

# **Clinical Short-Term Outcome of Severe Untreated Aortic Stenosis**

*Thesis*

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in Cardiology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ

فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا﴾

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# *List of Contents*

Title	Page No.
List of Tables .....	5
List of Figures.....	7
List of Abbreviations .....	10
Introduction .....	1
Aim of the Work .....	16
Review of Literature	
▪ Sclero-Calcific Aortic Valve.....	17
▪ Assessment and Risk Stratification .....	31
▪ Treatment Modalities .....	48
Patients and Methods.....	75
Results .....	80
Discussion.....	103
Study Limitations .....	109
Conclusion and Recommendations.....	110
Summary .....	112
References .....	115
Arabic summary	

## *List of Tables*

Table No.	Title	Page No.
<b>Table (1):</b>	Quantification of the severity of sclerocalcific aortic valve disease on a scale of 0 to 3 .....	35
<b>Table (2):</b>	Categories of aortic stenosis severity. ....	36
<b>Table (3):</b>	New aortic stenosis (AS) grading classification. ....	37
<b>Table (4):</b>	Recommended intervals for follow-up of adults with asymptomatic <sup>a</sup> aortic stenosis.....	50
<b>Table (5):</b>	ESC and ACC/AHA guidelines for management of aortic valve stenosis.....	51
<b>Table (6):</b>	Distribution of gender and age among studied patients. ....	80
<b>Table (7):</b>	The Distribution of smoking, DM, hypertension, dyslipidemia & CAD among studied patients. ....	81
<b>Table (8):</b>	Comparison between asymptomatic and symptomatic patients at baseline and follow up .....	82
<b>Table (9):</b>	Comparison between the total number of the patient both accidentally and symptomatically diagnosed based on symptom developed at baseline and follow up.....	83
<b>Table (10):</b>	The number of symptomatically diagnosed patients at baseline and follow up according to the symptom developed.....	85
<b>Table (11):</b>	Comparison between the number of accidentally diagnosed patients at baseline and follow.....	87
<b>Table (12):</b>	The number of accidentally discovered patients based on the symptom developed during follow up. ....	88

## *List of Tables cont...*

Table No.	Title	Page No.
<b>Table (13):</b>	The number of the patient hospitalized and not hospitalized throughout follow up period.....	89
<b>Table (14):</b>	Showing the relation between hospitalization and method of diagnosis.....	89
<b>Table (15):</b>	Relation between symptoms developed and hospitalization at follow up.....	90
<b>Table (16):</b>	Comparison between echocardiographic findings by M Mode at baseline and follow up.....	92
<b>Table (17):</b>	Comparison between echocardiographic findings by Doppler at baseline and follow up.....	94
<b>Table (18):</b>	Correlation between occurrence of syncope and echocardiographic data at follow up.....	96
<b>Table (19)</b>	Relation between occurrence of angina symptoms and echocardiographic data at follow up.....	97
<b>Table (20):</b>	Relation between occurrence of heart failure symptoms and echocardiographic data at follow u.....	98
<b>Table (21):</b>	Relation between occurrence of syncopal symptoms and demographic data at follow up.....	99
<b>Table (22):</b>	Relation between occurrence of angina symptoms and demographic data at follow up.....	100
<b>Table (23)</b>	Relation between occurrence of heart failure symptoms and demographic data at follow up.....	101

## *List of Figures*

Fig. No.	Title	Page No.
<b>Figure (1):</b>	Pathogenesis of valve calcification .....	20
<b>Figure (2):</b>	Gross specimen of sclerocalcific aortic valve disease .....	21
<b>Figure (3):</b>	Histological findings in early and late aortic valve calcification (AVC) lesions.....	23
<b>Figure (4):</b>	Important cellular pathways involved in development of aortic valve calcification, with potential targets for drug therapy outlined in red.....	28
<b>Figure (5):</b>	Echocardiographic images of sclerocalcific aortic valve.....	34
<b>Figure (6):</b>	(A) Normal aortic valve. (B) Mild aortic valve calcium (AVC); volumetric score 120. (C) Severe AVC; volumetric score 1020. (D) Magnified view of normal aortic valve. (E) Magnified view of mild AVC. (F) Magnified view of severe AVC. Arrows indicate AVC .....	40
<b>Figure (7):</b>	(A) Multislice computed tomography (CT): shows AVC in the short axis. (B) Reconstructed image to quantify the degree of calcification .....	41
<b>Figure (8):</b>	Management of severe aortic stenosis ESC/EACTS Guidelines 2012.....	48
<b>Figure (8):</b>	The EDWARDS SAPIEN system. ....	64
<b>Figure (9):</b>	The CoreValve ReValving System.....	64
<b>Figure (10):</b>	Gender distribution among studied population.....	80
<b>Figure (11):</b>	Distribution of risk factors among study population.....	81
<b>Figure (12):</b>	Comparison between asymptomatic and symptomatic patients at baseline and follow up.....	82

## *List of Figures cont...*

Fig. No.	Title	Page No.
<b>Figure (13):</b>	Comparison between the total number of the patient who developed syncope and angina symptoms at baseline and follow up.....	84
<b>Figure (14):</b>	Comparison between the total number of the patient who developed heart failure symptoms at baseline and follow up. ....	84
<b>Figure (15):</b>	The number of symptomatically diagnosed patients developed symptoms syncope and angina at baseline and follow up.....	86
<b>Figure (16):</b>	The number of symptomatically diagnosed patients developed symptoms of heart failure at baseline and follow up. ....	86
<b>Figure (17):</b>	Comparison between the number of accidentally diagnosed patients at baseline and follow.....	87
<b>Figure (18):</b>	The number of accidentally discovered patients who developed heart failure symptoms classified by NHYA during follow up.....	88
<b>Figure (19):</b>	Relation between method of diagnosis and hospitalization.....	89
<b>Figure (20):</b>	Relation between syncope and hospitalization at follow up .....	91
<b>Figure (21):</b>	Relation between heart failure symptoms and hospitalization at follow up .....	91
<b>Figure (22):</b>	Comparison between echocardiographic findings by EF, LVESD and LVEDD at baseline and follow up. ....	93



## *List of Figures cont...*

Fig. No.	Title	Page No.
<b>Figure (23):</b>	Comparison between echocardiographic findings by IVSD and PWDd at baseline and follow up.....	93
<b>Figure (24):</b>	Comparison between echocardiographic findings by PPG and MPG at baseline and follow up.....	95
<b>Figure (25):</b>	Comparison between echocardiographic findings by max. jet velocity and valve area at baseline and follow up. ....	95
<b>Figure (26):</b>	Relation between occurrence of angina symptoms and valve area at follow up.....	97
<b>Figure (27):</b>	Relation between occurrence of heart failure symptoms and max. jet velocity at follow up.....	98
<b>Figure (28):</b>	Relation between occurrence of syncopal symptoms and demographic data at follow up.....	99
<b>Figure (29):</b>	Relation between occurrence of heart failure symptoms and demographic data at follow up.....	102

## *List of Abbreviations*

<b>Abb.</b>	<b>Full term</b>
<i>ACC.....</i>	<i>American College of Cardiology</i>
<i>ACE.....</i>	<i>Angiotensin converting enzyme</i>
<i>AF .....</i>	<i>Atrial fibrillation</i>
<i>AHA .....</i>	<i>American Heart Association</i>
<i>ARBs.....</i>	<i>Angiotensin receptor blockers</i>
<i>AS .....</i>	<i>Aortic stenosis</i>
<i>AVR.....</i>	<i>Aortic valve replacement</i>
<i>BAV.....</i>	<i>Balloon aortic valvuloplasty</i>
<i>BP .....</i>	<i>Blood pressure</i>
<i>Ca<sup>2+</sup>.....</i>	<i>Calcium</i>
<i>CABG.....</i>	<i>Coronary artery bypass grafting</i>
<i>CAD .....</i>	<i>Coronary artery disease</i>
<i>CKD .....</i>	<i>Chronic kidney disease</i>
<i>CT .....</i>	<i>Computed tomography</i>
<i>CV.....</i>	<i>Cardiovascular</i>
<i>EF .....</i>	<i>Ejection fraction</i>
<i>ESC.....</i>	<i>European Society of Cardiology</i>
<i>ESRD.....</i>	<i>End-stage renal disease</i>
<i>HG.....</i>	<i>High gradient</i>
<i>HG.....</i>	<i>High gradient</i>
<i>IVSDd.....</i>	<i>Interventricular septum diastolic diameter</i>
<i>LDL-C .....</i>	<i>Low density lipoproteins -Cholesterol</i>
<i>LF.....</i>	<i>Low flow</i>
<i>LG .....</i>	<i>Low gradient</i>
<i>LTC.....</i>	<i>Long-term care</i>
<i>LV .....</i>	<i>Left ventricular</i>
<i>LVEDD .....</i>	<i>Left ventricular end diastolic diameter</i>
<i>LVESD.....</i>	<i>Left ventricular end systolic diameter</i>
<i>MI.....</i>	<i>Myocardial infarction</i>
<i>MMPs.....</i>	<i>Matrix-metalloproteinases</i>

*List of Abbreviations cont...*

Abb.	Full term
<i>MPG</i> .....	<i>Mean pressure gradient</i>
<i>NF</i> .....	<i>Normal flow</i>
<i>NP</i> .....	<i>Natriuretic peptide</i>
<i>PCI</i> .....	<i>Percutaneous coronary intervention</i>
<i>PPG</i> .....	<i>Peak pressure gradient</i>
<i>PWd</i> .....	<i>Posterior wall diameter</i>
<i>SAVR</i> .....	<i>Surgical aortic valve replacement</i>
<i>SCD</i> .....	<i>Sudden cardiac death</i>
<i>SD</i> .....	<i>Standard deviation</i>
<i>SEAS</i> .....	<i>Simvastatin and Ezetimibe in Aortic Stenosis</i>
<i>SPSS</i> .....	<i>Statistical Program for Social Science</i>
<i>STS-PROM</i> .....	<i>Society of Thoracic Surgeons Predicted Risk of Mortality</i>
<i>TAVI</i> .....	<i>Transcatheter aortic valve implantation</i>
<i>TIMPs</i> .....	<i>Tissue inhibitors of matrix metalloproteinases</i>
<i>TNF-<math>\alpha</math></i> .....	<i>Tumor necrosis factor alpha</i>
<i>V. Max</i> .....	<i>Maximum jet velocity</i>

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### Abstract

**Background:** Sclerocalcific aortic valve is a common condition. Risk stratification and decision making are particularly complex in adults with AS, because the disease mainly affects elderly patients who represent a heterogeneous population and require balanced and individualized analysis using a multidisciplinary collaboration. Further research is needed to provide better evidence in particular on spontaneous risk, earlier detection of LV dysfunction, and the results of transcatheter treatment and medical therapy.

**Objectives:** We studied the clinical short term outcome of the severe untreated severe sclerocalcific aortic valve stenosis and also we evaluated the correlation between echocardiography assessment of aortic stenosis and clinical history and examination.

**Methods:** In our study of 50 patients with severe sclerocalcific aortic stenosis, were subjected to full history taking along with full clinical examination and transthoracic echocardiography (2D, M mode & Doppler) at baseline and follow up. The TTE criteria for diagnosis of severe Sclero-calcific aortic stenosis are increased echogenicity and thickening of the aortic valve leaflets with mean gradient greater than 40 mm Hg, and maximum jet velocity greater than 4 m per second, valve area less than 1.0 cm<sup>2</sup>.

**Results:** At short term follow up of our patients (2 years), there were significant increase in the number of patients who developed symptoms of angina and heart failure ( $p < 0.01$ ) but there was no statistically significant increase in those who develop syncope ( $P = 0.106$ ). There were very evident echocardiographic findings in the form of highly significant ( $p < 0.01$ ) decrease in the EF & valve area and increase in the MPG, PPG, Max. Jet velocity.

**Conclusion:** 41.2% of previously asymptomatic patient developed symptoms at follow up. There were very evident and significant changes in the echocardiographic findings related to significant decrease in the EF & valve area and increase in the MPG, PPG, Max. jet velocity and intracardiac dimensions that is reflected in the clinical symptoms progression throughout the follow up period.

**Keywords:** Sclerocalcific - Severe aortic stenosis - Aortic valve replacement - Ejection fraction – aortic valve area- Max. Jet velocity-mean pressure gradient.

## INTRODUCTION

**A**ortic stenosis (AS) is the most common valvular disease in older adults. Aortic stenosis can be congenital or degenerative, with the latter resulting from calcification of the aortic valve over time. Although congenitally bicuspid valve with calcification is the most common form of AS overall, degenerative calcific AS of the trileaflet valve is the most common form observed in persons aged 60 years and older. Degenerative calcific (sclerocalcific) AS is the most common form of AS among older adults in the United States (*Hughes et al., 2005*).

Calcific AS is a chronic progressive disease. During a long latent period, patients remain asymptomatic. However, it should be emphasized that duration of the asymptomatic phase varies widely among individuals (*Bernacki and Alexander, 2013; Lancellotti et al., 2012*).

As the population continues to age, AS will be encountered more frequently in the long-term care setting. Patients may or may not have symptoms, but once symptoms manifest, AS has poor outcomes when left untreated (*Bernacki and Alexander, 2013; Lancellotti et al., 2012; Kang et al., 2010*).

AS usually has an asymptomatic latent period of 10-20 years. During this time, the LV outflow obstruction and the

pressure load on the myocardium gradually increase. Symptoms develop gradually. Exertional dyspnea is the most common initial complaint, even in patients with normal LV systolic function, and it often relates to abnormal LV diastolic function. In addition, patients may develop chest pain on exertion, effort dizziness or lightheadedness, easy fatigability, and progressive inability to exercise. Ultimately, the patient develops the classic triad of chest pain, heart failure, and syncope (*Hughes et al., 2005; Minners et al., 2010*).

Sudden cardiac death is a frequent cause of death in symptomatic patients but appears to be rare in the asymptomatic (1% per year) (*Lancellotti et al., 2012; Minners et al., 2010*).

As the severity of aortic stenosis worsen, the force the LV must generate to overcome the obstruction increases progressively. Although inotropic reserve and development of LV hypertrophy serve initially to compensate for this increase in demand, these double edged swords leads also to pathologic consequence, onset of symptoms, morbidity and mortality within 3years of the onset of the angina, syncope, or the symptoms of the heart failure, meanwhile the mortality reaches 75% of symptomatic patients unless the outflow obstruction is relieved by aortic valve replacement (AVR). Thus before aortic valve replacement there is a striking mortality risk of 2% a month in symptomatic patients (*Hachicha et al., 2007*).

Severe symptomatic calcific aortic valve stenosis (AS) is a proven indication for valve replacement according to the current guidelines. The therapeutic modality of choice is surgical aortic valve replacement (SAVR) (*Hachicha et al., 2007; Lancellotti et al., 2010*).

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative treatment for patients with severe AS considered at high surgical risk with promising early and mid-term results. In contrast to surgical replacement, this method forms a much less invasive approach, which therefore may be safely offered for high-risk surgical patients (*Lancellotti et al., 2010; Bergler-klein, 2009; Roberts et al., 2009*).