



# **Role of Beta-Blockers Following Percutaneous Balloon Pulmonary Valvuloplasty**

*Thesis*

*Submitted for Partial Fulfillment of Master  
Degree in Cardiology*

*By*

**Mohamed Ashraf Abdelsabour Abdelazeem**  
*M. B. B. Ch.*

*Supervised by*

**Prof. Dr. Ghada Samir El-Shahid**

*Professor of Cardiology  
Faculty of Medicine – Ain Shams University*

**Prof. Dr. Alaa Mahmoud Roushdy**

*Professor of Cardiology  
Faculty of Medicine – Ain Shams University*

**Dr. Tarek Khairy Moussa**

*Lecturer of Cardiology  
Faculty of Medicine – Ain Shams University*

*Faculty of Medicine  
Ain Shams University*

**2018**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

# Acknowledgment

*The vision for this thesis could only become a reality today because of the kind help and support of many; I would like to take the opportunity to extend my gratitude to them all.*

*First and foremost, all praise is to ALLAH Almighty for his daily blessings, beyond count or description, and beyond all attempts of thanks and gratitude.*

*For their relentless and continuous guidance, I am grateful to my supervisors. Their support and luminous feedback provided the backbone of this thesis.*

*I wish to express my deepest gratitude to **Prof. Dr. Ghada Samir El-Shahed**, Professor of Cardiology, Faculty of Medicine, Ain Shams University, for her invaluable mentorship and for her unrelenting leadership, evident at every step of this work. It has been an honor to complete this thesis under her direction.*

*I'm deeply indebted to **Dr. Alaa Mahmoud Roshdy**, Professor of Cardiology, Faculty of Medicine, Ain Shams University, for his priceless scientific assistance and the invaluable effort he provided during his supervision of this work.*

*I am delighted to have had **Dr. Tarek Khairy Mousa**, Lecturer of Cardiology, by my side during this endeavor, both as a mentor and as a friend.*

*My heartiest gratitude goes, of course, to my father and mother, always paving the path before me, never ceasing to believe in me. My past and my future are shaped by the warmth of your support.*

*To my wife, for her passionate encouragement and steadfast support.*

*My thanks also go to my brother and sister, my friends and my colleagues for their continuous support throughout my life.*

*Finally, I humbly extend my thanks to the patients who participated in this research, my department and to the great institution of Ain Shams University.*

# *List of Contents*

Title	Page No.
List of Tables .....	5
List of Figures .....	7
List of Abbreviations .....	10
Introduction .....	1
Aim of the Work.....	14
Review of Literature	
▪ Pulmonary Stenosis .....	15
▪ Balloon Pulmonary Valvuloplasty .....	32
▪ Infundibular Hypertrophy and Beta-Blockers .....	45
Patients and Methods .....	52
Results .....	66
Discussion .....	84
Limitations and Recommendations .....	92
Conclusion.....	93
Summary .....	94
References .....	96
Arabic Summary .....	—

## *List of Tables*

Table No.	Title	Page No.
<b>Table (1):</b>	Overview of the pharmacological and pharmacokinetic characteristics of the $\beta$ -blockers.....	46
<b>Table (2):</b>	Demographic and anthropometric data for the Placebo arm and the BB arm .....	66
<b>Table (3):</b>	Procedural data for the Placebo arm and the BB arm.....	68
<b>Table (4):</b>	Comparison between placebo arm and BB arm regarding functional capacity and echocardiographic data at 24 hours post-BPV.....	69
<b>Table (5):</b>	A Comparison between placebo arm and BB arm regarding functional capacity and echocardiographic data at 1 month post-BPV.....	71
<b>Table (6):</b>	A comparison regarding functional capacity and echocardiographic data obtained at 24 hours and at 1 month post-BPV for the placebo arm.....	73
<b>Table (7):</b>	A comparison regarding functional capacity and echocardiographic data obtained at 24 hours and at 1 month post-BPV for the BB arm. ....	75
<b>Table (8):</b>	A comparison between the two study arms regarding the percent change between FC and echocardiographic data obtained at 24 hours and at 1 month after BPV.....	77
<b>Table (9):</b>	Correlation of age and B/A ratio with percentage of change in FC and echocardiographic data in placebo Arm. ....	80
<b>Table (10):</b>	Correlation of participant sex with the percentage of change in FC and echocardiographic data in placebo Arm. ....	81

## *List of Tables Cont...*

Table No.	Title	Page No.
<b>Table (11):</b>	Correlation of age and B/A ratio with percentage of change in FC and echocardiographic data in BB Arm. ....	82
<b>Table (12):</b>	Correlation of participant sex with the percentage of change in FC and echocardiographic data in BB Arm. ....	83

## *List of Figures*

Fig. No.	Title	Page No.
<b>Figure (1):</b>	Drawing of pulmonary stenosis with atrial septal defect and left to right shunt well depicting the case of a 16-year-old girl reported by Morgagni.....	15
<b>Figure (2):</b>	(a) Dome-shaped pulmonary valve seen from the arterial aspect. (b) Dome-shaped valve with deep sinuses (s) opened to show the plication of the arterial wall at the sinutubular junction. (c) Dome-shaped valve with shallow sinuses (s).....	17
<b>Figure (3):</b>	(a) Dome-shaped valve with dysplastic leaflets (b) Histologic section shows fibrous dysplasia of the edge of the leaflets but a thinner component proximally (c) The sinutubular junction (arrowhead) is markedly accentuated in this section taken close to the raphé .....	18
<b>Figure (4):</b>	Fusion of the adjacent leaflets along their commissures in valvular pulmonary stenosis .....	19
<b>Figure (5):</b>	Right atrial abnormality is so obvious that the amplitude of the P wave in lead II is above than that of the following QRS complex.....	25
<b>Figure (6):</b>	ECG showing right axis deviation and right ventricular hypertrophy .....	26
<b>Figure (7):</b>	Chest radiograph reveals dilatation of the main pulmonary artery with relatively normal-sized right and left pulmonary arteries.....	27
<b>Figure (8):</b>	The thickened domed PV leaflets in the RV outflow view.....	28

## *List of Figures Cont...*

Fig. No.	Title	Page No.
<b>Figure (9):</b>	The echo shows post-stenotic dilation of the pulmonary trunk .....	29
<b>Figure (10):</b>	Continuous wave spectral Doppler across the pulmonary valve demonstrates a high velocity of flow, and calculated peak instantaneous and mean gradients across the valve .....	30
<b>Figure (11):</b>	Right ventricular outflow tract angiogram, demonstrating the domed and stenosed pulmonary valve, and allowing measurement of the ventriculo-arterial junction .....	34
<b>Figure (12):</b>	Right ventriculogram in antero-posterior .....	35
<b>Figure (13):</b>	Lateral projection showing an angioplasty balloon partially inflated across the pulmonary valve, with the characteristic hourglass impression imposed on the balloon by the stenosed pulmonary valve leaflets.....	36
<b>Figure (14):</b>	Mechanism of Beta-blockers action in myocytes.....	48
<b>Figure (15):</b>	Parasternal short axis view to measure pulmonary valve annulus and MPA. ....	55
<b>Figure (16):</b>	Suprasternal crab view to measure RPA.....	55
<b>Figure (17):</b>	Parasternal short axis view to assess severe PR. ....	56
<b>Figure (18):</b>	The RV dimensions measurement and tricuspid valve annulus measurement in the apical four chamber view. ....	57
<b>Figure (19):</b>	RV volume measurement at end-diastole.....	58
<b>Figure (20):</b>	RV volume measurement at end systole.....	59



## *List of Figures Cont...*

Fig. No.	Title	Page No.
<b>Figure (21):</b>	Upper panel shows tracing the end diastolic area of the RV in cm <sup>2</sup> and lower panel shows tracing the end systolic area of the RV to calculate the ECG gated FAC.....	60
<b>Figure (22):</b>	TAPSE measurement.....	61
<b>Figure (23):</b>	The peak pressure gradient (15 mmHg) across the PV recorded using CW Doppler.....	62
<b>Figure (24):</b>	A comparison regarding functional capacity and echocardiographic data obtained at 24 hours and at 1 month post-BPV for the placebo arm. ....	74
<b>Figure (25):</b>	A comparison regarding functional capacity and echocardiographic data obtained at 24 hours and at 1 month post-BPV for the BB arm. ....	76
<b>Figure (26):</b>	A comparison between the two study arms regarding the percent change in RVOT obtained at 24 hours and at 1 month after BPV. ....	78
<b>Figure (27):</b>	A comparison between the two study arms regarding the percent change in PG obtained at 24 hours and at 1 month after BPV. ....	78

## *List of Abbreviations*

Abb.	Full term
2D.....	Two-dimensional
AC .....	Adenylate cyclase
ATP .....	Adenosine triphosphate
AV .....	Atrio-ventricular
$\beta$ B.....	Beta-blockers
BPV.....	Balloon pulmonary valvuloplasty
BSA.....	Body surface area
Ca <sup>2+</sup> .....	Calcium
cAMP .....	Cyclic adenosine monophosphate
CRF .....	Case report form
ECG .....	Electrocardiogram
EDV .....	End diastolic volume
ESV .....	End systolic volume
FAC.....	Fractional area change
ICF.....	Informed consent form
ISA .....	Intrinsic sympathomimetic activity
L-VDCC .....	L-type or voltage-gated calcium channel
MPA .....	Main pulmonary artery
MSA .....	Membrane stabilizing activity
PA .....	Pulmonary artery
PDE.....	Phosphodiesterase
PKA.....	Protein kinase A
PLAX .....	Parasternal long axis
PS.....	Pulmonary stenosis
PR .....	Pulmonary regurgitation
PSAX.....	Parasternal short-axis
RVOT .....	Right ventricular outflow tract

RVOTO .....Right ventricular outflow tract obstruction

## *List of Abbreviations Cont...*

---

---

Abb.	Full term
RPA.....	Right pulmonary artery
RV .....	Right ventricle
RVH .....	Right ventricle hypertrophy
RVOT .....	Right ventricle outflow tract
RVOTO .....	Right ventricular outflow tract obstruction
RyR .....	Ryanodine receptor
SD .....	Standard deviations
TAPSE .....	Tricuspid annular plane systolic excursion
TR .....	Tricuspid regurgitation
VA .....	Ventriculo-arterial

## INTRODUCTION

**C**ongenital heart malformations are the most frequent of all major birth defects. Pulmonary stenosis (PS) accounts for approximately 8 - 12% of all congenital cardiac defects, with an incidence of about 1 per 2000 live births worldwide (*Mitchell and Mhlongo, 2018*).

Amongst congenital heart disease, PS is the second most common congenital cardiac malformation and is accompanied in approximately 20% of congenital heart disease cases (*Yang and Yi, 2005*). In Egypt, its prevalence is 2.3 per 10 000 school children (*Bassili et al., 2000*).

The traditional treatment for pulmonary valve stenosis prior to 1982 was surgical valvotomy. The relief of pulmonary valve stenosis by balloon dilatation during cardiac catheterization was first reported in 1982 (*Kan et al., 1982*). Since then, balloon pulmonary valvuloplasty has become the treatment of choice for relief of pulmonary valve stenosis (*Rao et al., 2007*).

It is theorized that dynamic right ventricular outflow tract obstruction plays a very crucial role in the immediate post operative period which can cause significant morbidity and mortality (*Subbarao et al., 1989*). A case study concerning a patient with worsening right ventricular outflow tract obstruction following BPV has emphasized the need for

preemptive hydration and beta-blocker therapy prior to balloon dilatation (*Khambatta et al., 2006*).

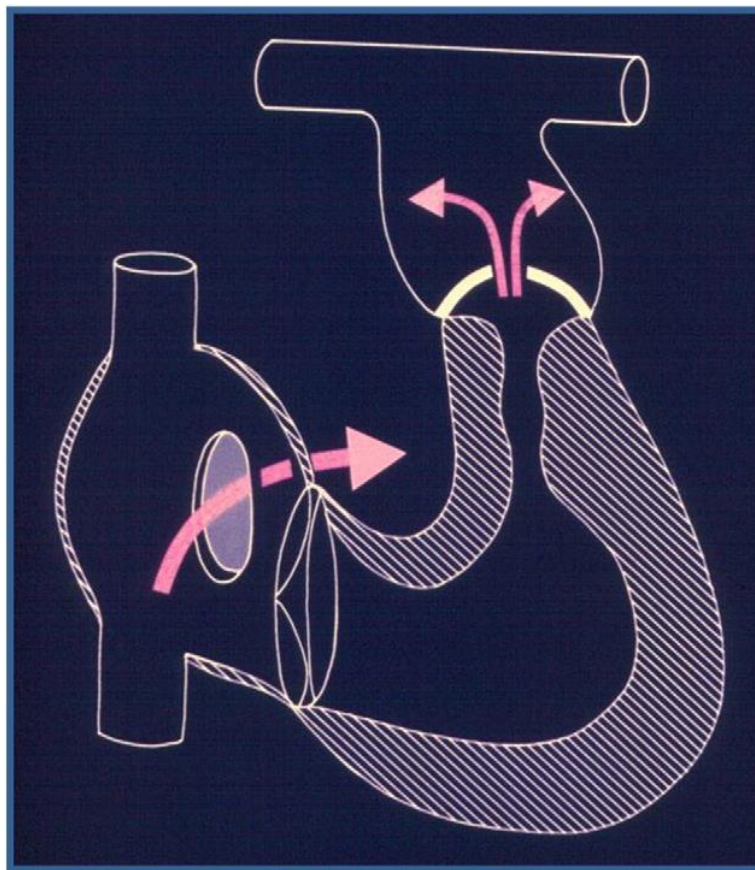
However, there is an absence of properly designed, randomized controlled trials to assess the role of routinely using beta blockers following BPV, hence the rationale of this study.

## **AIM OF THE STUDY**

**T**o assess the role of beta-blockers on functional capacity and cardiac hemodynamics following BPV in patients with congenital pulmonary stenosis.

**Chapter 1****PULMONARY STENOSIS**

**T**he first description of pulmonary stenosis as a separate pathological entity was in 1761 by Giovanni Battista Morgagni in Padova Italy, who is generally regarded as the father of modern anatomical pathology (*Zampieri et al., 2016*).



**Figure (1):** Drawing of pulmonary stenosis with atrial septal defect and left to right shunt well depicting the case of a 16-year-old girl reported by Morgagni. Note the right-to-left shunt at the level of patent foramen ovale (*Zampieri et al., 2016*).