Experimental model and anatomic principles of transapical mitral repair

Ph.D. Thesis

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1. Abbreviations

AML: anterior mitral leaflet

PML: posterior mitral leaflet

A1: A1 scallop of the anterior mitral leaflet

A2: A2 scallop of the anterior mitral leaflet

A3: A3 scallop of the anterior mitral leaflet

P1: P1 scallop of the posterior mitral leaflet

P2: P2 scallop of the posterior mitral leaflet

P3: P3 scallop of the posterior mitral leaflet

ALC: anterolateral commissure of the mitral valve

PMC: posteromedial commissure of the mitral valve

Ao1: right coronary cusp of the aortic valve

Ao2: noncoronary cusp of the aortic valve

Ao3: left coronary cusp of the aortic valve

Ant: anterior papillary muscle

Post: posterior papillary muscle

Ch: tendinous chords

2. Introduction

2.1. Anatomy of the mitral valvular complex

Numerous books and publications describe the classical anatomy of the mitral valve. But the mitral valvular complex is more than the strict mitral valve. On the basis of its functional parameters, structures of the left atrium as well left ventricle should also be added to the complex. The papillary muscles and tendinous chords are termed as the subvalvular apparatus of the mitral valve. *(Table 1)*

Table 1: Anatomy of the mitral valvular complex

<table>
<tr><td colspan="2">Valvular leaflets
(including the commissures)</td><td rowspan="4">Mitral
valve</td><td rowspan="8">Mitral
valvular
complex</td></tr>
<tr><td colspan="2">„Annulus”</td></tr>
<tr><td>Tendinous chords</td><td rowspan="2">Subvalvular
apparatus</td></tr>
<tr><td>Papillary muscles</td></tr>
<tr><td colspan="3">Left atrial myocardium</td></tr>
<tr><td colspan="3">Left ventricular myocardium</td></tr>
<tr><td colspan="3">Left atrial and ventricular endocardium</td></tr>
<tr><td colspan="3">Aorto-mitral curtain</td></tr>
</table>

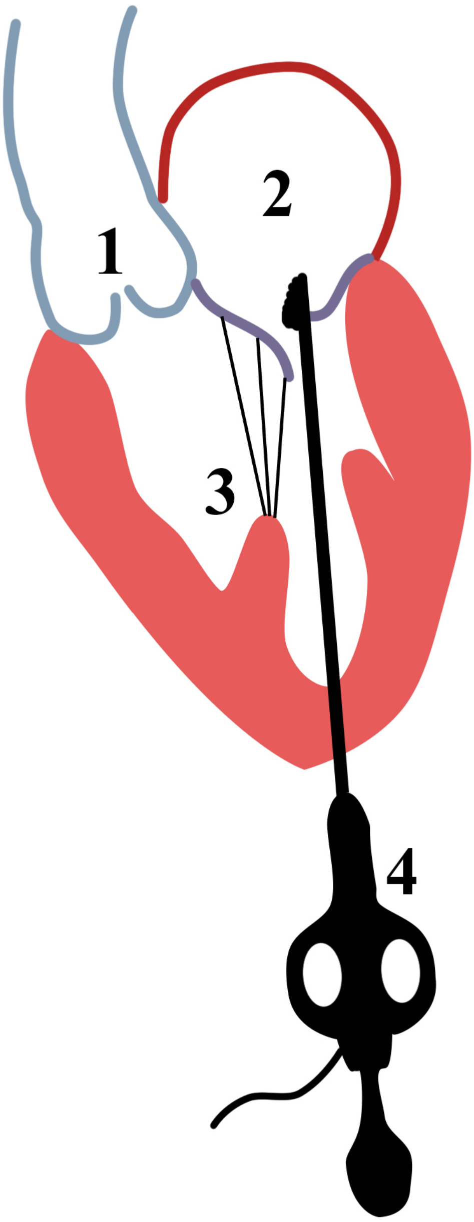
2.2. Mitral valve diseases

2.2.1. The „Functional Classification” of mitral valvular dysfunction

Due to better understanding of the pathophysiology of mitral valve dysfunction a more detailed so-called „Functional Classification” has been described by Carpentier. This classification is based on the leaflet motion and differentiate four functional types of mitral valve dysfunction.

2.3. The modern treatment strategy of mitral regurgitation

In the modern treatment of mitral regurgitation, valve repair techniques are preferred over valve replacement. The operative preservation of the valve is in the interest of the patients. In the last decades, development of surgical reconstructive techniques was supported by many innovative improvements which improved the results of mitral valve surgery. Besides classical median sternotomy, novel, minimally invasive techniques and approaches with endoscopic visualization emerged. The application of extracorporeal circulation and cardioplegy are furthermore indispensable by opening of the left atrium. However, in the case of mitral valve dysfunctions with various etiology the risks and morbidity of the intervention are different. Treatment of the high-risk patients, mostly with functional mitral regurgitation, with modern invasive cardiologic methods, show promising mid-term results. This methods prefer the performance of an edge-to-edge repair or an annuloplasty.



2.3.1. Echocardiography-guided transapical neochord implantation on beating heart

In the last years devices made possible to perform clinical transapical mitral valve repair procedures using polytetrafluoroethylen artificial chords on beating heart. Using the NeoChord© DS1000 device (NeoChord Inc, Minneapolis, Minnesota) real sutures are inserted on the free margin of the mitral leaflets. *(Figure 1)* Then the surgeon applies tension through manual pushing of the apical retracted suture while assessing the reduction of mitral regurgitation real time by color Doppler echocardiogram.

Figure 1: Surgical technique of NeoChord implantation: the instrument is introduced into the left ventricle using an apical approach.
1. aortic sinus, 2. left atrium, 3. left ventricle, 4. NeoChord device grasping the posterior mitral leaflet.

2.4. Experimental models for transapical mitral valve repair

2.4.1. Animal and human studies about fuctional anatomy of the mitral valve

The increasing number of minimally invasive mitral valve repair methods motivate the investigation of the endoscopic mitral valve visualisation. Multiple approaches have been used to describe the anatomy of this region. The left atrial method, which is the most commonly used in clinical practice, has generated extensive literature. The limitations of this approach have initiated research to provide a better visualisation of the subvalvular apparatus. Experimental in situ animal procedures have been described for transapical intracardiac imaging and mitral repair. In vitro animal and human studies have examined the functional anatomic parameters of the heart valves in the beating heart with endoscopic optics through the great vessels. To provide a more precise and detailed endoscopic anatomic description of the mitral valvular complex, we aimed to investigate the structures from multiple directions in human hearts in the first part of our cadaveric study.

2.4.2. Experimental animal mitral repair procedures

Various experimental in vivo animal studies have described transapical intracardiac imaging and simple operative repair procedures (clip-fixations, resection of the posterior leaflet) on the mitral valve. This beating heart methods or on-pump approaches using cardiopulmonary bypass were based on direct endoscopic visualization of the ventricular structures. The tansapical approach under beating heart conditions was also useful by self-expanding valved stent implantations under transesophageal echocardiographic and fluoroscopic guidance in the native mitral valve position. The aim of the second part of our study was to develop an experimental human cadaveric model for safe minimally invasive transapical endoscopic complex mitral repair procedures.

3. Aims

We aimed to provide a detailed endoscopic anatomic description of the human mitral valvular complex, which subsequently helped to develop an experimental human cadaveric model for novel transapical endoscopic complex mitral repair procedures.

1. We intended to investigate the endoscopic anatomy of the mitral valve from multiple directions in cadaveric hearts.

2. We needed to define standard anatomic landmarks of the views using endoscopic optics.

3. We aimed to outline exact step by step descriptions of different views from multiple directions and compare their advantages in mitral valve repair procedures.

4. We targeted the development of an apical port for safe surgical instrumental manipulations.

5. We needed suitable exposure of the collapsed left ventricle.

6. We aimed the development of a novel experimental model for complex mitral repair procedures.

4. Material and Methods

The endoscopic anatomic views of the mitral valvular complex were examined in 40 human cadaveric fresh hearts. In the second experimental surgical part of our study 20 human cadavers were investigated.

All hearts were obtained and dissected early after death at the Department of Anatomy Histology and Embryology (Semmelweis University, Budapest, Hungary).

4.1. Endoscopic anatomic investigation of the mitral valvular complex

We have used three approaches for the endoscopic examination: the aortic approach through the aortic valve, the atrial approach through the left atrium and the apical approach through the apex of the heart. Three different endoscopes were introduced into the left heart: 0, 30 and 70 degrees 4 mm rigid optics (Aesculap© PE 484A). The following exposures of the heart were performed for in situ investigation: partial upper sternotomy (aortic approach), right anterolateral mini-thoracotomy (atrial approach) and left anterolateral mini-thoracotomy (apical approach). In the other cases the hearts were completely removed from the thorax performing median sternotomy. The filling of the left ventricle was performed in all cases with the aorta clamped in the interest of optimal pressure and mitral valve closure.

4.2. Step-by-step description of transapical endoscopic visualization and experimental mitral valve repair procedures

4.2.1. Preparation of the cadavers

Using a conventional median sternotomy the left heart was rinsed out with saline injections through a transversal incision of the ascending aorta. After that the pulmonary veins and the ascending aorta were ligated. The pericardium was sutured and the sternum was closed in order to restore the original anatomic situation.

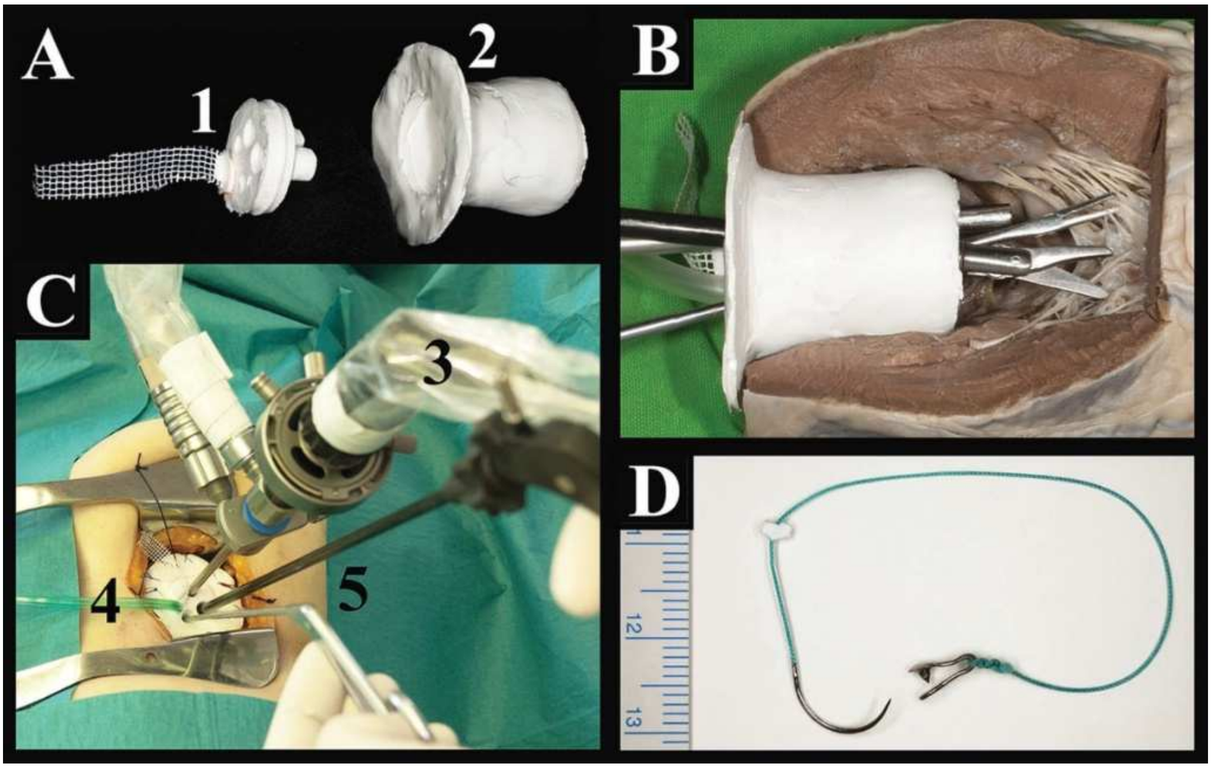


Figure 2: Instrument prototypes for transapical endoscopic mitral repair.
The used apical silicon port (A): 1. stopper with four holes, 2. funnel with an outer sheath. The intraventricular situation of the port in a formaline-fixed heart (B). The intraoperative situation of the placed port (C): 3. endoscopic optic (4 mm, 0 degrees), 4. silicon tube for suction, insufflation and saline-injection, 5. endoscopic instruments. The clip-chord (D).

4.2.2. Surgical technique

After standard left anterolateral mini-thoracotomy the pericardium was opened and retracted to expose the apex of the heart. A 2 cm transmural incision was performed close to the apex of the heart and lateral to the left anterior descending coronary artery. A self-designed apical silicon port was placed through the incision and fixed with sufficiently deep bites in the myocardium. (*Figure 2/A and 2/B)*

The rigid 4 mm 0 degrees endoscopic optic (©Aesculap PE 484A). *(Figure 2/C)* was introduced into the collapsed left ventricle *(Figure 3/A)*. The left heart was pressure-controlled insufflated with CO_2 (10 mmHg) restoring its natural three-dimensional shape. *(Figure 3/B)* Upon completion of CO_2-insufflation, the left ventricle was injected with saline *(Figure 3/C)*, allowing for assessing chordal length and coaptation area of the leaflets.

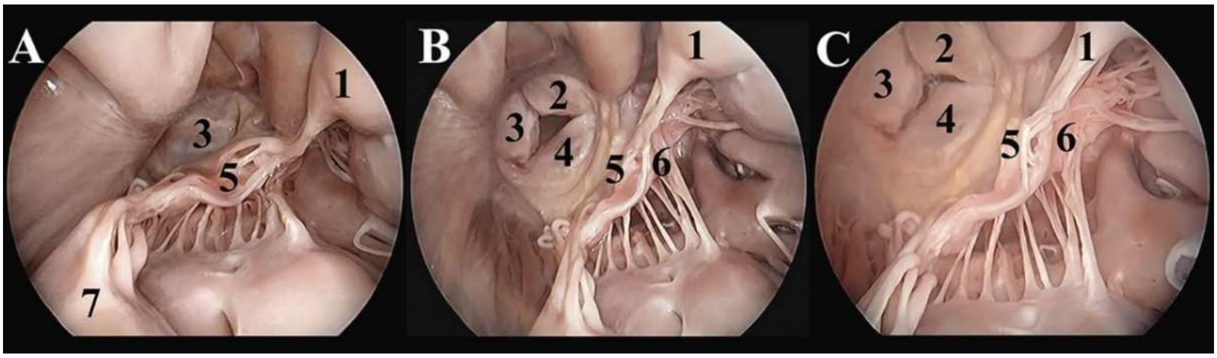


Figure 3: Anatomic structures of the left ventricle (apical endoscopic view). *The mitral valvular complex in the collapsed (A), insufflated (B) and saline-injected (C) left ventricle: 1. anterior papillary muscle, 2. left coronary cusp of the aortic valve, 3. right coronary cusp of the aortic valve, 4. noncoronary cusp of the aortic valve, 5. anterior mitral leaflet, 6. posterior mitral leaflet, 7. posterior papillary muscle.*

The left heart was insufflated again with CO_2 after suctioning the saline. Endoscopic scissors and forceps were introduced under visual control. One chord (running to the A2 scallop) was transsected by the investigator, resulting severe mitral valve insufficiency.

Figure 4: The steps of artificial chord implantation (apical endoscopic view). *The clip-chord fixation on the anterior mitral leaflet (A). The stich into the head of anterior papillary muscle (B). The saline-injected left ventricle after the clip-chord implantation (C).*

The first part of the endoscopic mitral valve repair consisted of the artificial chord implantation using self-designed clip-chords with a titanium-clip and a needle on the opposite end. *(Figure 2/D)* The clip was secured on the free edge of the A2 scallop at the original chord insertion site using an endoscopic clip-applier. *(Figure 4/A)*

The other end of the artificial chord was sutured to the head of the anterior papillary muscle. *(Figure 4/B)* Direct transapical visualization allowed for measuring the perfect length of the implanted chord after again filling the left ventricle with saline. The optimal length of the adjustable chord was secured using a patch and a clip. Following this step the mitral valve became competent again. *(Figure 4/C)*

The following step consisted of the quadrangular resection of the posterior mitral leaflet. The P2 scallop was incised twice beginning at the free edge of the leaflet towards the annulus and resected. *(Figure 5/A)* The chords were transsected. *(Figure 5/B)* The annulus was plicated at the resected part using plegeted stiches. *(Figure 5/C)* The gap in the posterior leaflet was closed with interruped sutures beginning at the annulus. The knots were tied on the ventricular side.

Figure 5: The steps of quadrangular resection and suture-annuloplasty (apical endoscopic view).
Incision of the posterior mitral leaflet (A). Cutting of the tendinous chords (B). The stich into the mitral annulus at the resected part of the posterior leaflet (C).

After completion of the valvuloplasty, a suture-annuloplasty was performed at the level of the angle between the ventricular surface of the posterior mitral leaflet and the left ventricular wall, also referred to as the aorto-mitral continuity. The mitral valve competence was tested with pressure-injection of the left ventricle after each individual step.

5. Results

5.1. Comparative endoscopic anatomic description of the mitral valvular complex

5.1.1. Aortic view

In this approach, we selected the 70 degrees optic based on the excellent visibility of the anterior and posterior mitral leaflets and the subvalvular apparatus. Three different views were described at three different depths with the mitral valve opened without filling and one view by closed valve after filling the left ventricle with saline under pressure. *(Table 2)*

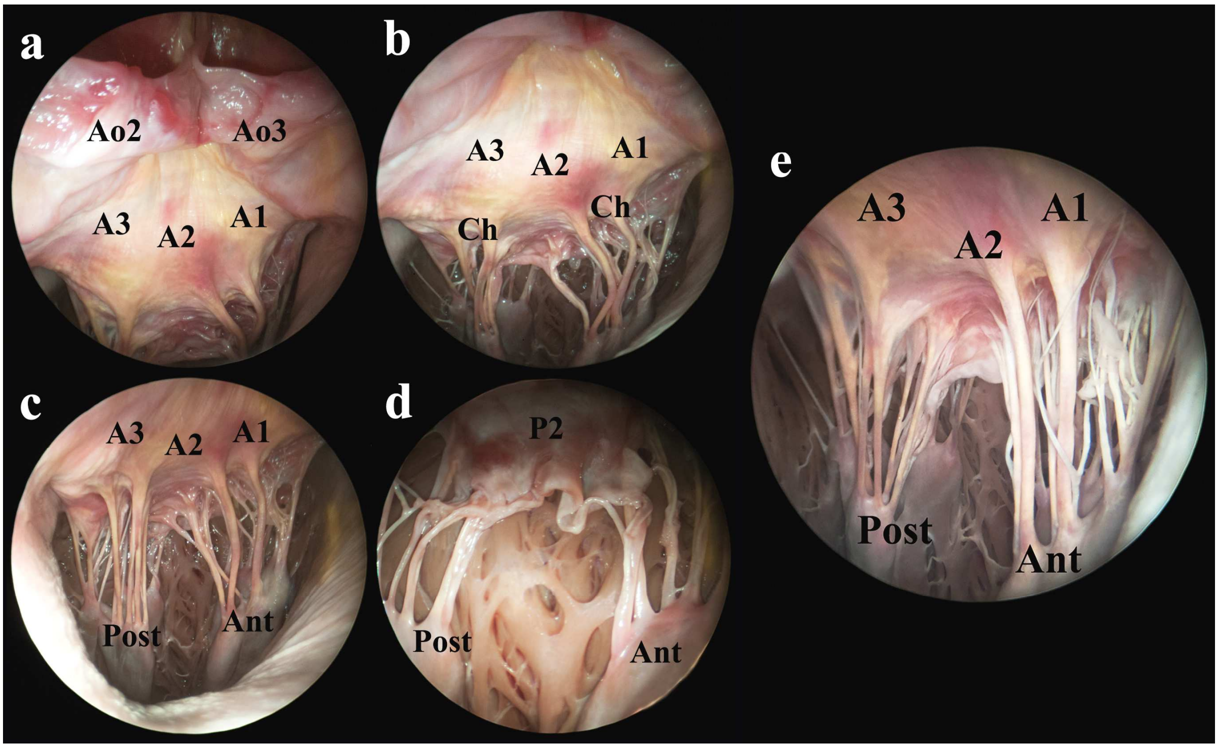


Figure 6: The endoscopic view of the mitral valve, introduced a 70 degrees rigid endoscope through the aortic valve without (a-d) and with saline-filling (e) of the left ventricle.

5.1.1.1. Unfilled heart

For the first view, the introduced endoscope was directed toward the anterior leaflet of the mitral valve situated the commissure between the noncoronary and left coronary aortic cusps at 12 o'clock. From the commissure downward straggling structures were identified as the ventricular surfaces of the posterior noncoronary aortic cusp on the left side, and the left coronary cusp on the right side. Underneath the aorto-mitral continuity and the ventricular surface of the anterior mitral leaflet was located. The inserting part of the anterior marginal chords appeared on that surface of leaflet. *(Figure 6/a)* Deeper, the whole length and the origins of the chords from the papillary muscles were visible on this view. The posterior papillary muscle was visible on the left side of the view and the anterior papillary muscle on the right side. *(Figure 6/b and Figure 6/c)* After that, as the endoscope was moved through the two chords running to the anterior leaflet of the mitral valve, the posterior leaflet became visible. The horizontal line of mitral annulus was situated at the upper part of this view. Under the annulus the atrial surface of the posterior mitral leaflet appeared. The posterior marginal chords were visible in their whole length. The posteromedial and anterolateral commissures could not be investigated yet. *(Figure 6/d)*

5.1.1.2. Filled left ventricle

After filling the left ventricle with saline, the closed mitral valve could be inspected from the aortic valve. All the anterior marginal ran with the posterior marginal, intermediate and basal chords, as two bands, from the papillary muscles to the leaflets. The chords were in a suspended state and the closing function of the valve could be investigated. *(Figure 6/e)*

5.1.2. Atrial view

During examination from the atrial approach, the 0 and 30 degrees endoscopes gave an optimal view of the mitral leaflets. To investigate the subvalvular apparatus with the mitral valve opened, the 70 degrees optic was more helpful. After filling the left ventricle with saline, the closed mitral valve could be examined optimally using the 0 and 30 degrees endoscopes. *(Table 2)*

5.1.2.1. Unfilled heart

Using the 0 degrees optic, the ring of the mitral annulus filled the view with the leaflets and the subvalvular apparatus. Positioning the A2 scallop at 12 o'clock, the anterior leaflet was visible between the commissures, under the line of the aorto-mitral continuity. The anterolateral commissure was situated on the left upper side of the view. From left to right, the atrial surfaces of the A1, A2 and A3 scallops were visualised, terminated by the posterolateral commissure. In the orifice, between the anterior and posterior mitral leaflets, the subvalvular apparatus was visible. The anterior and posterior marginal chords inserted on the free margins of the leaflets. The apical region of the anterior papillary muscle could be found on the left side and the posterior papillary muscle on the right side of the view. Under the mitral orifice, the atrial surface of the posterior leaflet was positioned, with, from left to right, the P1, P2 and P3 scallops. *(Figure 7/a and Figure 7/b)* Introducing the 70 degrees endoscope into the orifice of the mitral valve, the structures of the subvalvular apparatus and the commissures could be examined in richer detail. *(Figure 7/c and Figure 7/d)*

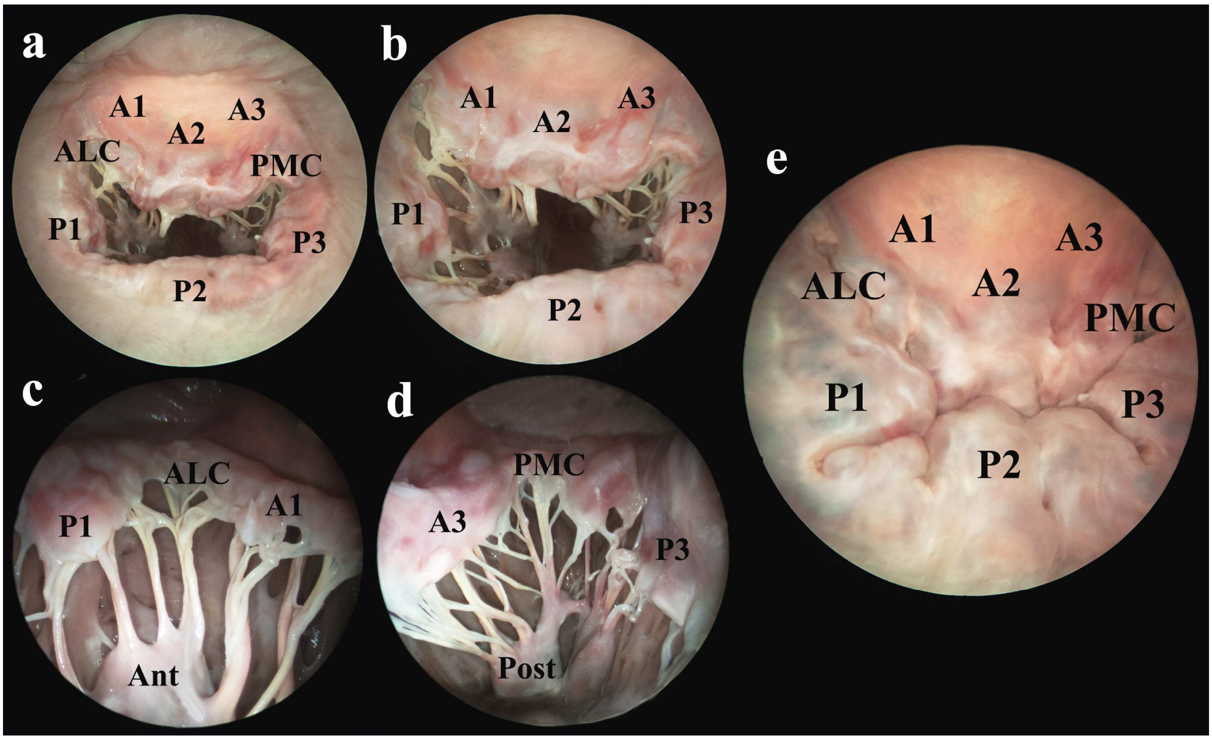


Figure 7: The endoscopic view of the mitral valve, introduced a 0 (a, b) and a 70 (c, d) degrees endoscope through the left atrium without (a-d) and with saline-filling (e) of the left ventricle.

5.1.2.2. Filled left ventricle

After filling the left ventricle with saline, the atrial surface of the closed mitral valve could be optimally visualised, but we did not get any direct visual information about the chords and papillary muscles. *(Figure 7/e)*

5.1.3. Apical view

Using the apical approach, the 0 degrees endoscope was found optimal for visualisation of the whole mitral valvular complex, with both opened and closed mitral valve. In the investigation of the smaller details, the 30 and 70 degrees optics proved themselves to be useful too. The description of the complex was given step by step in the left ventricle starting from the apex, with and without saline-filling. *(Table 2)*

5.1.3.1. Unfilled heart

Examining the mitral valve introducing the 0 degrees endoscope through the apical incision, all structures of the complex could be seen on the same view.

The ventricular surface of the aortic valve was positioned at 12 o'clock. The right coronary cusp of the aortic valve was located on the top, with the noncoronary cusp on the left side and the left coronary cusp on the right side under it. The line of the aorto-mitral continuity was situated exactly under the aortic valve. As the left angle of the mitral orifice, the posteromedial commissure could be visualised under the aforementioned anatomical structures. From left to right, the ventricular surfaces of the A3, A2 and A1 scallops of the anterior mitral leaflet were found, ending with the anterolateral commissure. The anterior marginal chords could be identified as they reached the free margin and the ventricular surface of the anterior leaflet, starting from their origin on the papillary muscles. The posterior papillary muscle was located on the left side of the orifice and the anterior papillary muscle on the right side. As the lower margin of the orifice, the posterior leaflet was to be seen. The whole length of the posterior marginal, intermediate and basal chords could be visualised, inserting on the P3 scallop on the left, P2 scallop in the middle and P1 scallop on the right. Both the atrial and ventricular surfaces of the leaflets could be investigated from the apex. Encircling the mitral orifice, the line of the mitral annulus could be followed, exactly in the angle of the posterior leaflet and the ventricular wall. *(Figure 8/a, Figure 8/b, Figure 8/c and Figure 8/d)*

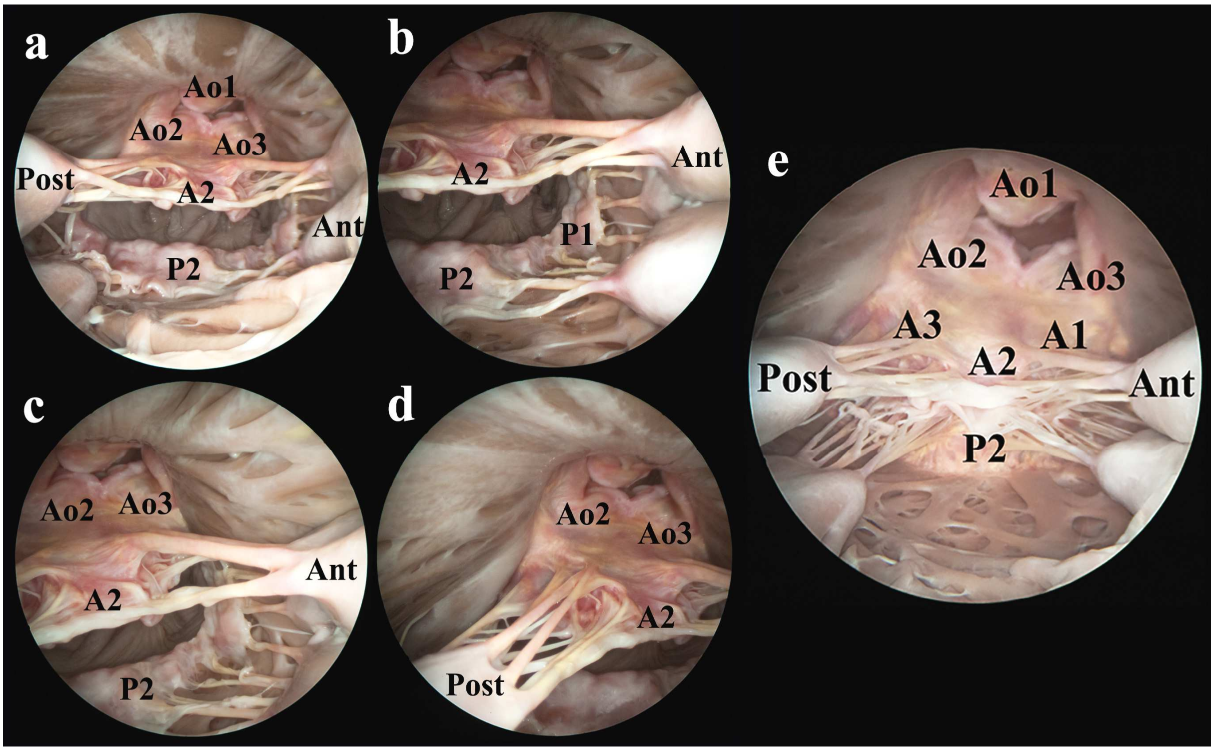


Figure 8: The endoscopic view of the mitral valve, introduced a 0 degrees rigide endoscope through the apex of the heart without (a-d) and with saline-filling (e) of the left ventricle.

5.1.3.2. Filled left ventricle

After filling the left ventricle with saline under pressure, the optimal visual and functional examination of the closed mitral leaflets and the subvalvular apparatus was possible with the 0 degrees endoscopic optic. *(Figure 8/e)*

Table 2: The visibility of the mitral valvular complex and the aortic valve using the investigated approaches

Visible structures	Aortic view		Atrial view		Apical view	
	Unfilled heart	Filled left ventricle	Unfilled heart	Filled left ventricle	Unfilled heart	Filled left ventricle
Mitral valvular complex: line of mitral annulus	+/-	+/-	+	+	++	++
atrial surface of the leaflets	+	-	++	++	++	-
ventricular surface of the leaflets	+	+	-	-	++	++
commissures	-	-	++	++	++	++
chords	++	++	+	-	++	++
papillary muscles	++	++	+	-	++	++
Aortic valve: aortic surface of the cusps	++	+	-	-	-	-
ventricular surface of the cusps	+	+	-	-	++	++

5.2. Results of the experimental mitral valve repair procedures

The apical view offered detailed information about potential mitral valve pathology by complex visualization of the entire mitral valvular complex, including the subvalvular apparatus. In addition to direct intracardiac imaging, the insufflated left ventricular cavity created sufficient space for safe instrumental manipulations. Successful complex mitral repair procedures (artificial chord implantation, valvuloplasty and annuloplasty) could be performed on each individual cadaver. The line of the mitral annulus is located exactly in the angle formed by the posterior leaflet and the ventricular wall. Performing running sutures in this line, a precise suture-annuloplasty could be carried out.

6. Discussion

Extensive literature on minimally invasive mitral valve repair procedures has been published in the last couple of years. In these partly clinical and experimental studies the anatomic structures were only described in general terms, but these publications outlined novel approaches and methods for future valve repair procedures.

The novel concept in our study consisted of investigating three dimensional anatomic structural confirmations by analysing and comparing various different approaches. We noticed that all of the directions (aortic, atrial and apical) used revealed new visual information on the examined structures. A thorough and complex knowledge of the anatomy of the mitral valve could help the surgeon in understanding and teaching various mitral valve repair techniques. The atrial endoscopic view is an optimal approach for annuloplasty ring replacement and leaflet resection. We prefer the aortic or apical view at the implantation of artificial chords as well as the functional investigation of the subvalvular apparatus by filling the left ventricle. For complex repair techniques the apical view is preferable since it allows for perfect visibility of the coaptation line as well.

On the basis of our anatomic study, we used this optimal approach for the investigation of novel mitral valve repair methods. Our self-designed apical port combined multiple advantages: the funnel of the port was soft and pliable to prevent injuries of the endocardium and also to allow for smooth manipulations of endoscopic instruments as well as the endoscopic camera. One of the most challenging problems of our technique was the collapsed left ventricle. This is the first description of pressure-controlled CO_2-insufflation of the left heart. The gained view was clear, the anatomic structures were visualized easily and the instrumental manipulations controllable and safe. The investigation of the mitral valve competence was performed by intermittent saline-injections to induce leaflet closure, and therefore much more precise when compared with an atrial approach. Our 4 mm 0 degree endoscopic optic delivered sufficient light for optimal visualization and the rigidity of the straight scope was helpful for stabilizing the view. The beating heart application of our transapical method is limited due to insufficient endoscopic visualization in non-transparent solutions such as blood. Maneuvering with the rigid instruments was certainly limited, but never the less even complex repair procedures could be performed with perfect results in all 20 cadavers included in our study. The clip we designed for our approach was made of titan and included a punching tooth in order to grasp the leaflet and assure safe fixation. Determining the correct length of the clip-chord was the most crucial step of the implantation. The experimental quadrangular resection of the posterior mitral leaflet resembled conventional surgical techniques. The annuloplasty can principally be performed on either the atrial side or on the ventricular side of the valve.

Further development of the currently only experimentally used transapical view could turn this approach into the most useful view since it allows for a perfect visualisation of the entire mitral valvular complex. The future will show if developments of the concepts will lead into clinical use of the novel techniques and improve outcomes of minimally invasive mitral valve repair procedures in patients suffering from complex mitral valve disease.

7. Novel findings

1. We gave detailed endoscopic anatomic description of the human mitral valvular complex using standardized views. We selected the conventional left atrial, the developing apical and the novel aortic approaches to visualize the valve and its related structures in the unfilled heart and the saline-filled left ventricle.

2. We defined standard anatomic landmarks using endoscopic optics. The described landmarks offer valuable help for the cardiac surgeon to identify the structures promptly in video-assisted surgery.

3. Our step-by-step anatomic descriptions of different endoscopic approaches allowed us to compare their advantages in mitral valve surgery. We found that the apical approach offers the most detailed view and the most promising opportunity for development of novel repair techniques.

4. A self-designed apical silicon port was placed through the incision and fixed with sufficiently deep bites in the myocardium. The port consisted of a funnel with a 1 cm wide outer sheath and a stopper with a total of four holes for the endoscopic optic, the endoscopic instruments and a silicon tube.

5. For suitable exposure the silicon tube of the apical port was connected to a system for suction, saline-injection and CO_2-insufflation. The insufflated cavity created sufficient space for safe instrumental manipulations.

6. Artificial chord implantation was performed using self-designed adjustable clip-chords with a titanium-clip and a needle on the opposite end. The following step was the quadrangular resection of the posterior mitral leaflet. A suture-annuloplasty was performed at the level of the angle between the ventricular surface of the posterior mitral leaflet and the left ventricular wall, also referred to as the aorto-mitral continuity.

8. Publications and presentations

8.1. Publications releated to the thesis

1. ***Ruttkay T****, Baksa G, Götte J, Glasz T, Patonay L, Galajda Z, Doll N, Czesla M.*
   Comparative endoscopic anatomic description of the mitral valvular complex: a cadaveric study.
   Thorac Cardiovasc Surg. 2015;63(3):231-237. **(IF: 0,957)**

2. ***Ruttkay T****, Czesla M, Nagy H, Götte J, Baksa G, Patonay L, Doll N, Galajda Z.*
   Experimental transapical endoscopic ventricular visualization and mitral repair.
   Thorac Cardiovasc Surg. 2015;63(3):238-242. **(IF: 0,957)**

3. ***Ruttkay T****, Jancsó G, Gombocz K, Gasz B.*
   A mitralis elégtelenség sebészi kezelésének új megközelítése: transapicalis ínhúrpótlás dobogó szíven.
   Orv Hetil. 2016;157(18):700-705. **(IF: 0,291)**

IF: 2,205

8.2. Publications not releated to the thesis

1. *Czesla M, Götte J, Weimar T,* ***Ruttkay T****, Doll N.*
   Safeguards and Pitfalls in minimally invasive mitral valve surgery.
   Ann Cardiothoracic Surg. 2013;2(6):849-852.

2. ***Ruttkay T****, Scheid M, Götte J, Doll N.*
   Endoscopic Resection of a Giant Left Atrial Appendage.
   Innovations (Phila). 2015;10(4):282-284.

3. ***Ruttkay T****, Götte J, Walle U, Doll N.*
   Minimally Invasive Cardiac Surgery Using a 3D High-Definition Endoscopic System.
   Innovations (Phila). 2015;10(6):431-434.

8.3. Abstracts

1. ***Ruttkay T,*** *Galajda Z, Patonay L.*
   Comparison of two approaches for biportal endoscope-assisted mitral valve repair: an anatomical study.
   Revista de Medicina si Farmacie / Orvosi és Gyógyszerészeti Szemle 2009, Vol. 55 supl 4; p121 (ISSN 1221-2229)

2. **Ruttkay T**, Baksa G, Glasz T, Patonay L, Galajda Z
   Transapical endoscopic mitral repair.
   Cardiologia Hungarica 2011, 41:N14 (ISSN 0133-5596)

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