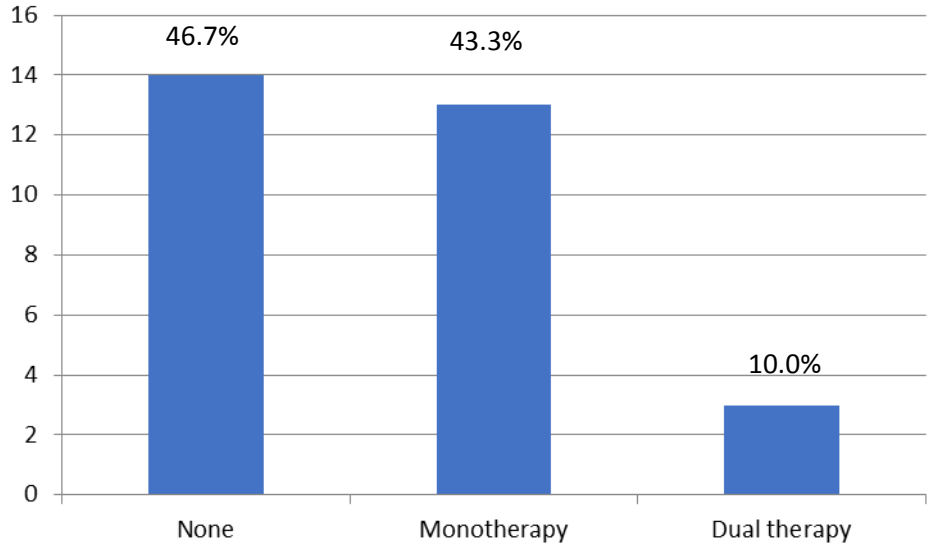


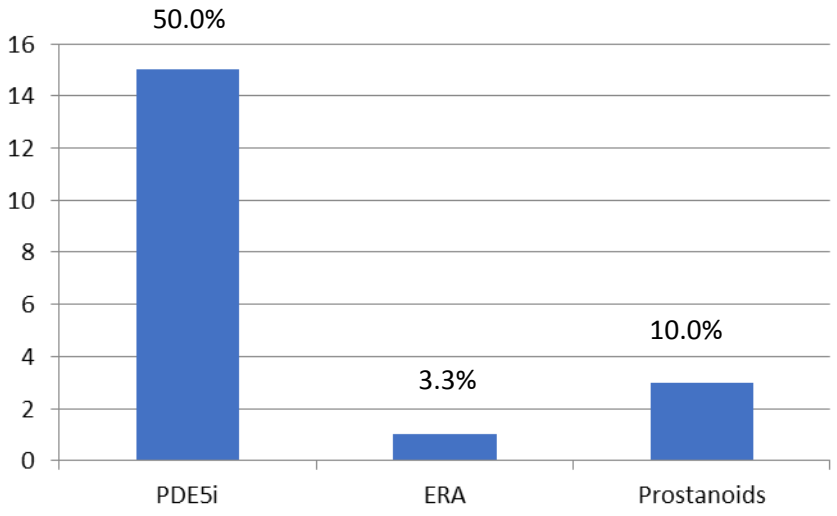
Results
Diagnostic parameters (GROUP 3)

Echocardiography	
	Baseline
TAPSE, mm	19.1±4.4
TR Vmax, m/s	4.0 ± 0.4
RVSP, mmHg	75.5 ±13.5

Hemodynamics	
	Baseline
mRAP, (mmHg)	8.6±5.0
sPAP, (mmHg)	65.1±19.5
dPAP, (mmHg)	29.1 ± 11.0
mPAP, (mmHg)	42.0±12.4
PAWP, (mmHg)	11.6±3.0
CO, (L/min)	4.6±1.4
CI, (L/min/m^2)	2.4±0.7
PVR, (WU)	7.5±4.3
SVO$_2$, (%)	67.6±7.1
HR, (bpm)	88.0 ± 21

Results
Medical therapy (baseline) (GROUP 3)





Non specific treatment, n (%)	
Oxygen therapy	5 (16.7)
OAC therapy	6 (20.0)
Diuretics	17 (56.7)

Conclusions and future perspectives
GROUP 4

- ✓ **82 consecutive patients with CTEPH were included**
- ✓ **Dyspnea and fatigue** were the most common presenting symptoms
- ✓ **History of PE was present in 53.7%** of patients
- ✓ **Half of patients were on WHO class II**
- ✓ **all patients underwent RHC** to confirm diagnosis
- ✓ V/Q scintigraphy was performed in 2/3 with 47.6% having abnormal lesions
- ✓ PA was performed in 1/5 of patients

- ✓ **About 72.6%** of patients received an **oral anticoagulant**
- ✓ **34.1% of patients screened, were considered operable, of which 67.9% PEA, while 4 patients underwent BPA**
- ✓ **inoperable** patients underwent **BPA**
- ✓ **65.8% received specific medical treatment for PAH**

Conclusions and future perspectives
GROUP 5

- ✓ **38 consecutive patients with haematological disorders were included**
- ✓ **Dyspnea and fatigue** were the most common presenting symptoms
- ✓ **B- thalassemia was the most common underline disorder (25.5%)**
- ✓ **Half of patients were on WHO class II**
- ✓ **All patients underwent RHC** to confirm diagnosis

- ✓ **About 72.6%** of patients received an **oral anticoagulant**
- ✓ **60.5% received specific medical treatment for PAH**

Thank you!

- **Α' Καρδιολογική Κλινική Αριστοτέλειο Πανεπιστήμιο, ΑΧΕΠΑ, Θεσσαλονίκη**: Αρβανιτάκη Αλεξάνδρα, Μουράτογλου Σοφία, Φελουκίδης Χρήστος, Φαρμάκης Δημήτριος, Καρβούνης Χαράλαμπος, Γιαννακούλας Γεώργιος
- **Καρδιολογική Κλινική Νοσοκομείο Mediterraneo, Γλυφάδα**: Μπούτσικου Μαρία, Παππά Λιλίκα, Μαγγίνας Αθανάσιος
- **Διακλινικό Ιατρείο Πνευμονικής Υπέρτασης ΠΓΝ Αττικόν, Αθήνα**: Σταγάκη Ελένη, Τσαγκάρης Ηρακλής, Λεκάκης Ιωάννης, Αρμαγανίδης Απόστολος, Άνθη Αναστασία, Ορφανός Στέλιος
- **Καρδιολογική-Παιδοκαρδιολογική Κλινική Ωνάσειο Καρδιοχειρουργικό Κέντρο**: Δεμερούτη Ευτυχία, Βούδρης Βασίλειος, Αποστολοπούλου Σωτηρία, Αθανασόπουλος Γεώργιος, Τσιάπρας Δημήτριος, Ράμμος Σπυρίδων Καρυοφίλλης Παναγιώτης
- **Μονάδα αναπνευστικής ανεπάρκειας, Γενικό Νοσοκομείο «Παπανικολάου», Θεσσαλονίκη**: Παναγιωτίδου Ευαγγελία, Στανόπουλος Ιωάννης, Πίτσιου Γεωργία
- **Πνευμονολογική Κλινική, ΠΑΓΝΗ, Ηράκλειο Κρήτη**: Φαναρίδης Μιχαήλ, Πρινιανάκης Γεώργιος, Μητρούσκα Ιωάννα
- **Καρδιολογική Κλινική Ιπποκράτειο ΓΝ Αθηνών**: Λεοντσίνης Ιωάννης, Πασχαλίδης Ελευθέριος, Αυγεροπούλου Αικατερίνη
- **Καρδιολογική Κλινική Δημοκρίτειου Πανεπιστημίου Θράκης**: Θωμαίδη Αντίνα, Κωνσταντινίδης Σταύρος
- **Β' Καρδιολογική Κλινική Πανεπιστημίου Ιωαννίνων**: Νάκα Αικατερίνη, Μιχάλης Λάμπρος