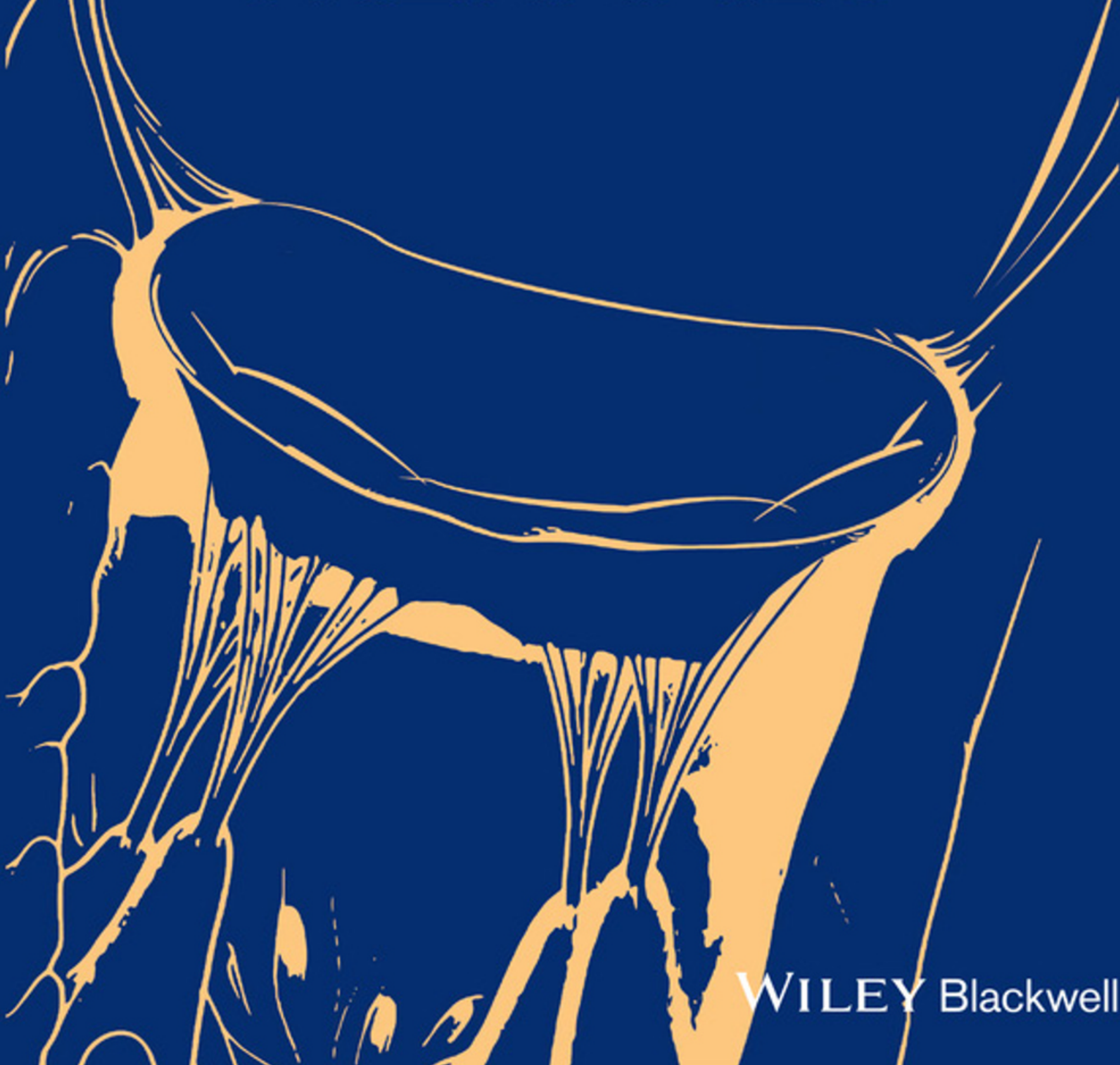
EDITED BY

RON WAKSMAN | TOBY ROGERS

TRANSCATHETER MITRAL VALVE THERAPIES



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Transcatheter Mitral Valve Therapies

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Introduction—The Mitral Book

Good God! How should the mitral valves prevent the regurgitation of air and not of blood?
—William Harvey (April 1578–June 1657).

The *mitral valve*, also known as the *bicuspid* or *atrioventricular valve*, plays a major role in controlling the transfer of blood from the left atrium to the left ventricle. There are two main types of mitral valve disease that can lead to mitral regurgitation: degenerative, in which the leaflets or the sub-valvular apparatus are deformed, and functional, in which cardiomyopathic dilatation of the ventricle or atrium results in malcoaptation of otherwise structurally normal leaflets. In reality, mitral regurgitation is often caused by a combination of both degenerative and functional processes. Therefore, it is essential to identify and understand the pathology and physiology of the valve to tailor the optimal therapeutic approach.

While there were sporadic attempts to surgically replace the faulty mitral valve at the beginning of the twentieth century, the breakthrough came after 1948 with open heart surgery and development of mechanical and bioprosthetic replacement valve devices. Since then, the quest for less-invasive valve repair has continued with the introduction of ring annuloplasty and chordal and leaflet repair. The desire to adapt open heart surgery to minimally invasive procedures and techniques did not stop with surgery. The success of converting from open heart surgery to catheter-based therapies for coronary artery disease and aortic valve replacement enthused inventors, physicians, and industry to develop catheter-based approaches to repair the mitral valve in a beating heart.

Thus, in the late 1990s, engineers and physicians teamed up to give birth to the first device to treat mitral regurgitation, known today as the MitraClip. The principle of the "edge-to-edge" repair technique was developed by an Italian surgeon Ottavio Alfieri and adopted by Mehmet Öz, who was visiting him at that time and proposed a device to deliver the surgical edge-to-edge repair via a catheter-based device. Over the past two decades, there has been a proliferation of new transcatheter solutions and approaches for the treatment of mitral valve disease, with a variety of edge-to-edge, spacer, annuloplasty, and chordal solutions all currently being tested in clinical trials. Most recently, the results of the COAPT study demonstrated the potential of mitral repair to grow the field and help to extend patients' lives with improved quality. As the field moves forward, it is increasingly apparent that there is no "one-size-fits-all" solution for mitral valve disease because there are many etiologies to the disease state, and a combination of different solutions is likely to be required for repair and replacement.

This book is an attempt to present the most recent technology and clinical trial updates in the transcatheter mitral valve repair and replacement space. We realize that this is a very dynamic field with growing interest and rapidly advancing innovative solutions, and so this edition will be followed by regular updates. Nevertheless, we assembled the content within the last 12 months and bring you the most up-to-date book in the field. In this book, you will find details on transcatheter repair and replacement devices for the treatment of mitral regurgitation. This field could not move forward without the collaborative Heart Team approach, including multimodality imaging and heart failure specialists, innovators, and industry. We would like to thank the contributors—including industry—who agreed to share with the readers their latest advances in the field. We would also like to acknowledge Wiley, the publisher, and Jason Wermers, the managing editor, for expediting the release of the book. We hope that you will find it useful and that it will get you enthused to be part of the mission to find simple and effective solutions for the treatment of mitral valve disease.

Ron Waksman
Toby Rogers

1

The Pathology of Mitral Valve Disease

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1.1 Introduction

Mitral valve (MV) insufficiency is a major causation of heart failure and cardiac death, with complications of arrhythmia, endocarditis, and sudden cardiac death [1, 2]. The most common clinical finding in degenerative valve disease is elongation and or rupture of the chordal apparatus resulting in leaflet prolapse, and varying degrees of mitral valve regurgitation due to abnormal leaflet coaptation during ventricular contraction [3]. Up to one third of all patients requiring mitral valve repair/replacement are at high operative risk for surgery [4]. Surgical mitral valve treatment is still the gold standard for treating severe mitral valve insufficiency; however, controversy exists as to whether early surgical intervention in asymptomatic patients before the onset of ventricular changes improves the outcome of patients with severe degenerative mitral valve disease [2, 5–7]. For patients with high surgical risk, transcatheter mitral valve device has become a therapeutic option [8]. This chapter highlights the mitral valve anatomy, pathophysiology of normal mitral valve, mitral stenosis (MS), and mitral regurgitation (MR).

1.2 General Anatomy of the Mitral Valve

The mitral valve is a two-leaflet valve with a saddle-shaped annulus and its valvular plane facing anteriorly, inferiorly, and to the left [9–12]. The mitral valve apparatus, both functionally and morphologically, consists of a constellation of individual structures, which consist of the annulus, anterior and posterior leaflets, chordae tendineae, papillary muscles (PMs), and also include the left ventricular wall and the left atrium which are essential for the valve to function normally. The valve is obliquely located in the heart and has a close relation to the aortic valve [13].

1.2.1 Mitral Annulus

The mitral annulus, the hinge line of the valvular leaflets, is “D”-shaped, unlike the aortic annulus which is circular (Figure 1.1a). The geometric “saddle shape” of the mitral annulus has the highest point of the saddle located in the middle of the anterior leaflet. During ventricular systolic phase, the mitral annulus folds at the intercommissural axis. This folding helps coaptation of the leaflet and prevents

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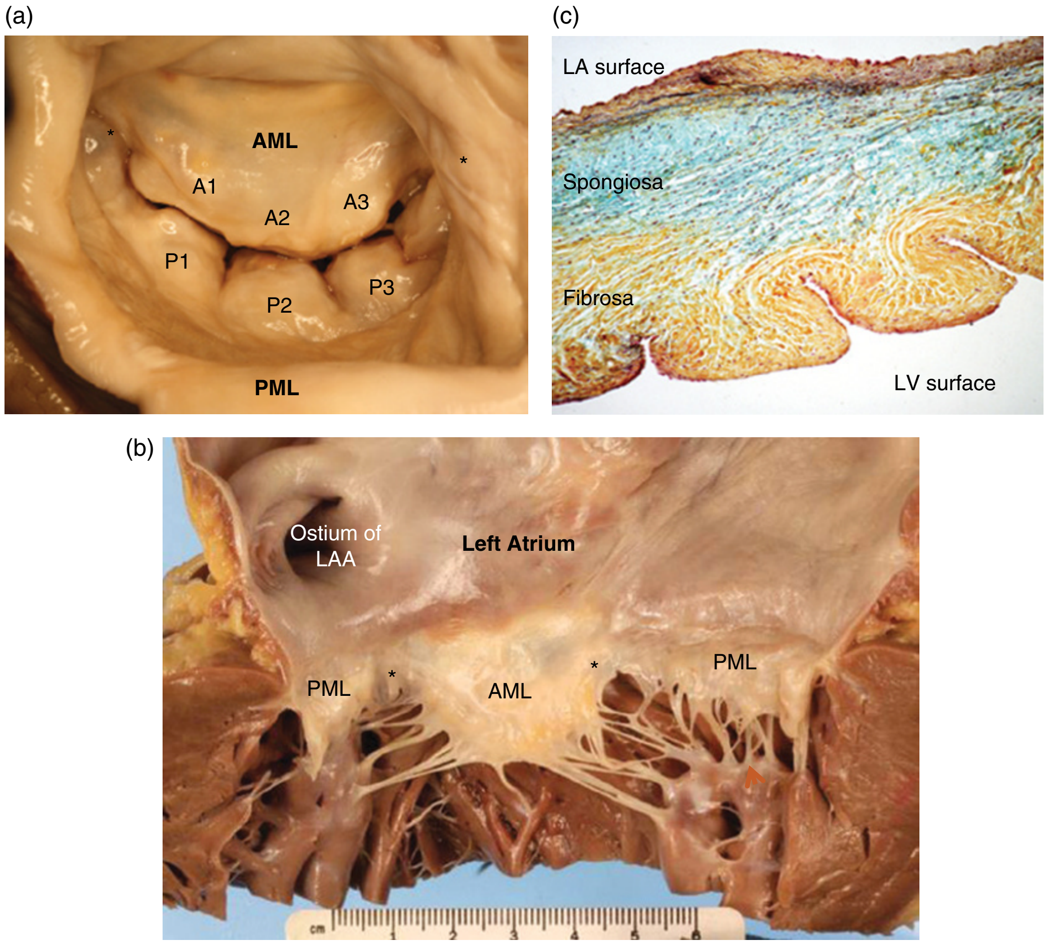

Figure 1.1 Normal mitral valve. (a) Gross atrial view of the mitral valve showing anterior and posterior leaflets. (b) The anterior leaflet is larger, and the chordae arise from the ventricular surface at 45° angle. The anterior leaflet is separated from the posterior leaflet by the commissures (*) with fan-shaped branching commissural chordae. The posterior leaflet has three, often poorly defined, scallops, each with chordal attachments. (c) A histological section of a mitral valve leaflet (Movat pentachrome stain) demonstrates the atrial surface which is rich in elastic fibers and collagen, glycosaminoglycans-rich spongiosa in the mid portion (green), and dense collagenous tissue (yellow) which is observed on the ventricular surface of the leaflet. Abbreviations: AML, anterior mitral leaflet; PML, posterior mitral leaflet. *Source:* Reproduced with permission from Torii et al. [14].

leaflet distortion along the lines of annular attachment, and reduces the pressure exerted on the mitral valve leaflets [15]. The normal annular circumference is <10 cm and the normal mitral valve orifice area is 4–6 cm^2. The anterior annulus spans the left and right fibrous trigones and is anatomically coupled to the aortic annulus (Figure 1.2). The right fibrous trigone is thicker with more fibrous tissue than left fibrous trigone; however, there is significant variability from heart to heart [16]. Both the trigones are extension of the fibrous tissue at the two ends of the aorto-mitral continuity. The central fibrous body is formed by the membranous septum together with the right trigone. The atrioventricular conduction bundle passes through the right fibrous trigone. There is a close relationship of

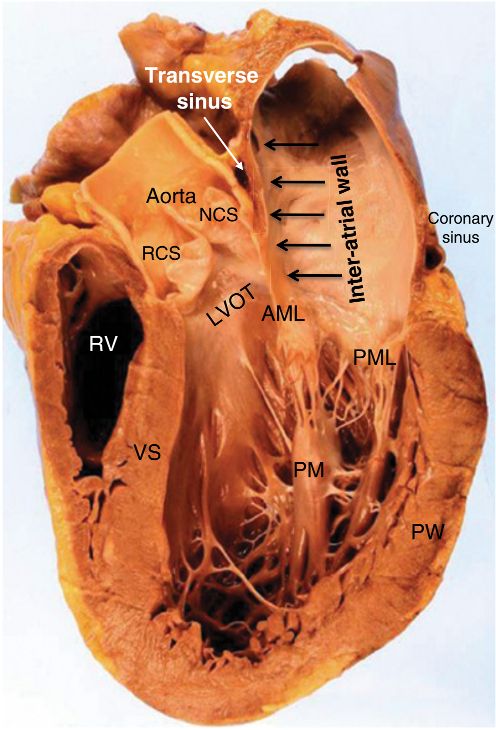

Figure 1.2 Long axis view of the heart demonstrating the fibrous continuity of the anterior leaflet with the non-coronary sinus. The atrioventricular junction is shown in the longitudinal view; the interatrial septal wall (arrows) is separated by the transverse sinus from the aorta. Note the fibrous continuity of the anterior leaflet with the non-coronary sinus. Abbreviations: AML, anterior mitral leaflet; NCS, non-coronary sinus; PML, posterior mitral leaflet; PM, papillary muscle; RCS, right coronary sinus; RV, right ventricle; VS; ventricular septum; PW, posterior wall; LVOT, left ventricular outflow tract. *Source:* Reproduced with permission from Torii et al. [14].

the coronary sinus to the posterior mitral annulus and the left circumflex artery lies adjacent to the left trigone and passes inferior to continuation of the coronary sinus (Figure 1.3). The annulus opposite the area of valvular fibrous continuity tends to be weaker in terms of lacking a well-formed fibrous cord. This is the area affected in annular dilatation and also most often involved in calcification of the annulus [13].

1.2.2 Leaflets

The normal mitral valve is comprised of an anterior leaflet connected by the commissures to a posterior leaflet. Owing to the oblique location of the valve, its two leaflets do not occupy anterior/posterior positions. The corresponding terms for anterior and posterior are "aortic" and "mural," respectively [13]. The latter usually consists of three scallops (92%) described as anterior, middle, and posterior, assigned as P1, P2, and P3, and is not equally in size, with a small percent (8%) of hearts having two or even five scallops [17]. Ranganathan and colleagues [17] found the middle scallops to be larger in the majority of hearts; in a floppy valve when the mural leaflet is deformed, the middle scallop is likely to prolapse [13]. The anterior leaflet (1.5–2.5 cm [mean 2.0 cm]) is semicircular occupying 1/3 of the circumference, whereas the posterior leaflet (0.8–1.4 cm [mean 1.1 cm]) is long and narrow forming 2/3 of the circumference. The mean anterior leaflet width is 3.3 ± 0.5 cm, and the mean posterior leaflet width is 4.9 ± 0.9 cm. When the mitral valve is closed, 2/3 of the floor of the atrium is formed by the anterior leaflet, while the other 1/3 is formed by the posterior leaflet (Figure 1.1a) [14]. The anterior mitral leaflet is in direct continuity (without an intervening myocardium, in contrast to the tricuspid valve) with the non-coronary and the left coronary cusps of the aortic valve (Figure 1.4). The closure line of the mitral valve is just above the free edge of the leaflets and is thicker than the free margins of the leaflets (Figure 1.1b) [14].

The mitral valve leaflets are thin, pliable, delicate, and translucent structures with an atrial and a ventricular surface. Grossly, two zones can be distinguished on the anterior leaflet, whereas three zones can be distinguished on the posterior leaflet according to the insertion of the chordae tendineae. There are three orders of chordae tendineae: (i) inserted on the free edge, (ii) inserted on the ventricular surface of the leaflet beyond the

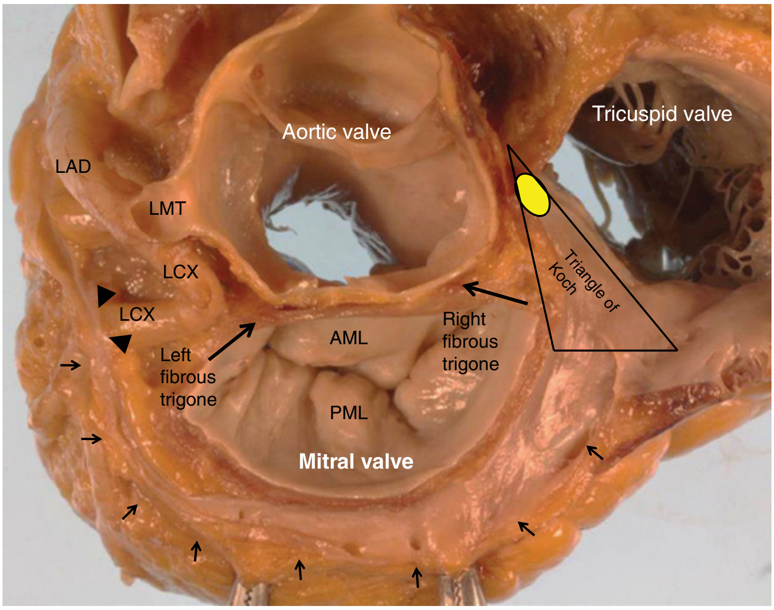

Figure 1.3 Adjoining structure around the mitral valve. Superior view of the base of the heart shows the spatial relations of the three cardiac valves (aortic, mitral, and tricuspid). The left heart valves are close together and the right heart valves are separated by interatrial septum and the base of the ventricular septum. Atrioventricular node is located within the triangle of Koch near its apex and lies close to the junction of the septal and anterior tricuspid leaflets. Note that the coronary sinus hugs the posterior mitral annulus with an intervening posterior left atrial wall. The left circumflex artery lies adjacent to the left trigone and passes inferior to the continuation of the coronary sinus (arrowheads). The aortic valve is separated from the anterior mitral leaflet by fibrous tissue, and on the right and left are located the fibrous trigones (the non-coronary and the left coronary cusps have been removed). Abbreviations: AML, anterior mitral leaflet; PML, posterior mitral leaflet; LMT, left main trunk; LAD, left anterior descending artery; LCX, left circumflex artery. *Source:* Reproduced with permission from Torii et al. [14].

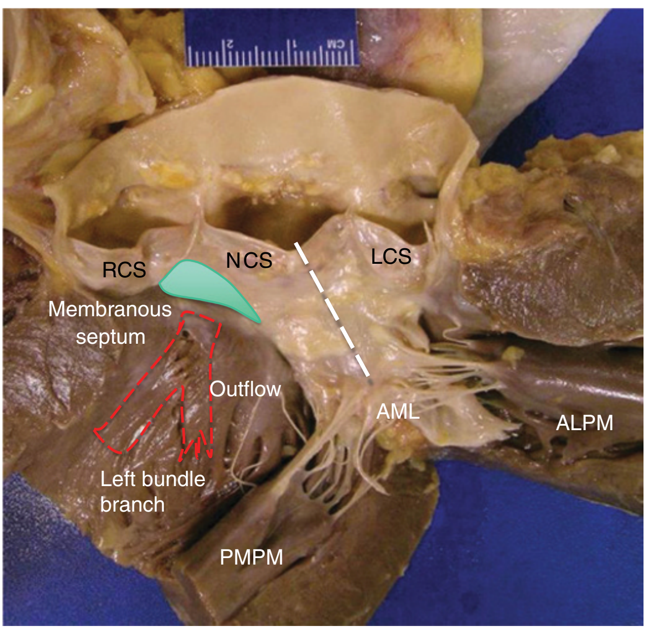

Figure 1.4 Fibrous continuity of the anterior mitral leaflet with the aortic valve. Note the fibrous continuity between the anterior mitral valves and the non-coronary and the left coronary sinuses (white dotted line) of the aorta. The membranous septum is located inferiorly and proximal between the non-coronary and the right coronary sinus. The location of the left bundle branch has been outlined in red dotted lines. Also, the chordae tendineae arising from the two papillary muscle heads inserting into the anterior mitral leaflet at 45° angle. Abbreviations: AML, anterior mitral leaflet; ALPM, anterolateral papillary muscle; PMPM, posteromedial papillary muscle; RCS, right coronary cusp; LCS, left coronary cusp; NCS, non-coronary cusp. *Source:* Reproduced with permission from Torii et al. [14].