Estimated Mean Pulmonary Artery Pressure in Cases of Cryptogenic Fibrosing Alveolitis

Thesis submitted for partial fulfillment for the master degree in chest diseases

Presented by

Rana Mohamed Taha M.B.B.Ch.

Supervised by Prof. / Mohamed Ali Farrag

Professor of Chest Diseases Ain Shams University

Prof. / Mohsen Fahmy Metwali

Professor of Cardiology Ain Shams University

Dr. / Nehad Mohammed Osman

Lecturer of Chest Diseases Ain shams University

Department of Chest Diseases Faculty of Medicine Ain Shams University 2013

Acknowledgement

In the beginning, I would like to thank God above all for accomplishing this work.

I would like to express my profound gratitude to Prof. / Mohamed Ali Farrag, Professor of Chest Diseases, Faculty of Medicine - Ain Shams University, for his valuable advises and support all through the whole work and for dedicating much of his precious time, constant support, general help, great interest to accomplish this work.

My special thanks to Prof. / Mohsen Fahmy Metwali, Professor of Cardiology, Faculty of Medicine -Ain Shams University, for his help and kind cooperation throughout the work.

I am also grateful to Dr. /Nehad Mohammed Osman, Lecturer of Chest Diseases, Faculty of Medicine -Ain Shams University for her great support and kind guidance, considerable help and valuable advice throughout the work.

Finally I would like to thank all my Professors, teachers, colleagues and all members of the Chest Department, Ain Shams University for their encouragement.

Contents

	Page
Introduction	1
Aim of the work	3
Review of Literature	4
- Idiopathic pulmonary Fibrosis	4
- Pulmonary Hypertension	64
- Diagnostic Evaluation Of	96
Pulmonary Hypertension	
- Pulmonary Hypertension	104
Associated With Idiopathic	
Pulmonary Fibrosis	
Subjects and methods	118
Results	130
Discussion	151
Summary	159
Conclusions and Recommendations	161
References	163

List of Abbreviations

5HTT	5-Hydroxytryptamine Transporter
6MWD	Six Minute Walk Distance
6MWT	Six Minute Walk Test
^{99m} Tc- DTPA	Technetium-99m Labelled Diethylenetriamine Penta- Acetate
aaPo ₂	Alveolar–Arterial Pressure Difference for Oxygen
ACE	Angiotensin-Converting Enzyme
AIDS	Acquired Immune Deficiency Syndrome
AIP	Acute Interstitial Pneumonia
ANA	Anti-Nuclear Antibody
ANAs	Anti-Nuclear Antibodies
ANCA	Antineutrophil Cytoplasmic Antibody
Anti DNA	Anti-Deoxyribonucleic Acid
APAH	Associated Pulmonary Arterial Hypertension
ASD	Atrial Septal Defects
ATS	American Thoracic Society
BAL	Bronchoalveolar Lavage
BAS	Balloon Atrial Septostomy
BMPR2	Bone Morphogenetic Protein Receptor Type II

BNP	Brain Natriuretic Peptide
ВООР	Bronchiolitis Obliterans Organizing Pneumonia
ССВ	Calcium Channel Blocker
CFA	Cryptogenic Fibrosing Alveolitis
CI	Confidence Interval
CMV	Cytomegalovirus
CO	Carbon Monoxide
COPD	Chronic Obstructive Pulmonary Disease
СРК	Creatine Phosphokinase
cPLA2	Cytosolic Phospholipase A2
CPR	Cardiopulmonary Resuscitation
CRP	Clinical-Radiographic-Physiologic Scoring System
CT	Computed Tomography
CTDs	Connective Tissue Diseases
СТЕРН	Chronic Thromboembolic Pulmonary Hypertension
DAD	Diffuse Alveolar Damage
DIP	Desquamative Interstitial Pneumonia
DL _{CO}	Diffusing Capacity Of The Lung For Carbon Monoxide
DL _{CO} SB	Diffusing Lung Capacity For Carbon Monoxide Single Breath

EBV	Epistein Barr Virus
ECG	Electrocardiography
eNOS	Endothelial Nitric Oxide Synthase
ERA	Endothelin Receptor Antagonist
ERS	European Respiratory Society
ESC	European Society Of Cardiology
FDA	United States Food And Drug Administration
FEF ₂₅₋₇₅	Forced Expiratory Flow 25-75
FEV ₁	Forced Expiratory Volume In One Second
FEV ₁ /FVC	FEV ₁ -To-FVC Ratio (Tiffeneau-Pinelli Index)
FPF	Familial Idiopathic Pulmonary Fibrosis
FRC	Functional Residual Capacity
FVC	Forced Vital Capacity
HHV-8	Herpesvirus-8
HIV	Human Immunodeficiency Virus
HIV-1	Human Immunodeficiency Virus-1
HLA	Human Leukocyte Antigen
HRCT	High-Resolution Computed Tomography
HS	Highly Significant
IBW	Ideal Body Weight

ILD	Interstitial Lung Disease
ILO	International Labor Organization
INR	International Normalized Ratio
IPAH	Idiopathic Pulmonary Arterial Hypertension
IPF	Idiopathic Pulmonary Fibrosis
IV	Intravenous
kPa	Kilopascal
Kv	Voltage-Gated Potassium Channel
LAM	Lymphangioleiomyomatosis
LBW	Lean Body Weight
LDH	Lactate Dehydrogenase
LIP	Lymphocytic Interstitial Pneumonia
LV	Left Ventricle
LVEDP	Left Ventricular End Diastolic Pressure
mmHg	Millimeter Mercury
Mo(s)	Month (s)
MPAP	Mean Pulmonary Artery Pressure
mPAP	Mean Pulmonary Artery Pressure
MRI	Magnetic Resonance Imaging
N	Number

N.S.	Non Significant
NSIP	Nonspecific Interstitial Pneumonia
NT-proBNP	N-Terminal Pro-Brain Natriuretic Peptide
Num	Number
NYHA	New York Heart Association
\mathbf{O}_2	Oxygen
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
P(A-a)O2	Alveolar-Arterial Oxygen Gradient
PAH	Pulmonary Arterial Hypertension
Pa _{O2}	Partial Pressure of Oxygen in Arterial Blood
PASP	Pulmonary Artery Systolic Pressure
PCO ₂	Partial Pressure of Carbon Dioxide
PCWP	Pulmonary Capillary Wedge Pressure
Pde-5 I	Phosphodiesterase Type-5 Inhibitor
PFF	Pulmonary Fibrosis Foundation
PFTs	Pulmonary Function Tests
PH	Pulmonary Hypertension
PLCH	Pulmonary Langerhans Cell Histiocytosis
PMNs	Polymorphonuclear Leukocytes

Po ₂	Partial Pressure of Oxygen
Ppa	Pulmonary Artery Mean Pressure
Ppv	Pulmonary Vein Mean Pressure
PVR	Pulmonary Vascular Resistance
Q	Right-Sided Cardiac Output
RAP	Right Atrial Pressure
RBILD	Respiratory Bronchiolitis-Associated Interstitial Lung
	Disease
RF	Rheumatoid Factor
RV	Right Ventricle
RV	Residual Volume
RVSP	Right Ventricular Systolic Pressure
S.	Significant
S.C	Subcutaneously
Sa _{O2}	Arterial Oxygen Saturation
SD	Standard Deviation
Sig	Significance
SLE	Systemic Lupus Erythromatosis
sPAP	Systolic Pulmonary Artery Pressure
SSc	Systemic Sclerosis

TBBs	Transbronchial Lung Biopsies
TEE	Transesophageal Echocardiography
TLC	Total Lung Capacity
TRV	Maximum Tricuspid Regurgitant Jet Velocity
U-4-E-uh	4-Methylaminorex
UIP	Usual Interstitial Pneumonia
V/Q	Ventilation-Perfusion
VATS	Video-Assisted Thoracoscopic Lung Biopsy
VC	Vital Capacity
Vd	Dead Space Ventilation
VSD	Ventricular Septal Defect
Vt	Total Volume
WBC	White Blood Cell
WHO	World Health Organization
WHO-FC	World Health Organization Functional Class
Yr (s)	Year (s)

List of Tables

Table	Title	Page
No.		
	Descriptive criteria of patients included in the	130
1	study.	130
	· ·	120
2	Descriptive statistics of duration of co	130
	morbidities in the study population.	
_	Description of number of IPF patients included	131
3	in the study and the mean pulmonary artery	
	pressure.	
	Relation between the age of IPF patients in years	132
4	and their mean pulmonary artery pressure.	
	- v v -	100
5	Relation between the sex of the IPF patients and	133
	their mean pulmonary artery pressure.	
	Relation between patients' special habits who	134
6	were diagnosed with IPF and their mean	
	pulmonary artery pressure.	
	Correlation between patients' mean duration of	135
7	illness with IPF and their mean pulmonary	
	artery pressure.	
	Correlation between co morbid diseases	136
8	(Diabetes Mellitus) in patients diagnosed with	
	IPF and their mean pulmonary artery pressure.	
9	Correlation between co morbid diseases	137
	(Hypertension) in patients diagnosed with IPF	

	and their mean pulmonary artery pressure.	
10	Correlation between honey comb appearances in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	138
11	Correlation between fibrotic changes in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	139
12	Correlation between bronchiectatic changes in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	140
13	Correlation between sites of affection in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	141
14	Correlation between DL_{CO} SB in patients diagnosed with IPF and their mean pulmonary artery pressure.	143
15	Correlation between oxygen saturation percentages at rest in patients diagnosed with IPF and their mean pulmonary artery pressure.	144
16	Correlation between oxygen saturation percentages after 6 minute walking test in patients diagnosed with IPF and their mean pulmonary artery pressure.	145
17	Comparison between difference in oxygen saturation percentages at rest and after 6 minute walk test in patients diagnosed with IPF and	146

	their mean pulmonary artery pressure.	
18	Correlation between distances walked in meters in 6 minute walking test in patients diagnosed with IPF and their mean pulmonary artery pressure.	147
19	Correlation between FVC in patients diagnosed with IPF and their mean pulmonary artery pressure.	148
20	Correlation between FVC/FEV ₁ in patients diagnosed with IPF and their mean pulmonary artery pressure.	149
21	Correlation between presence and absence of small airway affection (FEF ₂₅₋₇₅) in patients diagnosed with IPF and their mean pulmonary artery pressure.	150

List of Figures

Figure No.	Title	Page
1	Evidence-based treatment algorithm for pulmonary arterial hypertension patients (for group 1 patients only).	94
2	Description of number of IPF patients included in the study.	131
3	Relation between the age of IPF patients in years and their mean pulmonary artery pressure.	132
4	Relation between the sex of IPF patients and their mean pulmonary artery pressure.	133
5	Relation between patients' special habits who were diagnosed with IPF and their mean pulmonary artery pressure.	134
6	Correlation between patients' mean duration of illness with IPF and their mean pulmonary artery pressure.	135
7	Correlation between co morbid diseases (Diabetes Mellitus) in patients diagnosed with IPF and their mean pulmonary artery pressure.	136
8	Correlation between co morbid diseases (Hypertension) in patients diagnosed with IPF and their mean pulmonary artery	137

	pressure.	
9	Correlation between honeycomb appearances in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	138
10	Correlation between fibrotic changes in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	139
11	Correlation between bronchiectatic changes in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	140
12	Correlation between sites of affection in HRCT scan in patients diagnosed with IPF and their mean pulmonary artery pressure.	141
13	Correlation between DL_{co} SB in patients diagnosed with IPF and their mean pulmonary artery pressure.	143
14	Correlation between oxygen saturation percentages at rest in patients diagnosed with IPF and their mean pulmonary artery pressure.	144
15	Correlation between oxygen saturation percentages after 6 minute walking test in patients diagnosed with IPF and their mean pulmonary artery pressure.	145