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

CL: standard clefts of the posterior 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 valve and its nomenclature applied in the thesis

Numerous books and publications describe the classical anatomy of the mitral valve. The recent extensive knowledge about the valve is based on the modern functional, pathological and surgical descriptions. 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 [1-3]. Therefore, the mitral valve consists of the anterior and posterior leaflets including the anterolateral and posteromedial commissures, the annulus, the tendinous chords and papillary muscles. The last two structures are termed as the subvalvular apparatus of the mitral valve. The endocardium and the myocardium of the left atrium and left ventricle, as well as the aorto-mitral curtain complete the valve to mitral valvular complex. *(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>

After the classical anatomic description of the mitral leaflets [4], the worldwide used nomenclature is based on Carpentier’s modern surgical description [5]. *(Figure 1)* The anterior leaflet and the posterior leaflet are separated by two transitional areas, the anterolateral and the posteromedial commissures. Two standard clefts divide the posterior mitral leaflet (from the anterolateral to the posteromedial commissure) into three scallops, namely P1, P2 and P3. The anterior mitral leaflet has no standard clefts normally, but the scallops of it can be distinguished similarly to the scallops of posterior leaflet as A1, A2 and A3. Other clefts, namely deviant clefts are deviated from Carpentier's description [6]. They are located within scallop areas. The corresponding marginal surfaces of the leaflets coapt in systole according to the closure line of the valve.

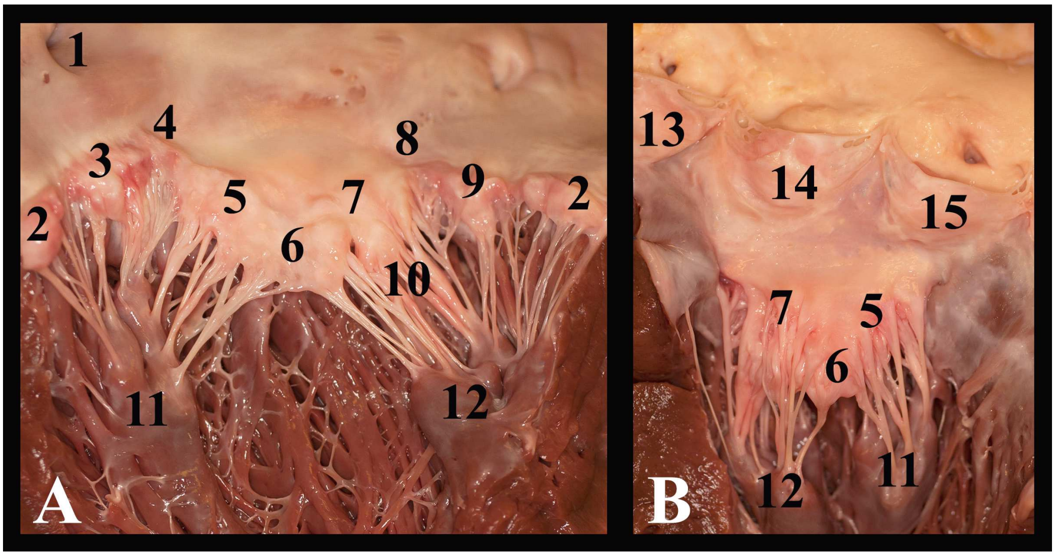

Figure 1: Atrial surface of the mitral valve (A) and ventricular surface of the anterior mitral leaflet (B) on a dissected non-fixed human cadaveric heart.

1: left auricle, 2: P2 scallop of the posterior mitral leaflet, 3: P1 scallop of the posterior mitral leaflet, 4: anterolateral commissure of the mitral valve, 5: A1 scallop of the anterior mitral leaflet, 6: A2 scallop of the anterior mitral leaflet, 7: A3 scallop of the anterior mitral leaflet, 8: posteromedial commissure of the mitral valve, 10: tendinous chords, 11: anterior papillary muscle, 12: posterior papillary muscle, 13: right coronary cusp of the aortic valve, 14: noncoronary cusp of the aortic valve, 15: left coronary cusp of the aortic valve.

Ten years ago Ritchie et al. published a reversed nomenclature of the tendinous chords [7]. The commissural, posterior marginal and anterior marginal chords are differentiated according to the previous first order inserting on the free edge of the leaflet as well as the commissural areas [8]. As previous second order the posterior intermediate chords and the anterior strut chords are distinguished inserting on the ventricular surface of the leaflet. On the posterior leaflet basal posterior chords are originated from the posterior left ventricular wall and inserted on the leaflet next to the annulus.

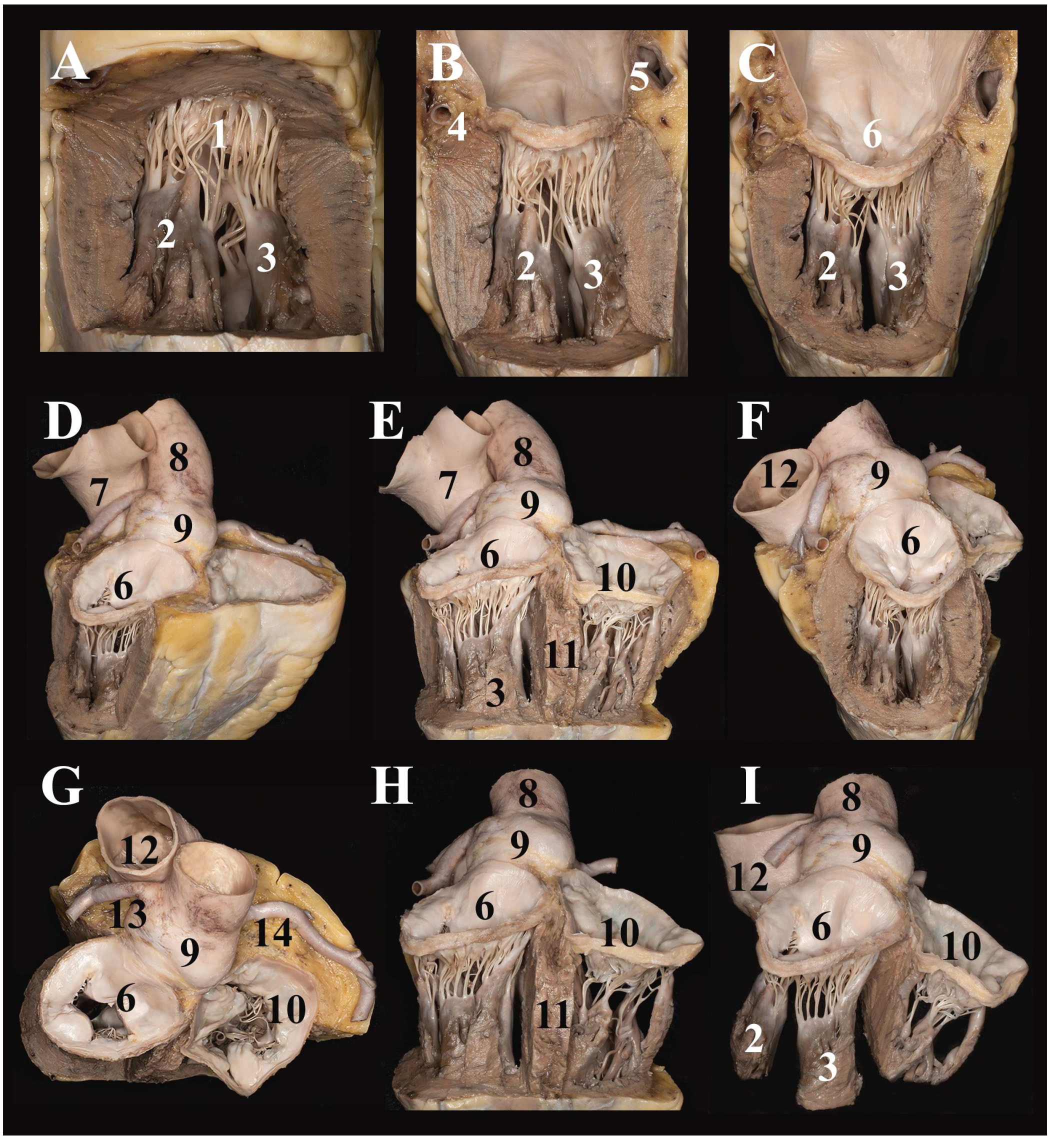

Figure 2: Topography of the mitral valvular structures in a human formaline-fixed cadaveric heart.

1: tendinous chords, 2: anterior papillary muscle, 3: posterior papillary muscle, 4: circumflex branch of the left coronary artery, 5: coronary sinus, 6: mitral valve, 7: pulmonary trunk, 8: ascending aorta, 9: aortic sinus, 10: tricuspid valve, 11: interventricular septum, 12: pulmonary valve, 13: left coronary artery, 14: right coronary artery.

Anterior and posterior papillary muscles are distinguished in the left ventricle with origins of the various tendinous chords on their heads running to the leaflets [9]. *(Figure 2)* Berdajs defined three main groups of anatomic variants of the papillary muscles on the ground of the morphology of their head [10]. In the first group the head of the papillary muscle is undivided. The papillary muscles in the second group form two individual heads. Last but not least, three separated heads are described in the third group. Further subtypes are distinguished according to common or separated origin of the papillary muscle heads, however the morphological properties have no direct influence on the role of the global mitral valve function.

2.2. The apex of the heart

The definition for the ,,apex of the heart" can be formulated in various ways [11]. It is the vertex, the pointed end, the top, the tip or peak of the cardiac pyramid or cone. With the goal of a more precise definition of the structure, three summarizing concepts were defined. The anatomical, the amplified anatomical and the geometric concepts of the apex of the heart were distinguished. The anatomical apex is located with its base at the *incisura apicis cordis*. The double of the previous defined segments of the heart is described as amplified anatomical apex. The geometric apex consists of the distal third of the ventricles. Numerous superficial blood supply variants are described in this region. The number of the coronary artery branches depends upon the concept and it decreases from the base to the apex. The branches of the anterior interventricular branch of the left coronary artery are generally found in all apex types. The incidence of the posterior interventricular branch is increasing from the anatomic to the geometric apex. The left ventricular myocardium is built from different muscular layers. The external left-handed helix continues uninterrupted through the apical vortex into the internal longitudinal fibres. The middle, almost circular right-handed helix layer is located between the aforementioned muscular fibres. On the basal part of the ventricle, all three layers take part in the formation of the muscular wall as opposed to the apex, which is not reached through the middle fibres.

2.3. Mitral valve diseases

2.3.1. Mitral stenosis

In the case of mitral stenosis the transvalvular gradient increases significantly in diastole between the left atrium and the left ventricle [12]. The majority of mitral stenosis is a typical consequence of rheumatic heart disease. Classic morphological alterations include commissural fusion, chordal shortening and fibrosis of the leaflets with retraction. The minority of mitral stenosis can be the result of severe annular or leaflet calcification, congenital deformities, carcinoid syndrome, neoplasm and atrial thrombus.

2.3.2. Mitral regurgitation

Based on its etiology, mitral regurgitation can be devided into two groups. We can distinguish organic and functional mitral regurgitation [12]. Functional mitral regurgitation evolves due to the pathological morphology or function of the left ventricle in the presence of healthy valvular structures (leaflets, tendinous chords, papillary muscles), often as a result of dilatation of the mitral annulus. Among others we can describe this type by annular dilatation due to dilatative or ischaemic cardiomyopathy. In the case of organic mitral regurgitation, the pathological alterations of the valvular structures lead to valve dysfunction. The most common pathological morphology is the prolapse of the leaflets due to chordae rupture or chordae elongation by degenerative diseases [13, 14]. Additionally, bacterial endocarditis can cause mitral insufficiency by the destruction of the valve structures.

2.3.3. 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 [5, 15]. This classification is based on the leaflet motion and differentiate four functional types of mitral valve regurgitation. *(Figure 3)*

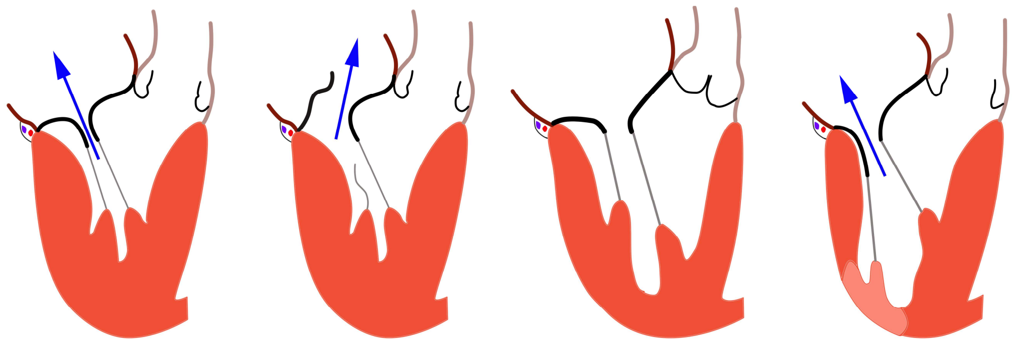

Figure 3: The „Functional classification" of mitral valvular dysfunction.
Type I: normal leaflet motion, Type II: excess leaflet motion, Type IIIa and Type IIIb: limited leaflet motion during diastole or systole.

In mitral regurgitation with normal leaflet motion (Type I) the free edges of the leaflets are normally positioned 5 to 10 mm under the plane of the anulus. The insufficiency is a result of a coptation gap between the leaflets due to annular dilatation, a leaflet perforation, tear or vegetation by endocarditis. In the case of mitral regurgitation with excess leaflet motion, leaflet prolapse (Type II) the free edge of the leaflet is located over the plane of the annulus during systole. The resulting insufficiency jet runs above the nonprolapsing leaflet because of chordae rupture, elongation or papillary muscle rupture, elongation. The incidence of prolapse of the posterior mitral leaflet at the P2 segment is dominant [16, 17]. Mitral valve prolapse due to degenerative disease is defined by a wide spectrum of lesions. This spectrum is ranging from fibroelastic deficiency to Barlow's disease. In the spectrum of fibroelastic deficiency, the rate of isolated segmental pathological leaflet tissue (myxomatous changes) is variable. In contrast to fibroelastic deficiency, in Barlow's disease diffuse excess tissue causes a generally large valve size, thickened and distended leaflets as well as elongated chordae. In mitral regurgitation with restricted leaflet motion (Type III), two subtypes can be distinguished on the basis of the heart cycle. The movement of one mitral leaflet or both mitral leaflets can be limited primarily during diastole (Type IIIa) or systole (Type IIIb). In Type IIIa, the movement of the valve is limited either due to thickening and fusion of chordae or fusion of commissures in rheumatic valve disease. This type, also known as valve stenosis, which can be further divided into two subgroups based on the pliability of leaflet tissue (pliable or rigid leaflets), and the two subgroups depend on the severity of subvalvular lesions (minimal or severe subvalvular lesions and classification). In the case of Type IIIb, mitral insufficieny is a consequence of papillary muscle displacement in ischemic cardiomyopathy with regional ventricular dyskinesie or global dilatation of the left ventricle in dilatative cardiomyopathy.

2.4. 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. 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.

2.4.1. Invasive cardiologic methods

2.4.1.1. Percutaneous edge-to-edge mitral repair

MitraClip (Abbott Vascular ©) system enables percutaneous edge-to-edge mitral repair procedures with polyester-covered cobalt-chromium clips [18-20]. Using transfemoral venous access and performing transseptal puncture, the device is introduced into the left atrium. The clip is opened and positioned directly above the insufficient jet under multiplane 2-dimensional and 3-dimensional echocardiography guidance. After insertion in the left ventricle, the free edges of the mitral leaflets can be grasped and the clip can be closed. Multiple clip implantations can be performed under continuous color Doppler quantification of mitral regurgitation.

The studies describe at 12 months follow-up the mitral regurgitation equal or less than second grade in 84 % of the patients after percutaneous edge-to-edge repair. This method shows currently the best results according to safety and feasibility among other invasive cardiologic procedures.

2.4.1.2. Percutaneous mitral annuloplasty with fixed-length double-anchor implant in the coronary sinus

The fixed-length double-anchor implant with mirror-image hoop-shaped helical anchors helps with plication of the periannular tissue by the treatment of functional mitral regurgitation through indirect annuloplasty [21, 22]. After puncture of the right internal jugular vein, the Carillon® Mitral Contour System™ (Cardiac Dimension Inc., Kirkland, WA, USA) can be introduced into the coronary sinus. The geometry of the device (length, proximal and distal anchor sizes) is appropriately selected based upon the measurements of the coronary sinus dimensions. Under fluoroscopy-guidance, the system can be implanted precisely and the resulted reduction of mitral regurgitation controlled with transoesophageal echocardiography.

An acute reduction of approximately one grade in mean mitral regurgitation is described in current studies with small patient groups, and a further improvement after 3 months is also observed because of the left ventricular remodeling.

2.4.1.3. Percutaneous adjustable direct annuloplasty system

The Cardioband system (Valtech Cardio ©, OrYehuda, Israel) implanted on the posterior annulus of the mitral valve using transfemoral venous access and transseptal puncture allows a percutaneous direct surgical-like annuloplasty from the left atrium [23, 24]. With the help of the anchor delivery system the polyester sleeve with radiopaque markers spaced 8 mm apart can be fixed to the annulus with 6 mm long anchors begining at the anterolateral commissure and ending at the posteromedial commissure. After fixation of the device the desired degree of the contraction and with that the implant size can be regulated under color Doppler control of the mitral regurgitation.

The clinical studies with relatively small cases show, that approximately 89,3 % of the patients has none or mild mitral regurgitation 1 month after the procedure and the rate of equal or less than third grade mitral regurgitation was 86,4 % at 7 months.

Currently other interventional cardiologic mitral valve repair and mitral valve replacement techniques are investigated as well in the preclinical or early clinical stages. This is a highly dynamic field of cardiovascular medicine.

2.4.2. Surgical repair techniques

In the last decades, development of surgical reconstructive techniques for the correction of organic regurgitation was supported by many innovative improvements which improved the results of mitral valve surgery [25]. Published data support the view that the surgical correction should be performed as soon as possible and mitral repair is curative in 95-99 % of the patients with excellent long-term results [26, 27]. Currently, the following operative repair methods are used during routine reconstruction:

2.4.2.1. Annuloplasty

The aim of mitral valve annuloplasty is the reduction of pathologically altered, generally dilated diameter of the annulus and the stabilization of its pathological changed structure. Suture annuloplasty enables the long-term reduction of the diameter through simple running suture in the whole circle of the mitral annulus. In these days, most of the implanted rigide or semirigide annuloplasty rings are selected individually based on the pathological alterations of the valve [28, 29]. The special ring forms are developed and produced for ideal surgery of organic and functional valve diseases. The most modern annuloplasty rings for treatment of mainly functional mitral regurgitation are adjustable after surgery [30].

2.4.2.2. Triangular and quadrangular resection

The pathologically changed extended leaflet tissue or flail leaflet, which is due to chordal rupture, is excised in a trigonal or trapezoidal shape during successful triangular or quadrangular resection [5, 15]. The resection is performed with two incisions from the free margin of the leaflet to the mitral annulus. The identical part of the annulus is plicated with a pledget suture and the resection lines of the leaflet are joined with running suture. Nowadays these methods will be replaced by artificial chord implantation.

2.4.2.3. Artificial chord implantation

The most effective method to restore the structure of the mitral valvular complex is the artificial neochord implantation by ruptured or elongated nativ chords [31-34]. One end of the artificial chord is stabilized with a surgical stich to the apical part of the papillary muscle, while the other end is fixed to the free margin of the leaflet tissue. Multiple neochord implantations can be performed at the same time. The developed surgical polytetrafluoroethylen cords are flexible, but not elastic and enable excellent long-term reconstructive results by mitral repair procedures.

All of the reconstructive, valve preserver surgical techniques, wich achieve excellent outcomes, apply a left atrial approach. Special intruments and new surgical method through right anterolateral mini-thoracotomy were developed in the middle of the 1990s for the first endoscope-assisted mitral valve operations in order to have less operative risk [35-44]. The use of surgical robots in cardiac surgery (for example Da Vinci) showed equisite results during mitral repairs [45-48]. 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.

Summarizing the main points of optimal reconstructive strategy of mitral valve prolapse, the clinic needs a method which provides reliable neochord implantation using a simple surgical approach on the beating heart without cardiopulmonary bypass and its harmful pathophysiological effects. The implantation of polytetrafluoroethylen chords show excellent long-term results. The apical incision recently became a safe approach during transapical aortic valve replacement procedures [49]. State-of-the-art 3-dimensional echocardiographic imaging enabled the real-time representation of the left ventricular structures including the mitral valve. Taking advantage of recent technical innovations, the novel transapical neochord implantation method meets the above mentioned requirements for the optimal treatment of isolated mitral valve prolapse.

2.4.2.4. Echocardiography-guided transapical neochord implantation on beating heart

In the last years two devices made possible to perform clinical transapical mitral valve repair procedures using polytetrafluoroethylen artificial chords. One of the devices (TSH-5© device, Harpoon Medical Inc) allows to implant preformed knots on the free margin of the mitral leaflet [50]. Using the other one (NeoChord© DS1000, NeoChord Inc, Minneapolis, Minnesota) real sutures are inserted on the mitral valve. We describe the second method detailed, because it has more extended literature about clinical trials worldwide. The precise performance of transapical neochord implantation requires 2-dimensional and 3-dimensional transoesophageal echocardiography [51, 52]. Real-time echocardiographic visualization is indispensable during the course of detailed preoperative assessment, safe intraoperative guidance and final evaluation of the surgical result.

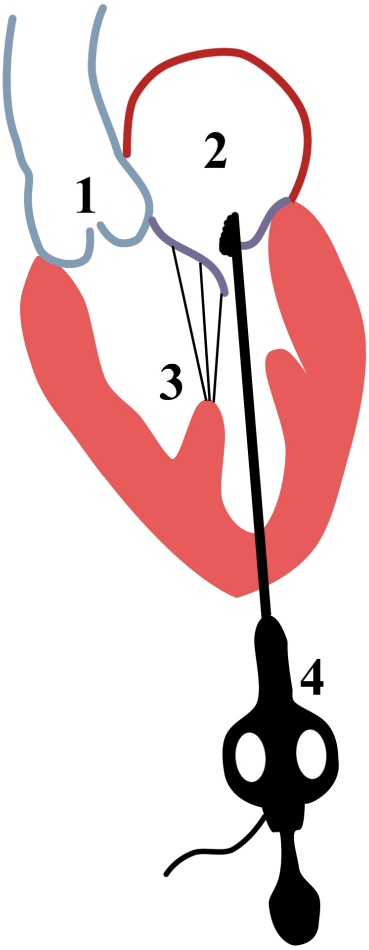

Figure 4: Surgical technique of NeoChord implantation: the instrument is introduced into the left ventricle using an apical approach.
1. aortic sinus, 2. left atrium, 3. left ventricle, 4. NeoChord device grasping the posterior mitral leaflet.

As surgical approach for implantation, a 4-5 cm left anterolateral mini-thoracotomy placed in the fifth intercostal space is applied. *(Figure 4)* During the development of the operative device (NeoChord© DS1000, NeoChord Inc, Minneapolis, Minnesota) *(Figure 5)*, constructors aimed to achieve the secure grasp of the mitral leaflet. That is why the device sytem consists of two main components connected with a cable: the hand-held delivery instrument and the device monitor for visualization of leaflet capture. In most cases, the optimal apical transmural incision is located 2-4 cm posterolateral from the apex of the left ventricle. The correct position of the incision should be probed by visualization of the finger impression of the operateur using multiplane echocardiography to prevent papillary muscle injuries. After optimal ventriculotomy, the shaft of the device (8 mm diameter, 24 F) is introduced into the left ventricle and left atrium. Intracardiac movements, manipulations and grasping of the mitral leaflet are performed with a handle. Two channels are included in the introduced shaft. One channel contains the loop of a polytetrafluoroethylen suture. The other one contains a harpoon-tipped needle for grab the suture and pulling it through the leaflet. In the same part of the device, four parallel fiberoptic sensors are built as well, which help to distinguish blood and leaflet tissue connected to the monitor. The echocardiographer changes into zoom mode for precise 2-dimensional multiplane and 3-dimensional echocardiographic visualization of the tip of the instrument to determine its exact position to the leaflets. At the grasp of the mitral leaflet, the four fiberoptic channels around the needle send information to the other main component of the device, the monitor. The four dots are red in the monitor when the introduced device has no connection with the heart valve. After achievement of the appropriate position the jaws are opened and the valve is grasped. When no leaflet tissue is grasped, four red dots light on the monitor. The valve is correctly captured, when all four fiberoptic red lights turn to white. In the case of two white and two red signals a new grasp is necessary, beacause not enough leaflet tissue is grasped for the safe neochord implantation and sufficient line of coaptation. After confirmation of optimal polytetrafluoroethylen suture insertion point at a depth of 3 to 4 mm from the free edge of the leaflet, the needle is pushed forward carefully to pierce the prolapsing valve scallop. After retraction of the needle, the subsequent fixation of the created loop is performed. 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. In most cases, to achieve intraoperative success with suitable reduced mitral regurgitation, generally more neochords should be implanted. With no residual or significantly reduced insufficiency, the sutures are fixed at their optimal length apical to the epicardium over a pledget adjacent to the ventriculotomy with a knot.

This procedure is appropriate for surgical treatment of the anterior, as well as the posterior mitral leaflet prolapse.

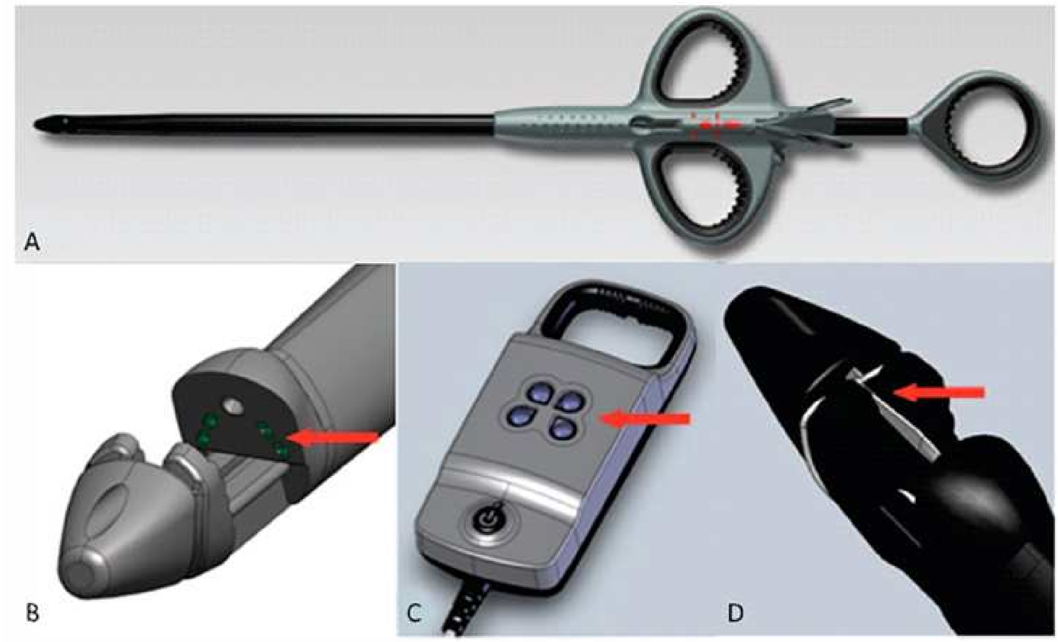

Figure 5: ***The Neochord DS1000 © transapical device (A)*** *consist of the tip with expandable jaws as well fiberoptic channels* ***(B)*** *connected to the device monitor* ***(C)*** *to confirm optimal leaflet capture and the needle* ***(D)*** *to perform the suture at the free margin of the mitral leaflet.*
(http://www.neochord.com/index.php/neochord-ds1000)

Severe mitral regurgitation due to prolapse of the valve demands early surgical intervention. Recently artificial chord implantation is the prefered solution, which requires cardioplegia and application of cardiopulmonary bypass using the left atrial approach. Transoesophageal echocardiography guided transapical neochord implantation is an emerging new technique for the treatment of mitral regurgitation. It enables the operation through the left minithoracotomy on beating heart using a special instrument introduced into the left ventricle. After the development of the procedure for transapical neochord implantation on beating heart, animal studies with promising results were published [53-55]. Based on these results, the first human procedures were performed under strict professional control. Besides numerous case reports [56-60], relevant clinical trials [61-64] were described and published with good early outcomes. Acute procedural success rates in different clinics vary between 86 and 100%. According to reports, 92% of the patients do not require additional intervention at the 3 month follow-up. Continuous integration of data results improving outcomes supporting the hope that this novel, less-invasive technique will be applied widely for the treatment of mitral regurgitation. In years to come further dynamic development of this innovative method is likely to accomplish more exquisite acute and long-term outcomes.

With the increasing number of neochord implantation on the prolapsing mitral valve segment, the intraprocedural success rate improved. In this case, the tension is appropriately distributed, reducing the risk of leaflet-chordal dehiscence and providing a more extended coaptation area. Initially, patients with narrow prolapsing area were prefered regarding primary selection criteria for surgery, but subsequently these patients have shown higher difficulty with placement of neochords and achievement of stable operative result was more difficult too. The grasp of marginal part of the prolapsing leaflet was significantly easier in patients with wide P2 or P3 segment prolapse and the best results were achieved in these cases. The correction of the apical incision 2-4 cm posterolateral from the classical apex of the heart resulted further improvement of procedural outcomes [61]. The mechanical tension on the posterior leaflet can be reduced with this approach by using shorter neochords with an anchoring vector similar to native tendinous chords [62]. The implanted neochords of the anterior leaflet ruptured more frequently, than in the case of the posterior leaflet. Therefore, development of a new approach is required to support the implantation of anterior neochords with ideal longitudinal axis. In the following days after surgery, relative elongation of the implanted neochords due to early left ventricular remodelling and volume reduction may occur, which can be solved by the apical re-tension of the sutures according to clinical experience. During conventional mitral repairs with widely applied rigide and semirigide annuloplasty ring implantations, the natural structure of the valve annulus is affected. Transapical neochord implantations restore normal leaflet motion and additionally preserve the vantriculo-annular continuity 3-dimensional dynamics [63].

It is an additional advantage that the applied apical surgical approach does not make significant tissue alterations which allow the exploration of the left atrium during a potencial subsequent conventional reoperation [64]. The conventional correction of an inappropriate operative result is still performed by intact anatomic properties using right anterolateral minithoracotomy.

Future studies integrating previous results will probably describe more precise surgeries and improved procedural results, since optimal patient selection and the experience of the surgeon as well as echocardiographer are two major determinants of the success of this innovative method [61].

2.5. Experimental models for transapical mitral valve repair

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

The increasing number of aforementioned minimally invasive mitral valve repair methods motivate the investigation of the endoscopic mitral valve visualisation and the anatomic description. 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 describing both the anatomic findings as well as the mitral repair techniques [5, 25, 35-47]. 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 repairs [65-69]. In vitro animal [70] and human [71] 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.

2.5.2. Experimental animal mitral repair procedures

Various experimental in vivo animal studies have described transapical intracardiac imaging and simple operative repair procedures on the mitral valve. This method was based on endoscopic visualization of the ventricular structures. Beating heart approaches were performed by using two separate circles: a transparent solution circulation for the left heart and the conventional extracorporal hemocirculation for peripheral organ perfusion [65, 67]. Mitral clip-fixations were carried out on the beating heart with flexible instruments [66]. In other cases off-pump endoscopic visualization of mitral valve apparatus structures was possible using a convex plexiglass covered optic [68]. Using cardiopulmonary bypass and a self-made left ventricular expander triangular resection of the posterior leaflet could be performed in a pig model [69]. 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 [72, 73]. The aim of the second part of our human cadaveric study was to develop an experimental 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 (22 female, 18 male; aged 49 to 88 years). Thirty of them were removed from the chest before the investigation and 10 were observed in situ, within the thorax. The mitral valves did not demonstrate any pathological findings. In the second experimental surgical part of our study 20 human cadavers (10 female, 10 male; aged 45 to 84 years) were investigated.

All hearts were obtained and dissected early after death at the Department of Anatomy Histology and Embryology (Semmelweis University, Budapest, Hungary) and no ethical approval for this study was necessary.

4.1. Endoscopic anatomic investigation of the mitral valvular complex

In this study 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. *(Figure 6)* Three different endoscopes were used: 0, 30 and 70 degrees 4 mm rigid optics (Aesculap© PE 484A). The following exposures of the heart were performed for in situ investigation. *(Figure 7)*

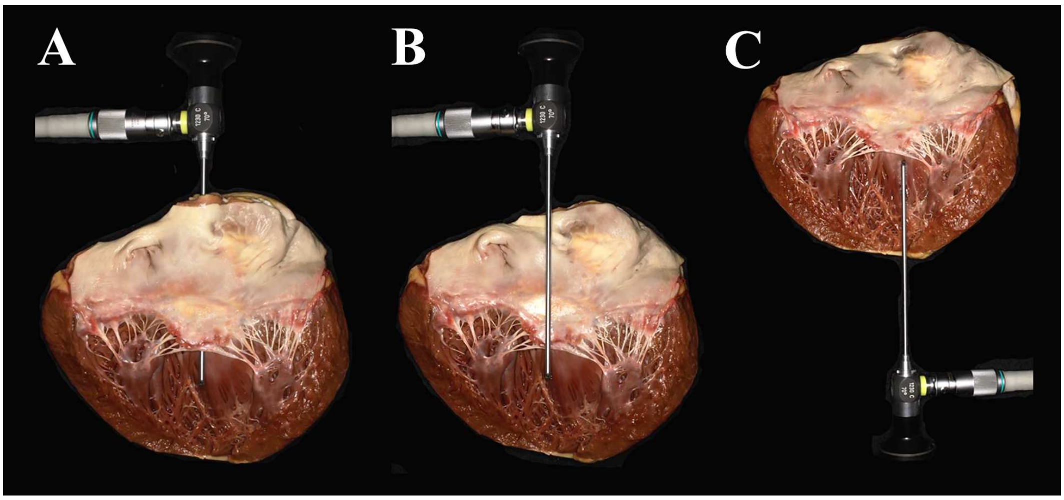

Figure 6: Itroduction points of the endoscopic optics on a dissected fresh heart: *through the aortic valve (A), the left atrium (B) and the apex of the heart (C).*

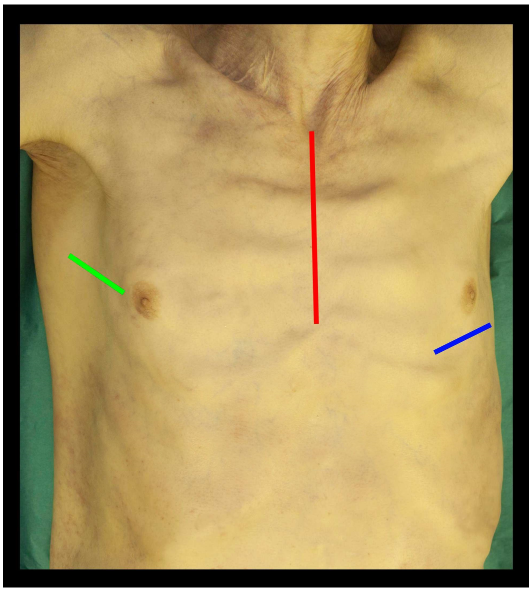

Figure 7: Skin incisions for in situ endoscopic anatomic investigation: *partial upper sternotomy (red), right anterolateral mini-thoracotomy (green), left anterolateral mini-thoracotomy (blue).*

Aortic approach: After standard partial upper sternotomy and pericardiotomy a 2 cm long transversal incision was performed at the aortic root 1 cm superiorly to the aortic valve. *(Figure 8)* Using a sucker and saline-injection, the blood was washed out from the left heart. The 4 mm endoscopes were inserted through the leaflets of the aortic valve under direct visual control. After clamping the aorta, the left ventricle was injected with saline solution under pressure using a silicon tube.

Atrial approach: After standard right anterolateral mini-thoracotomy in the third intercostal space and pericardial incision a 3 cm long transmural incision was made on the left atrium 1 cm anteriorly and parallel to the line between the right superior and inferior pulmonary veins. *(Figure 9)* An atrial retractor was placed to have an optimal exposure of the mitral valve. The structures of the mitral valvular complex were investigated with the rigid, 4 mm endoscopic optics. The left ventricle was filled with saline solution.

Apical approach: After standard left anterolateral mini-thoracotomy in the fifth intercostal space the pericardium was opened and a 1 cm long transmural incision was carried out on the apex of the heart lateral to the left anterior descending coronary artery branch. *(Figure 10)* The apex of the heart was pulled with patch-sutures to the skin incision. Introducing the rigid, 4 mm endoscopes into the left ventricle, the structures within it were inspected. Then the left ventricle was injected with saline solution under pressure using a simple silicon tube.

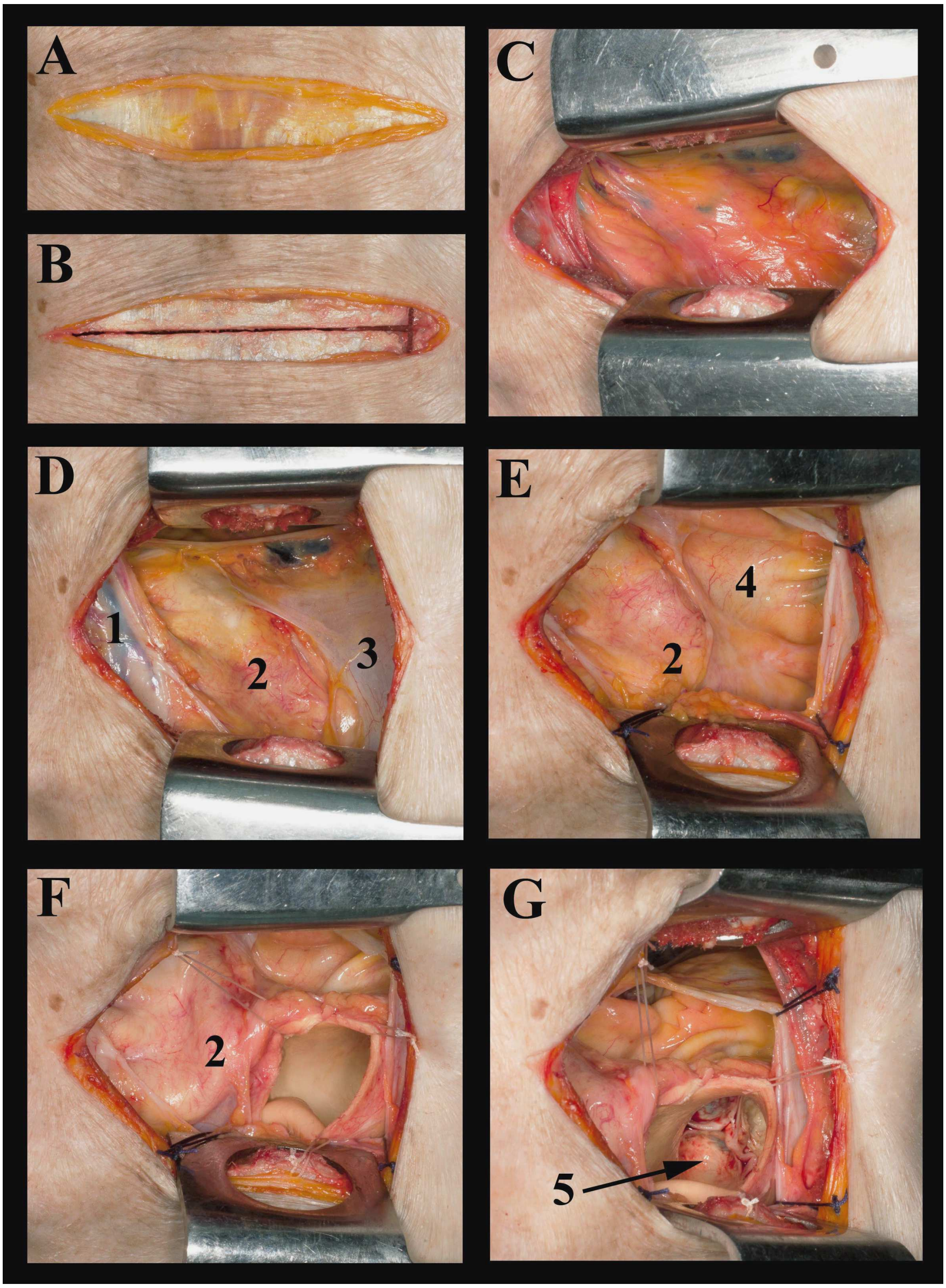

Figure 8: Steps of partial upper sternotomy (cranial direction on the left side). *1: left brachiocephalic vein, 2: ascending aorta, 3: pericardium, 4: pulmonary trunk, 5: aortic valve.*

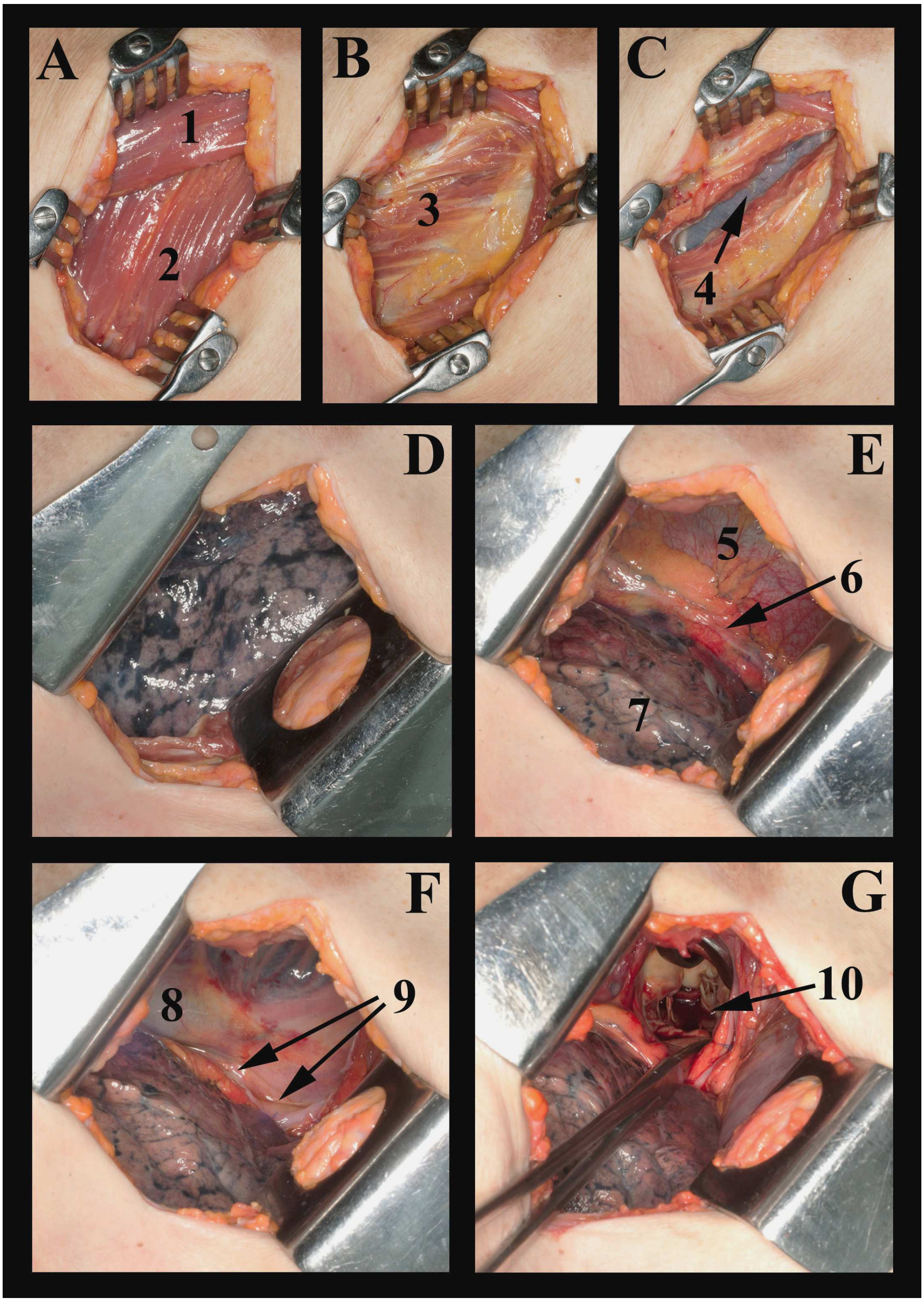

Figure 9: Steps of right anterolateral mini-thoracotomy (cranial direction on the left side).

1: pectoralis major, 2: serratus anterior, 3: intercostal muscles, 4: parietal pleura, 5: pericardium, 6: phrenic nerve, 7: right lung, 8: superior vena cava, 9: right pulmonary veins, 10: mitral valve.

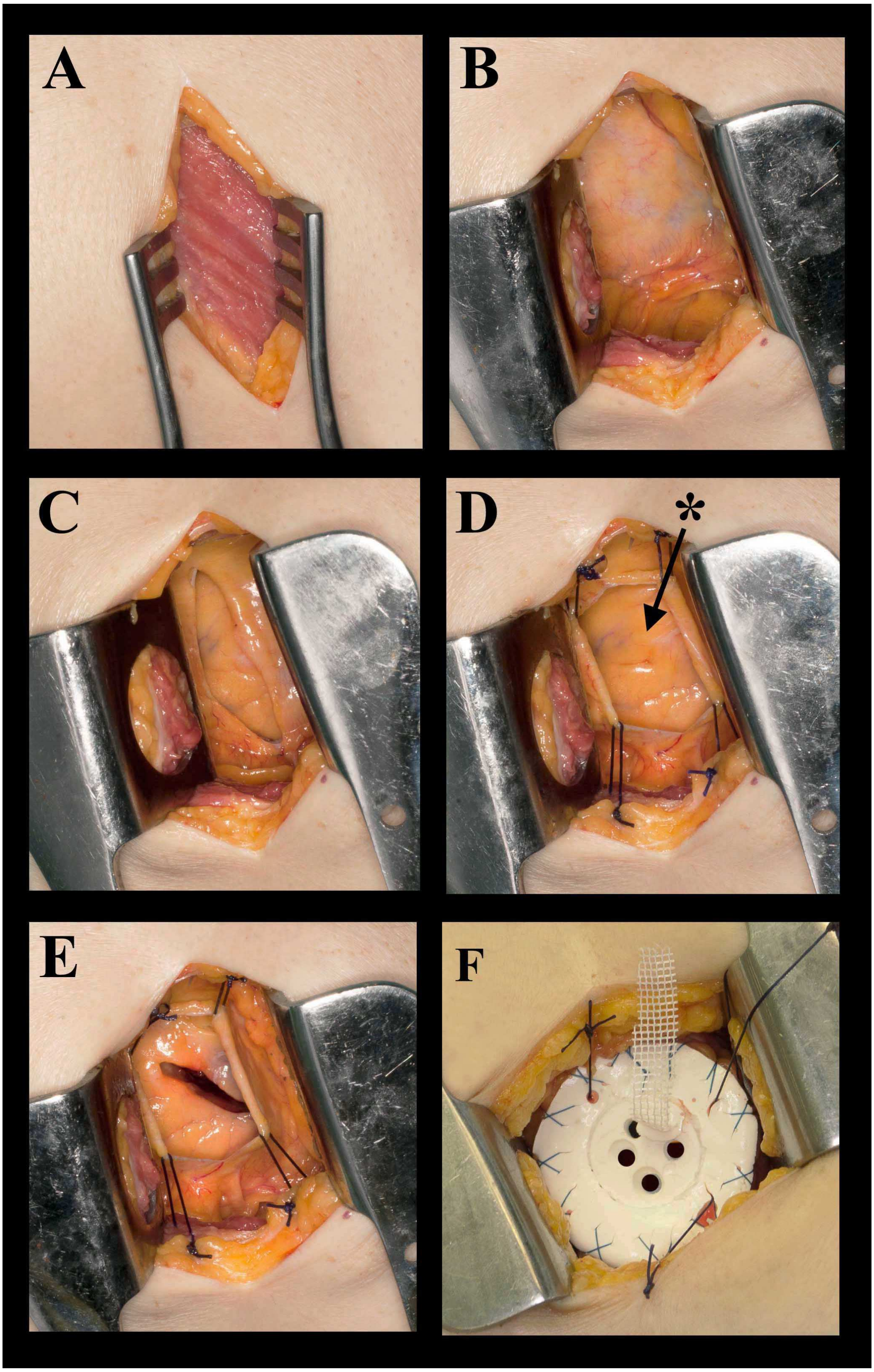

Figure 10: Steps of left anterolateral mini-thoracotomy with an apical silicon port (cranial direction on the right side). * anterior interventricular branch.

The heart and the aformentioned layers of the chest were closed after each approaches with running sutures, reconstructing the original situation. This step gave us the possibility for a real in situ anatomic investigation of the next approaches. The filling of the left ventricle was performed in all cases with the aorta clamped in the interest of optimal pressure and valve closure.

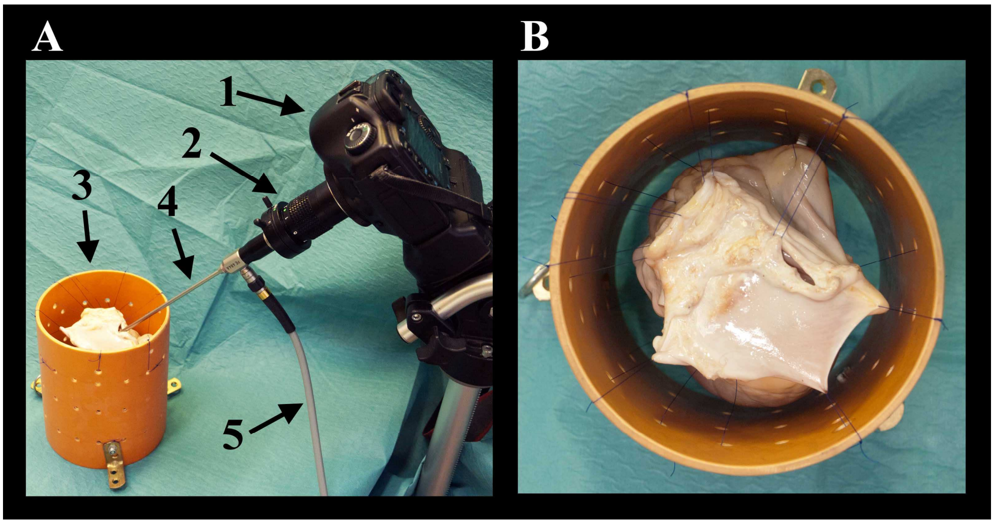

Figure 11: Endoscopic anatomic investigation of the cadaveric hearts removed from the thorax.

1: digital camera (Canon EOS 5D), 2: endoscopic adapter of the camera, 3: plastic cylinder for the hearts, 4: endoscopic optic, 5: light cable.

In the other 30 cases, the hearts were removed from the thorax performing median sternotomy. The aorta and pulmonary artery were resected 2 cm superiorly to the valve commissures. The superior and inferior caval veins and each pulmonary vein were transsected from the right and left atrium leaving a 1 cm cuff. Before endoscopic examination each heart was rinsed in saline solution. The removed hearts were suspended by using a plastic cylinder (20 cm long and 12 cm diameter) with 5 mm holes on it, 2 cm apart. *(Figure 11)* Making stitches around the apex of the heart, the mitral annulus and the left atrium, the natural forms of the atrial and ventricular cavity were simulated. The endoscopic optics were inserted through the three aformentioned incisions: aortic approach, atrial approach and apical approach. The anatomical investigation of the mitral valvular complex was carried out first without filling of the left ventricle, then it was injected under pressure with saline resulting in closure of the mitral leaflets. During this step the aorta was clamped. All views of the mitral valvular complex were documented with colour photographs using a Canon 5D camera with a Canon endoscopic adapter and the rigid, 4 mm endoscopic optics (0, 30, 70 degrees, Aesculap©).

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

4.2.1. Preparation of the cadavers

A conventional median sternotomy was performed and the pericardium was opened. The pulmonary veins were exposed and ligated 1 cm lateral to the left atrium. The left heart was rinsed out with saline injections through a transversal incision of the ascending aorta (1,5 cm distally to the valve commissures). The ascending aorta was ligated. After completing the above steps, the left heart was isolated. The pericardium was sutured and the sternum was closed in order to restore the original anatomic situation.

4.2.2. Surgical technique

After standard left anterolateral mini-thoracotomy in the fifth intercostal space, the pericardium was opened with a 6 cm longitudinal incision 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. The port (*Figure 12/A and 12/B)* consisted of a funnel (outside diameter apical 2 cm, basal 3 cm) with a 1 cm wide outer sheath and a stopper with a total of four holes for the endoscopic optic (4 mm), the endoscopic instruments (2 mm and 4 mm) and a silicon tube (4 mm).

The tube was connected to a system for suction of blood and fluid, saline-injection and CO_2-insufflation.

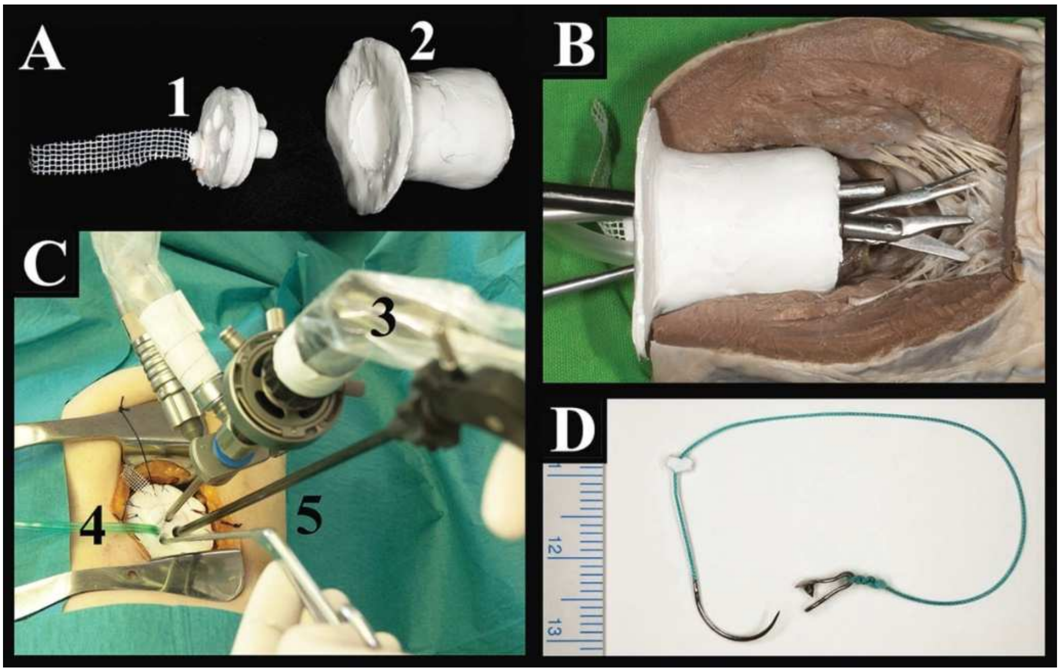

Figure 12: Instrument prototypes for transapical endoscopic mitral repair.
The used apical silicon port (A): 1. stopper with four holes, 2. funnel with an outer sheath. The intraventricular situation of the port in a formaline-fixed heart (B). The intraoperative situation of the placed port (C): 3. endoscopic optic (4 mm, 0 degrees), 4. silicon tube for suction, insufflation and saline-injection, 5. endoscopic instruments. The clip-chord (D).

The endoscope was a rigid 4 mm 0 degrees optic (©Aesculap PE 484A). *(Figure 12/C)* It was introduced into the collapsed left ventricle *(Figure 13/A)* through the first hole of the port. The left heart was pressure-controlled insufflated with CO_2 (10 mmHg) restoring its natural three-dimensional shape. *(Figure 13/B)* The inner site of the silicon port, the walls of the left ventricle, the apical third of the papillary muscles including the origins of the tendinous chords, the anterior and posterior mitral leaflets and the aortic valve were visible. Upon completion of CO_2-insufflation, the left ventricle was injected with saline *(Figure 13/C)*, allowing for assessing chordal length and coaptation area of the leaflets.

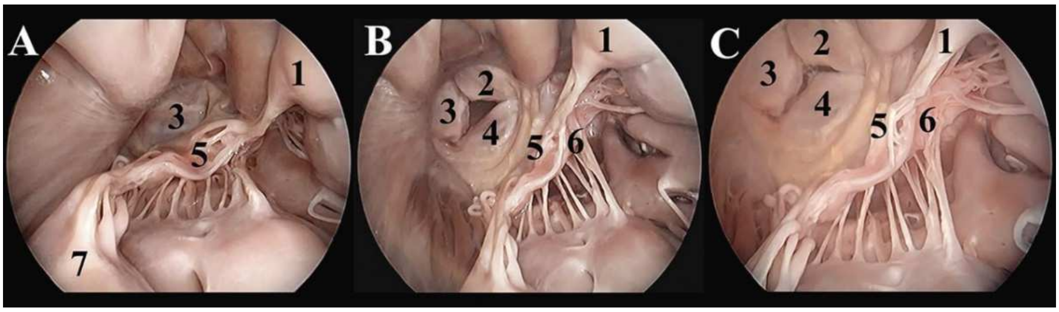

Figure 13: Anatomic structures of the left ventricle (apical endoscopic view). *The mitral valvular complex in the collapsed (A), insufflated (B) and saline-injected (C) left ventricle: 1. anterior papillary muscle, 2. left conary cusp of the aortic valve, 3. right coronary cusp of the aortic valve, 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. 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 12/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 14/A)*

Figure 14: 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 other end of the artificial chord was sutured to the head of the anterior papillary muscle. *(Figure 14/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 14/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, similar to the method of conventional mitral repair procedures. *(Figure 15/A)* The chords were transsected. *(Figure 15/B)* The annulus was plicated at the resected part using plegeted stiches. *(Figure 15/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 15: 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 running suture stitches were begun at the anterolateral commissure. The knots at different steps of the procedure were thrown extracorporeally and tightened with a knot pusher.

The mitral valve competence was tested with pressure-injection of the left ventricle after each individual step. The 1 cm wide outer sheath of the apical silicon-port was separated from its inner parts and the apical closure stiches were placed through this sheath.

5. Results

5.1. Comparative endoscopic anatomic description of the mitral valvular complex

For the sake of the plasticity of the heart and great vessels, determination of parameters for the introduction of the endoscopes was limited. The aforementioned exact anatomic locations for the introduction were clear and by using fixed landmarks, the momentary position of the optic could be determined. Variations in the introducing angle and the accurate deepness were variable and caused by different measures of the individual hearts investigated.

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.

5.1.1.1. Unfilled heart, aortic view 1

For the first view, the introduced 70 degrees 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 was located forming a convex line. The entire ventricular surface of the anterior mitral leaflet could be seen under the aforementioned line. From left to right the A3, A2 and A1 scallops were distinguished. The inserting part of the anterior marginal chords and the two thicker strut chords appeared on that surface of the anterior mitral leaflet. *(Figure 16/a)*

5.1.1.2. Unfilled heart, aortic view 2

For the second view, introducing the endoscopic optic deeper, the upper structure was the line of the aorto-mitral continuity. Under this line one could see the ventricular surface of the anterior mitral leaflet with the insertions of the anterior marginal and strut chords. In addition, the whole length and the origins of the chords were visible on this view. The two bands of chords were convergent on the left and the right half of the picture and originated from the papillary muscles. One could recognize the apical part of the posterior and anterior papillary muscles at 7 o'clock and 5 o'clock, respectively. *(Figure 16/b and Figure 16/c)*

5.1.1.3. Unfilled heart, aortic view 3

On the third view, 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 line of the annulus the atrial surface of the posterior mitral leaflet appeared. From left to right the P3, P2 and P1 scallops could be seen. The chords running to the posterior leaflet converged downward to the posterior papillary muscle on the left side and to the anterior papillary muscle on the right side. The posterior marginal chords were visible in their whole length from the papillary muscles to the margin of the posterior leaflet. However, the insertions of intermediate and basal chords on the ventricular surface were hidden. The P3 and P1 scallops could be examined closely rotating the optic at 30 degrees to both directions around its longitudinal axis, but the posteromedial and anterolateral commissures could not be investigated yet. *(Figure 16/d)*

5.1.1.4. Filled left ventricle, aortic view 4

After filling the left ventricle with saline, the closed mitral valve could be inspected from the aortic valve. In this case, similarly to the open valve, the ventricular surface of the anterior mitral leaflet, as well as, from left to right, the A3, A2 and A1 scallops were represented on the upper half of the view. All the anterior marginal and strut chords 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 because of the closing of the mitral valve. The posterior papillary muscle was visible on the left side of the view at 7 o'clock and the anterior papillary muscle on the right side at 5 o'clock. The commissures and the coaptation line could not bee seen directly. The entire distended subvalvular apparatus, as well as the closing function of the valve could be investigated. *(Figure 16/e)*

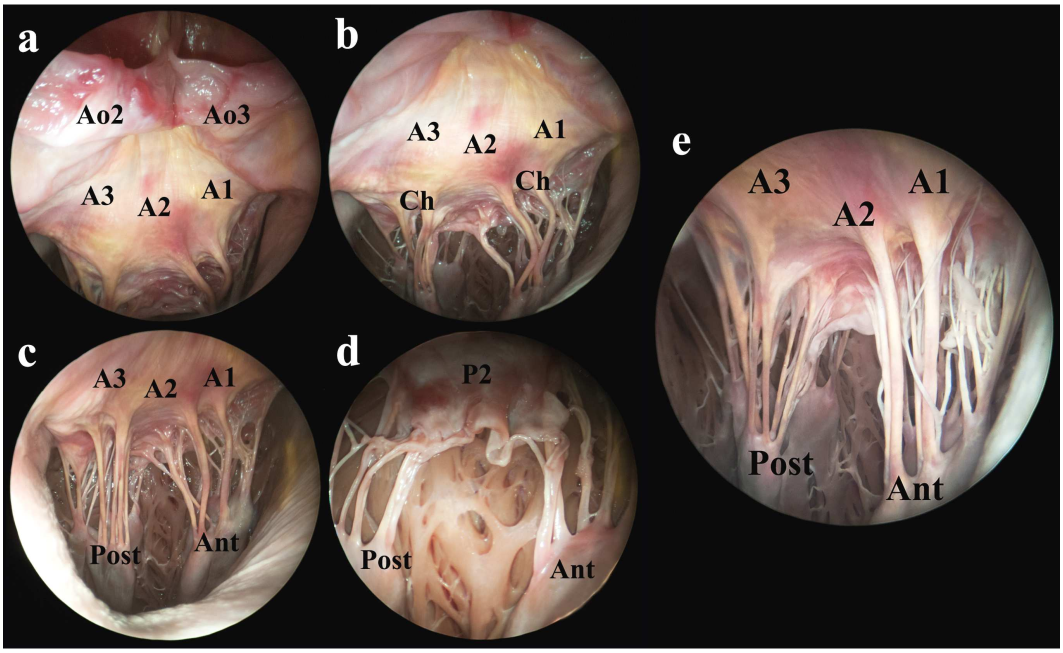

Figure 16: The endoscopic view of the mitral valve, introduced a 70 degrees rigid endoscope through the aortic valve without (a-d) and with saline-filling (e) of the left ventricle.

5.1.2. 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. These two optics gave about the same views.

5.1.2.1. Unfilled heart, atrial view 1

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, at 10 o'clock. From left to right, the atrial surfaces of the A1, A2 and A3 scallops were visualised, terminated by the posterolateral commissure at 2 o'clock. 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. Conversely, the visibility of strut, posterior intermediate and basal chords were limited. These chords could be followed from their origins on the papillary muscles, but their insertions on the ventricular surface of the leaflets could not be seen. 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. The standard and deviant clefts of the posterior leaflet were located between the scallops, as small fissures. *(Figure 17/a and Figure 17/b)*

5.1.2.2. Unfilled heart, atrial view 2

Introducing the 70 degrees endoscope into the orifice of the mitral valve, the structures of the subvalvular apparatus could be examined in richer detail. The anterolateral commissure was positioned at 12 o'clock. The P1, P2 scallops of the posterior leaflet, as well as the A1, A2 scallop of the anterior leaflet could be followed straggling downwards from the high middle located commissure, with P1, P2 on the left side of the view and A1, A2 on the right side. The chords, originating from the anterior papillary muscle, were seen in the central zone of the view, encircled by the atrial surfaces of the leaflets. The commissural chords were located on the main vertical axis of the view, surrounded by the posterior marginal chords on the left and the anterior marginal chords on the right. While the marginal chords could be visualised in their whole length, the visualisation of the insertions of the posterior intermedier and basal chords was limited. The anterior papillary muscle was situated in the middle on the bottom of the view. *(Figure 17/c)*

5.1.2.3. Unfilled heart, atrial view 3

After a 90 degree rightward rotation of the endoscope around its longitudinal axis, the atrial surface of the anterior mitral leaflet became visible, as well as its upper border, the line of aorto-mitral continuity. On the surface of the tongue-shaped anterior leaflet all three scallops, such as, from left to right, A1, A2 and A3 could be characterized. Under the free margin of the leaflet, the downward straggling anterior chords could be investigated.

5.1.2.4. Unfilled heart, atrial view 4

Rotating the optic by another 90 degrees, the posteromedial commissure could be seen, offering a similar view as before described by the anterolateral commissure, just with opposite directions. The posteromedial commissure was situated at 12 o'clock. The atrial surfaces of the leaflets were downwards straggling, with the A3 scallop on the left side of the view and the P3 scallop on the right side. In the middle zone of the view, the aforementioned commissural, anterior marginal, posterior marginal, intermediate and basal chords could be visualised. The posterior papillary muscle was positioned in the middle in the bottom part of the view. *(Figure 17/d)*

5.1.2.5. Unfilled heart, atrial view 5

After another 90 degrees right rotation of the endoscope around its longitudinal axis, the atrial surface of the posterior leaflet filled in the field of vision with its subvalvular apparatus. Under the line of the mitral annulus, all three scallops of the leaflet could be seen, with the P3 scallop on the left side, the P2 scallop in the middle and the P1 scallop on the right side of the view. Under the free margin of the leaflet, few detailes of the subvalvular apparatus, especially the posterior marginal chords were found.

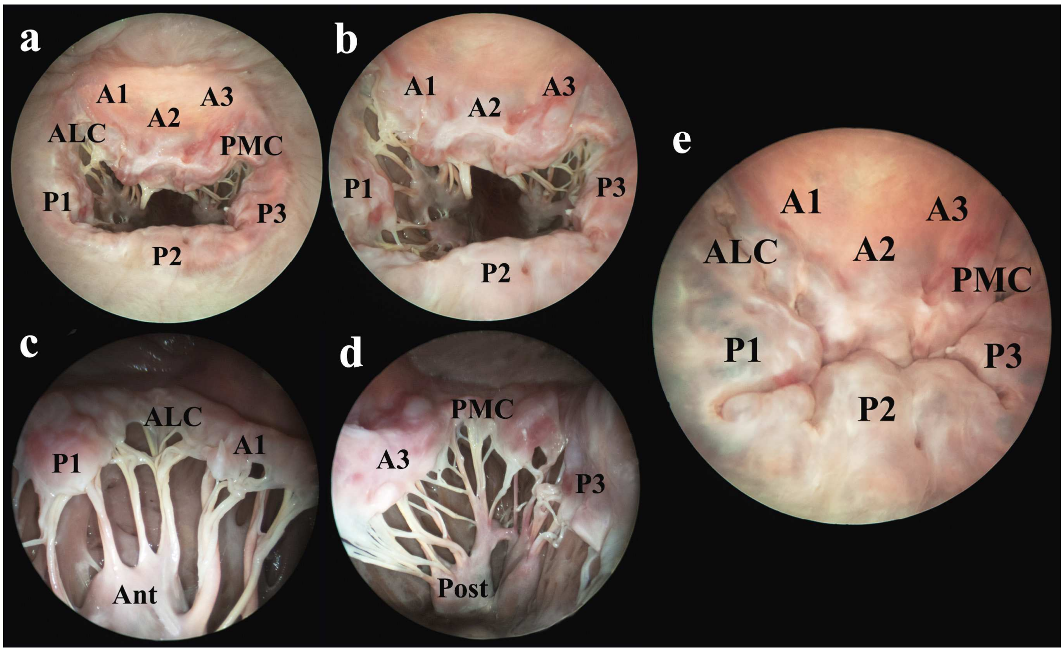

Figure 17: The endoscopic view of the mitral valve, introduced a 0 (a, b) and a 70 (c, d) degrees endoscope through the left atrium without (a-d) and with saline-filling (e) of the left ventricle.

5.1.2.6. Filled left ventricle, atrial view 6

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. On the upper side of the view, the A1, A2 and A3 scallops of the anterior leaflet were situated between the anterolateral commissure on the left and the posteromedial commissure on the right. Under the semilunar coaptation line, the P1, P2 and P3 scallops of the posterior leaflet could be characterized, as well as the bordering standard and deviant clefts on its surface. *(Figure 17/e)*

5.1.3. Apical view

After testing the apical approach with different endoscopic optics, 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.

5.1.3.1. Unfilled heart, apical view 1

Introducing the 0 degrees endoscope through the apical incision, the trabecules of the left ventricle were the first to appear in the field of vision. Directing the anterior wall of the left ventricle in the upper part of the view, the interventricular septum was situated on the left, the left marginal wall on the right and the posterior wall in the bottom part of the view. The different anatomical variations of the trabecules filled in the foreground of the view as myocardial bridges. The mitral valve was suspected in the deep.

5.1.3.2. Unfilled heart, apical view 2

Examining the mitral valve deeper in the left ventricle, 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 and the two strut chords could be identified as they reached the free margin and the ventricular surface of the anterior leaflet, starting from their origin on the posterior and anterior 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 not 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 18/a, Figure 18/b, Figure 18/c and Figure 18/d)*

5.1.3.3. Filled left ventricle, apical view 3

After filling the left ventricle with saline under pressure, the optimal visual examination of the closed mitral leaflets and the subvalvular apparatus was possible with the 0 degrees endoscopic optic. The view was just the same as without saline-filling. Under the three leaflets of the aortic valve and the aorto-mitral continuity, from left to right, the posteromedial commissure, the A3, A2, A1 scallops of the anterior leaflet and the anterolateral commissure were situated.

Under the coaptation line, similarly from left to right, the P3, P2 and P1 scallops of the posterior leaflet, along with their bordering clefts were positioned. The posterior papillary muscle was located on the left side and the anterior papillary muscle on the right side of the coaptation line. All the distended anterior and posterior chords could be visualised in their whole length, originating from the papillary muscles and the free wall of the left ventricle, and inserting on the free margins and the ventricular surfaces of the leaflets. The line of the mitral annulus was located in the angle of the posterior leaflet and the wall of the left ventricle. *(Figure 18/e)*

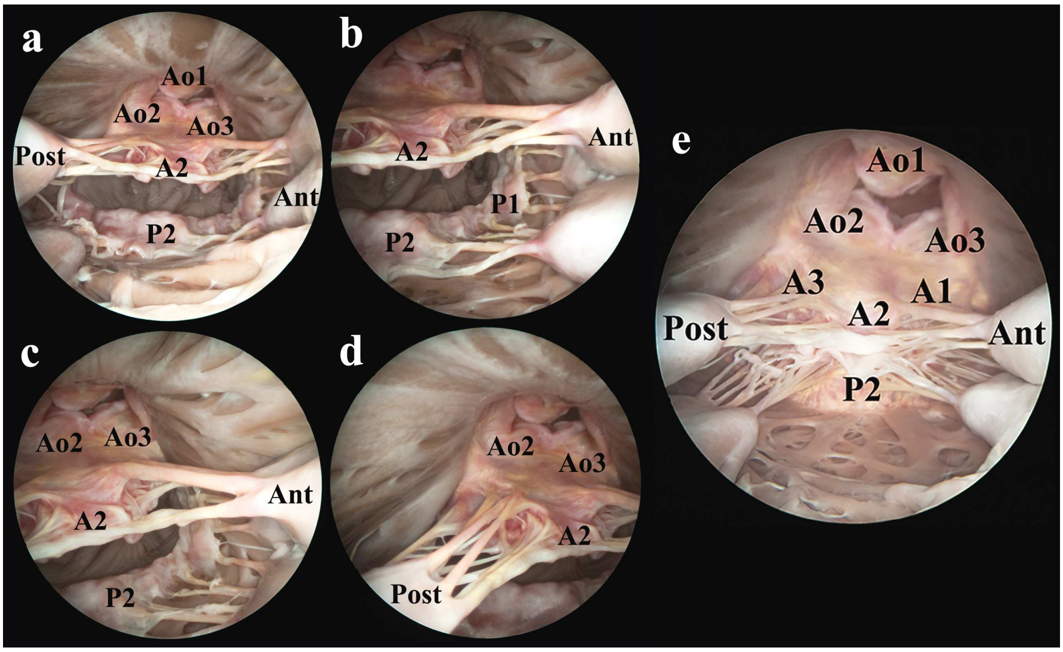

Figure 18: The endoscopic view of the mitral valve, introduced a 0 degrees rigide endoscope through the apex of the heart without (a-d) and with saline-filling (e) of the left ventricle.

Generally all mitral valves could be visualised perfectly using any of the described methods without any significant difficulties. The techniqually easiest approach was the atrial. Using the aortic and apical approaches some anatomical variations such as pathological findings influenced the investigation. We refer to two important aspects: first, the left ventricular hypertrophy and second, the length of the chords. Left ventricular hypertrophy resulting in smaller cavity measures limited free movement of the optics and thus the visualisation of all details in case of the aortic and exspecially the apical approaches. In case of the aortic approach, relatively short chords resulted in difficulties when the endoscope was introduced between the chords of the anterior mitral leaflet to observe the posterior leaflet. The visibility of the mitral valvular complex and the aortic valve generally using the investigated approaches was summerized in *Table 2*.

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 using the left atrial approach has been published in the last couple of years [35-47]. Publications focusing on anatomic aspects as well as methodical issues reported overall good results of this procedure. The left atrial approach offers optimal visualisation of the mitral valve leaflets. The subvalvular apparatus can only be visualised when the valve is opened. At the sealing probe surgeons do not become any direct visual information about the status of the papillary muscles and tendinous chords. To solve this problem in other previous publications an impressive transapical in vivo endoscopic imaging of the mitral and tricuspid valves has been described [65-67]. In these cases a cardiopulmonary bypass circuit supported the systemic organ perfusion and a separate transparent fluid circuit in the left heart allowed for visualisation of intracardiac structures. Anatomic structures were only described in general terms, but these publications outlined a novel approach and method for future valve repair procedures under beating heart conditions. The endoscopic investigation through blood was described by a beating heart animal model [68]. The top of the endoscope introduced into the left ventricle was covered with a convex Plexiglass and the tissues in front of the cardioscope could be seen. Other animal and human studies were using beating heart models to investigate the movement of intracardiac structures by explanted hearts [70, 71]. An endoscopic optic was introduced through the great vessels. Dynamic images of the motion of different valves during contraction and relaxation phases of the cardiac cycle will lead to a more profound understanding of cardiac physiology, pathology and pathophysiology. Under echocardiography guidance it was possible to implant transapical neochords in off-pump animal and clinical studies [53-55]. Using the complex, apically introduced NeoChord© DS1000 system (NeoChord Inc, Minneapolis, Minnesota) after fixing on the leaflet margin the length of the neochords was adjustable from the outside [51, 52]. Transapical mitral valved stent implantations were described in native valves under transoesophageal echocardiography guidance in animal experiments [72, 73], clinical studies [74], as well as clinical valve-in-valve implantations by deteriorated bioprotheses [75, 76]. Both the neochord implantations and mitral valve stent implantations outline the real possibility and importance of transapical procedures in mitral valve surgery.

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 used revealed new visual information on the examined structures. The description of those three different entries studied in this publication highlights their individual advantages and drawbacks in detail. 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. For artificial chord replacement we prefer a complementary view near the conventional atrial approach. The aortic or apical view could help at the implantation of chords as well as the functional investigation of the subvalvular apparatus by filling the left ventricle. For edge-to-edge repair techniques the apical view using biportal endoscopic control is preferable since it allows for perfect visibility of the coaptation line. The in vivo intraoperative transapical introduction of an additional endoscope requires a separate left mini-thoracotomy in standard minimally invasive mitral repairs or the displacement of the heart including distorsion of the anatomy in median sternotomy cases. The introduction of an additional optic through the aortic valve is possible by just performing a small aortotomy in median sternotomy approaches. The surgeon has to decide in each case weather perfect visualisation or minimal access surgery is more important.

Various concepts of endoscopic port access for different clinical applications have been described in the literature. On the basis of our anatomic study, the transapical approach offers the most complex view of the mitral valve with its subvalvular apparatus. In experimental transapical mitral valve surgery the endoscope has been introduced through a translucent outer sheath. Continuous saline infusion was applied between the cardioscope and the sheath to facilitate manoeuvering the scope [65-67]. In single-port laparoscopic surgery various umbilical ports are used, to allow for unobstructed instrumental manipulations in the abdominal cavity [77, 78]. Closure of the port site can be approached in different ways. In transapical aortic valve implantations two plegeted purse-strings of transmural deep bites are prepared prior to introducing the apical port. Upon closure of the port site the actual port is removed entirely [49]. Our self-designed 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. The movable stopper in the funnel was particularly useful for the insertion of needles, cords and clips. Beyond that, efficient CO_2-insufflation, suctioning, and pressure-injection of saline and elaborate endoscopic intraventricular imaging are additional features of the port we designed for our experimental study. In this study a 2 cm apical port was placed. In order to minimize myocardial injuries in vivo the diameter of the port should be reduced.

Beating heart experimental animal studies were performed in blood-filled ventricles [68] or by using two separated circles with transparent solutions in the left heart [65-67]. One of the most challenging problems of our technique was the collapsed left ventricle. This is the first description of gas-insufflation of the left heart. Pressure-controlled CO_2-insufflation in the beginning of the procedure allowed us to restore the geometry of the collapsed left ventricle. 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.

A flexible gastroscope with a clip-applier has been described to perform edge-to-edge repairs in beating heart studies [66]. 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. 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.

In recent publications on animal studies simple clips without an attached cord have been implanted [66]. In other off-pump animal studies the length of the implanted neo-chord was adjustable from the outside using echocardiography guidance [53-55]. 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. The cord connected to the clip was inserted into the papillary muscle with an attached needle. Determining the correct length of the clip-chord was the most crucial step of the implantation. The measurement was performed after filling the left ventricle with saline to simulate its natural shape under direct endoscopic visual control.

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. Our approach allows for a ring implantation from the ventricular side based on identifying the angle between the posterior leaflet and ventricular wall and hence after visualizing the exact outline of the mitral annulus.

Our repair procedures were carried out in the isolated left heart, the pulmonary veins and the aorta were ligated. How could this experimental cadaveric model be applied by in vivo models? In-vivo animal studies are required to demonstrate the advantages of our strategy in the context of extracoporeal circulation. Femoro-femoral cannulation using an endoaortic clamp for aortic occlusion, aortic root venting and delivery of antegrade cardioplegia, as well as endopulmonary venting and decompression of the pulmonary circulation have been described [38]. The beating heart application of our transapical method is limited due to insufficient endoscopic visualization in non-transparent solutions such as blood.

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. At this point we are convinced that the findings of our experimental studies have demonstrated significant advantages for minimal invasive mitral valve repair procedures. 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.

7. References

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9. Publications and presentations

9.1. 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

9.2. 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.

9.3. 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)

9.4. Presentations

1. ***Ruttkay T***, *Galajda Z, Patonay L*
Comparison of two approaches for biportal endoscope-assisted mitral valve repair: an anatomical study.
X. National Congress of Anatomy with International Participation
Marosvásárhely, Romania (2009)

2. ***Ruttkay T***, *Galajda Z, Patonay L*
Morphologic investigation of the mitral subvalvular apparatus, specifically the endoscope-assisted mitral valve repairs.
XV. Congress of the Society of Hungarian Anatomists
Budapest, Hungary (2009)

3. ***Ruttkay T.***
   Surgical anatomy of the heart and its importance.
   Congress for normal and pathologic development of the cardiovascular system, actual questions of the modern congenital cardiac surgery
   Debrecen, Hungary (2010)

4. *Grimm A,* ***Ruttkay T****, Baksa G, Glasz T, Galajda Z, Patonay L.*
   The anatomic bases of the greater omentum autotransplantation applied by arterial circulation disorders of the lower limb.
   XVI. Congress of the Society of Hungarian Anatomists
   Pécs, Hungary (2011)

5. ***Ruttkay T****, Baksa G, Glasz T, Patonay L, Galajda Z.*
   Transapical endoscopic mitral repair.
   XVIII. Congress of the Society of Hungarian Cardiac Surgeons
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6. *Nagy H,* ***Ruttkay T****, Czeibert K, Baksa G, Patonay L.*
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