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CICLO XXVII

MITRAL VALVE POSTERIOR LEAFLET MORPHOLOGY REVISITED FROM PATHOLOGICAL ANATOMY TO THREE-DIMENSIONAL ECHOCARDIOGRAPHY EVALUATION: IMPLICATIONS IN PATIENTS WITH MYXOMATOUS DISEASE FOR SURGICAL PROCEDURES

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Dedica

Vorrei dedicare questa tesi dapprima ai miei genitori che purtroppo non sono riusciti a vedermi realizzata e oggi non potranno gioire con me di questo grande e nuovo risultato: "***a mio Padre***" che mi ha lasciato a 18 anni dopo un tragico incidente e che quando i primi tempi mi vedeva spaventata dalle prime esperienze in università mi diceva sempre: "Hai voluto la bicicletta adesso devi pedalare", che è stato il modello migliore di entusiasmo della vita e di Amore per il lavoro e "***a mia madre***" che non è riuscita a vedermi specializzata ma che è stata la silenziosa colonna portante di quasi tutti gli anni dell'università a Roma, lavoratrice indefessa, piena d'amore per suo marito e per i suoi figli che amava definire " il suo gioiello più bello".

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ABSTRACT IN INGLESE

MITRAL VALVE POSTERIOR LEAFLET MORPHOLOGY REVISITED FROM PATHOLOGICAL ANATOMY TO THREE-DIMENSIONAL ECHOCARDIOGRAPHY EVALUATION: IMPLICATIONS IN PATIENTS WITH MYXOMATOUS DISEASE FOR SURGICAL PROCEDURES

Key words: mitral valve, echocardiography, anatomy, leaflet morphology, three-dimensional

BACKGROUND

The perfect function of the mitral valve is linked to the anatomical conformation and physiological interaction of all the component of the mitral valve complex (leaflets, annulus, chordae, papillary muscles, left ventricle). The most important component of the valve are the leaflets. The nomenclature and the number of the leaflets are divergent in different studies. Usually the clinical Carpentier's Classification is used, which identifies three posterior leaflet scallops: from antero-lateral (P1) to central (P2) and postero-medial (P3). The terminology of mitral valve leaflet is a lot debated in the scientific literature. The aim of the study is to analyze the variability of the anatomy of posterior leaflet in normal subjects (Autoptic and cardiectomy specimens) and patients with myxomatous disease (three dimensional echocardiography) for assess possible difference and similarity. In patient with myxomatous disease we evaluate the clinical influence of the anatomy of the posterior leaflet on the planning of the mitral valve surgical repair strategy.

MATERIALS AND METHODS

Thirty normal heart specimens without mitral valve disease, were examined by three independent observers (two pathologists and 1 cardiologist). The specimens which had been fixed in formalin following autopsy or cardiectomy, were selected in the anatomo-pathological heart collection of Padua University. The mitral valve was opened along the optus margin of the heart and evaluated. It was used a new terminology and call the normal physiological indentation, deep more than 50% of the leaflet high, "subcommisure" and the simple indentation ,deep less than 50% ,"incisure". The subcommissure and incisure with relative chordae tendineae were studied in detail. Special attention was given to (1) the number of the scallops of posterior leaflet with (2) the characterization of the subcommisure and incisure, to (3) the high and the width of every single scallop, and to (4) to the high of the leaflet in correspondence of subcommisure, incisure and commisure; to (5) the morphology of the chordae tendineae at the sites of insertion in the commisure, subcommisure and incisure. In all specimens the total annular circumference was measured . From a large database of 706 patients (pts) consecutively admitted to the Cardiovascular Department of San Raffaele Hospital, from January 2008 to December 2012 with a diagnosis of severe mitral regurgitation, we analysed the first 238 consecutively enrolled. All the patients were studied with pre-operative two dimensional (2D) and three dimensional (3D)

Trans-oesophageal echocardiography (TOE) and submitted to surgical repair of the mitral valve.
We analyzed also the 3D TOE imaging (zoom 3D acquisitions) in order to establish the presence of subcommisure and incisure in patients affected by myxomatous disease. All examinations were stored in TomTec system and analyzed retrospectively with 3D dedicated software. Eighty eight examination were excluded: 1) for low quality of imaging and/or absence of 3D acquisition, 2) left anterior prolapse with no good evaluation of posterior leaflet anatomy.
In 163 pts I reconstructed with Tomtec system the zoom 3D morphology of the mitral valve in order to study the leaflet's characteristics and to establish a clinical correlation with the type of surgical repair. The total patients population was divided in two groups A and B according to the type of surgical repair technique used , respectively simple and complex.

RESULTS

"Anatomic results"

There were variability in the number of scallop of posterior leaflet (PL): only 1 sample has 1 scallop (mono-scallop, 3,3%) and another one has 5 scallop, 2 samples have 2 scallops (bi-scallop, 6,6%), the major number of posterior leaflets are three scallops (63%) and 7 samples have 4 scallops (23%).Mean total annulus circumference was 9,6 ±1,25 cm. We identified a subcommisure as an indentation between two leaflets deeper than 50% of the high of the leaflets with fun like chordae very similar to the commissures, an incisure as an indentation in a scallop with an high less than 50% of the leaflets high and with or without small marginal chordae. In all sample we found: 23 total number of incisure, 4 incisure with chordae fun like and 19 incisure without chordae. The major number of incisure were on the posterior leaflet (19) and less on anterior (4). In the PL they were present more frequently in the central scallop P2 (9, 47%) and less on P3 ad P1 (5 and 3, 26% and 16 %, respectively).

"Echocardiographic results": at the first analysis there is a predominant incidence of posterior leaflet prolapse. In the total population analyzed I found 46 bileaflet prolapse (28%), 117 posterior leaflet prolapse (72%), Ninety five pts with flail (58%). The Type of posterior prolapse was: P2 involvement 142 pts (87%), other than P2 21 pts (13%), monolobate P2 45 pts (31%), bilobate P2 48 (33%), biscallop P2 62 (44%), number of incisure 61 (on posterior and anterior leaflet), number of pts with 2 subcommisure 99 (60%), number of pts with >2 subcommisure 65 (40%), intercommissural extension of the prolapse lesion: 2D evaluation 18,4 mm (±5,5) and 3D evaluation 28,5 mm (±11,12). The patients were divided in two groups according to the presence of simple (group A 49 pts) and complex surgical repair (group B 114) In the **Group A** (49 pts) the type of lesion and morphology were: 15 bileaflet prolapse (30%), type of posterior prolapse P2 involvement 39 pts (79%), other than P2 10 pts (20%), monolobate P2 20 pts (41%), bilobate P2 13 (26%), biscallop P2 18 (36%), number of incisure 11(18%, on posterior and anterior leaflet), number of pts with 2 subcommisure 36 (73%), number of pts with >2 subcommisure 13 (26%), intercommissural extension of the prolapse lesion: 3D evaluation 25,7 mm. In the **Group B** (114 pts): Type of lesion and morphology were: 31 bileaflet prolapse (27%) , type of posterior prolapse: P2 involvement 101 pts (89%), other than P2 13 pts (11%), monolobate P2 25 pts (22%), bilobate P2 35 (30%), biscallop P2 50 (44%), number of incisure: 50 (44%, on posterior and anterior leaflet), number of pts with 2 subcommisure 63 (55%), number of pts with >2 subcommisure 51 (45%), intercommissural extension of the prolapse lesion: 3D evaluation 29,5 mm. I found the same prevalence in normal valves and in the myxomatous mitral valve diseases of the of three scallop morphology (about 30%), the posterior scallops are more wide and long in the myxomatous valve than in normal valve examined, according to the past literature. Also the annulus has more high dimension in myxomatous pts vs normal subjects. In the group B submitted to a complex surgical repair of the mitral valve prolapse I have found a major incidence of incisure (50/61) and a major incidence of bilobate P2 lesion and biscallop P2 (major incidence also of more than 2 commisure). I have found also a significative difference in the evaluation of intercommisural prolapse lesion extension with two-dimensional vs three-dimensional echocardiography, due to the different power of the two imaging technology (18,4 vs 28, 5 mm, mean values). In the group B submitted to a complex mitral valve surgery repair there is a major intercommissural extension of the prolapse lesion (29,8 vs 25,8 mm, mean values). In the group A there is a prevalence of three scallops with monolobate morphology of the posterior leaflet (with 2 subcommissure 73%).

CONCLUSIONS: This study analyzed deeply the anatomy of the normal leaflets in order to establish the incidence of the presence of subcommisure and incisure. In the field of very debated past literature, this study introduce a new terminology and call the normal physiological indentation, deep more than 50% of the leaflet high, “subcommisure” and the simple indentation ,deep less than 50% ,“incisure”. This nomenclature is supported by the insertion on the subcommissure of tendineae chordae funny like very similar to the commissure ones. The main results of my PhD thesis are: 1° the same prevalence in normal valves and in the myxomatous mitral valve diseases of the of three scallop morphology (about 30%); 2° the posterior scallops are more wide and long in the myxomatous valve than in normal valve examined, according to the past literature; 3° The annulus ‘ dimensions are major in the myxomatous disease vs normal mitral valve; 4° in the group B submitted to a complex surgical repair of the mitral valve prolapse I have found a major incidence of incisure (50/61) and a major incidence of bilobate P2 lesion and biscallop P2 (major incidence also of more than 2 commissure); 5° I have found also a significative difference in the evaluation of intercommisural prolapse lesion extension with two dimensional vs three-dimensional echocardiography, due to the different power of the two imaging technology; 6° In the group B submitted to a complex mitral valve surgery repair there is a major intercommissural extension of the prolapse lesion (29,8 vs 25,8 mm, mean value); 7° in the group A there is a prevalence of three scallops with monolobate morphology of the posterior leaflet (with 2 subcommissure 73%).
This study assess that in the analysis of severe myxomatous mitral valve incompetence, is essential to establish with a pre-operative three-dimensional echocardiography the presence of the subcommissure and the incisure, and the intercommissural extension of the prolapse lesion, those elements are important determinants to guide an optimal surgical repair treatment .

ABSTRACT IN ITALIANO

MORFOLOGIA DEL LEMBO POSTERIORE MITRALICO DALL'ANATOMIA PATOLOGICA ALLA VALUTAZIONE CON ECOCARDIOGRAFIA TRIDIMENSIONALE: IMPLICAZIONI NELLA SCELTA DELLA TECNICA CHIRUGICA RIPARATIVA NEI PAZIENTI CON MALATTIA MIXOMATOSA.

Parole chiavi : valvola mitrale, ecocardiografia, anatomia, morfologia del lembo. Tridimensionale.

Introduzione

La corretta funzione della valvola mitrale è legata alla conformazione anatomica e all'interazione di tutte le componenti del complesso valvolare mitralico (lembi, anello, corde tendinee, muscoli papillari, ventricolo sinistro). La componente più importante della valvola sono i lembi. La nomenclatura ed il numero dei lembi è diversa in studi presenti in letteratura. La classificazione piu' comunemente utilizzata è quella di Carpentier, che identifica nel lembo posteriore tre scallop: dall'antero-laterale (P1) al centrale (P2) e il postero-mediale (P3). La terminologia della morfologia descrittiva dei lembi mitralici è molto dibattuta nella letteratura scientifica. Lo scopo dello studio è analizzazre la variabilità anatomica del lembo posteriore nei soggetti normali (campioni da cuori autoptici e donatori per trapianto) e in pazienti con malattia mixomatosa (ecocardiografia tridimensionale) per stabilire possibili differenza. Nei pazienti con malattia mixomatosa vogliamo valutare inoltre la possibile influenza dell'anatomia del lembo posteriore sulla pianificazione della strategia chirurgica riparativa.

Materiali e Metodi

Nello studio anatomo patologico sono stati selezionati ed esaminati da tre osservatori indipedenti (2 anatomopatologi ed un cardiologo) trenta campioni di cuori normali, senza patologia della valvola mitrale.
I campioni erano stati fissati in formalina dopo autopsia o donazione da espianto, e sono stati selezionati dalla collezione anatomopatologica della Università di Padova.
La valvola mitrale è stata aperta lungo il margine ottuso del cuore e valutata. E' stata usata una nuova terminologia che definisce le fisiologiche indentature con altezza maggiore del 50% rispetto al lembo adiacente "subcommissure" e le indentature con altezza inferiore al 50% "incisure". Sono state studiate in dettaglio le subcommissure e le incisure con le relative corde tenidinee.
E' stata effettuata una attenta valutazione al (1) numero degli scallop del lembo posteriore con (2) la caratterizzazione delle subcommisure e delle incisure, (3) all'altezza e all'ampiezza di ogni singolo scallop e (4) all'altezza dei lembi in corrispondenza delle subcommissure , delle incisure e delle commissure; (5) alla mrofologia delle corde tendinee nel sito di inserzione a livello delle commissure, subcommissure ed incisure. In tutti I campioni è stata misurata la lunghezza della circonferenza dell'anello. Da un grande database di 706 pazienti consecutivamente ricoverati copn diagnosi di insufficienza mitralica severa, da gennaio 2008 a Dicembre 2009 nel dipartimento Cardiovascolare dell'ospedale San Raffaele, sono stati analizzati I primi 238 paziente arruolati consecutivamente. Tutti i pazienti sono stati valutati

con ecocardiogramma transesofageo (TEE) bidimensionale (2D) e tridimensionale (3D) e sottoposti successivamente ad intervento cardiochirurgico di riparazione della valvola mitrale.
Abbiamo analizzato le acquisizioni zoom 3D transesofagee per stabilire la presenza di subcommissure e incisure in pazienti affetti da malattia mixomatosa. Tutti gli esami sono stati salvati sul sistema di archivio e analisi Tomtec e analizzati retrospettivamente con programmi tridimensionali dedicati all'analisi valvolare. Ottantotto esami sono stati esclusi per : 1) bassa qualità delle immagini o assenza delle acquisizioni tridimensionali, 2) prolasso dominante del lembo anteriore con scadente visualizzazione dell'anatomia del lembo posteriore.
In 163 pazienti sono state ricostruite le immagini delle acquisizioni zoom 3D della valvola mitrale con il sistema Tomtec, per studiare le caratteristiche dei lembi e stabilire una correlazione clinica con il tipo di tecnica chirurgica riparativa usata. Il gruppo di pazienti della popolazione totale è stato diviso in due sottogruppi A e B in base alla tecnica riparativa usata, semplice (A) e complessa (B) rispettivamente.

Risultati

"Risultati Anatomici" :

Abbiamo troavto la seguente variabilità morfologica nel numero di scallop del lembo posteriore: solo 1 campione aveva uno scallop (mono-scallop, 3,3%) e un solo campione aveva 5 scallop (3,3%), 2 campioni avevano 2 scallop (6,6%), il numero maggiore di campioni (19) aveva 3 scallop (63%) e 7 campioni avevano 4 scallop (23%). La media della circonferenza totale dell'anello era 9,6 ±1,25 cm. Abbiamo identificato come subcommissura una indentatura profonda più del 50% dell'altezza del lembo con corde a festone molto simili alle corde commissurali, una incisura come un'indentatura in uno scallop con un'altezza inferiore al 50% dell'altezza del lembo con o senza piccole corde marginali. In tutti I campioni abbiamo trovato un totale di 23 incisure, 4 incisure con corde e 19 incisure senza corde. Il maggior numero delle incisure era sul lembo posteriore (19) e meno sull'anteriore (4). Nel lembo posteriore erano presenti più frequentemente nello scallop central P2 (9,47%) e meno sugli scallop P3 e P1 (5 e 3 , 26% e 16% rispettivamente).

"Risultati Ecocardiografici": ad una prima analisi risulta una incidenza predominante del prolasso del lembo posteriore ed in particolare dello scallop central P2. Nella popolazione totale ho trovato 46 prolassi bilembo (28%), 117 prolassi del lembo posterior (72%), 95 pazienti con flail (58%). Il tipo di prolasso del lembo posteriore era: conivolgente lo scallop P2 142 pts (87%), altro che P2 21 pz (13%), con morfologia di P2 monolobato: 45 pts (31%), P2 bilobato 48 (33%), P2 biscallop 62 (44%) , un numero di incisure: 61 sui due lembi, numero di pz con 2 subcommissure: 99 (60%), numero di pz con più di 2 subcommissure : 65 (40%), l'estensione intercommissurale della lesion prolassante era: alla valutazione bidimensionale 18,4 mm (±5,5) e alla valutazione tridimensionale 28,5 mm (±11,12). I pazienti sono stati divisi in 2 gruppi in base alla presenza di chirurgia semplice (gruppo A 49 pz) e chirurgia complessa (Gruppo B 114 pz). Nel gruppo A (49 pz) il tipo di lesione e la morfologia erano: 15 pz con prolasso bi-lembo (30%), tipo di prolasso posteriore: coinvolgente P2 in 39 pz (79%), altro tipo non P2 10 pz (20%), P2 monolobato 20 pz (41%), P2 bilobato 13 pz (26%), P2 biscallop 18 pz (36%), numero si incisure : 11 (18% sui due lembi), numero di pz con 2 subcommissure 36 (73%), pz con più di 2 subcommissure 13 (26%), estensione intercommissurale del prolasso in 3D 25,7 mm. Nel gruppo B (114 pz) il tipo di lesione e la morfologia erano: coinvolgimento di P2 101 pz (89%), altro scallop non

P2 13 pz (11%), P2 monolobato 25 pz (22%), P2 bilobato 35 (30%), P2 biscallop 50 pz (44%), numero di incisure 50 (44% sui due lembi), numero di pz con 2 subcommissure 63 (55%), numero di pz con più d 2 subcommissure 51 (45%), estensione intercommissurale della lesione prolassante alla valutazione tridimensionale 29,5 mm. È stata trovata la stessa prevalenza della mrofologia con 3 scallop (30% circa) sia nella popolazione dei campioni normali che nei pz con malattia mitralica mixomatosa, gli scallop del lembo posterior sono più ampi e lunghi nella valvola mixomatosa rispetto alla valvola mitrale normale, in accorso con la letteratura esistente. Anche l'anello ha dimensioni maggiori nei pazienti mixomatosi. Nel gruppo B sottoposto a chirurgia riparativa complessa è stata trovata una maggiot incidenza di incisure (50/61) e una maggior incidenza di P2 bilobati e biscallop con più di 2 subcommissure, inoltre vi è anche una maggior estensione 3D intercommissurale della lesione prolassante (29,8 vs 25,8 mm). Nel gruppo generale è stata trovata una significative differenza nella valutazione ecocardiografica intercommissurale con 2D versus 3D (18,4 vs 28, 5 mm, mean values) legata al diverso potere delle due tecniche. Nel gruppo A vi è una prevalenza della morfologia monolobato di P2 con due subcommissure (73%).

Conclusioni: Lo studio analizza in dettaglio l'anatomia dei lembi mitralici in valvole normali per stabilire l'incidenza e la presenza di subcommissure ed incisure. In un campo molto dibattuto nella letteratura scientifica esistente , introduce una nuova terminologia chiamando "subcommissure" indentature con altezza maggiore del 50% ed "incisure" indentature con altezza inferiore al 50% dell'altezza del lembo. Questa nomenclatura è supportata dall'inserzione sulle subcommisure di corde a festone molto simili a quelle commissurali. I principali risultati della mia tesi sono: 1° la stessa prevalenza della morfologia a 3 scallop nelle valvole normali e mixomatouse (circa 30%); 2° ampiezza e lunghezza maggiore degli scallop del lembo posteriore nelle valvole mixomatose; 3° anello con dimensioni maggiori nelle valvole mixomatose, 4° nel gruppo B sottoposto a chirurgia riparativa complessa maggiore incidenza di incisure e di lesioni bilobate e biscallop con più di 2 subcommissure; 5° è stata trovata inoltre una significativa differenza nella valutazione ecocardiografica 2D vs 3D della estensione intercommissurale del prolasso; 6° inoltre nel gruppo B vi è una maggiore estensione intercommissurale del prolasso rispetto al gruppo A; 7° nel gruppo A vi è una prevalenza maggiore della morfologia monolobata con 2 subcommissure (73%). Questo studio afferma che nell'analisi pre-operatoria di una insufficienza mitralica severa mixomatosa è essenziale eseguire un ecocardiogramma tridimensionale transesofageo per stabilire la presenza di subcommissure ed incisure, e valutare la estensione intercommissurale della lesione prolassante, essi sono elementi determinanti per la scelta della complessità della tecnica chirurgica riparativa.

Index

1. Introduction

1.1 History of the Mitral Valve 's anatomy description

Leonardo Da Vinci was one of the first "scientists" to describe the anatomy of the mitral valve.

Leonardo da Vinci's Heart drawings made him one of the first anatomists, described with a great coincidence to the real anatomy, some characteristics of the heart and the heart's valves.

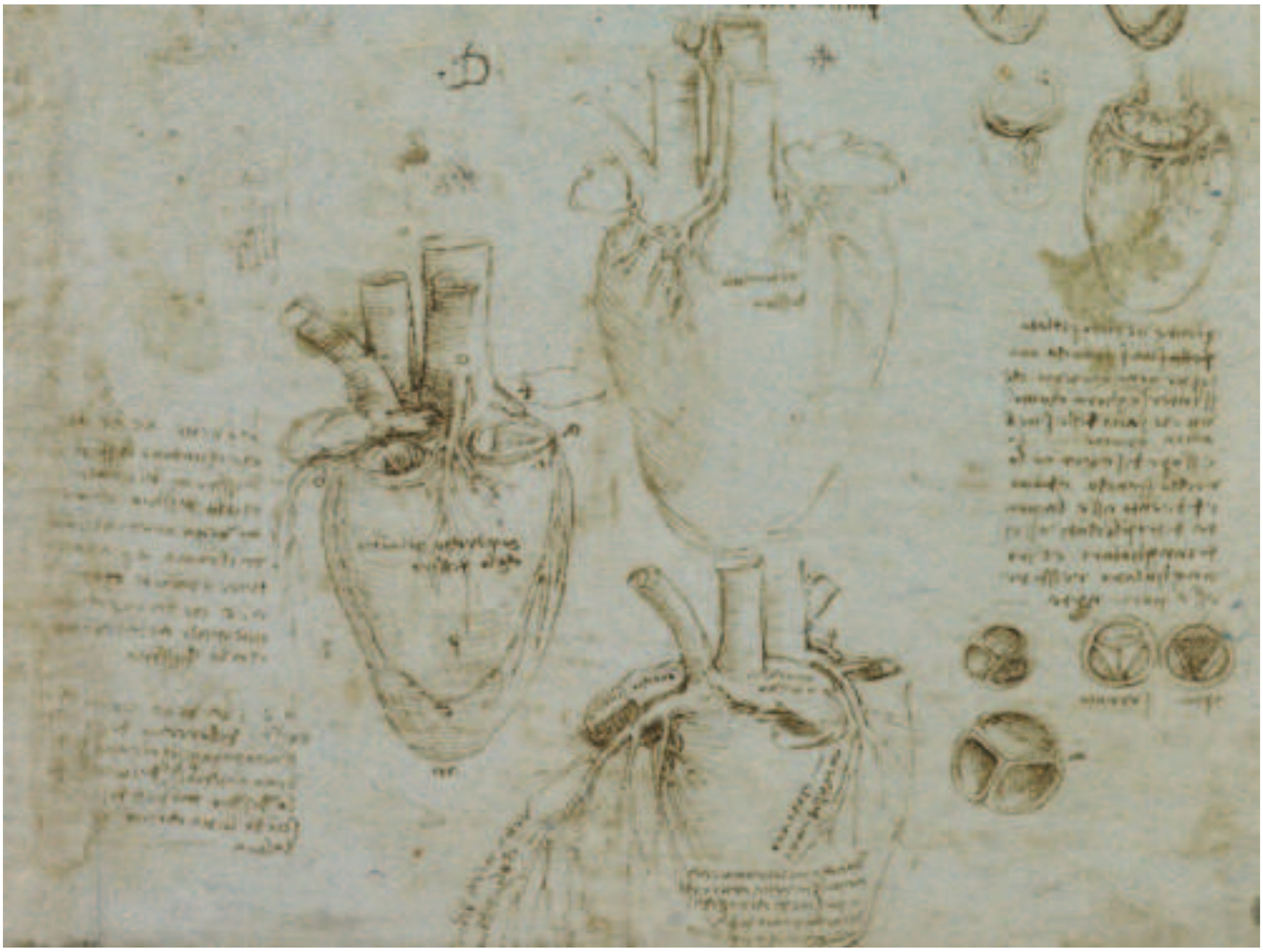


Figure 1.1.1: *Leonardo Da Vinci' s drawings of the heart and some heart valve details, first anatomical descriptions made by observation of necroscopic specimens.*

Around 1513, Leonardo da Vinci made detailed drawings of the heart and wrote nearly 2000 words of notes on the organ in his characteristic mirror handwriting.

Intrigued by the way the aortic valve opens and closes to ensure blood flows in only one direction, he set about constructing a model.

Figure 1.1.2 A : Details about aortic valve cusps anatomy and openening. Leonardo da Vinci's drawing.

Figure 1.1.2 B: Details about aortic valve cusps anatomy and openening. Leonardo da Vinci's drawing.

He also drew some details about the tendineae chordae of the mitral valve. Cartoon by Leonardo da Vinci, believed to have been drawn around 1513, and showed the different features of the tendineae chordae supporting the aortic and mural leaflets of the mitral valve. Note in particular the laminated appearance that Leonardo da Vinci depicted for the ventricular surface of the aortic leaflet and the representation of the tendinous chordae like the arches of the church (1).

The first Leonardo's representation of the mitral leaflets was with four festonatures.

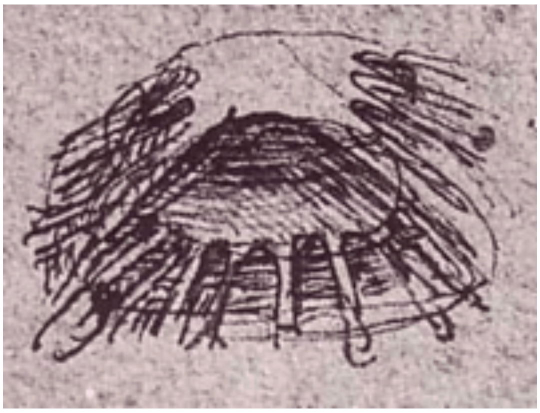


Figure 1.1.3: *Mitral valve details, leaflet and chordae Leonardo Da Vinci's drawings*

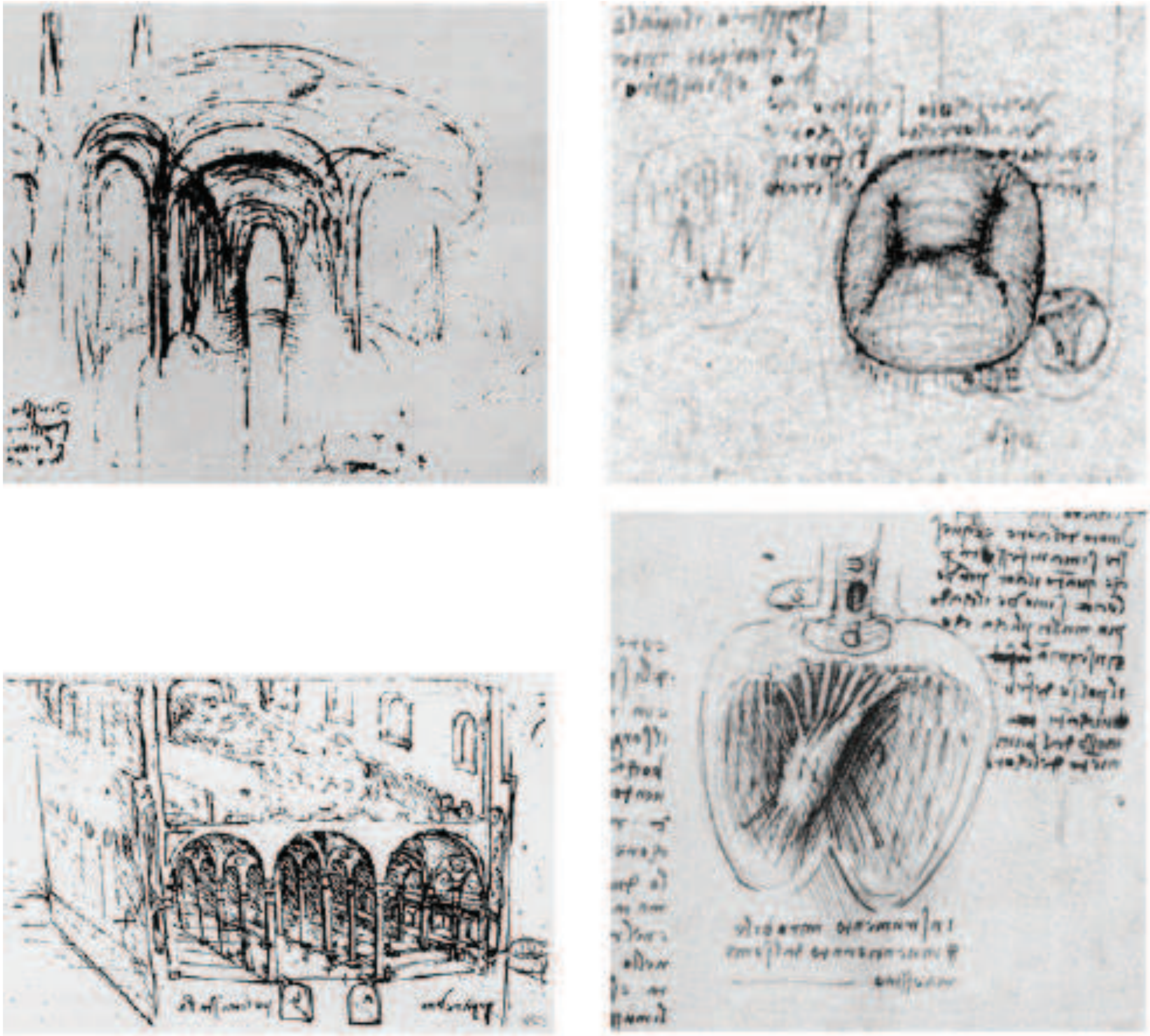


Figure 1.1.4: Leonardo Da Vinci's drawings about detail of mitral valve, chordae, papillary muscles, Quadri scallops description of the mitral leaflets.

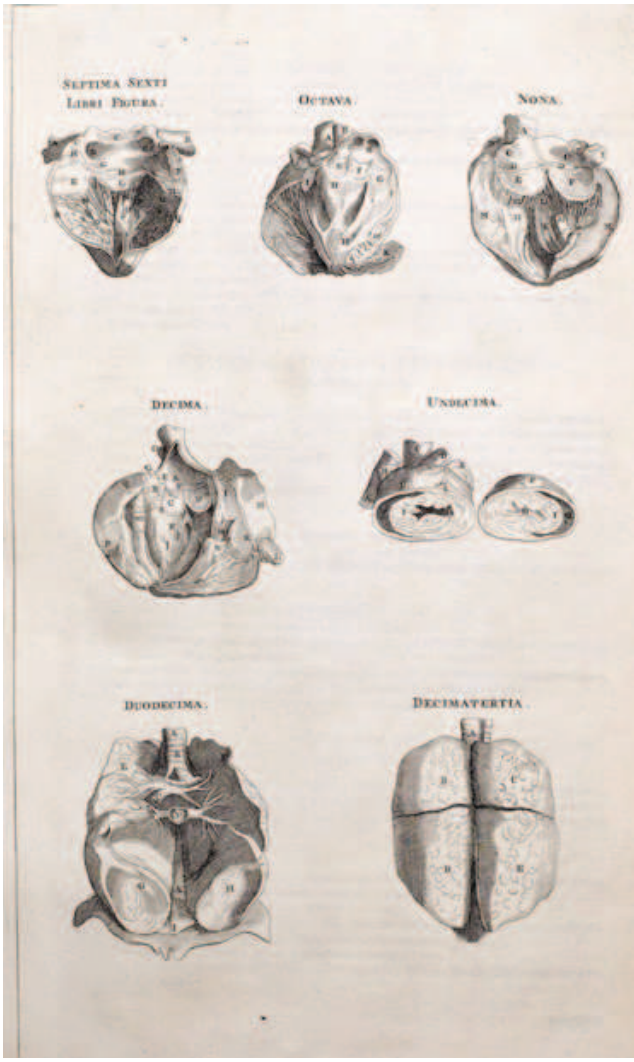
The name of Mitral Valve for the left atrioventricular valve, as far as we know, it was created by Andreas Vesalius, the famous anatomist who worked in Padova, who first linked the shape of the valve to the Episcopal mitre.

Figure 1.1.5: *Andrea Vesalius, emeritus of patavinum anatomic school was the first who called the left atrio-ventricle valve as mitral valve for its similarity with the episcopal mitre.*

Also according to Walmsley (2), it was Andreas Vesalius who suggested the picturesque term "mitral" to describe the left atrioventricular valve due to its resemblance to a plan view of the bishop's mitre. He corrected many mistakes of Galen due to his observation upon animal dissection.

In the text of De Corporis Humani Fabrica Vesalius gave an accurate description of the structural anatomy of the Valves.

Andrea Vesalius assessed also that the mitral valve has been presumed to have two leaflets, hence its alternative title of the bicuspid valve (3).



ANDREAE VESALII,

DE

CORPORIS HUMANI FABRICA

LIBER SEXTUS,

Cordi ipsique famulantibus organis dedicatus, ac mox in fronte figuras sibi proprias offerens, quo minus & hic quoque eaedem figurae variis Capitibus passim praefigantur.

PRIMAE FIGVRAE, EJVSDEMQVE characterum Index.

Figure 1.1. 6: Pictures of the Corporis Humani Fabrica's Vesalius Opera (Website photos).

1.2 The Classical Anatomy Description of the Mitral Valve Leaflets

The Mitral Valve Complex comprises two leaflets, annular attachment at the atrioventricular junction, tendinous chords and the papillary muscles (PMs). The mitral valvular complex is made of several individual parts, which need to function in harmony to maintain the competence of the valve. The fundamental parts are: the annulus, the leaflets, the tendinous cords, and the papillary muscles (4-14).

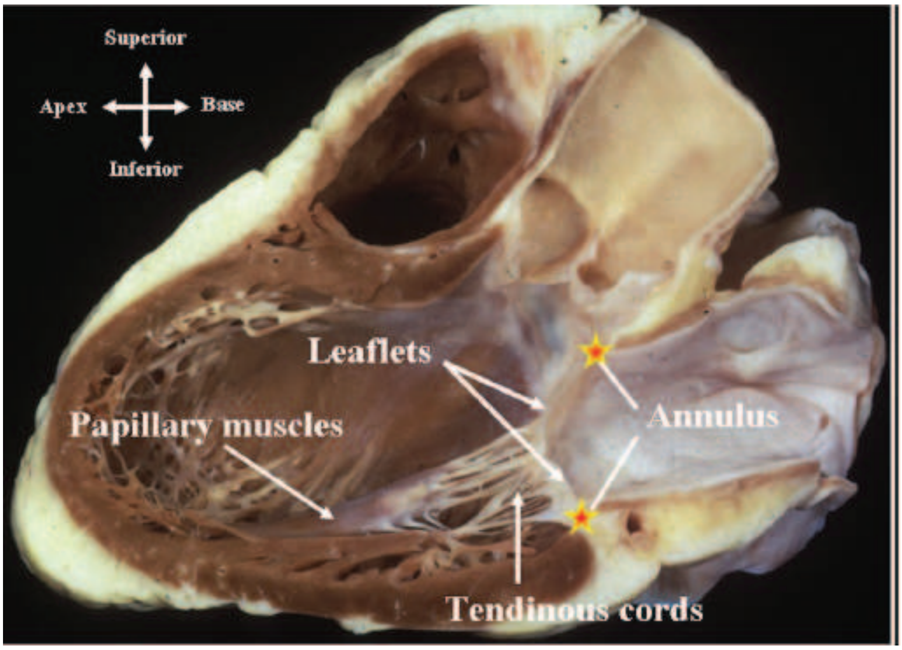


Figure 1.2.1: *a complete view of the mitral valve complex, composed by: leaflet, annulus, chordae, papillary muscles, left ventricle and left atrium. (R. H. Anderson)*

Traditionally, according to the ancient anatomic description (ie Vesalius) the mitral valve has been presumed to have two leaflets, hence its alternative title of the bicuspid valve.

The Leaflets are also the parts that attract the greatest divergence in description, particularly their number, albeit that this largely reflects the criterions used to define them .

The two leaflets of the MV are very different in structure and are usually referred to as the anterior and posterior leaflets by clinicians. Although is still debate the best nomenclature for the mitral leaflets, in the past literature the terms of aortic and mural leaflets were also used. The so-called anterior leaflet is named the aortic leaflet according to its anatomic relation. The aortic leaflet is attached to the aortic annulus through the mitral-aortic courtain. The aortic leaflet is in anterior position when vieuwed through the atrial incision. For thir reason is named anterior. Its rounded leading edge hangs free as a curtain that separates the inflow and outflow components of the left ventricle.

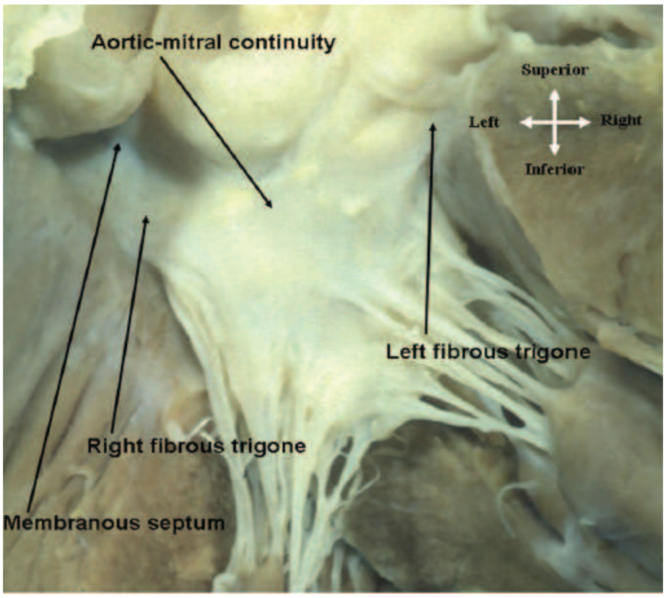


Figure 1.2.2. *The left ventricular outflow tract has been opened from the front, showing how the area of fibrous continuity between the leaflets of the aortic and mitral valves is anchored at its ends by the fibrous trigones. Note the layered attachment of the ventricular aspect of the aortic leaflet of the mitral valve.*

The mural (posterior) leaflet is narrow and extends two-thirds around the left atrioventricular junction, it usually has indentations (sometimes called ‘clefts’, we explain in the next chapter the co1rrect terminology) that generally form three scallops (segments) along the elongated free edge.

The “Cleft” do not usually extend all the way through the leaflet to the annulus; if this is seen, or if there is an enlargement of the gap between the two scallops,this is usually associated with pathological valve regurgitation.

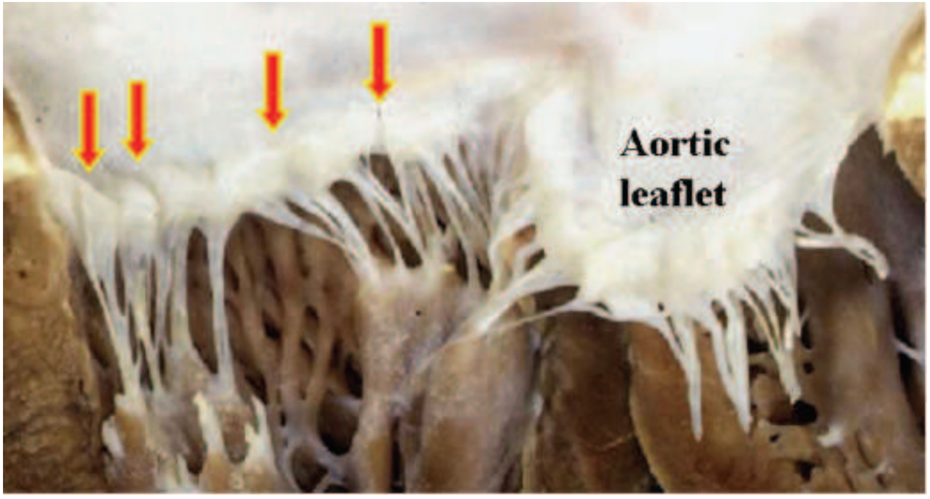


Figure 1.2.3. *The mitral valve is photographed in open position, showing the indentations (arrows) in the mural leaflet that extend towards the annulus, albeit not quite reaching the atrioventricular junction. This arrangement gives the mural leaflet its scalloped appearance.*

In the surgical and echocardiographic language is usually used the Carpentier’s nomenclature, that devide the posterior/mural leaflet in three segments: P1, which lies adjacent to the anterolateral commisure, P2 central and can significantly vary in size, and the most medial defined P3 segment, which lies adjacent to the posteromedial commissure (Figure 1.2.1) . The anterior or aortic leaflet of the MV is much broader than the mural leaflet and comprises one third of the annular circumference, it is also divided conventionally into three regions labelled A1, A2 and A3 corresponding to the adjacent regions of the mural leaflet (Figure 1.2.4).

This classification was used for many years and in the last years. Dr. Duran modified only the central Scallop P2 and A2 in two segment: M1 (antero-lateral) and M2 (poster-medial) regarding the insertion of the tendinous chordae from the antero-lateral and postero-medial papillary muscles (Figure 1.2.7).

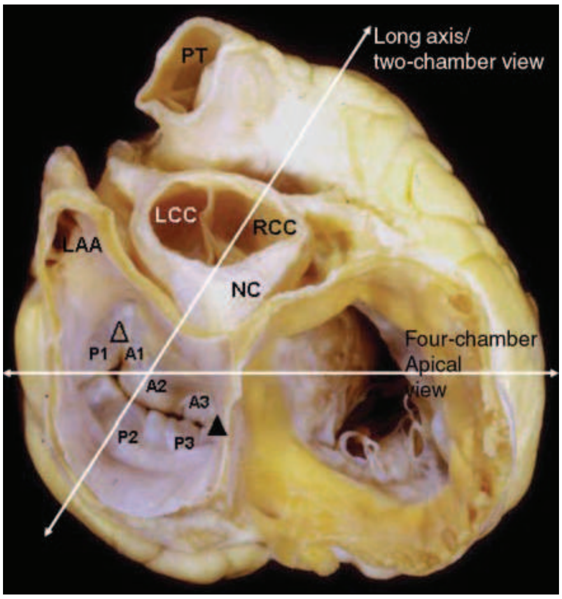


Figure 1.2. 4. *Specimen picture showing the base of the heart with the location of two- and four-chamber echocardiographic views superimposed (double-headed arrows). (1) Base of the adult heart specimen showing the mitral valve with double-headed arrows superimposed demonstrating the two- and four-chamber echocardiographic approach. D, anterolateral commissure; O,posteromedial commissure; A1–A3, divisions of the aortic mitral leaflet; P1–P3, divisions of the mural leaflet of the mitral valve; LAA, left atrial appendage; PT, pulmonary trunk; NC, non coronary cusp of the aorta; LCC, left coronary cusp of the aorta;RCC, right coronary cusp of the aorta(15)*

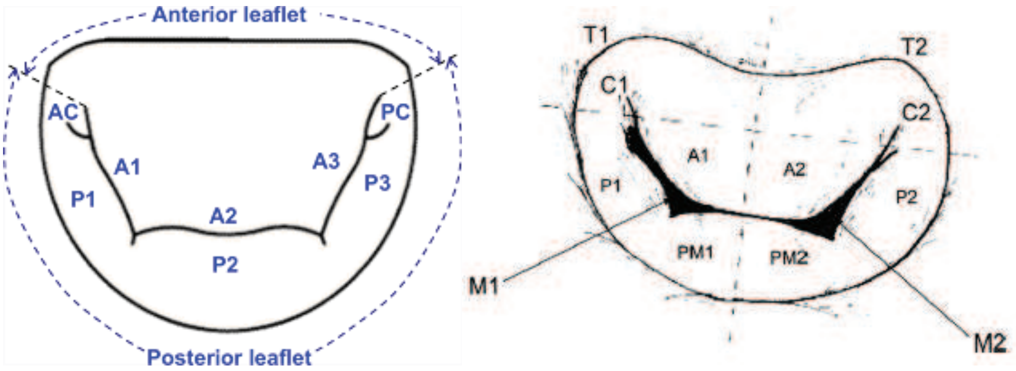


Figure 1.2.5: Classical Carpentier nomenclature of the mitral valve leaflets and on the right Revisited classification by Duran.

The annulus or atrioventricular junction is a complete fibrous entity, which serves to anchor the leaflets. It isn't a planar structure,, but it has a distinct saddle shaped configuration that can be elicited with 3-D model of reconstruction.

Its parietal component coincides with the atrioventricular junction.

The flattened portion of the D, however, extends away from the junction, incorporating as it does, the region of continuity with two of the leaflets of the aortic valve.

The two ends of this area of fibrous continuity anchor the overall valvular complex to the walls of the left ventricle. These ends are called the fibrous trigones, with the right trigone being larger and firmer than the left. The remainder of the annulus then continues around the parietal part of the left atrioventricular junction, where it provides a flexible rather than a rigid support for the valvular leaflet.

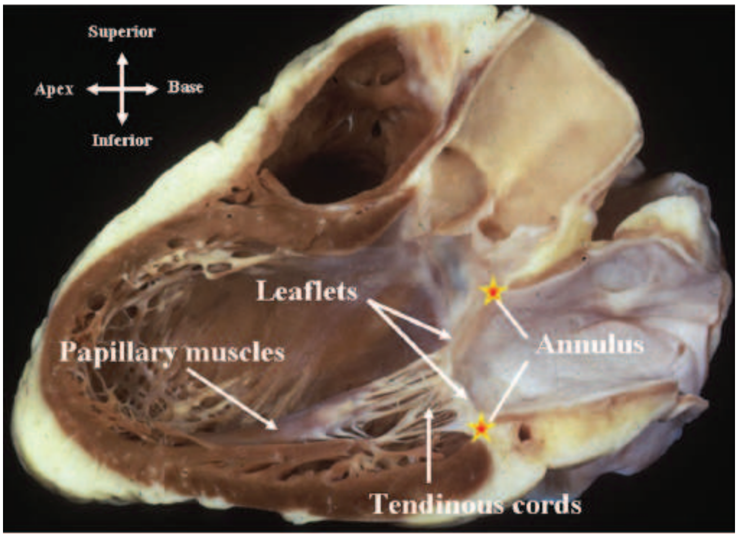


Figure 1.2.6. *As shown in this section of the human heart taken to simulate the parasternal long axis, echocardiographic cut, the mitral valve is a complex structure made up of the annulus, the leaflets, the tendinous chords, and the papillary muscles. Note that the superior leaflet of the valve, in fibrous continuity with the leaflets of the aortic valve, has greater depth than the inferior leaflet, which ishinged from the atrioventricular junction.*

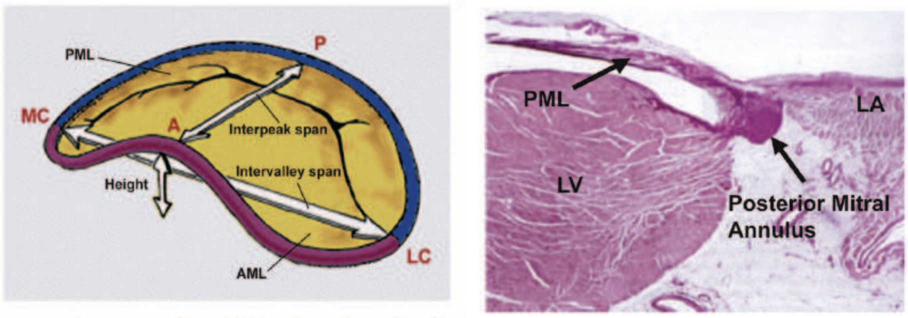


Figure 1.2.7: schematic representation of saddle shape mitral valve anulus and detail of istologic composition of the atrio-ventricular junction

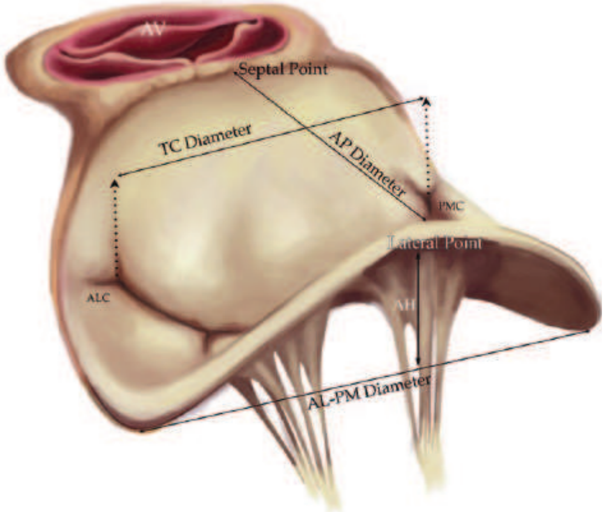


Figure 1.2.8: The mitral valve annulus isn't a planar structure, it has a three dimensional saddle shape with two different diameter intercommissural major than the antero-posterior one.

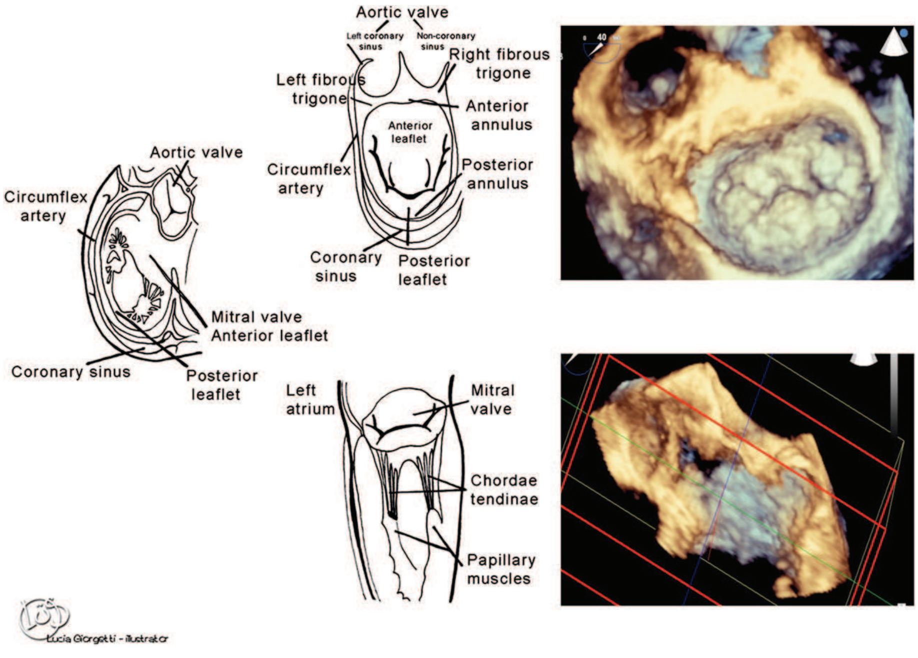


Figure 1.2.9: Three dimensional echocardiography acquisition zoon 3D and full volume for annulus visualization

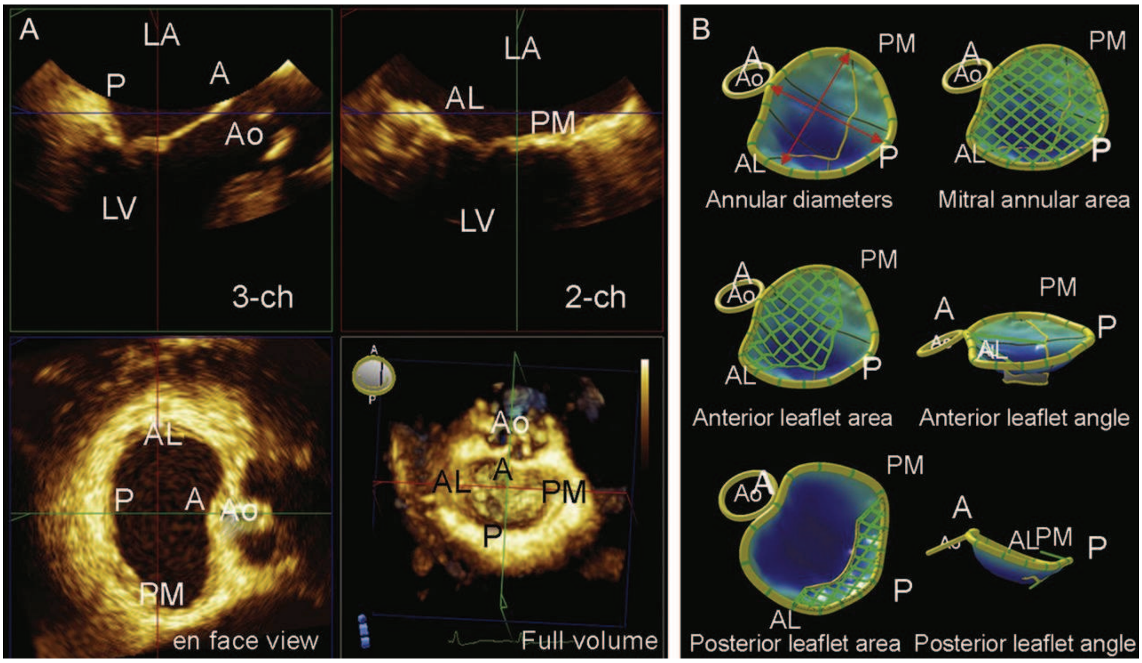


Figure 1.2.10: 3D reconstruction of annulus anatomy

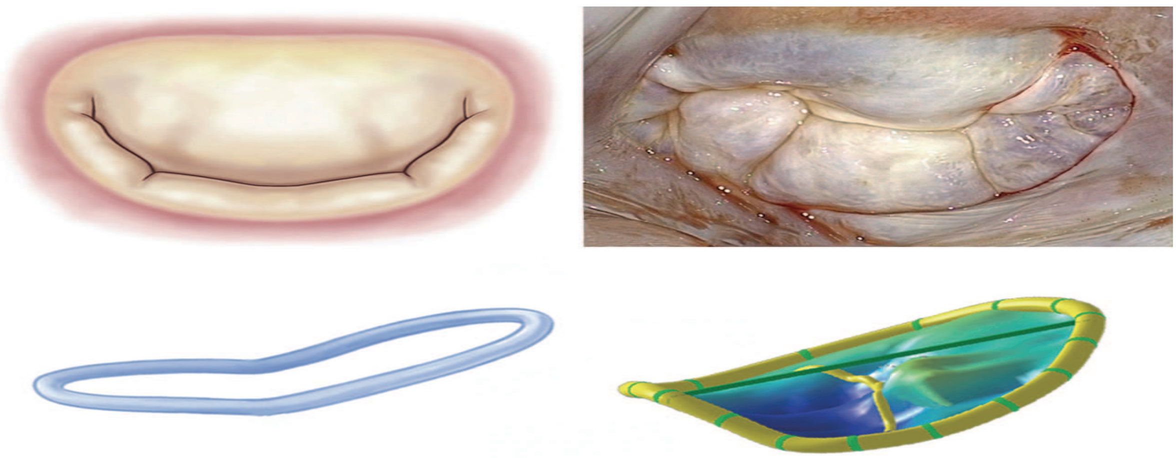


Figure 1.2.11: *Comparison between Netters' drawing and intraoperative photo of a mitral valve, the same exposition and same suddivision in scallop of the posterior leaflet.*

Since the earliest days, beginning with Leonardo da Vinci, investigators have understood that the competence of the mitral valve related to a correct interaction between the leaflet and the tendinous chords that support them. Over the last decades, these structures were studied in detail the morphology of these structures.

It is the location of the insertions of the chords on the leaflets that provides the basis for classification. Primary chords, or chords of the first order, normally insert in uniform fashion along the free edge of both leaflets. Secondary chords, or chords of the second order, insert in layered fashion along the rough zone of the aortic leaflet, as illustrated so long ago by Leonardo da Vinci. They ensure that the coapting surfaces meet during systolic closure. Some of these secondary chords inserting into the ventricular aspect of the aortic leaflet are thickened, and are appropriately described as the strut chords. There are also chords supporting the ventricular aspect of the

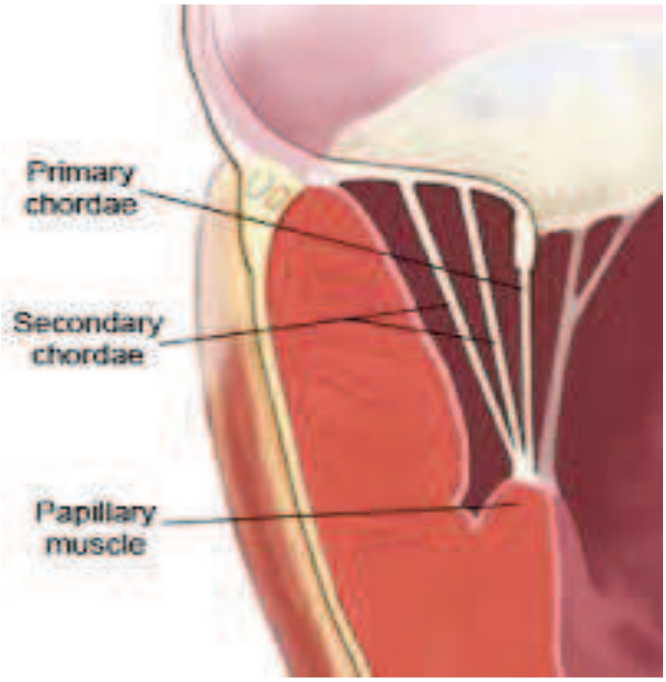
mural leaflet, the so-called basal chords. These chords, however, differ from all the others in that they do not take origin from the papillary muscles, but rather possess their own small muscular bellies, or else extend directly from the parietal ventricular wall to insert on to the under surface of the mural leaflet. In the past, the basal chords have been considered to represent chords of a third order.

Groups of chords sprout from both papillary muscles, and support the leading edges of both leaflets. Fan-shaped chords are found beneath the two ends of the solitary line of apposition between the aortic and mural leaflets, and also beneath the subsidiary zones of apposition of the components of the mural leaflet.

The papillary muscles and left ventricle are important componente of the mitral valve complex, moreover for the correct function of the mitral valve. Groups of chords sprout from both papillary muscles, and support the leading edges of both leaflets. The papillary muscles themselves lie directly beneath the two ends of the solitary zone of apposition between the leaflets. Contrary to the names usually given to them nowadays, they are located inferiorly and septally, and superiorly and parietally.

Their positions ensure that the chords arising from the tips of the two muscles are able to provide support to the adjacent parts of both leaflets.

The mural part of the annulus, an integral part of the left atrioventricular junction, is in continuity antero-superiorly with the aortic root. The mitral valve has crucial relationships to the left atrium the left ventricle, the atrial septum, the coronary vasculature, and the atrioventricular axis of conduction tissue. For a correct unction of the mitral valve it is very important the normal function of the left ventricle. A complete left bundle block or an ischemia of the infero-lateral wall can induce some modification of the pattern of contractility that can lead to mitral regurgitation.



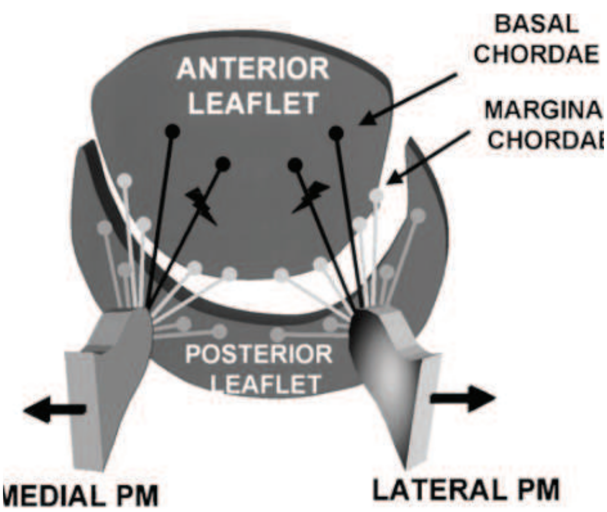


Figure 1.2.12: Tendineae Chordae classification: First order or marginal chords that insert on the free edge of the leaflet, Second order or Struct chordae that insert on the rough zone, Third order or basal chord.

1.3 Diatribe about the leaflets description

At the state of the art there is some debate about the leaflets' anatomy description. Some famous surgeons have created a different anatomical characterization.

According the more widespread anatomical description of Carpentier the mitral valve is labelled with an alphanumerical description: the mitral's posterior leaflet is divided in three scallops named P1 the antero-lateral, P2 the central one and P3 the postero-medial, there are two commissure antero-lateral and postero-medial. There is only a one anterior leaflet without scallop and divided in three imaginary portion A1 antero-lateral, A2 central and A3 antero-medial facing to the corresponding posterior scallops (Fig 1.3.1 C).

Sir M. Yacoub described the mitral valve has having four leaflets: one anterior and three posteriors. (22).

Kumar and colleagues give another description identifying six leaflets in the mitral valve, considering also the two commissural areas like a leaflet (21).

The Carpentier's classification is the more widespread used, in the last years it is rivisited by Duran that modified only the central Scallop P2 and A2 in two segment: M1 (antero-lateral) and M2 (poster-medial) regarding the respectively origin of the tendinous chords, from the antero-lateral and postero-medial papillary muscles (Fig 1.3.2 D, 17,18,19).

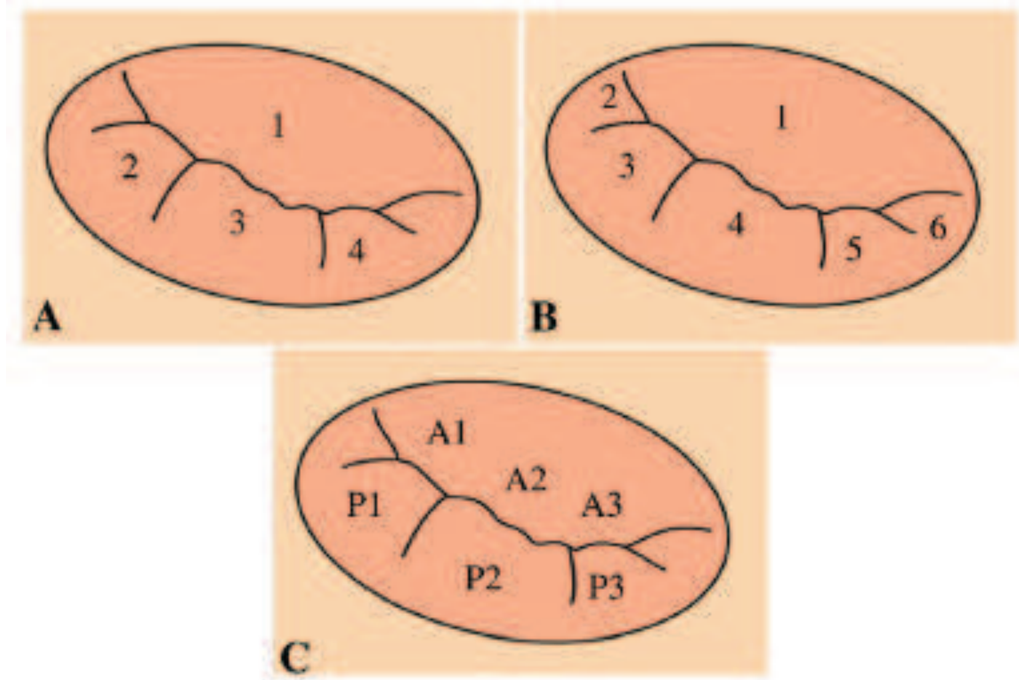
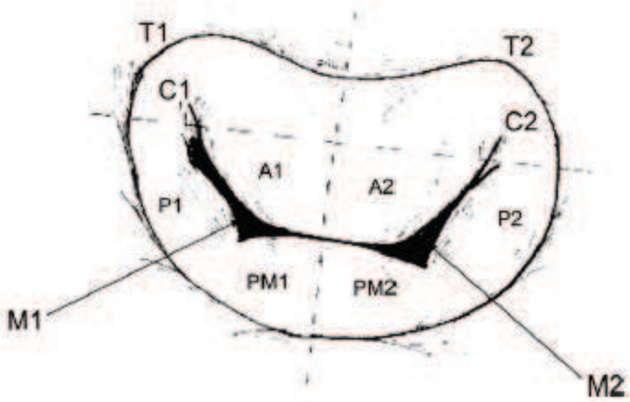
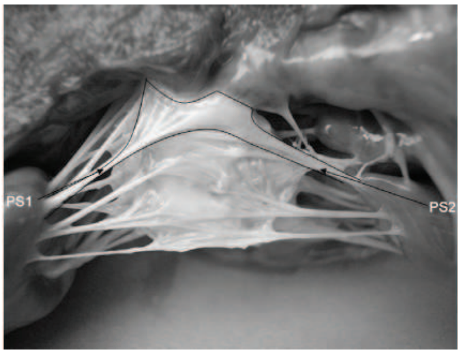


Figure 1.3.1: *The Picture illustrates the concept for description suggested by Yacoub (Panel A), arguing that the valve has four leaflets, and Kumar and colleagues (Panel B), who suggest that there are six leaflets including the commissural areas like leaflets. More commonly, however surgeons adopt the description of Carpentier (Panel C) who labelled the three scallop of the posterior leaflets with alphanumeric fashion.*

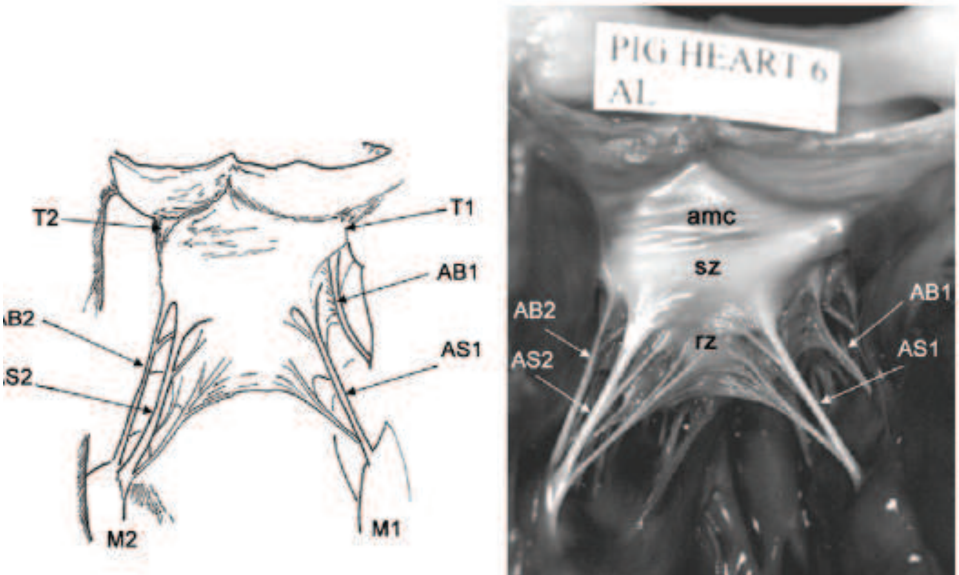
D1



D 2



D3



D4

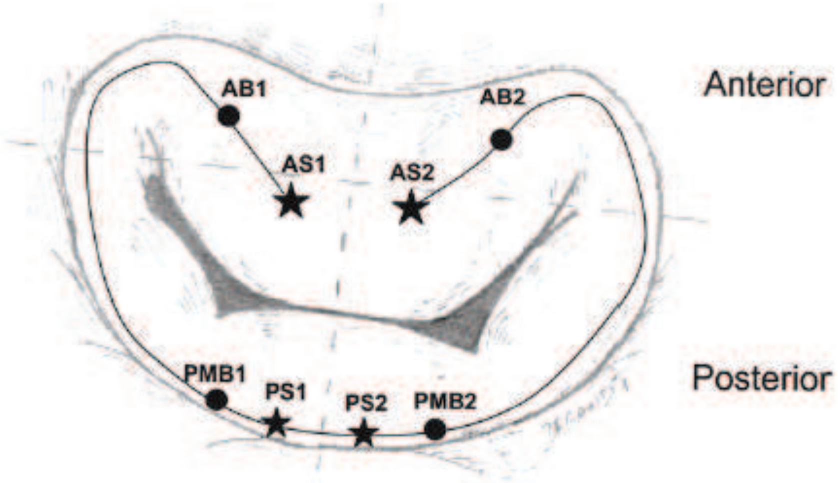


Figure 1.3.2 D 1,2,3, 4 *Drawings and pictures show Duran modified Carpentier's Classification (19), the posterior leaflt central scallop and the facing anterior leaflet was divided in two portion, P1M1 antero-lateral and P2M2 postero-medial , they received chordae from the two corresponding papillary muscles. (17)*

1.4 Terminology

There is a confusion and discussion, in the past literature, on the number and the morphological description of the mitral valve leaflets, between clinicians, surgeons and anatomopathologists (21,22,25).

The two leaflets of the mitral valve were named anterior and posterior leaflet, but also aortic (AM) and mural leaflet (PL); other scientist believe it is more correct to speak of left and right leaflet (25).

Usually the anterior leaflet is a continued veil between the two commissure, while the posterior leaflet is variably divided by two or more incisura in more scallops.

A scallop is a piece of leaflet tissue between two incisure with a high major than 50% of leaflet’s high.

We prefer to use the term “subcommisure” rather than the classical surgical and clinical nomenclature of “Cleft”.

From an anatomopathologist point of view “Cleft” is the name of a congenital disease, which involve the anterior leaflet and derives from a defect of the cushion fusion (81-87).

In the literature founded on pubmed the terminology of “Cleft” is usually used only for pathological V-shaped fissure on the leaflet and not for the physiological scallops’ division.

An isolated cleft of the mitral valve, not associated with some form of endocardial cushion defect, is a very uncommon (but not rare) congenital malformation of the septal leaflet and sometimes of the posterior leaflet.

This condition was first described in 1987 by Petitalot and colleagues. Subsequent reports have concerned cases of 1 to 5 patients who have displayed severe regurgitation.

The morphology of the mitral valve and the “cleft” in the septal leaflet have been well defined by echocardiographic and pathological studies (26,27).

This “cleft” can be wide and extend to the mitral annulus, but it can also be only a few millimetres deep and display minimal regurgitation. A similar cleft has been described in the posterior leaflet of the mitral valve.

The edges of the mitral valve tend to be thicker and more retracted in older patients. The isolated mitral cleft is oriented towards the LVOT rather than towards the inlet septum, as is seen in the “cleft” between the anterior and posterior bridging mitral leaflets of patients who have endocardial cushion defects.

In order to respect this definition, we prefer calling “subcommissure” the incisure with an high major than 50% of the leaflet’s high, between two scallop of the posterior leaflet.

The incisure of an high minor than 50% of the leaflet’s high was called “pseudocleft” or more simple “incisure”.

We also called the central scallop P2 of the posterior leaflet in presence of a subcommissure “biscallops” while in presence of an incisure “Bilobate” (Figures 1.4.1 A, 1.4.2 and 1.4.3) or if it is a single scallop “monolobate” (Figure 1.4.1 B).

The incisure can be present on every scallop of the posterior leaflet and also on the anterior leaflet..

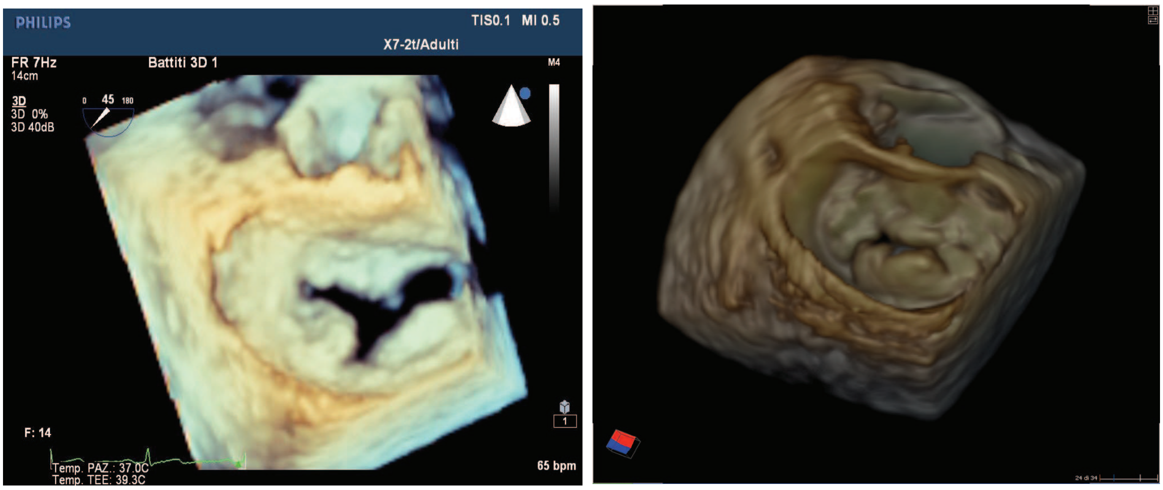


Figure 1.4.1 A: Three dimensional imaging of mitral valve in the left panel presence presence of subcommissure and “biscallop” posterior leaflet on the right a presence of an incisure of P2 that is “bilobate”.

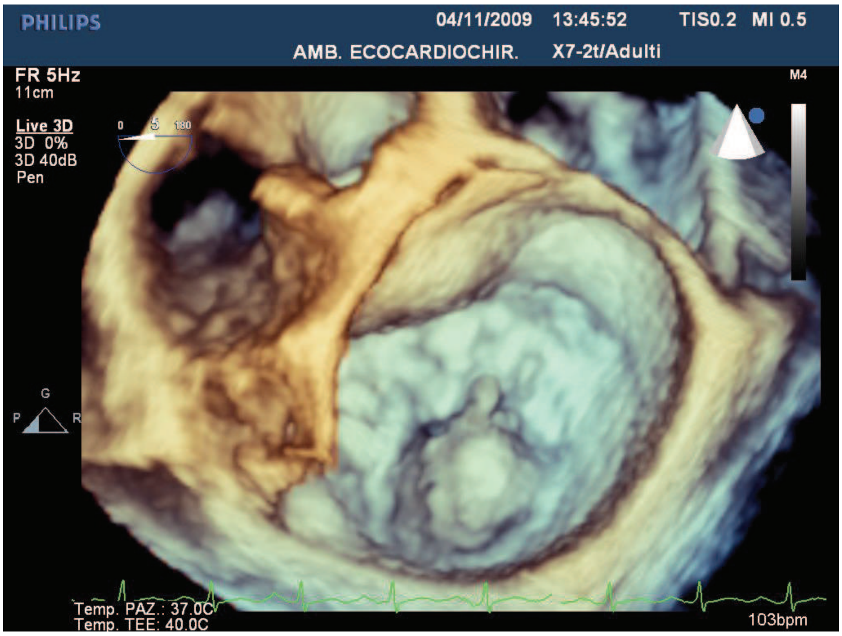


Figure 1.4.1 B: Three dimensional imaging of mitral valve anatomical description like Carpentier’s classification, prolapse of P2 that is a single scallop “monolobate”

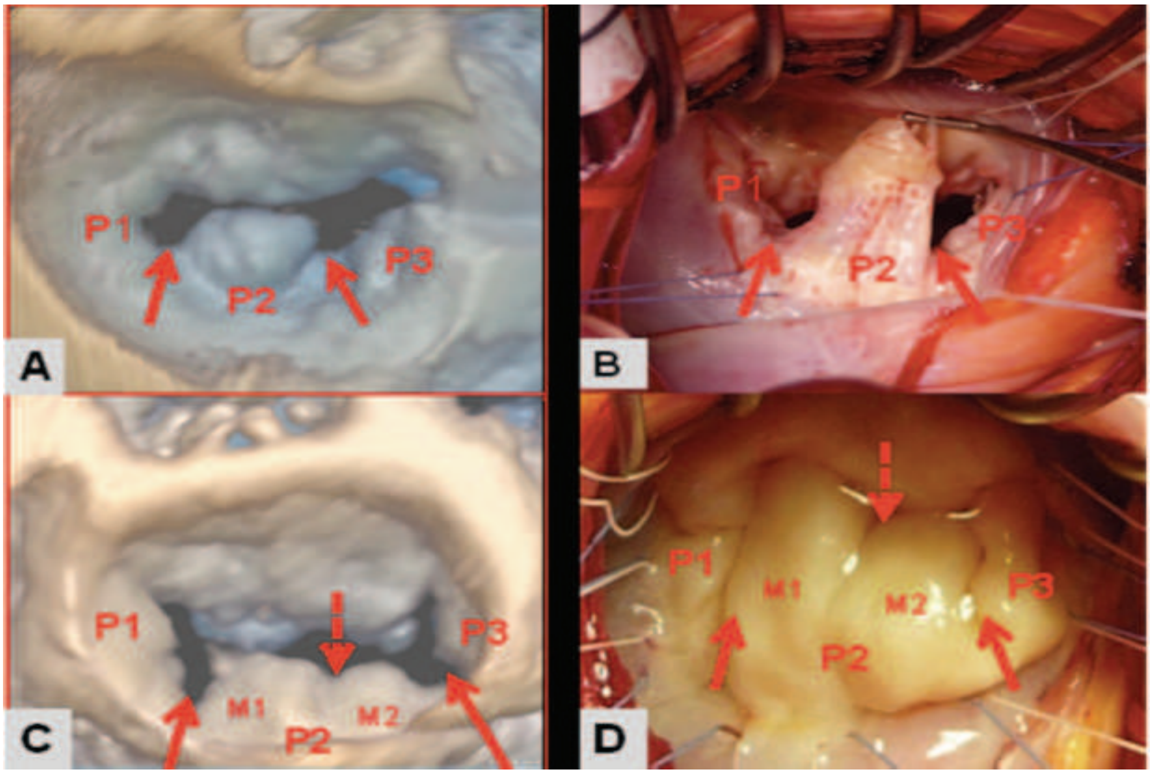


Figure 1.4.2 : Double imaging of degenerative mitral valve disease, correspondence of the three dimensional zoom acquisition with the intraoperative picture.

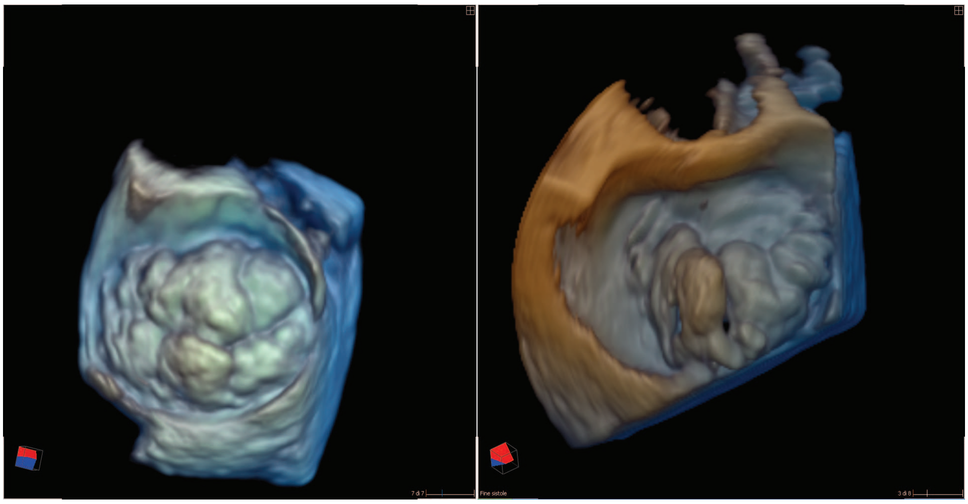


Figure 1.4.3 : zoom acquisition, on the left classical anatomical segmentation of the posterior leaflet according Carpentier's one, on the right multi scallops posterior leaflet (4 scallops).

1.5 Literature Review

Several pubblications examine the anatomy of the mitral valve, in particular the first articles were written in the 1970^{th} . Ranghatan and Lam performed necroscopic specimens observation of the mitral valve apparatus, classifying the tendinous chordae (5,16) .

Other important findings were made by the group of Roberts and Y. Ho, who analysed the anatomy-pathology of the normal mitral valve (6,9-10).

Angelini and coll. analysed the atrioventricular junction in 13 necroscopic specimens, 7 of normal subjects and 6 of patient with degenerative disease.

Serial sections of the heart were cut perpendicular to the valve ring along the atrioventricular Junction.

For each valve, it was studied the structure of the annulus and the presence of "disjunction".

The relation between atrium, ventricle, and annulus is similar to that shown in the normal valves. The leaflets of myxomatousatous valves are thickened, producing "disjunction" with a junction as "a separation between the atrial and left ventricle wall (6).

Two studies of Indian anatomopathologist investigated the anatomy of mitral valve on necroscopic specimens.

The study of Deopujari on 34 adult Indian cadavers, assessed the presence of incisure on the posterior mitral leaflet; they suggested that the number of leaflets my vary depending on the annular circumferences.

The criterion used in the present study was based on indentation of valve leaflets.

This criterion was formulated with the hypothesis that deeper indentations increase independence in functionality (movement of leaflets) and hence can be appropriately called extra commissures delineating extra leaflets.

Although, descriptions of such deep indentation do exist, especially in clinical literature (Fuster et al ; Anderson & Kanani) and have also been implicated as the cause of mitral valve prolapse. In a recent study Ring et al did not describe them as commissures but as extra leaflet.

However Yacoub & Kumar et al (as quoted by Anderson & Kanani) have suggested that the number of leaflets are 4 and 6 respectively.

Anderson & Kanani in their critical analysis of mitral valve have discussed the various descriptions about the variability in number of leaflets and conclude that interpretations may vary depending upon criteria used to define them.

The criterion used, in the present study, for delineating different leaflets differs from that of previous studies. Previous studies have used the attachment of chordae tendinae arising from apex of papillary muscle (Victor & Nayak, 1995, Anderson & Kanani), and ii) type of Chordae (Ranganathan et al, 1970). Both these criteria are not dependable due to great variability of papillary muscle (Rusted et al., 1952, as quoted by Ho, 2002) and chordae (Lam et al, 1970; Becker & de Witt, 1980, as quoted by Anderson & Kanani).

Gunnal et al considered every scallops of the posterior leaflet like a single leaflet, according to Yacoub classification, so they finded in their 116 necroscopic specimens different morphology bicuspid, esacuspid, pentacuspid etc.

From the studies of the Carpentier's group, the most famous cardiac surgeon that create the first technique of mitral valve repair (the dad of the mitral valve repair), it derived the most used classification of the mitral valve posterior leaflet anatomy (17,18).

The Carpentier Classification assessed the presence for two leaflet anterior and posterior, two commissure and only the posterior leaflet was divided in three scallops.

The mitral valve leaflet posterior scallops are identified as P1 (anterior scallop), P2 (middle scallop), and P3 (posterior scallop) as viewed by the surgeon though a left atriotomy. The three corresponding segments of the anterior leaflet are termed A1 (anterior part), A2 (middle part), and A3 (posterior part). The remaining two segments are the anterior commissure (Ac) and posterior commissure (Pc).

The regions of the mitral valve leaflets are defined surgically through a left atriotomy by taking nerve hooks and lifting each posterior leaflet scallop and their corresponding, coapting anterior leaflet. The posterior leaflet P1 scallop coapts with A1. The posterior leaflet P2 scallop coapts with A2. The posterior leaflet P3 scallop coapts with A3. Surgical pathology was then defined by leaflet section: P1/A1, P2/A2, P3/A3. (Functionally this is what we do today using echocardiography).

In the recent years this classification was modified by Duran divided the central scallop P2 and facing zone A2 in two portion P2M1 (antero-lateral) and P2M2 postero-medial following the distribution of mitral chordae from the two papillary muscles.

Nowadays the new three-dimensional transoesophageal echocardiography allows the same surgical view of the atrial side of the mitral valve (surgical view). For this reason there has been a new interest in the anatomy and function of the mitral valve.

Recent studies have analysed the anatomy of myxomatousatous mitral valve with three-dimensional echocardiography, and assessed the importance of the mitral valve functional anatomy, the presence of the “cleft” in the planning of the mitral valve repair .

In particular, Real Time 3 D echocardiography allows the determination of dominant and secondary lesion that can be useful in term of surgical strategy and long term follow up of the patients.

Moreover in the Papworth Hospital study the evidence of “cleft” is important for the surgical planning.

Article	Journal	Year	Author	Number of patients
Anatomy of the mitral valve: understanding the mitral valve complex in mitral regurgitation	European Journal of Echocardiography (2010) 11, i3–i9	2010	Karen P. McCarthy1*, Liam Ring2, and Bushra S. Rana	0 Review
Anatomy of Left Atrioventricular Valve (Mitral Valve) Leaflets in Adult Indian Cadavers	Intern journal morphology (impact fact 1,5)	2013	Deopujari, R.*; Sinha, U.* & Athavale, S. A.**	34 necroscopic hearts
Study of mitral valve in human cadaveric hearts	Heart Views Official Journal of gulf Heart association	2012	SA Gunnal, MS Farooqui, RN Wabale	116 necroscopic hearts
Morphology of the Human Mitral Valve: II. The Valve Leaflets	Circulation	1970	N.RANGANATHAN, J. H. C. LAM, E. D. WIGLE and M. D. SILVER	50 necroscopic hearts
Morphology of the Human Mitral Valve: I. Chordae Tendineae: A New Classification	Circulation	1970	J. H. C. LAM ,N.RANGANATHAN,M. D. SILVER	50 necroscopic hearts
Anatomy of the mitral Valve	Heart	2002	S. Ho	0 Review
The mitral apparatus. Functional anatomy of mitral regurgitation.	Circulation	1972	Perloff JK, Roberts WC	0 Review
A histological study of the atrioventricular junction in hearts with normal and prolapsed leaflets of the mitral valve.	Br Heart J	1988	Angelini A, Ho SY, Anderson RH, Davies MJ, Becker AE.	13 necroscopic hearts (7 normal and 6 mitral valve prolapse)
A new reconstructive operation for correction of mitral and tricuspid insufficiency	J Thoracic Cardiovascul surg	1971	Carpentier A, Deloche A, Dauptain J, Soyer R, Blondeau P, Piwnica A, Dubost C, McGoon DC	Prolapse patients
Mitral valve apparatus. A spectrum of normality relevant to mitral valve prolapse.	Br Heart J	1979	Beker , De wit	140 pts (100 normal subject, 40 mitral valve prolapse)
The prevalence and impact of deep clefts in the mitral leaflets in mitral valve prolapse.	European heart cardiovasc j imaging	2013	Ring L, Rana BS, Ho SY, Wells FC.	176 pts, 76 prolapse , 57 control, 43 other mitral valve disease
Real-time three-dimensional transesophageal echocardiography for assessment of mitral valve functional anatomy in patients with prolapse-related regurgitation.	Am journal Cardiology	2011	La Canna G[1], Arendar I, Maisano F, Monaco F, Collu E, Benussi S, De Bonis M, Castiglioni A, Alfieri O.	222 pts with mitral valve (prolaspe/ Cleft subcleft)

Table 1.5.1: A review about some anatomical studies that analyzed the mitral valve anatomy in vivo and on necroscopic specimens, and recent study about the analysis of the mitral leaflet with three-dimensional echocardiography.

1.6 The echocardiography of the mitral valve

Mitral valve disease is the second most common valvular heart disease after the aortic valve. Mitral valve has historically been a structure of interest by pioneers in echocardiography. One of the earliest applications of echocardiography was in the diagnosis of valvular heart disease, particularly mitral stenosis. The transthoracic and trans-oesophageal echocardiography allow structural and hemodynamic evaluation of the normal and pathological mitral valve.

Echocardiographic assessment of normal mitral valve: transthoracic and trans-oesophageal echocardiography

Transthoracic echocardiography is the main tool to assess mitral valve pathology in day to day practice of cardiology. The following views are essential for assessment of mitral valve: (a) Parasternal long axis view is the first view to assess MV. In this view thickness of leaflets and their motion during the cardiac cycle can be evaluated. Dimension of the left atrium, which will be affected by MV pathology, is evaluated in this view as well (Fig. 1.6.1). Applying the colour Doppler adds more information about mitral inflow in diastole and eventual regurgitation, sometime is also possible to see flail of ruptured chordae. Although M-mode echo is used less frequently nowadays, it is still important in terms of accurate timing of mitral events during the cardiac cycle (Fig. 1.6.2) and for the estimation of left ventricle dimensions.

(b) Parasternal short axis view reveals mitral leaflets motion and their attachment to the chordae. Short axis view at the level of mitral leaflets shows their restrictions and splitting of commissures. Mitral valve area can be measured in this view by planimetry at the level of leaflets tip. At the mid-ventricular level, were are located two papillary muscles, their orientation, and the number of their heads can be illustrated (Fig. 1.6.3). This view is very important to establish the wall motion of all mid-ventricular left ventricle walls.

Apical four chamber view visualizes both mitral leaflets and their coaptation, which should be at the level of the plain of the mitral annulus (Fig. 1.6.4). MV area by pressure-half time and LV diastolic parameters including mitral inflow Doppler can be assessed in this view (Fig. 1.6.5).

Apical long axis view (three chamber view) and apical two chamber view are necessary to evaluate different segments of mitral leaflets and the degree of possible mitral regurgitation (Fig. 1.6.6).

Moreover, the vena contracta diameter and the regurgitant volume must be measured only in the three chamber view.

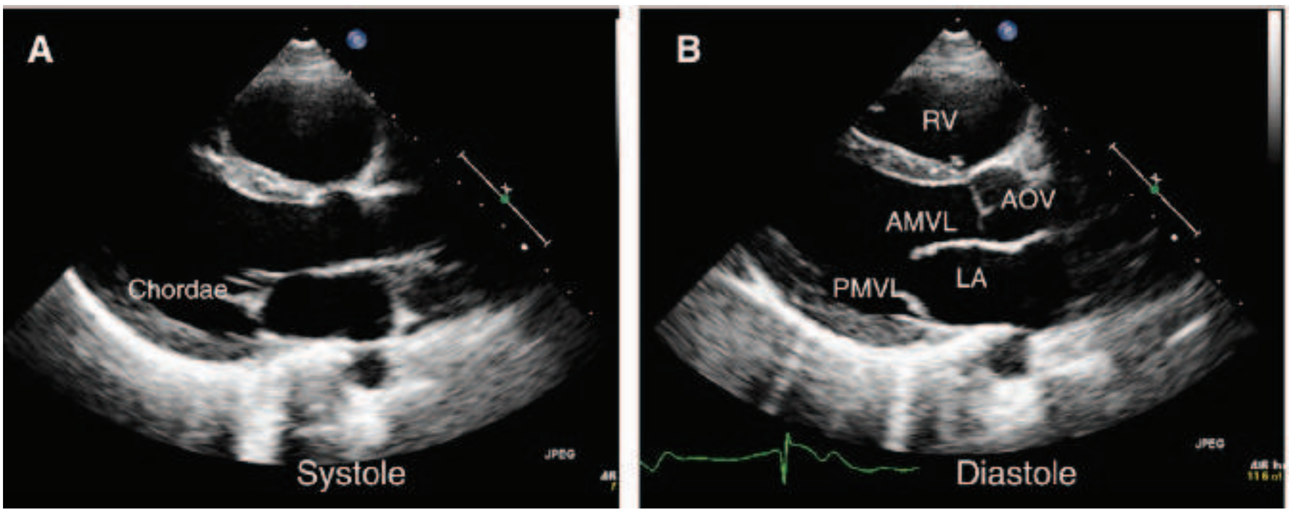


Figure 1.6.1 *Parasternal view of normal mitral valve. (A) In systole, leaflets are closed and chordae are barely visible. (B) In diastole, leaflets are open. RV = right ventricle; AOV = aortic valve; AMVL = anterior mitral leaflet; PMVL = posterior mitral leaflet*

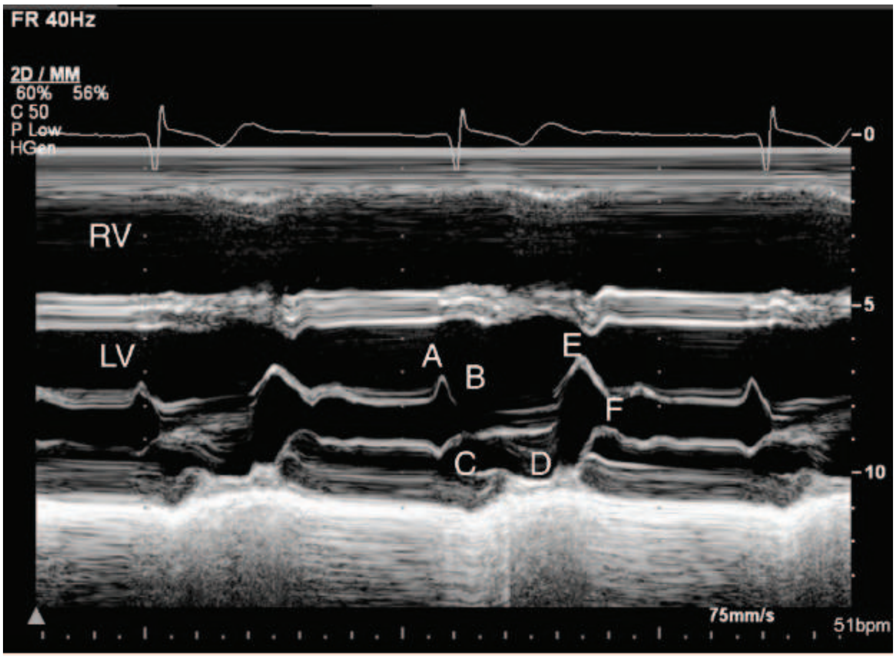


Figure 1.6.2 *M-mode display of mitral valve. Anterior mitral valve leaflet (AMVL) during diastole moves anteriorly like letter of ''M'' and posterior mitral valve leaflet moves backward like letter of ''W''. Mitral leaflets motion during one cardiac cycle is labeled as A–E, and F. Note: leaflet closure line (C–D line) in systole is straight and towards the interventricular septum*

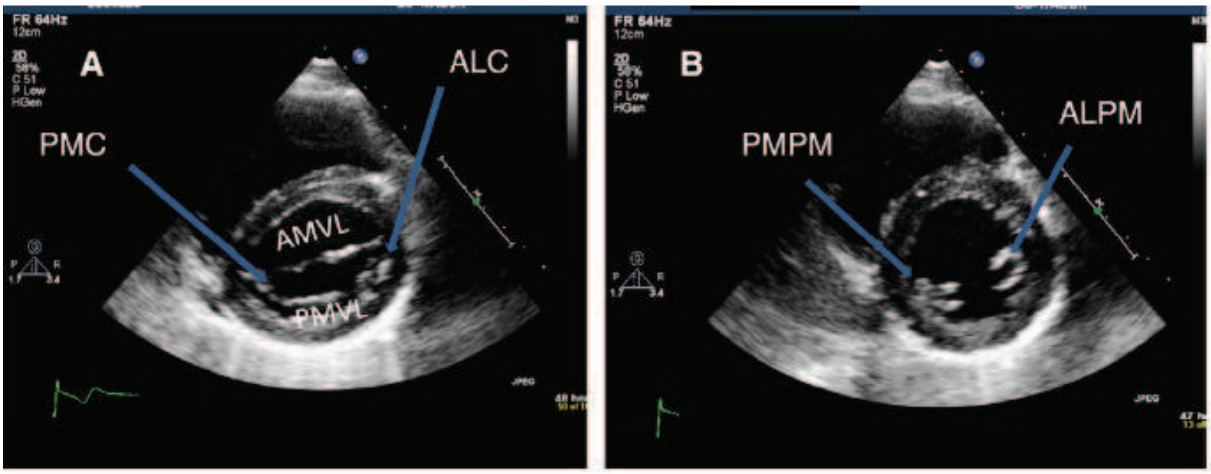


Figure 1.6.3 *Parasternal short axis views. (A) At the level of mitral valve showing anterior (AMVL) and posterior (PMVL) leaflets. Anterolateral (ALC) and posteromedial (PMC) commissures (arrows) are widely open. (B) At the level of papillary muscle showing anterolateral (ALPM) and posteromedial (PMPM) papillary muscles.*

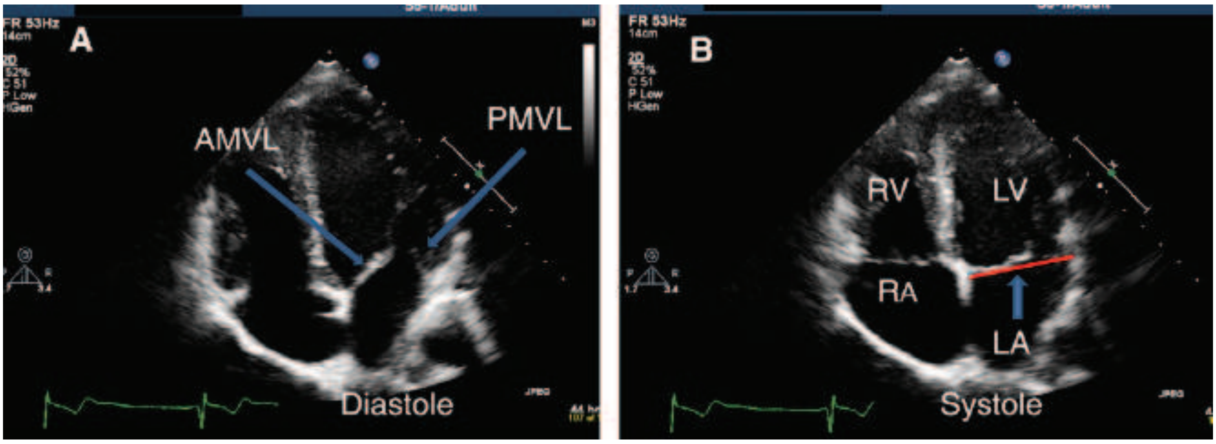


Figure 1.6.4 *Apical four chamber view. (A) In diastole, mitral leaflets are open. Anterior mitral leaflet (AMVL) and posterior mitral leafletare shown (arrows). (B) In systole, leaflets are closed. Note: coaptation line of leaflets are at LV side of mitral annular plane (arrow).*

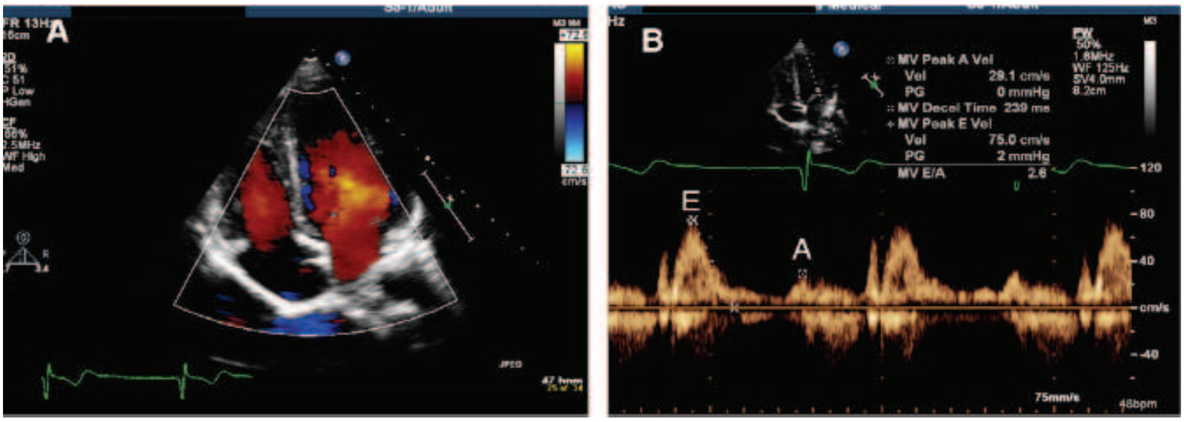


Figure 1.6.5 (A) *Apical four chamber view in diastole, showing laminar flow from LA to LV. (B) Spectral Doppler of mitral inflow at the level of leaflets tip showing early rapid filling (E) and late filling after atrial contraction* (A).

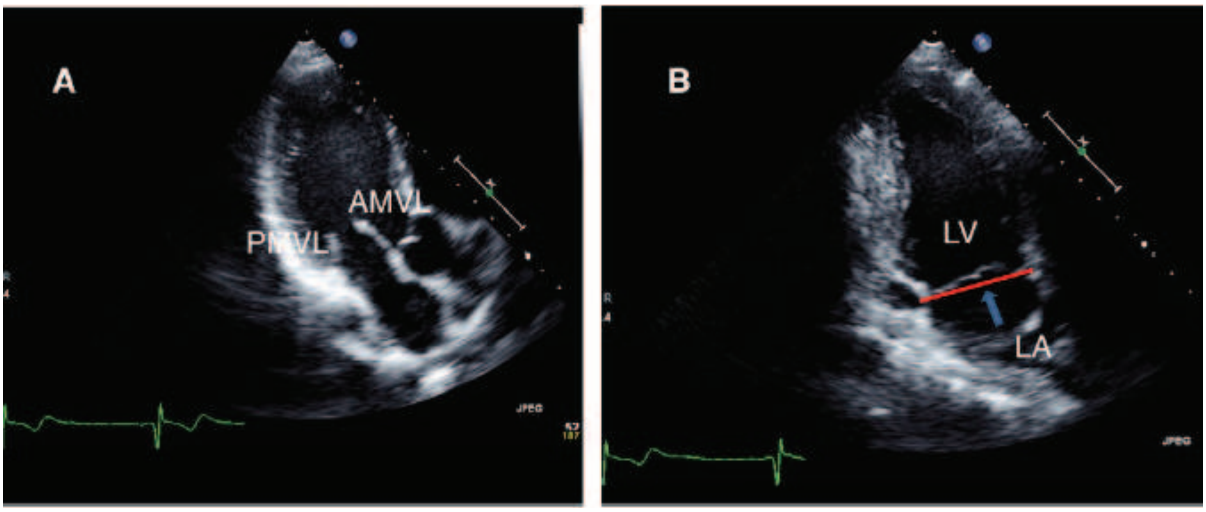


Figure 1.6.6 *(A) Apical three chamber view showing mitral leaflets. (B) Apical two-chamber view showing level of leaflets coaptation and mitral annulus (arrow).*

Trans-oesophageal echocardiography (TEE) has a great role in accurately predicting mitral valve anatomy and decision making for possible intervention. Multiplanar TEE allows imagining numerous scan planes, which can be optimally aligned to specific anatomy orientations to provide detailed information about pathology of mitral valve. Schematic diagram of mitral valve in Figs. 1.6.7–1.6.8 shows how scallops and segments of mitral valve can be investigated by different angle orientations (Omran et al., 2002).

3-D TEE is an emerging modality, which offers comprehensive evaluation of MV by providing surgical views and common language between cardiologists and cardiac surgeons in the operating room (Salcedo et al., 2009). The use of 3-D has facilitated the preoperative surgical planning of treating complex mitral pathology. Fig. 1.6.8-9 and 1.6.13 shows example of a patient with degenerative mitral valve, flail A2 with ruptured chordae and severe prolapse of A3 causing severe mitral regurgitation.

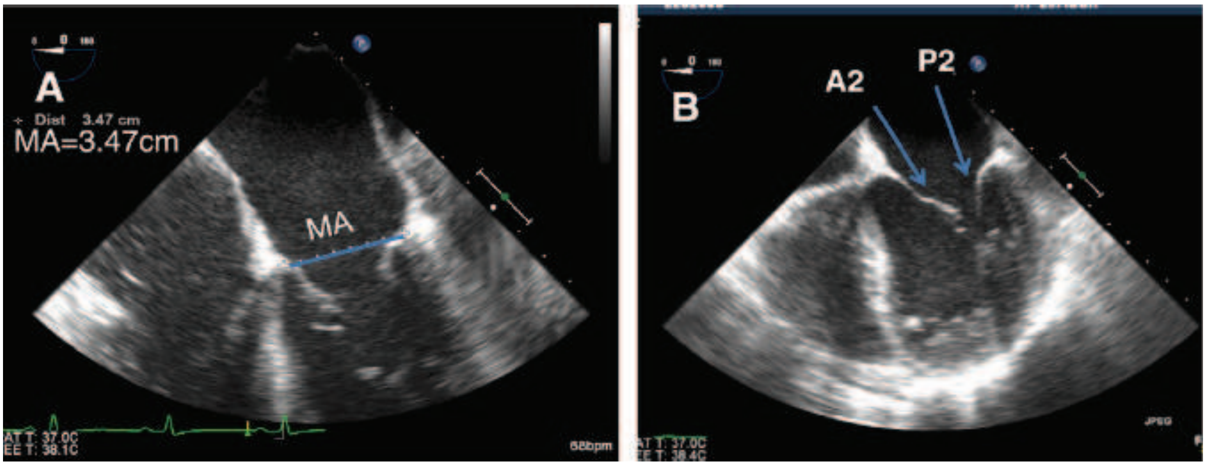


Figure 1.6.7 *(A) Mid oesophageal TEE view of mitral valve in four chamber view (0) to measure mitral annulus (MA). (B) Mitral leaflets at 0 visualizing A2 and P2 segments.*

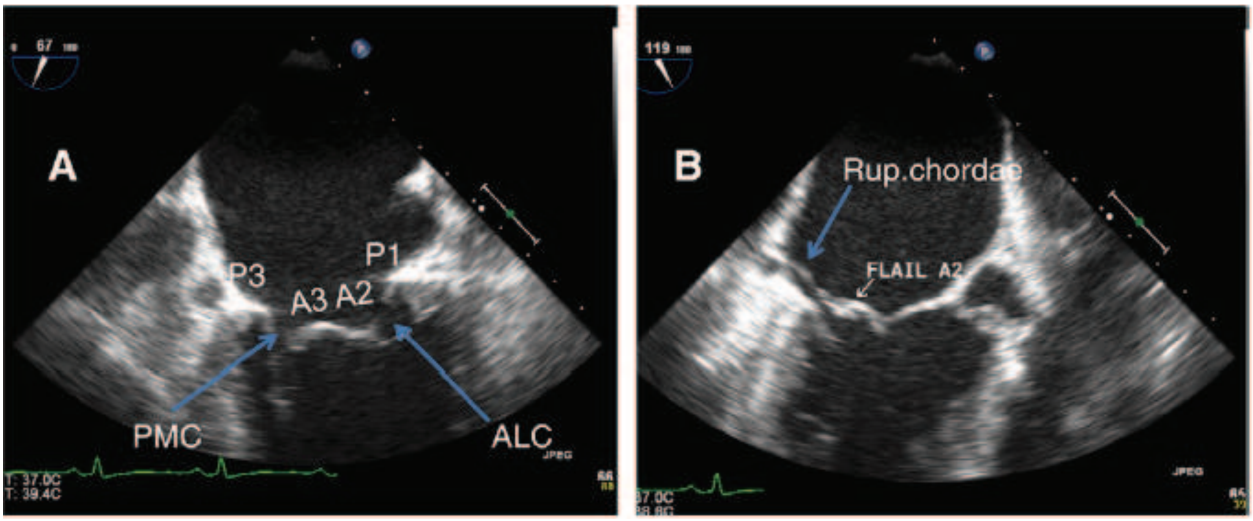


Figure 1.6.8 *(A) Mid oesophageal TEE view (bicommissural view, 75) showing P1, P3, A2, A3 and both commissures (ALC and PMC). (B) Long axis view at 120 showing flail A2 and ruptured chorda of A2.*

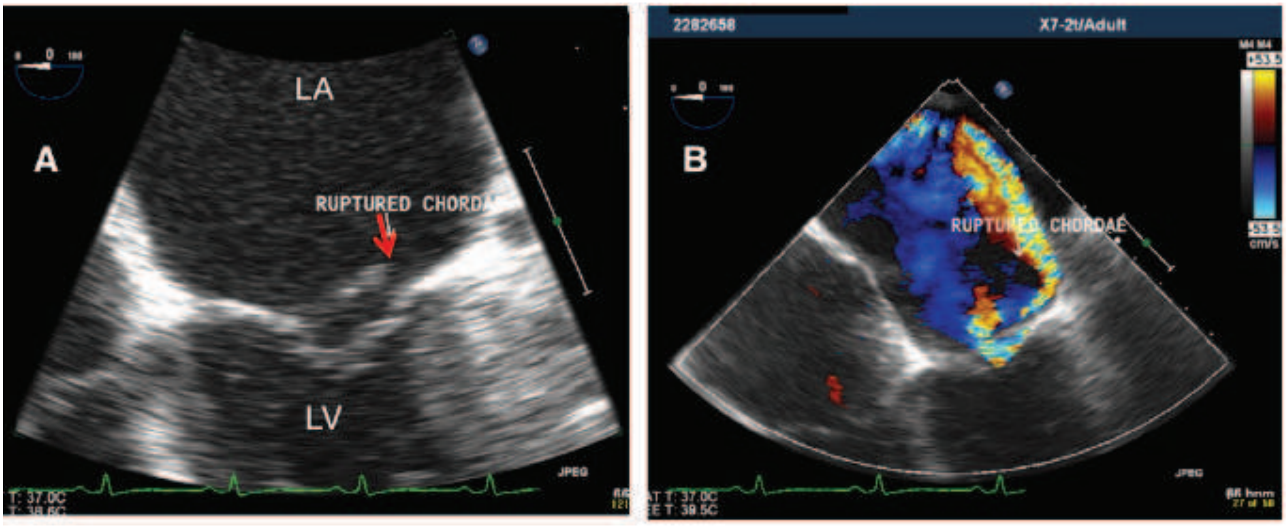


Figure 1.6.9*(A) TEE zoom view of mitral valve at 0 , showing flail A2 with ruptured chordae (red arrow). (B) Same view with colour, showing severe very eccentric (hugging jet) of posteriorly directed MR.*

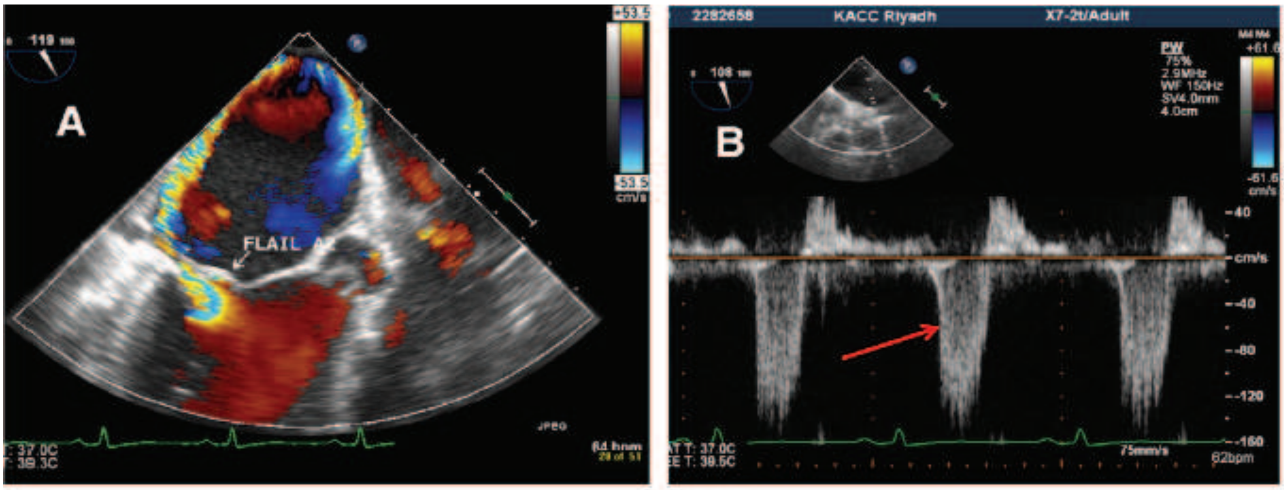


Figure 1.6.10 *(A) Midesophageal long axis view of mitral valve showing flail A2 with severe MR. (B) Mitral inflow Doppler sampling from right upper pulmonary vein showing systolic reversal flow confirming severe MR (red arrow).*

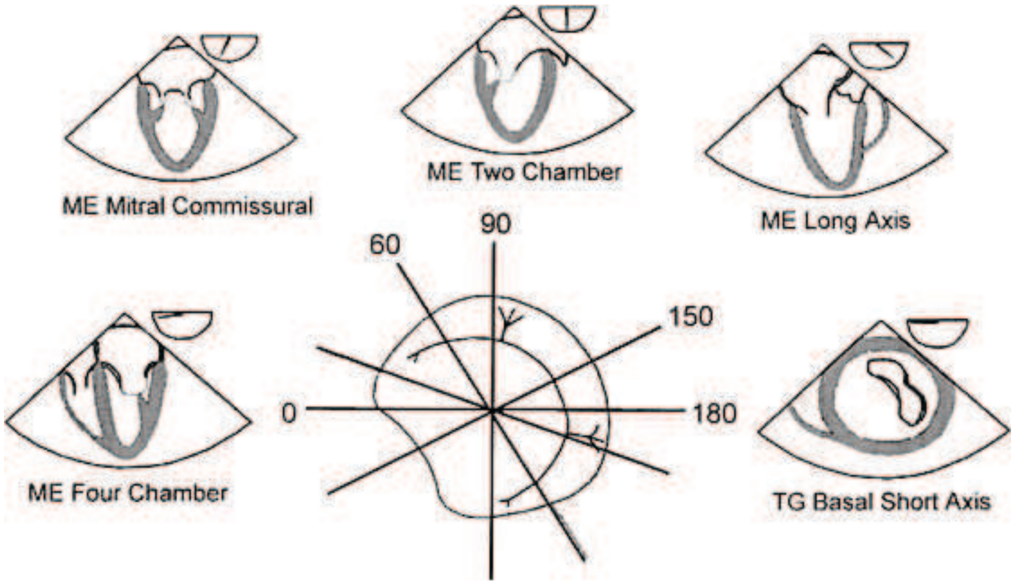


Figure 1.6.11 Cross sections of the mitral valve as described in the American Society of Echocardiography/Society of Cardiovascular Anesthesiologists guidelines for performing comprehensive intraoperative transesophageal echocardiographic examinations. (Adapted from Shanewise JS, Cheung AT, Aronson S, et al. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. *Anesth Analg* 1999;89:870–884,

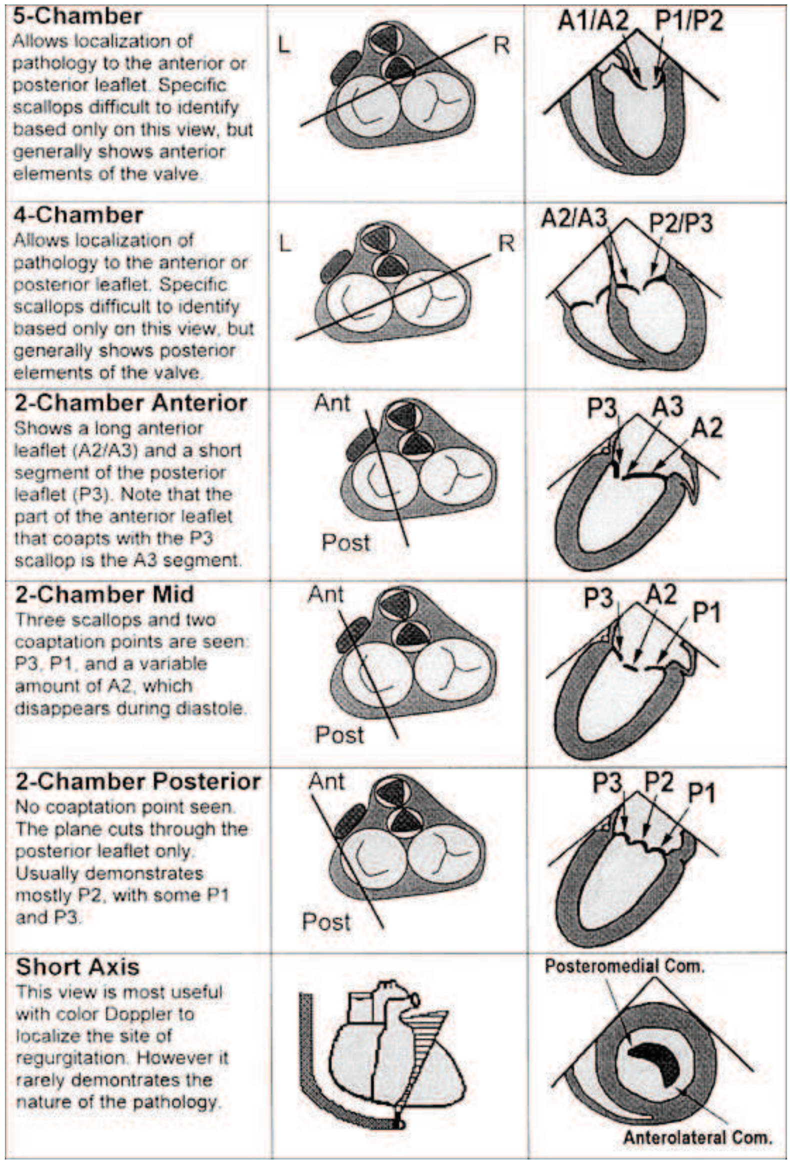


Figure 1.6.12 Systemic transesophageal echocardiographic examination of the mitral valve. (From Lambert AS, Miller JP, Merrick SH, et al. Improved evaluation of the location and mechanism of mitral valve regurgitation with a systematic transesophageal echocardiography examination. *Anesth Analg* 1999;88:1205–1212

The new advanced technology in echocardiography it is represented by three dimensional (3D) echocardiography. The use of new 3D probe has increased our ability to see the mitral valve anatomy like the surgeon sees it in the open chest with the 3 D zoom acquisition named also " surgical view". So the multiplane acquisition of 2D TEE echocardiography can be substituted with a simple one 3D acquisition and give the same and more accurate and specific informations about mitral valve anatomy also in relation to the surrounding structures.

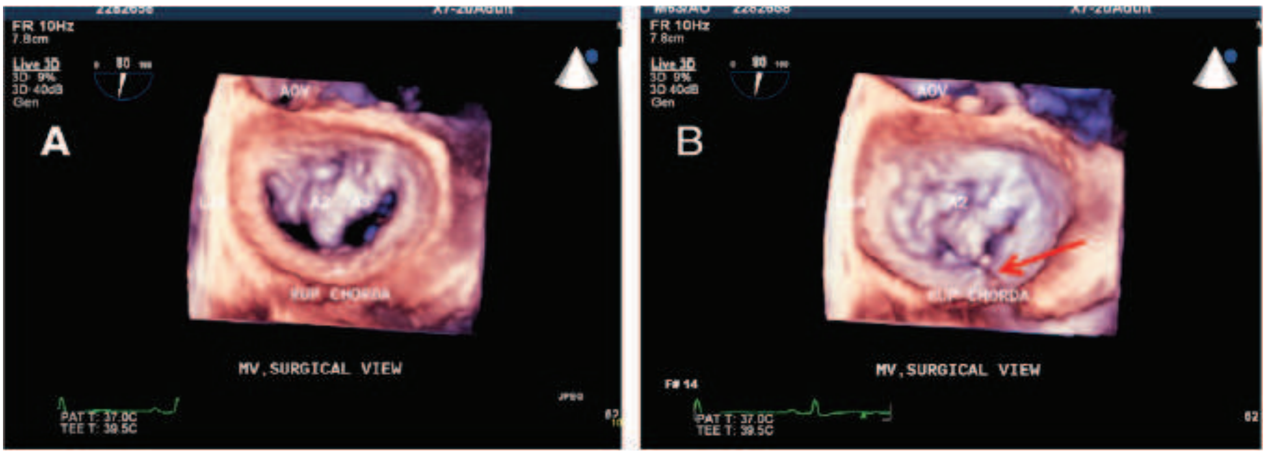


Figure 1.6.13 (A) 3-D zoom mode acquisition showing en-face surgical view of mitral valve with flail A2 and severe prolapse of A3. (B) Same mitral valve at the end of systole showing ruptured chorda attached to the A2 (red arrow).

1.7 The three-dimensional evaluation of mitral valve anatomy

Three-dimensional (3D) echocardiography has changed the view to see the heart structures, offers the ability to improve and expand the diagnostic capabilities of cardiac ultrasound.

Ultrasound technology has improved markedly in the past 10 to 15 years, prompting echocardiographs to extend its use in studying cardiac structure and function. New ultrasound equipment and techniques offer superior image quality, greater accuracy, and expanding capabilities.

Attempts to record and display ultrasound images in 3D format were first reported in the 1960s. One of the earliest studies described the acquisition of a series of parallel scans of a human orbit to reconstruct 3D anatomy.

More than a decade later, investigators began to obtain 3D ultrasound images of the heart.

Through he careful tracking of a transducer, a sequence of 2-dimensional (2D) echocardiograms could be recorded, aligned, and reconstructed into a 3D data set. This methodology was limited by the need for offline data processing to create and display the 3D images. In the early 1990s, von Ramm and colleagues developed the first real-time 3D (RT3D) echocardiographic scanner, capable of acquiring volumetric data at frame rates sufficient to depict cardiac motion. More recently, further improvements in design and engineering have led to the commercialization of RT3D echocardiography. The 3D real time echocardiography allows to see all the heart structures in three dimension .

Different types of 3D acquisition:

1) Real-Time 3D Mode—Narrow Sector

Live 3D using the matrix array transducer permits a real-time display of a 300 x 600 pyramidal volume. While the size of the sector is usually insufficient to visualize the entirety of a single structure in any one imaging plane, the superior spatial and temporal resolution permits accurate diagnoses of complex pathologies while preserving optimal temporal resolution.

2) Focused Wide Sector—"ZOOM"

The "ZOOM" mode permits a focused, wide sector view of cardiac structures. It must be noted that enlarging the region of interest excessively will result in a further detrimental decrease of the spatial and temporal resolution relative to real-time 3DE.

3) Full Volume—Gated Acquisition

The full volume mode has the largest acquisition sector possible, which is ideal when imaging specific structures such as the mitral valve or aortic root. This mode also has optimal spatial resolution, which permits detailed diagnosis of complex pathologies. As well, it has high temporal resolution (>30 Hz). Similar to the real-time 3D and the focused wide sector—"ZOOM" modalities, the gated full volume can also be rotated to orient structures such as valves in unique en face views. Furthermore, the full volume data set can be cropped or multiplane transected to remove tissue planes in order to identify components of valvular structures within the volume or to visualize 2D cross-sectional x, y, and orthogonal planes using off-line analysis software.

4) Full Volume with Color Flow Doppler

When 3DE color flow Doppler imaging was first introduced using a matrix array transducer, it could only be displayed using a full volume, gated reconstruction technique. This required the incorporation/"stitching" of 7-14 individual pyramidal volume slabs gated to the ECG, to create a 3D composite volume, in the upper-end range of a 400 x 400 sector at a frame rate of 15-25 Hz depending upon the selected line density. However, currently 3D color full volume can be acquired with less than the 7-14 individual gated volumes and the most recently developed software allows acquisition of as low as 2 beats, albeit at the cost of temporal resolution.

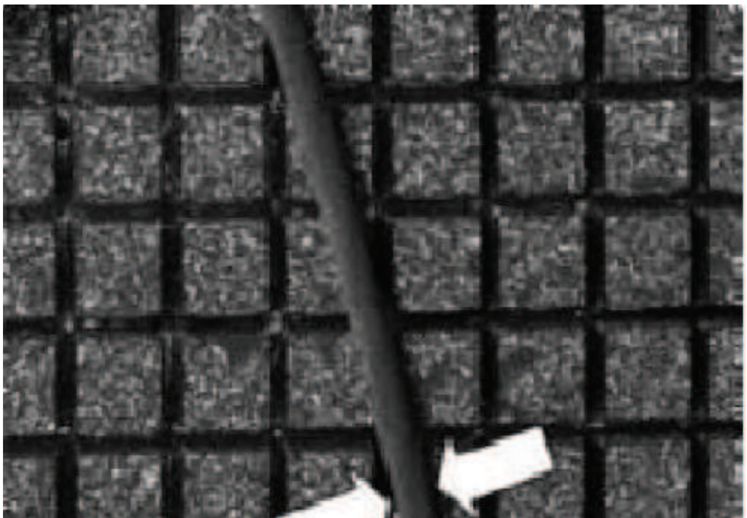


Figure 1.7.1: *Multiple transducer elements arranged in a grid like fashion in a matrix phased-array transducer. A human hair is shown for a size comparison.*

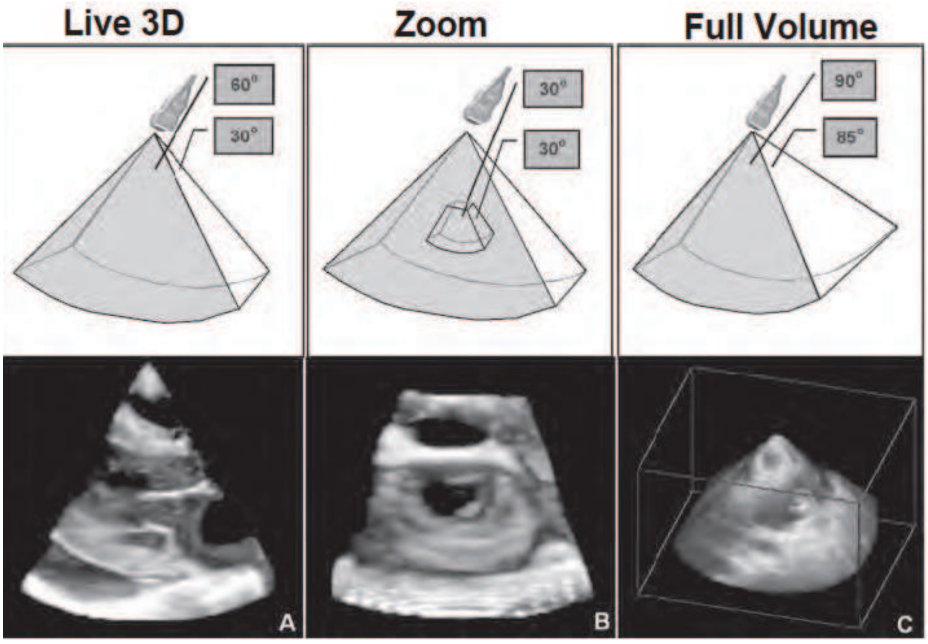


Figure 1.7.2: *different types of three dimensional acquisitions: Live 3D sector of acquisition regulable in width for anatomical details, Zoom 3D acquisition focused on a section, Full volume acquisition a slice of tissue.*

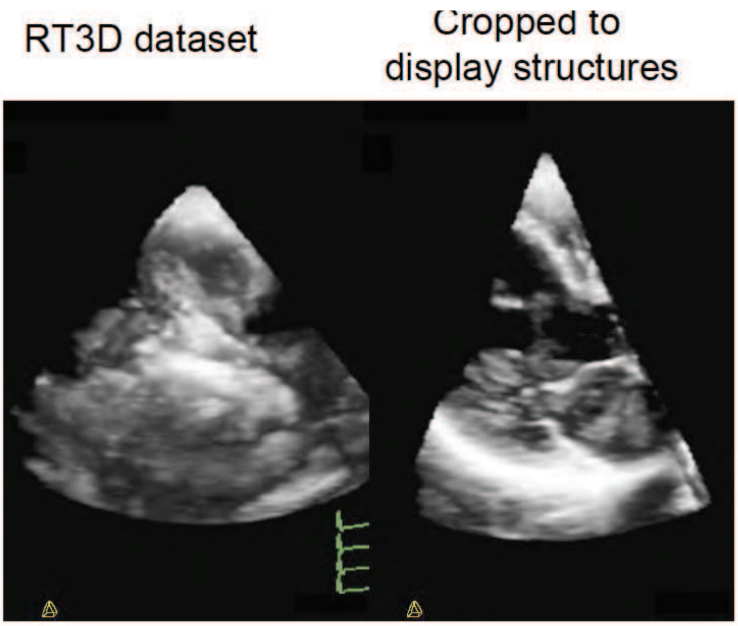


Figure 1.7.3: *Zoom 3D acquisition and Full volume acquisition can be sliced with dedicate software Qlab or other in order to obtain the optimal plane of observation.*

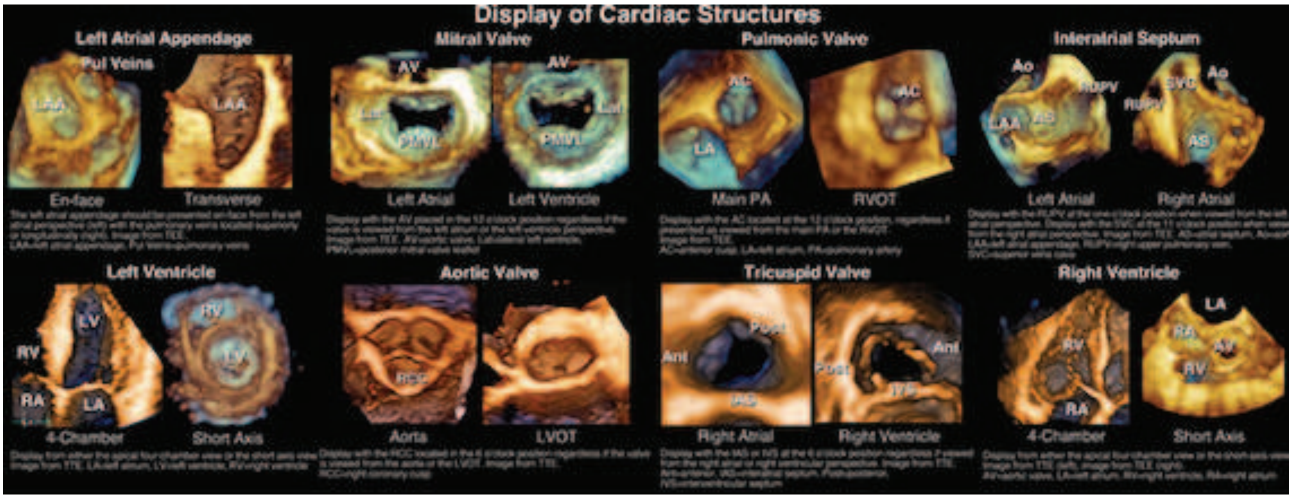


Figure 1.7.4 : *3D revolution and most important change in the visualization of heart structures.*

Three-dimensional (3D) echocardiography has been conceived as one of the most promising and essential methods for the diagnosis of valvular heart disease, and recently has become an integral clinical tool thanks to the development of high quality real-time transesophageal echocardiography (TEE). In particular, for mitral valve diseases, this new approach has proven to be the most unique, powerful, and convincing method for understanding the complicated anatomy of the mitral valve and its dynamism. The method has been useful for anatomy characterization before surgical management.

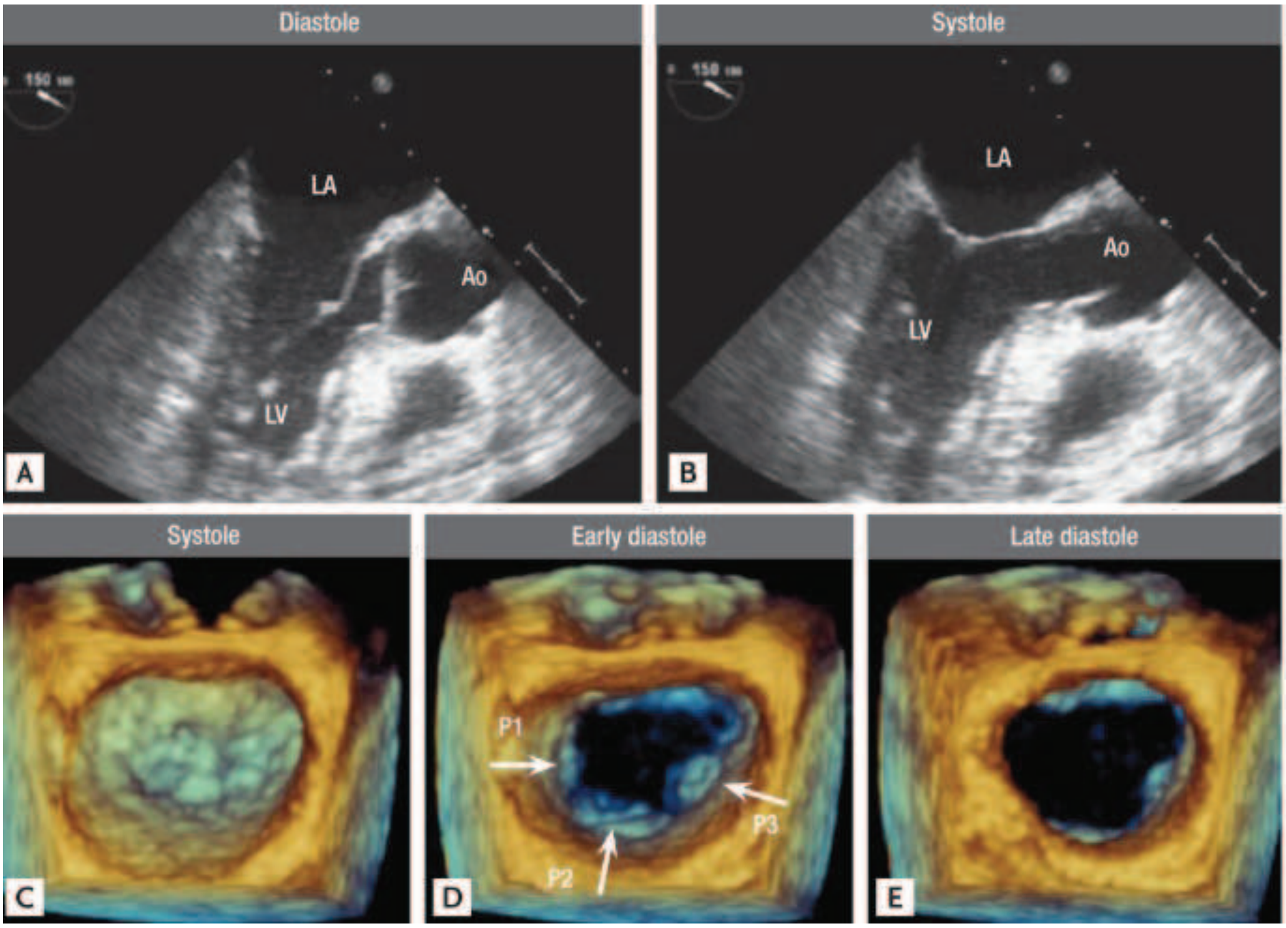


Figure 1.7.5 **:***Normal mitral valve imaged by 2-dimensional (D) echo (A, a long axis view in diastole; B, in systole) and real-time 3D transesophageal echocardiography (C, a view from the left atrium in systole; D, in eerily diastole; E, in late diastole).*

Image resolution remains a concern for transthoracic 3D imaging, but the recent development of 3D transesophageal echocardiography (TEE) (either real-time or reconstructed) has made this less of an issue. Development of 3D echocardiography has made vast contributions to the understanding of mitral valve function. Although in the majority of patients with mitral stenosis, comprehensive 2D and Doppler echocardiography is sufficient, several clinical trials have demonstrated that 3D echocardiographic mitral valve planimetry can provide better correlation with invasively determined mitral valve area. An example of this technique using 3D transthoracic imaging is shown in Figure 1.7.1. With the advent of real-time 3D TEE, rapidly obtainable views of the mitral valve, either from the left atrial perspective ("surgeon's view") or from the left ventricular perspective, are now possible with intraoperative TEE during mitral valve surgery.

I order to see better mitral valve leaflets details it is possible to crop the valve , with different cutting planes. Otherwise it is possible to do a reconstruction with 3D software dedicated to tha valve analysis (47-60).

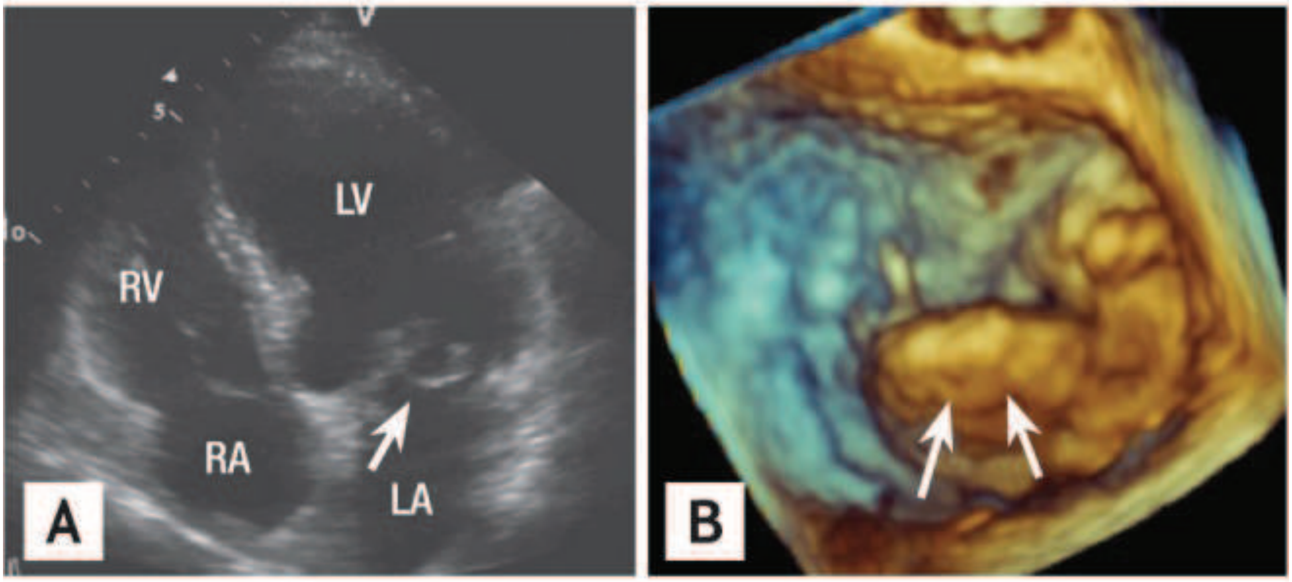


Figure 1.7.6: *Mitral valve prolapse imaged by (A) 2-dimensional (D) transthoracic echocardiography (arrow) and (B) real-time 3D transesophageal echocardiography (arrows). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.*

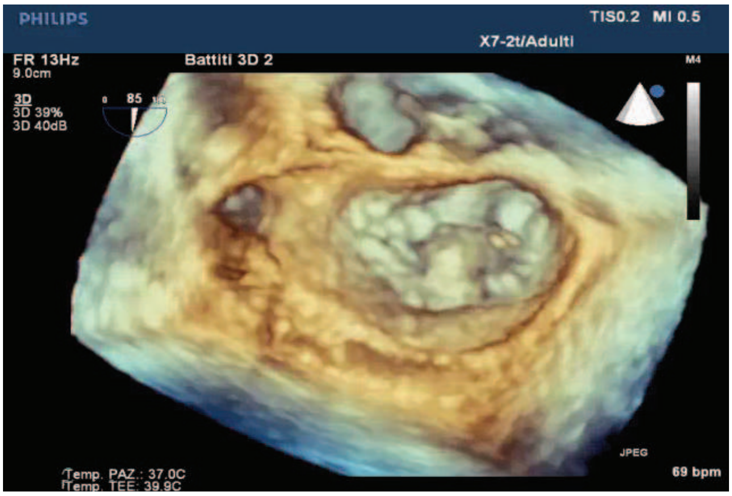


Figure 1.7.8 *Zoom 3D of the mitral valve with prolapse flail of P2*

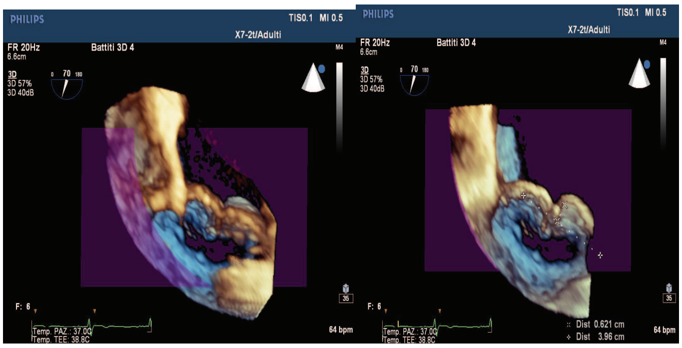


Figure 1.7.9 : *Croped slice of mitral valve with myxomatousatouse disease*

Figure 1.7.10: full volume of left ventricle and mitral valve , it is possible to see also right chambers

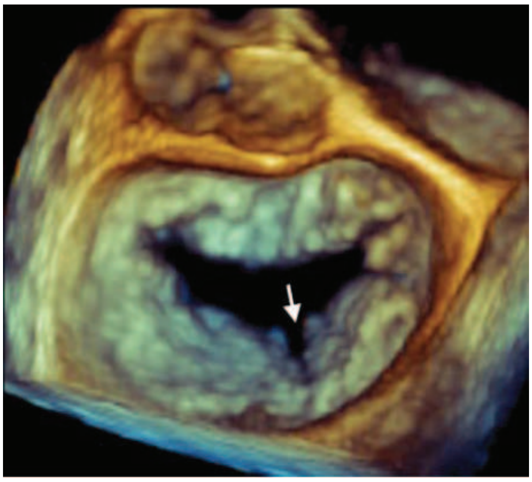


Figure 1.7.11: 3D zoom acquisition with a detail of a "Cleft " or subcommissure enlargement in the posterior leaflet between P2 and P3.

The myxomatousatous Mitral Valve Disease

In western countries the most common etiology of mitral valve pathology is the degenerative disease, affecting around 2% of the population, with a wide spectrum of anatomic lesions, from fibroelastic deficiency (localized prolapse segment, often associated with ruptured chordae), to extensive myxomatous degeneration and Barlow's disease (with multiple valvular segments involved) . In the last decade, three-dimensional transesophageal echocardiography has improved imaging power to identify anatomical and functional problems, and has become an indispensable instrument of cardiological diagnosis and management in the field of mitral valve disease. It also simplifies the language between physicians and surgeons, introducing, with 3D zoom acquisition the opportunity to have the “surgical view”, as it represents the intraoperative image of the mitral valve after the surgeon, standing on the patient’s right side, opens the left atrium.

It is very important characterize the lesion, by identifying the wide spectrum of lesions, from fibroelastic deficiency to myxomatous disease and Barlow’s syndrome, and identify the presence of chordae rupture (“flail”).

Identification of the lesion: whether it is monoleaflet (anterior or posterior located) or bileaflet, and which segment (for the anterior Leaflet) or scallop (for the posterior leaflet) of the leaflets is enveloped. The posterior leaflet is usually divided by the intra-leaflet cleft into three scallops: P1 (anterolateral), P2 (central, possibly divided into two subunits: P2 M1 more antero-lateral and P2M2 postero-medial according Duran Classification) and P3 (postero-medial), normally in the anterior leaflet there are no clefts and we can identify three corresponding facing segments (A1-A2-A3) .

In the case of bileaflet prolapse, it is necessary to describe if the lesions are facing or non facing. We can also identify two commissures: anterolateral (near the left appendage between P1 and A1) and posteromedial (between P3 and A3) rarely they can be involved in the degenerative disease.

This anatomical characterization helps to identify whether the mitral valve lesion is simple or complex, whose surgical repairs have different grades of efficacy and durability.

In the last decade 3-Dimensional transesophageal echocardiography has changed the physician's ability to describe the mitral valve anatomy in the degenerative disease, and it has simplified communication with the cardiac surgeon through the 3D zoom acquisition with " surgical view" (61-70).

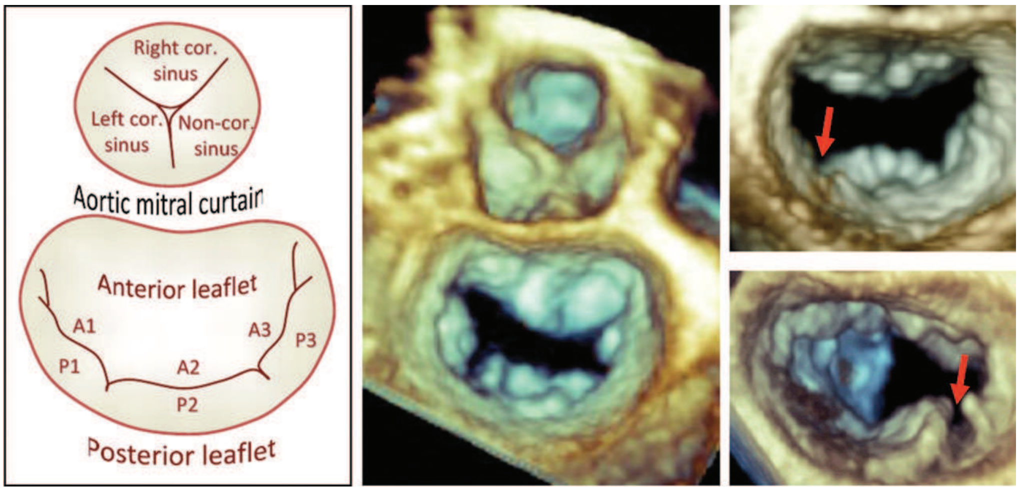


Figure 1.7.12: The Surgical View

3D transesophageal echocardiography is the most powerful technique with high sensibility and specificity to identify the site and the types of lesion that our study group(La Canna *et al*) has divided in primary and secondary prolapses.

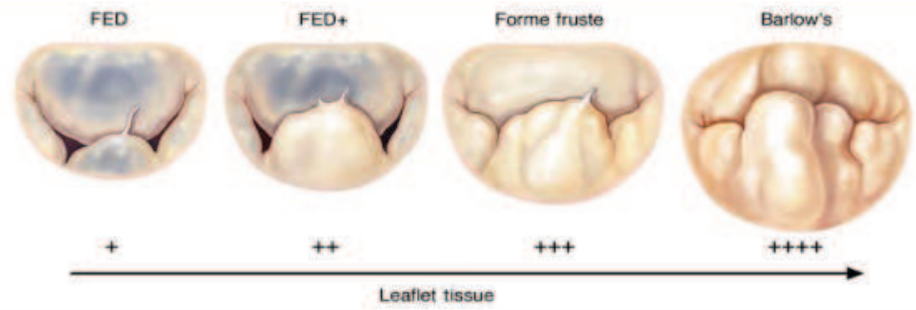
In this study the echocardiographic data were compared with the surgical findings, and per-patient analysis of RT3D-TEE identified prolapse more accurately (92%) than 2D-TEE (78%), RT3D-TTE (80%), and 2D-TTE (54%), the multiplanar reconstruction enabled RT3D-TEE to differentiate dominant (≥5-mm displacement) and secondary (2 to <5-mm displacement) prolapsed according to surgically recognized dominant lesions (100%), but with a low predictive value (34%) for secondary prolapses.

There are many ideal lesions to perform E-to-E technique: a little prolapse of P2 in myxomatous degenerative mitral valve disease, prolapse/flail of P2 in fibroelastic deficiency, or bileaflet prolapse facing (i.e. A2P2) with a good starting valve area, sometimes also in the isolated prolapse of commissure (anterolateral or posteromedial) it is possible to apply an asymmetrical E-to-E closure of the commissure with a good result and durability.

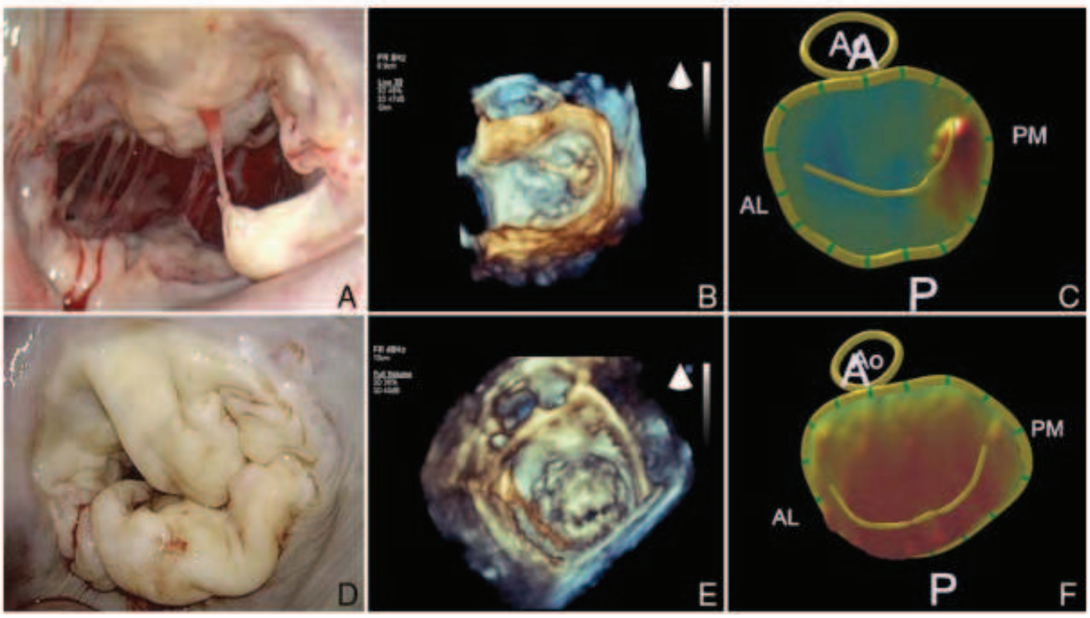
The annulus is normally saddle-shaped, but in the degenerative disease, and in Barlow's Syndrome, its three dimensional shape changes becoming more enlarged and flat, with a tendency to assume a circular form. It is important to stress its dimension, because many studies have assessed that E-to-E technique has a more favourable outcome if stabilized with an annular ring.

Surgical experience with edge-to-edge technique indicates significant recurrent MR if the procedure is not accompanied by annuloplasty, resulting in a need for reoperation in 30% of patients at 5 years (versus 8% in those with annuloplasty; P=0.02).

The annulus may often be affected by calcification, therefore it is important to define the entity of the calcification and if it extends to the leaflet or to the left ventricle wall.. It is also mandatory to identify the presence and localization of calcium. The calcification of the mitral apparatus is frequently associated to Barlow's disease, therefore it is mandatory to establish possible calcification of the annulus (mild or severe, spot or circumferential) and its possible extension to the leaflets' tissue and to the target lesion in order to choose the correct surgical treatment (111-118).



A



B

Figure 1.7.13 Ae B: *Wide spectrum of mitral valve's degenerative disease importance of Three-dimensional evaluation and 3D software reconstraction.*

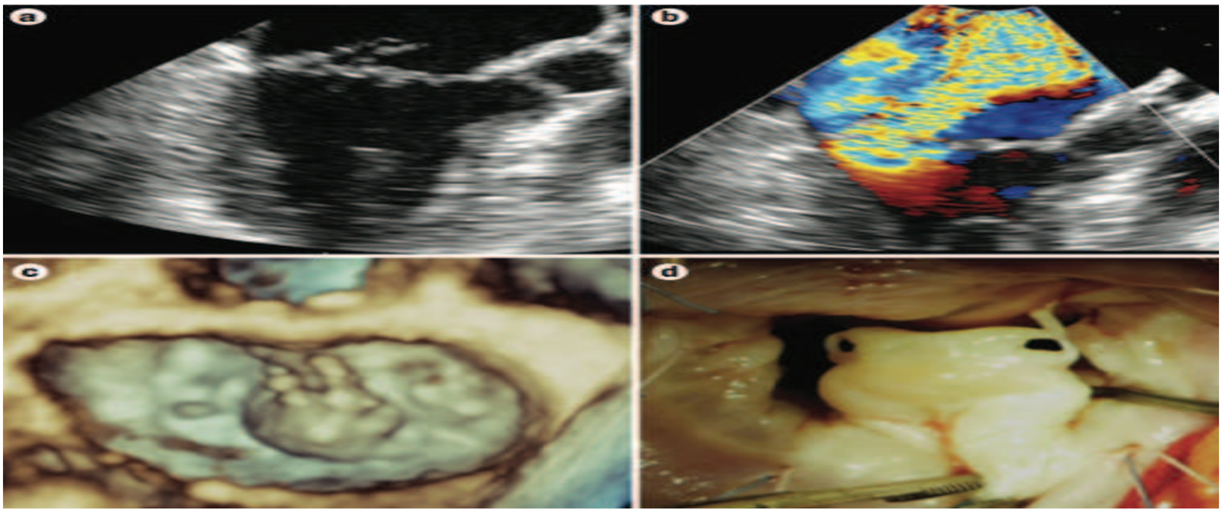


Figure 1.7.14 : *Comparison between 3D echocardiography imaging and real intraoperative pictures of mitral valve disease with P2 prolapse/flail*

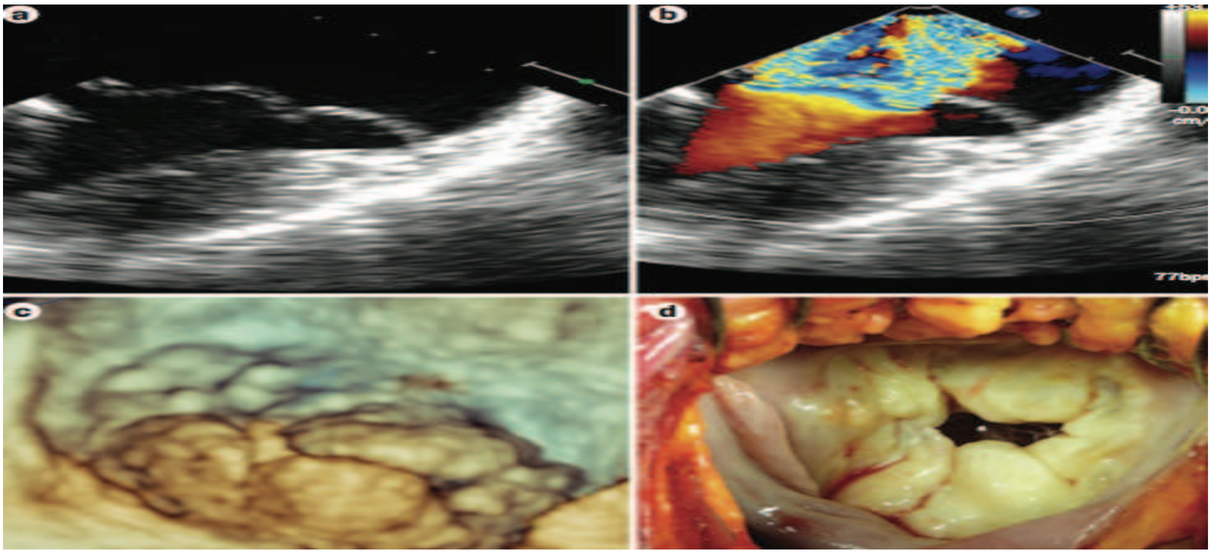


Figure 1.7.15 : *Comparison between 3D echocardiography imaging and real intraoperative pictures of myxomatousatous mitral valve disease Barlow disease with multiscallops iprolaps*

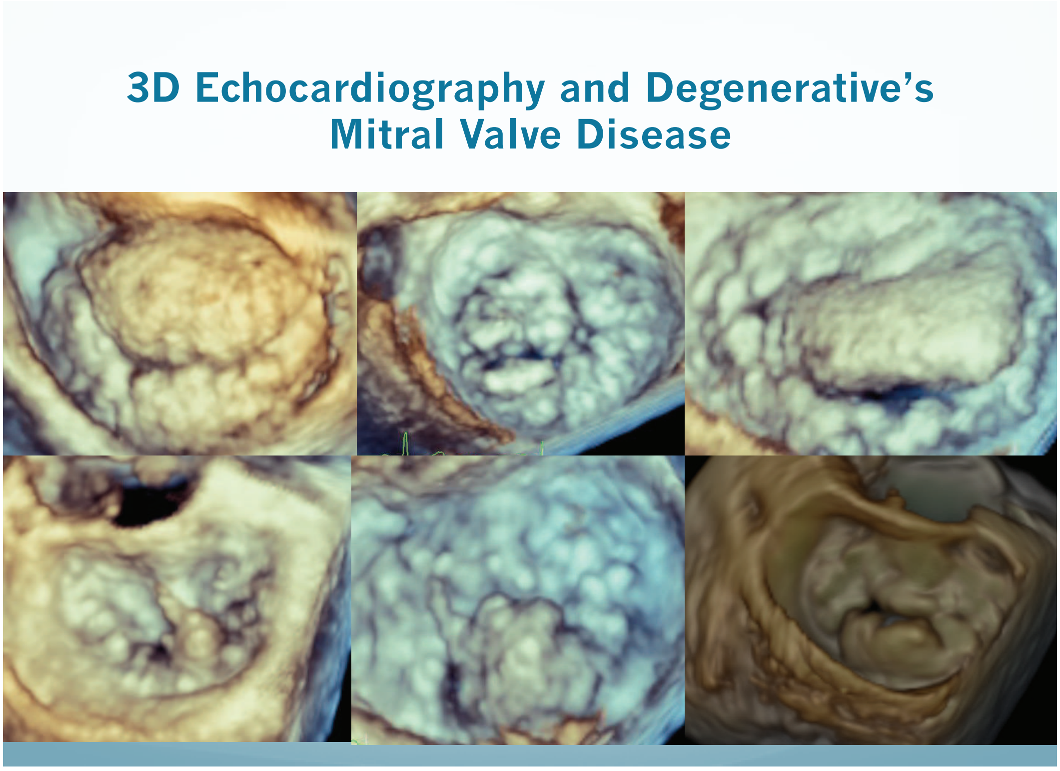


Figure 1.7.16 : *three dimensional imaging of the mitral valve with different type of degenerative disease, from the simple prolapse of P2 with fibroelastic deficiency, degenerative prolapse of the posterior leaflet and myxomatousautouse disease Barlow disease with multiscallop prolapse.*

	Simple lesions	Complex lesions	Lesions at high-risk of unsuccessful repair
Type of lesion	Posterior leaflet prolapse or flail (isolated mid-scallop involvement [P2], with or without redundant tissue [leaflet height ≥15 mm]) Annular dilation Leaflet perforation	Complex posterior leaflet lesions Anterior prolapse or flail Bileaflet prolapse or flail Commissural prolapse or flail Combined lesions Deviant anatomy	Prolapse and extensive annular calcification Prolapse with hypoplasia of opposite leaflet Extreme fibroelastic deficiency Post-endocarditis extensive destruction Rheumatic disease
Probability of successful and durable repair	High	Depends on experience of the surgical team	Low
Surgical techniques	Quadrangular or triangular resection (including sliding plasty according to leaflet height) Annuloplasty Patch or direct suture	Artificial chordae Chordal transposition Edge-to-edge technique	Very technically demanding techniques (including artificial chordae, leaflet enlargement, and annular decalcification)
Necessary expertise of surgical team	Low	High	Very high

*Judged by echocardiography. Abbreviation: MV, mitral valve.

Table 1.7.2: *the lesions can be calssificated in simple and complex mitral valve lesions, this can have an important impact on the surgical mitral valve repair*

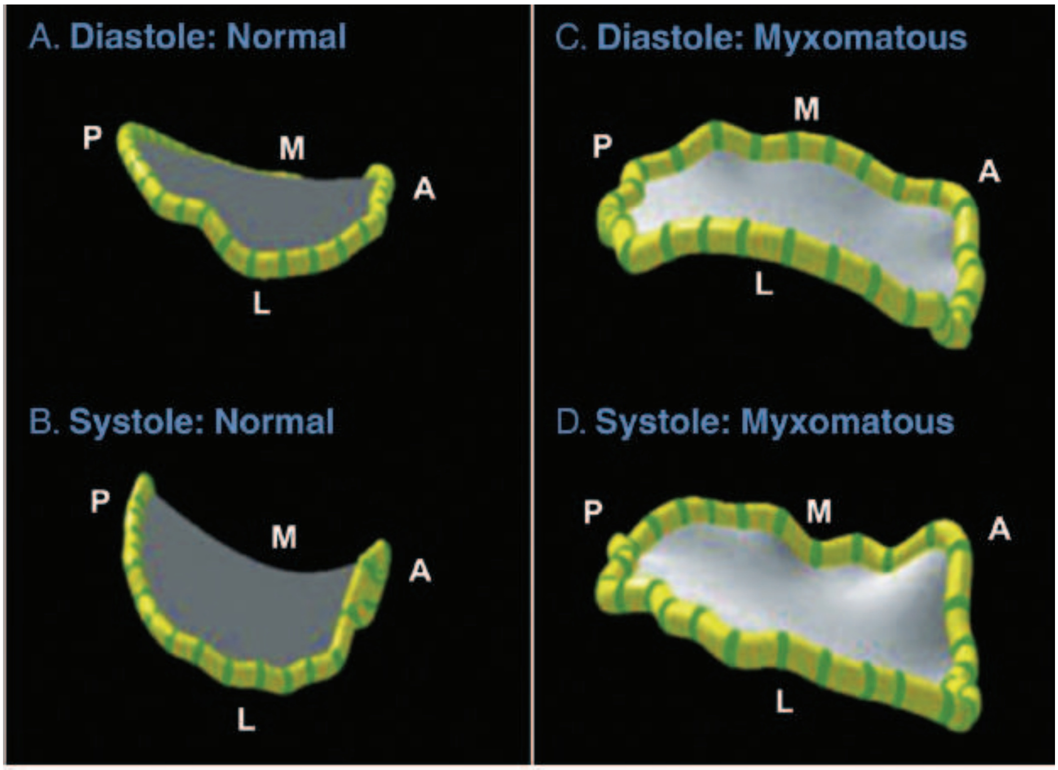


Figure 1.7.17: 3D reconstruction of mitral valve annulus with dedicated software.

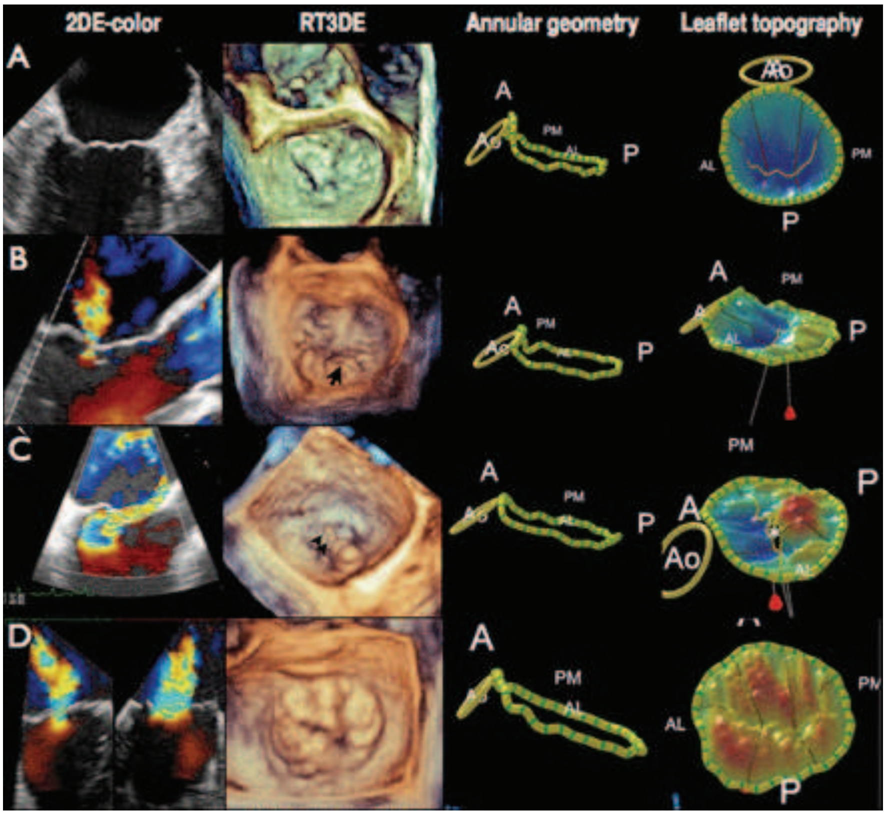


Figure 1.7.18: *3D reconstruction of mitral valve annulus with dedicated software, modification in different setting of degenerative disease. Illustrative examples of mitral valve deformation in mitral valve prolapse.* ***A****, A control subject with a saddle-shaped annulus (annular high to commissural width ratio [AHCWR]=23%).* ***B****, A patient with mild posterior leaflet billowing with mild mitral regurgitation (MR) on 2-dimensional echocardiography (2DE). Real-time 3-dimensional echocardiography (RT3DE) reveals isolated P2 billowing (arrow). The saddle shape of mitral annulus decreases , and the leaflet topography shows a light-red hue localized to P2 with a leaflet billow volume of 0.2 mL. C, A patient with chordal rupture resulting in flail P2 segment and severe eccentric MR on 2DE. The ruptured chord can be clearly visualized on RT3DE. Leaflet topography shows a deep-red hue at P2, indicating P2 prolapse with a large coaptation gap (asterisk). Leaflet billow volume=0.8 mL.* ***Bottom****, A patient with bileaflet billowing and severe MR. The MR jet is central and large with an elongated vena contracta, as shown on biplane imaging. Substantial leaflet billowing and increased total leaflet surface area are well appreciated on RT3DE. The mitral annulus is large and extremely flat (AHCWR=10%), and the leaflet topography shows diffuse deep-red discoloration over multiple segments, illustrating extensive leaflet billowing. A indicates anterior; AL, anterolateral; Ao, aortic annulus; P, posterior; and PM, posteromedial.*

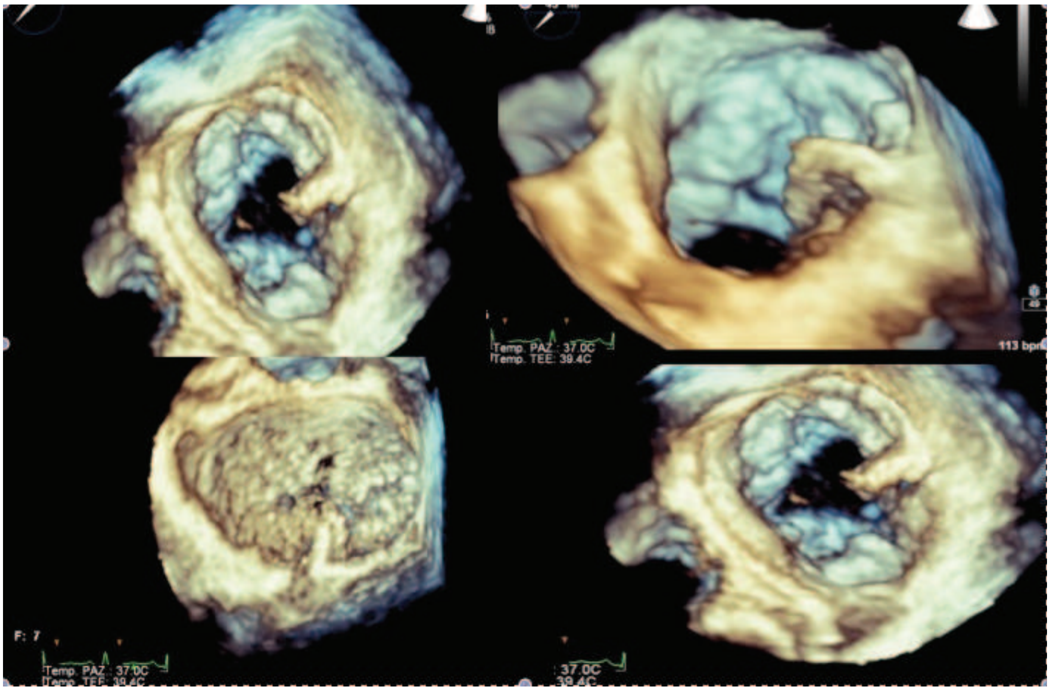


Figure 1.7.19: 3*D real time visualizzation of anulus calcification, localizzation and extension to the annulus and to the posterior leaflet*

1.8 Mitral Valve Repair for Degenerative's Mitral Disease: type of surgical interventions

The atrioventricular valve is the most commonly repaired valve of the heart.

Over the past few decades, it has become apparent that mitral valve repair is preferable to mitral valve replacement for the majority of patients undergoing surgery for mitral regurgitation (MR).

The advantages of mitral valve repair include low rates of thromboembolism, resistance to endocarditis, excellent late durability reported for as long as 25 years, and no need for anticoagulation in the majority of patients.

Because of these advantages of repair over replacement, the threshold for performing mitral valve repair has been lowered to include patients with MR who have early symptoms or even those who are asymptomatic, assuming that the chance of successful repair is ≥90% according to the latest American College of Cardiology/American Heart Association guidelines.

Myxomatous MR affects 1% to 2% of the population and therefore is a common pathology for mitral valve surgery, but the complexity of the operation may be difficult, which leads to generally low rates of repair. In a recent review, only 44.3% of patients in the United States who required mitral valve surgery for MR received a mitral valve repair, and in the Euro Heart Survey, repair rates were similarly low (46.5%). The goals of mitral repair are to maintain leaflet mobility, remodel the annulus, and allow normal coaptation of the anterior and posterior leaflets.

Interventional procedures like annuloplasty, valvotomy/valvuloplasty, repair/replacement of the valve for regurgitation or prolapse are increasing by the day. This necessitates a clear understanding of the mitral valve anatomy. Nowadays the mitral valve repair is the best choice for young asymptomatic patients affect by severe organic mitral regurgitation.

In this last 20 years a lots of technique were developed and they can be divided in simple and complex in order to their technical complexity and time consumption. Complex leaflet reconstruction techniques, such as sliding plasty or reduction of anterior leaflet high, are technically more difficult than annuloplasty alone, and this is thought to be one of the important reasons why repair rates are low in this condition.

Prolapse of the posterior leaflet (PPL) is the most frequent dysfunction of the mitral valve in the western world. Quadrangular resection, first proposed by Alain Carpentier, has progressed to become the gold standard modality to repair posterior leaflet prolapse. Although this "resection technique" is safe, reproducible, and offers favorable long term results, it presents major drawbacks. Firstly, it leads to a reduced surface of coaptation, the ultimate goal of mitral valve repair; secondly, it does not respect the anatomy of the mitral valve; thirdly, it leads to a deformation of the base of the ventricle; and finally, degenerative disease of the mitral valve is a spectrum of lesions depending on the amount of excess tissue, and hence, a one technique-fits-all strategy cannot meet the absolute necessity to repair all mitral valve patients with PPL. Therefore, new approaches which have been proposed place greater emphasis on respecting, rather than only resecting, the leaflet tissue in order to avoid the drawbacks of the "resection" approach. The use of artificial chordae to correct the leaflet prolapse restores the normal anatomy and physiology of the mitral valve, thus producing an optimal surface of coaptation. However, this approach is limited by anatomical variances.

The choice of the best surgical technique depend by the experience of the surgeon and by the anatomy of the myxomatousatous mitral valve (88-110).

- Triangular Resection (s)

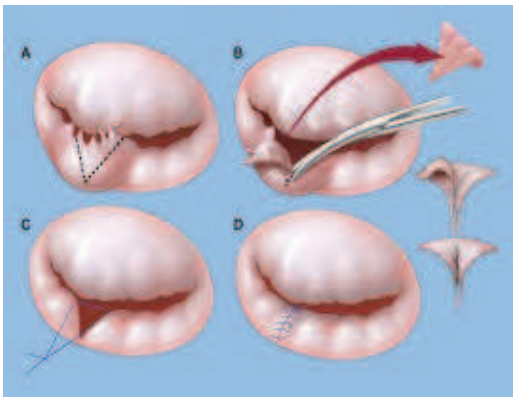
- Quadrangular Resection (s)
- Quadrangular resection +Sliding plasty ©
- Folding plasty ©

- Annuloplasty (s)
- Neochordae implantation ©
- Edge to Edge (s)
- Cleft Closure (s)

The triangular resection

This technique has been promoted by the Mayo Clinic . It is the logical evolution of the original technique used by MacGoon . Long-term results of this technique are very satisfactory . The triangular resection has several distinct benefits over quadrangular resection. Triangular resection does not alter the geometry of the base of the left ventricle. Triangular resection removes less normal tissue, and is technically less demanding.

Nonetheless, the triangular resection has obvious limitations: (I) in cases of extensive PPL involving more than one scallop; (II) in cases of excess leaflet tissue, the reduction of the high of the posterior leaflet may require additional steps that have been described .



Drawing of The Triangular Resection Technique

The quadrangular resection

This approach has been developed and promoted by Carpentier *et al.* , to repair PPL, whether the result of ruptured or elongated chordae is treated by extensive quadrangular resection of the prolapsed area.There is no doubt that this technique is easily reproducible, especially in the case of standard prolapse of P2 with no excess of tissue. Long term results have been very gratifying, showing a minimal operative mortality, an excellent long term survival equal to the survival rate for a normal age- and sex-matched population and a long-lasting durability (On the other hand, unexpected technical difficulties, due to special anatomical conditions may be encountered leading to a non-satisfactory result.

I. The loss of surface of coaptation, secondary to leaflet prolapse may lead to excess tension and stress on the chordae adjacent to the prolapsed area. In case of a long-standing mitral regurgitation, these chordae may become elongated. In such a situation, blindly applying the technique may lead to a certain degree of residual prolapse and the possibility of excess motion of the free edge of the posterior leaflet;

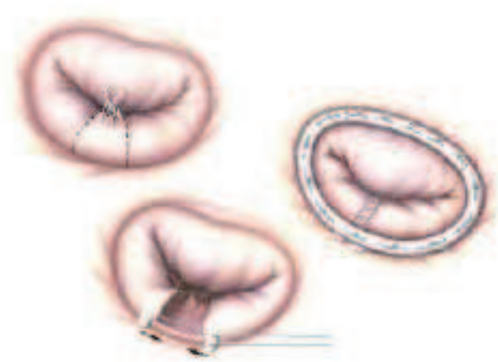
II. Numerous chordae may be ruptured or elongated and thus responsible for a very large prolapse. Leaflet resection of the prolapsed area would leave insignificant remnants of the posterior leaflet to satisfactorily repair the mitral valve;

III. Annulus plication induces a deformation of the sub annular region of the left ventricle. This may be responsible for a temporary dysfunction of the base of the left ventricle;

IV. In case of extensive resection and lengthy annulus plication, cases of kinking of the circumflex artery have been described ;

V. PPL frequently involves P2, which by nature is the highest and most developed scallop. This portion of the posterior leaflet is the one sustaining the greatest stress during systole . Resection of this area decreases the high of the posterior leaflet precisely where it is the most needed;

VI. Mucoid degeneration associated with degenerative mitral valve may lead to excess of tissue. Mihaileanu has shown that excess of tissue predominantly involving the posterior leaflet in one of the main factors responsible for left outflow tract obstruction (LVOT) with systolic anterior motion (SAM) . Carpentier has subsequently described the “sliding plasty” to reduce the high of the posterior leaflet and subsequently prevent SAM

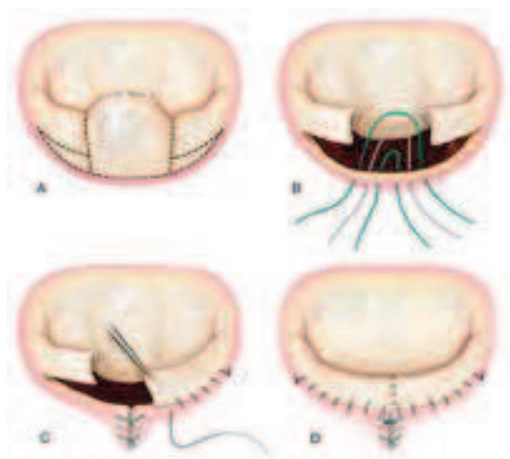


Drawing of The Quadrangular Resection Technique

Sliding plasty

The goal of the sliding plasty is to reduce the high of the posterior leaflet, in circumstances where there is excess tissue, to restore the normal two-thirds to one-third ratio between the respective high of the anterior and posterior leaflets. This technique has proved to be efficient to prevent or treat LVOT with SAM . The main advantages of this technique include: (I) it allows the resection of any amount of excess tissue of the posterior leaflet; and (II) it achieves a regular and progressive narrowing of the annulus, thereby avoiding any major changes in the geometry of the left ventricle.

Drawbacks of this technique are identical to these of leaflet resection presented with the quadrangular resection technique.



Drawing of The Sliding Resection Technique

Other repair techniques

The folding technique has been described by Grossi *et al*. and the butterfly technique by Asai *et al*.

The need for annulus plication is reduced with the use of these techniques. The high of the posterior leaflet is reduced and leaflet coaptation is moved posteriorly. These techniques share the disadvantages of the "resection techniques".

The "respect approach" Neochordae implantation

The rationale of this approach is to preserve the leaflet tissue that is critically important for the coaptation surface and to correct the prolapse by using expanded polytetrafluoroethylene (e-PTFE) suture neochordae without the employment of leaflet resection to resuspend the free edge of the posterior leaflet (). The goal of the RRR approach is to intentionally transform the posterior leaflet into a smooth, flat and regular buttress hanging vertically from the mitral annulus and against which the anterior leaflet will come in apposition.

Long-term results have shown that this approach presents the same durability and stability as the gold standard "quadrangular resection" . This technique offers numerous advantages:

I. The goal of mitral valve repair is to restore a good surface of coaptation to ensure a satisfactory function of the mitral valve. Leaflet tissue is the primary component defining the surface of coaptation and thus it may be more logical to preserve as much of the leaflet tissue, as opposed to resecting a large portion of it;

II. Respecting the leaflet tissue allows for a high surface of coaptation, especially when P2 is involved, as shown in a previous study ;

III. It is a safe method, allowing pursuit of another technique at any time, as nothing is resected or irreversibly altered;

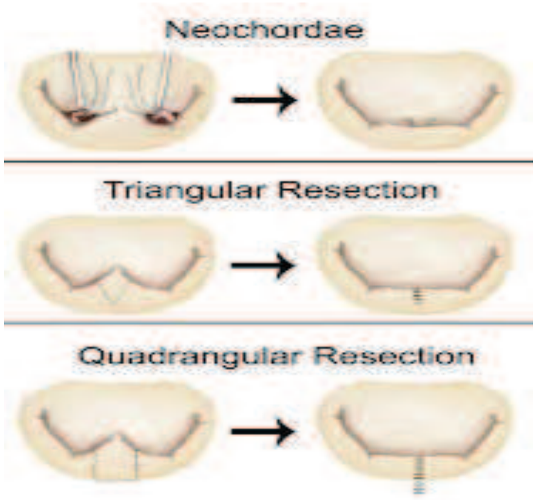
IV. Artificial chordae have been used to repair mitral valve for 25 years, and excellent long-term durability has been reported ;

V. From time to time, lesions are extensive with involvement of more than one scallop. This situation is easily addressed by the use of as many artificial chordae as necessary to resuspend all the prolapsed area;

VI. Not only does this approach correct the leaflet prolapse, but it also helps to prevent the occurrence of postoperative SAM. As seen above, at the time of adjusting the length of the artificial chordae it is necessary to take into account any excess of tissue so that the free edge of the posterior leaflet cannot move anteriorly and push the surface of coaptation in the outflow tract. Simply stated, if the excess tissue is large, the resulting artificial chordae should be made shorter. It is important to ensure that the surface of coaptation remains in the inflow parallel to the wall of the left ventricle;

VII. Artificial chordae not only correct the leaflet prolapse, but also maintain the posterior leaflet and the surface of coaptation in the inflow of the left ventricle.

The RRR approach may be the technique of choice when quality and quantity of posterior leaflet tissue is adequate to achieve a smooth and regular surface. However, there are some limitations to this technique. Excessive and exuberant myxomatous degeneration can render the posterior leaflet irregular with bulging deformations that need to be resected to obtain a regular surface of coaptation. Excess of tissue affects not only the high if the posterior leaflet, but more importantly its width, and may transform the normally rectangular P2 into a trapezoidal element. The placement of the annuloplasty ring may result in folds of the posterior leaflet that alter the coaptation surface smoothness. Again in this situation, a localized resection is necessary to reshape the posterior leaflet. Accumulation of myxomatous material at the base of the posterior leaflet should be removed with leaflet resection, as it deforms and prevents the leaflet from hanging vertically, causing it to protrude anteriorly and increasing the risk of SAM.



Drawing of Neochordae Implantation Technique

The Edge to Edge Techique

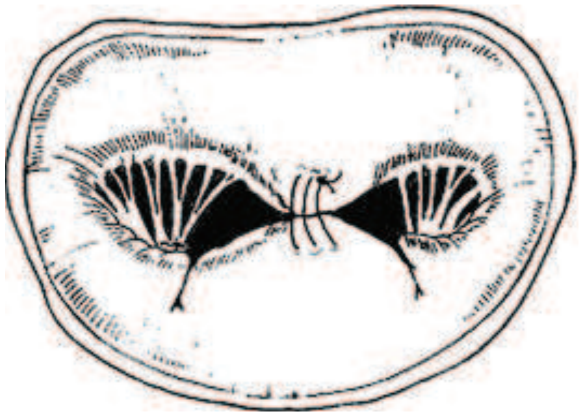
The edge-to-edge (EtoE) approximation (“Alfieri “repair) consists of suturing the anterior and posterior leaflets together to create a “double orifice” mitral valve. It is a method to treat mitral valve regurgitation by suturing the edges of the leaflet s at the site of regurgitation. Sometime the EtoE can be applyed not int he central scallop P2 ore central segment A2, but also in asymmetrical position and to the commissure (paracommissural EtoE in which the repaired mitral valve has a finale single orefice.)

It is worldwide considered a reproducipble and simple technique as possible for native mitral valve repair , sistolic anterior movement and for a rescue surgery after a suboptimal repair. Different scientific reports assess a goog long term follow up of patients treated with surgical EtoE technique up to 20 years (71-74).

According to the general princiles of mitral valve reconstructive surgery, a prosthetic ring annuloplasty is considered an important step of the operation and it is routinely added to the repair at the level of the leaflets.

From this surgical technique it takes inspiration the born of a percutaneus device “ the MitraClip system” that is a growing and promising transcatheter device used in a high risk patient .

Today the Mitraclip system, with around 20,000 procedures performed worldwide, has already received the CE mark in Europe and FDA approval in the USA and it is included in heart valve guidlines since 2012.



Drawing of surgical Edege to Edge tecnique , double orefice with asuturing and central approssimation of the two mitral leaflets.

Drawing and pictures of Mitraclip Implantation Technique

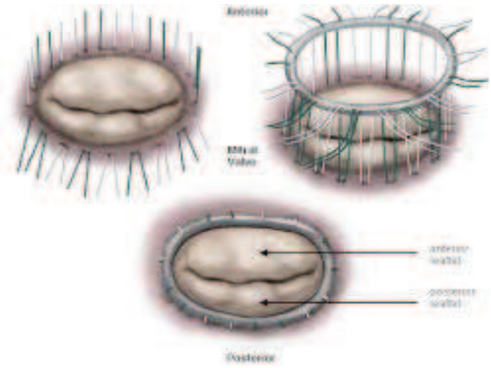
The Annuloplasty

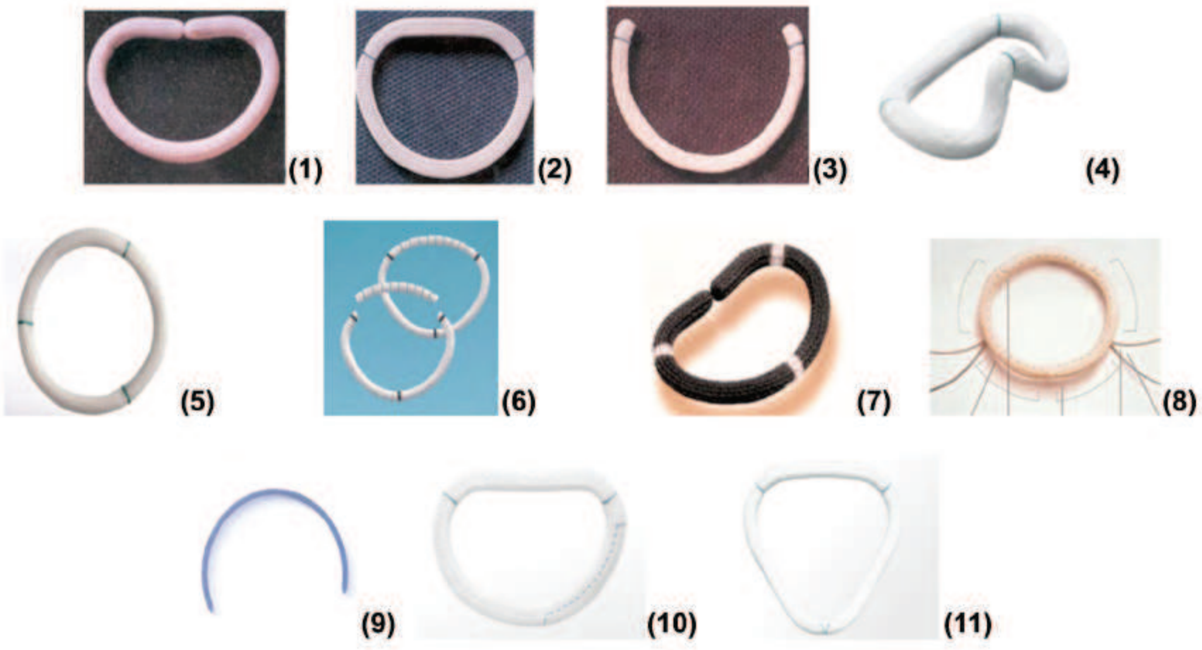
The mitral annulus is a dynamic, saddle-shaped structure with the maximum high of the saddle in the middle of the anterior part of the annulus and another rise along the posterior leaflet .

Annuloplasty can be an isolated treatment or associated with the resection technique or Edege to edge technique in order to stabilize the repair.

Accordingly, the next-generation “physio-ring” had selective flexibility and a slight 3D shape to conform better to the normal mitral annulus.Newer mitral rings have increasingly attempted to replicate this “normal” saddle shape, and “flexibility” has also been built into the design of various rings. Yet, despite a more “normal” valve physiology, superior long-term clinical results with flexible rings have not been demonstrated.The most recent annuloplasty rings are cause-specific, geometrically shaped to accommodate the underlying pathology, not to replicate the “normal” mitral annulus . A large variety of rings or bands are now available for mitral repair.

Degenerative MR can be treated with a variety of techniques. If the valve leaflets are normal, either after resection of the only abnormal area (fibroelastic deficiency) or after complex leaflet reconstruction to reduce leaflet length, then a normal size and shape ring may be appropriate (B and C). This could be either with a complete remodeling ring or a partial band or ring. Alternatively, if the remaining leaflets are elongated and complex reconstruction is not desired, then a larger ring to accommodate the larger leaflets represents a new approach.





Drawing and Pictures of Annuloplastic Technique and different annular devices

Successful mitral valve repair is achieved in ≈80% of all surgical cases of chronic MR.84 The importance of intraoperative transesophageal echocardiography cannot be overstated, and its use should be considered routine. The surgeon and echocardiographer discuss the severity of MR, the mechanism, the lesion, segmental valve pathology, subvalvular pathology and calcification, left ventricular size and function, left atrial size and thrombus, and other pathology, especially other valve lesions such as tricuspid regurgitation, aortic pathology such as atherosclerosis, a patent foramen ovale, and right ventricular dysfunction.

The advantages of mitral valve repair over replacement with a valve prosthesis are no longer debated, and mitral valve repair is the standard of care whenever it is feasible. Repair has been demonstrated to be superior in the setting of combined coronary bypass procedures, reoperations, double-valve procedures, and in elderly patients. However, no prospective randomized trial of repair versus replacement has been performed, and all reports contain some statistical shortcomings that may not be able to account for bias and heterogeneity.

In asymptomatic young patients an early surgery strategy can be usefull in order to avoid the oral anticoagulation therapy and the left ventricle deterioration, it have demonstrated improved measures of exercise tolerance after repair. The early strategy can be justify only if there is a 98% probability of repair success without residual regurgitation .

2. Aim of the Study

The aim of the study is to analyze the variability of the anatomy of posterior leaflet in normal subjects (Autoptic and cardiectomy specimens) and patients with myxomatous disease (three dimensional echocardiography) for assess possible difference and similarity. In patient with myxomatous disease we evaluate the clinical influence of the anatomy of the posterior leaflet on the planning of the mitral valve surgical repair strategy.

To Analyze the variability of the posterior leaflet in normal subjects we use heart specimen in wich we evaluate the anatomy of posterior leaflet

- In order to assess:
  1) The number of scallops,
  2) The dimensions width and eight of each scallop
  3) The number and presence of the subcommissure and incisure
  4) The morphology of the commissures
  5) The annular dimension

To analyze of the posterior leaflet's anatomy in patient with mitral valve myxomatous disease and severe mitral regurgitation and its influence on the reconstructive surgery , we analyze 3D transesophageal echocardiography.

- In order to assess:
  1) The number of scallops,
  2) The dimensions width and high of each scallop in 2D and 3D TOE
  3) The number and presence of the subcommissure and incisure
  4) The morphology and extension of the prolapse leasion, that was measured in 2D

TOE and 3D echocardiographic view.

5) The annular dimension in 2D and 3D TOE.

The mitral valve surgical repair techniques are divided in two groups: simple (simple surgery, that is technically reproducible and feasible) and complex (complex surgery is more difficult and needs of an high surgical expertise, usually performed in high volume center). We evaluate a correlation between anatomical characterists (presence of more subcommisure and incisure, echocardiographic measurements) and the type of surgery.

3. Materials and methods

3.1 Anatomic sample Selection

Thirty normal autoptic heart specimens without mitral valve disease, were examined by three independent observers (two pathologists and 1 cardiologist).

The specimens, fixed in formalin following necropsy, were selected in the anatomo-pathological heart collection of Padua University.

All specimens were from people who died for non major cardiac disease, like pulmonary or other organ pathology, and some specimens were not utilized donor hearts.

Heart with any grossly identifiable mitral valve anomaly or disease were escluded from the study.

The hearts were extracted from the formalin, washed with water cleaned and cleared from any clots within the chamber , and then sectionated for the mitral valve exploration.

The left atrium and left ventricle were opened.

3.2 Anatomic measurements

First of all an observation cutting the left atrial wall was performed with the mitral valve in situ, extracting all blood clots, we take some pictures.

The mitral valve was opened and evaluated along the obtuse margin of the heart. The Commisure, Subcommissure and incisure with relative chordae tendineae were studied in detail.

Special attention was given to: (1) the number of the scallops of posterior leaflet, (2) the characterization of the subcommisure and incisure, (3) the high and the width of every single scallop, (4) the high of the leaflet in corrispondence of subcommisure, incisure and commissure, (5) the morphology of the chordae tendinea at the sites of insertion in the commisure, subcommissure and incisure. In all specimens the total annular circumference was measured.

All the measure were taken with a dedicate centimeter and the leaflets were examined with a surgical probe (“specillum”).

Final Morphologic Evaluations

Based on the newly defined criteria, observations were made on:

1) Number of commissures and their positions,

2) Number and position of leaflets,

3) Number and position of subcommisure and commissures,

4) Number and position of incisure;

5) Length of annular attachment of each leaflet,

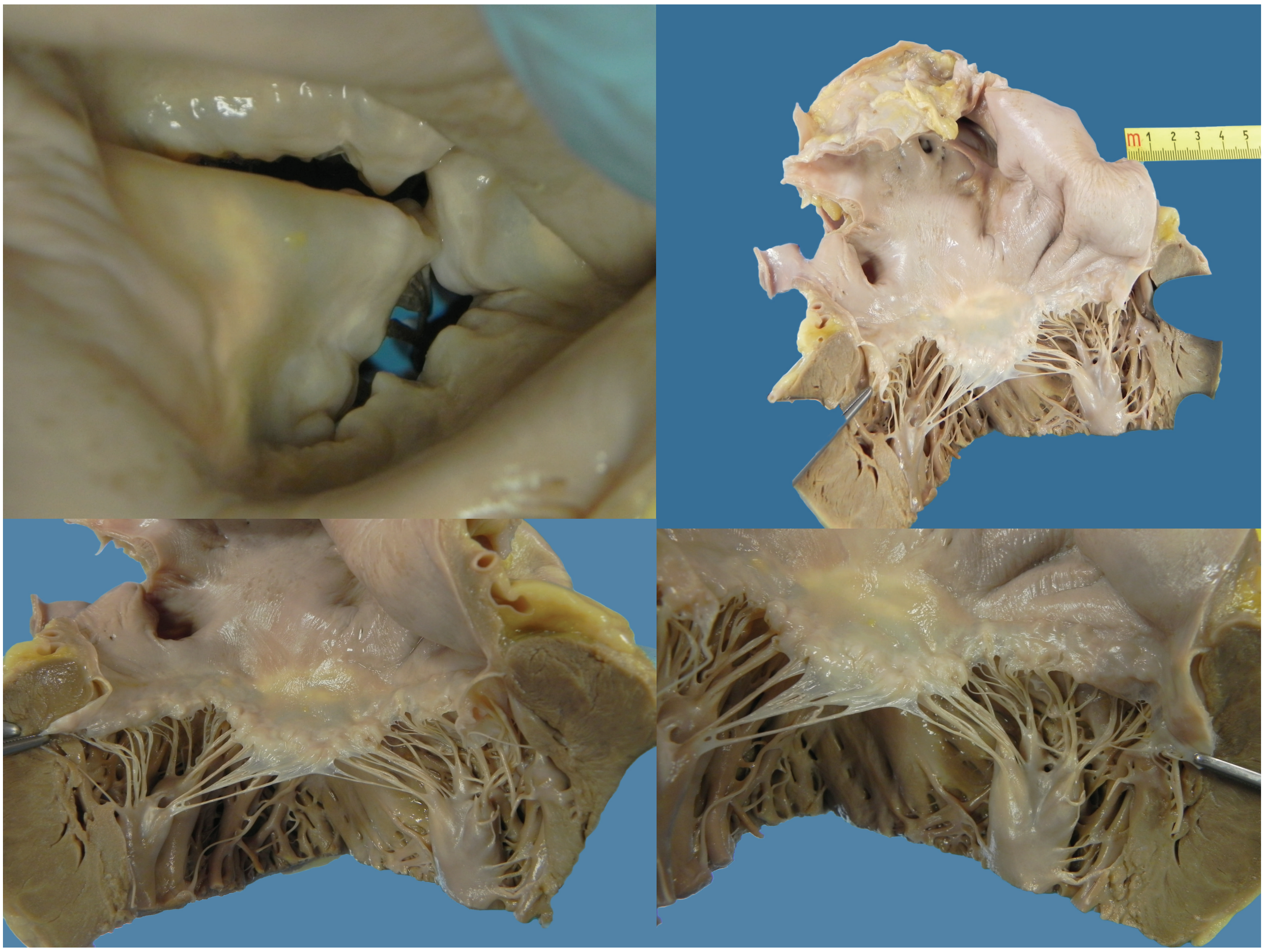
6) Annular circumference (AC),

7) Maximum width of each scallop

8) The maximum eight of each scallop .

The observations were recorded on a database and together with the anatomical picture of every analyzed specimen. The results were analyzed wtih descriptive statistical test (percentual and prevalence).

A B



C D

Figures 3.2.1 with macroscopic view of the atrial side of the mitral valve A, Mitral valve opened to take measurements and to study details B and C, analysis of chordae details and incisure distribution D.

The following measurements were made: 1) the circumference of the opened valve orifice at the base of the leaflets; 2) the high of each leaflet measured at its center, from free edge to base; 3) the width of each leaflet measured at its base.
Measurements were made with a caliper, a metric rule graduated to 1 mm.

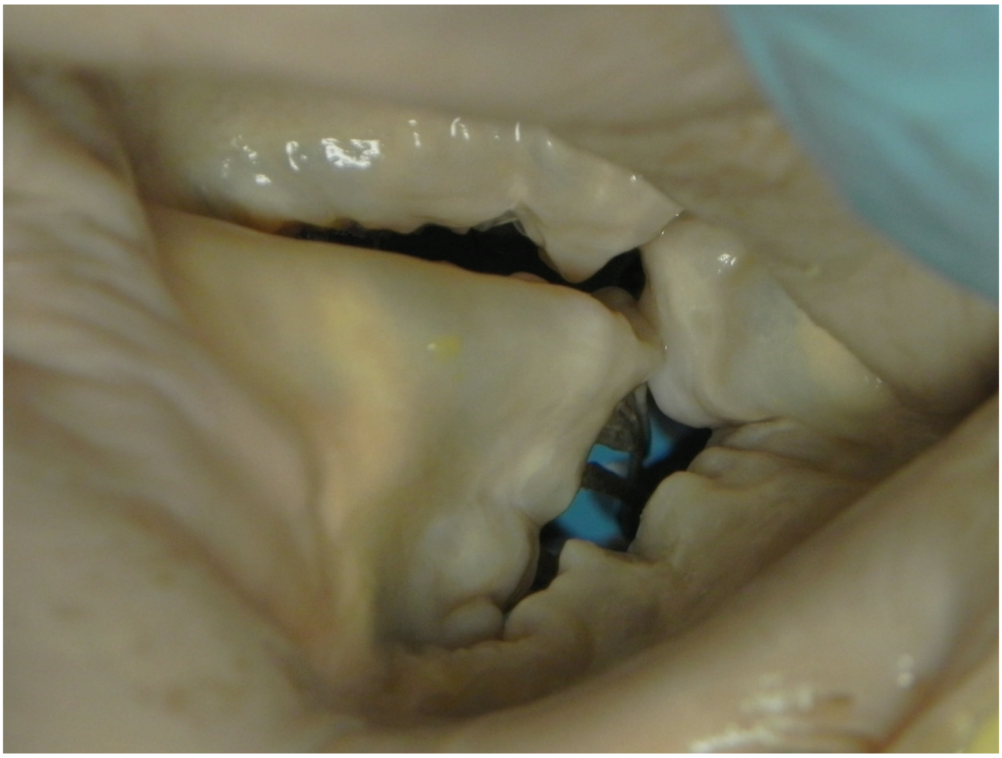


Figure 3.2.2 Specimen 1

Macroscopic View of mitral valve (not opened and not cutted) from above see by the atrial face after the opening of the left atrium roof.

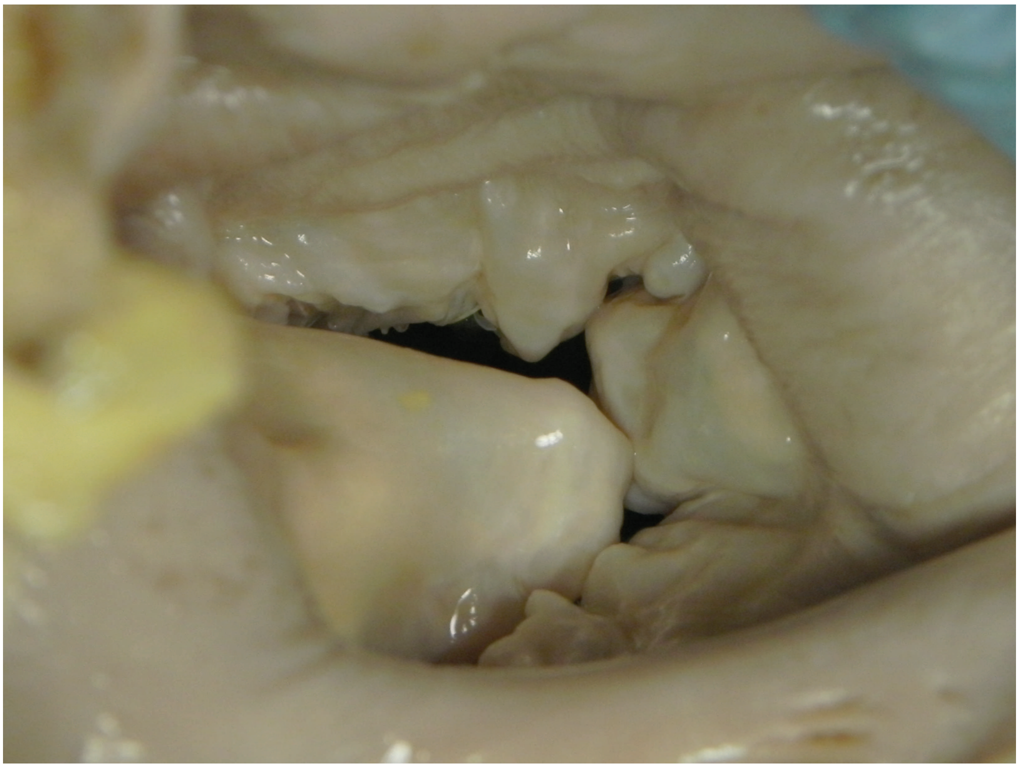


Figure 3.2.3 Specimen 2

Macroscopi View of the mitral Valve from above.

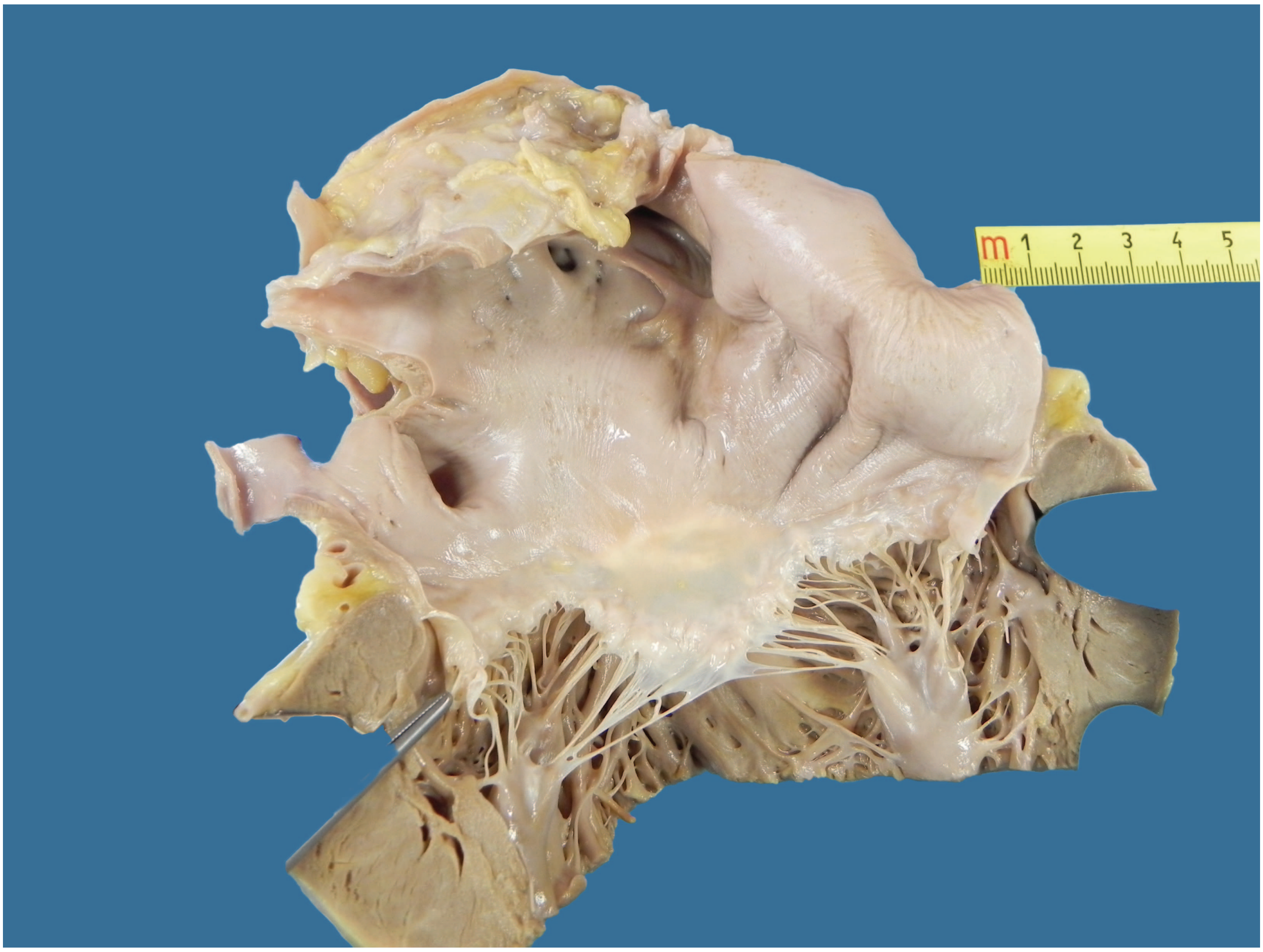


Figure 3.2.4

Macroscopic view of the opened mitral valve

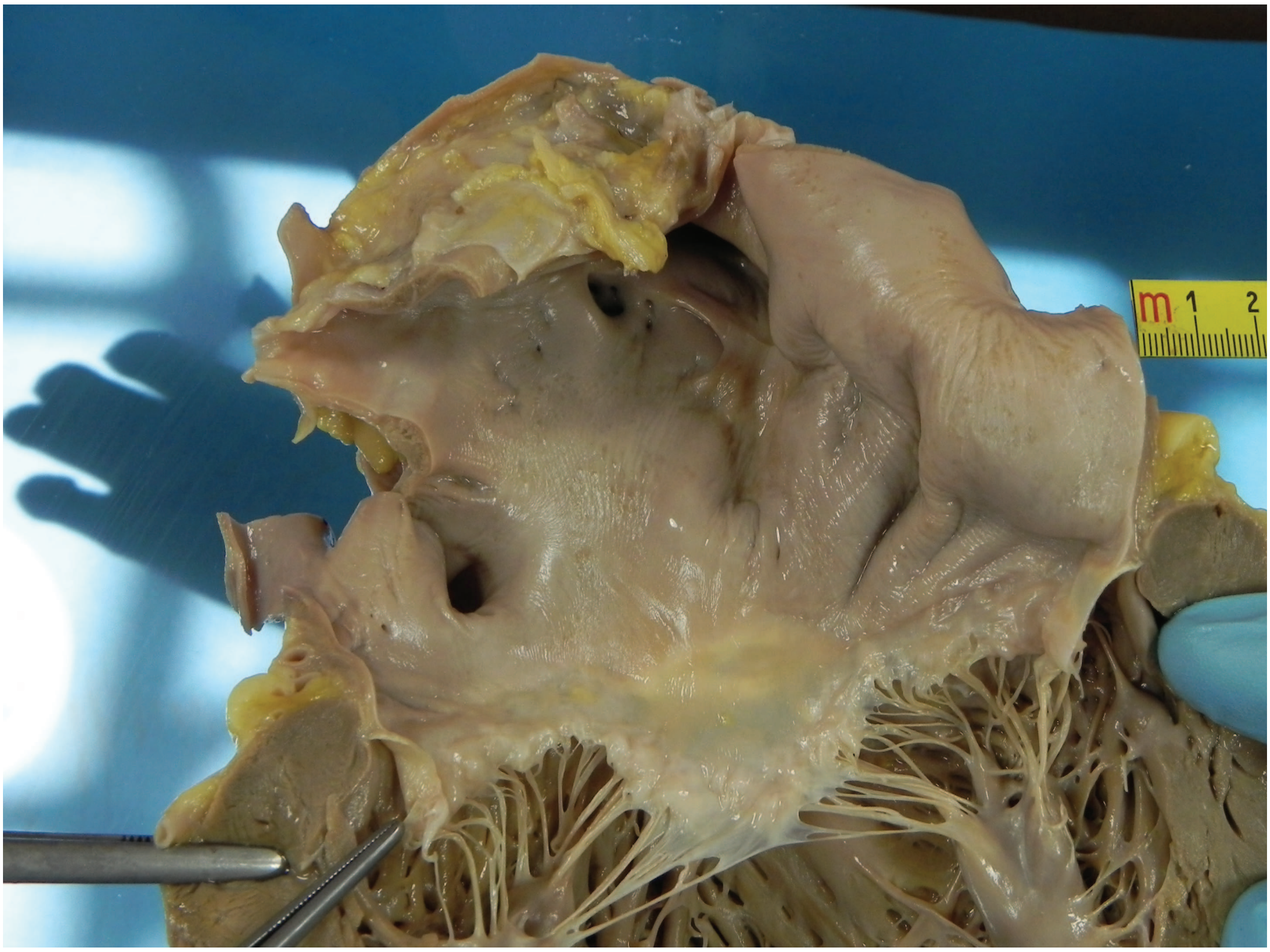


Figure 3.2.5

Macroscopic view of the opened mitral valve of two specimens .

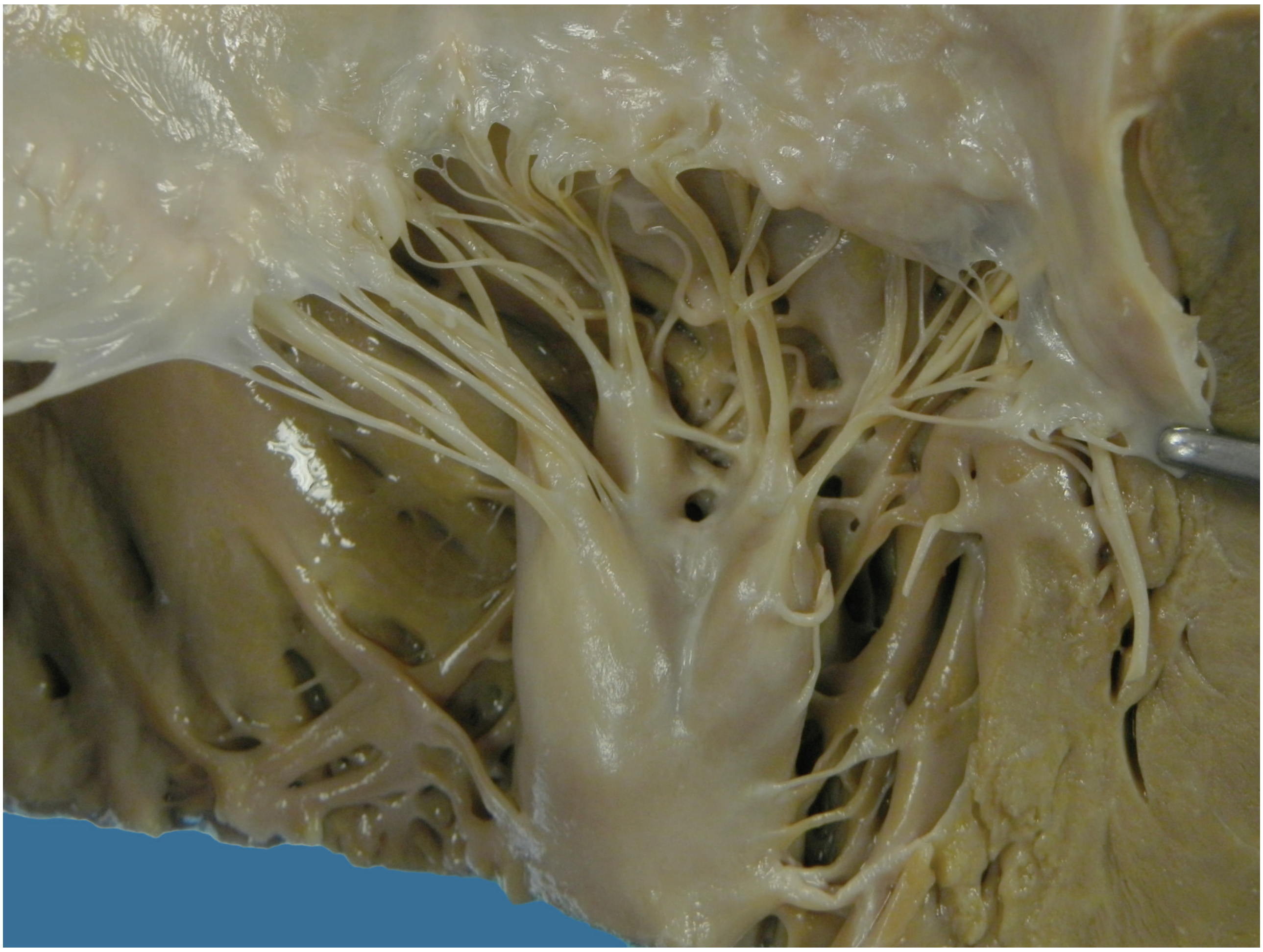


Figure 3.2.6

Macroscopic view: Details of tendineae Chordae

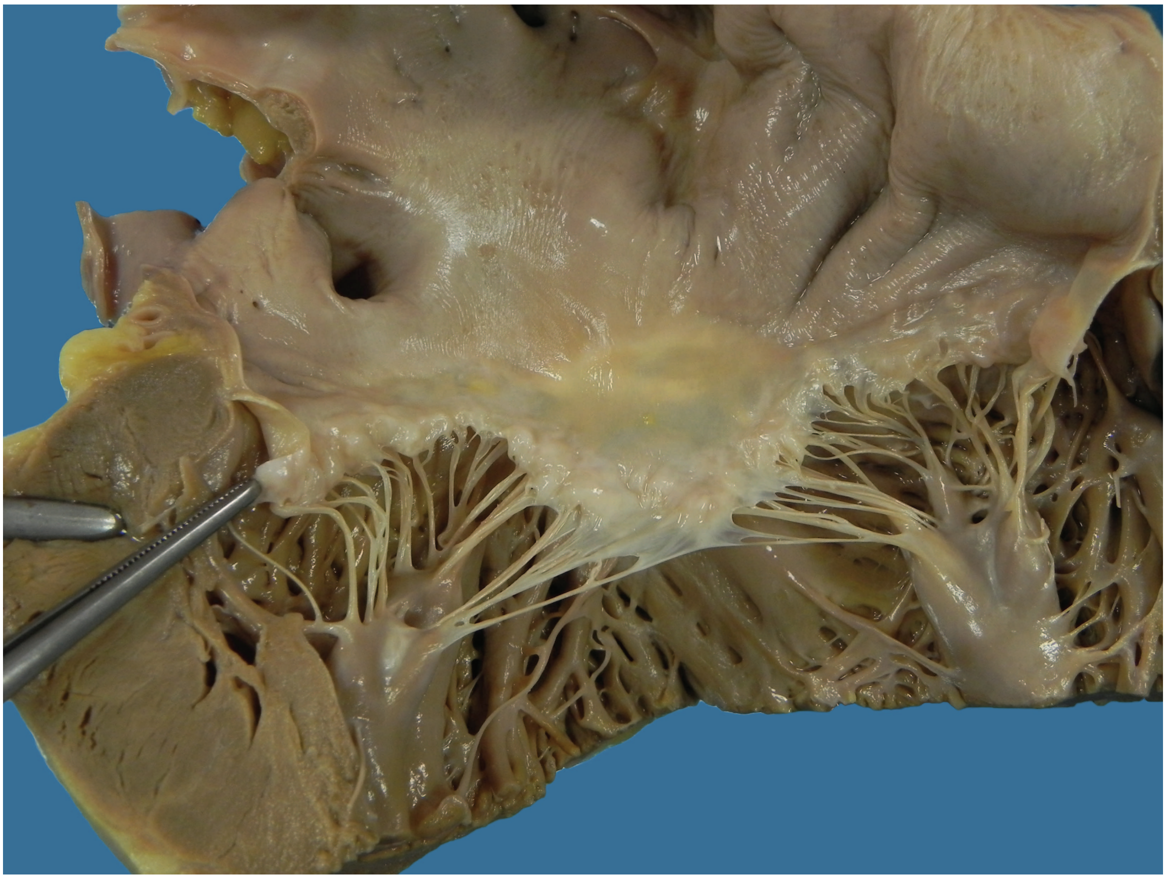


Figure 3.2.7 Macroscopic view opened mitral valve

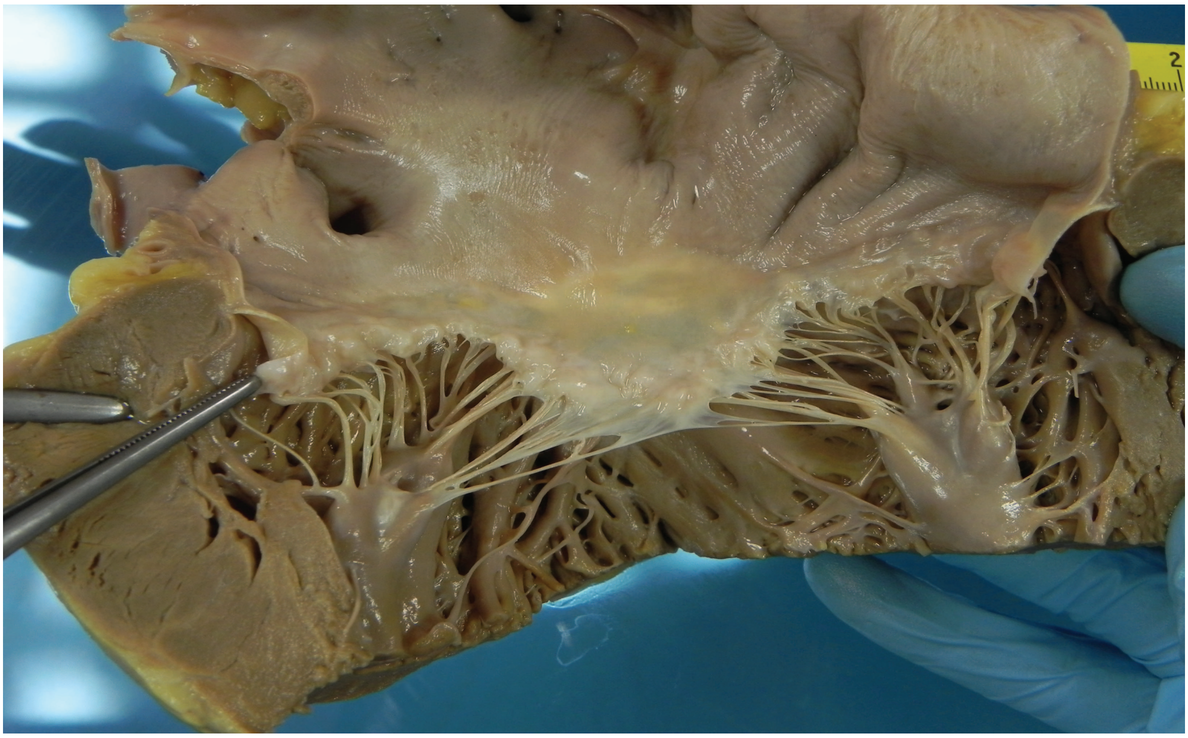


Figure 3.2.8

Macroscopic View opened Mitral Valve

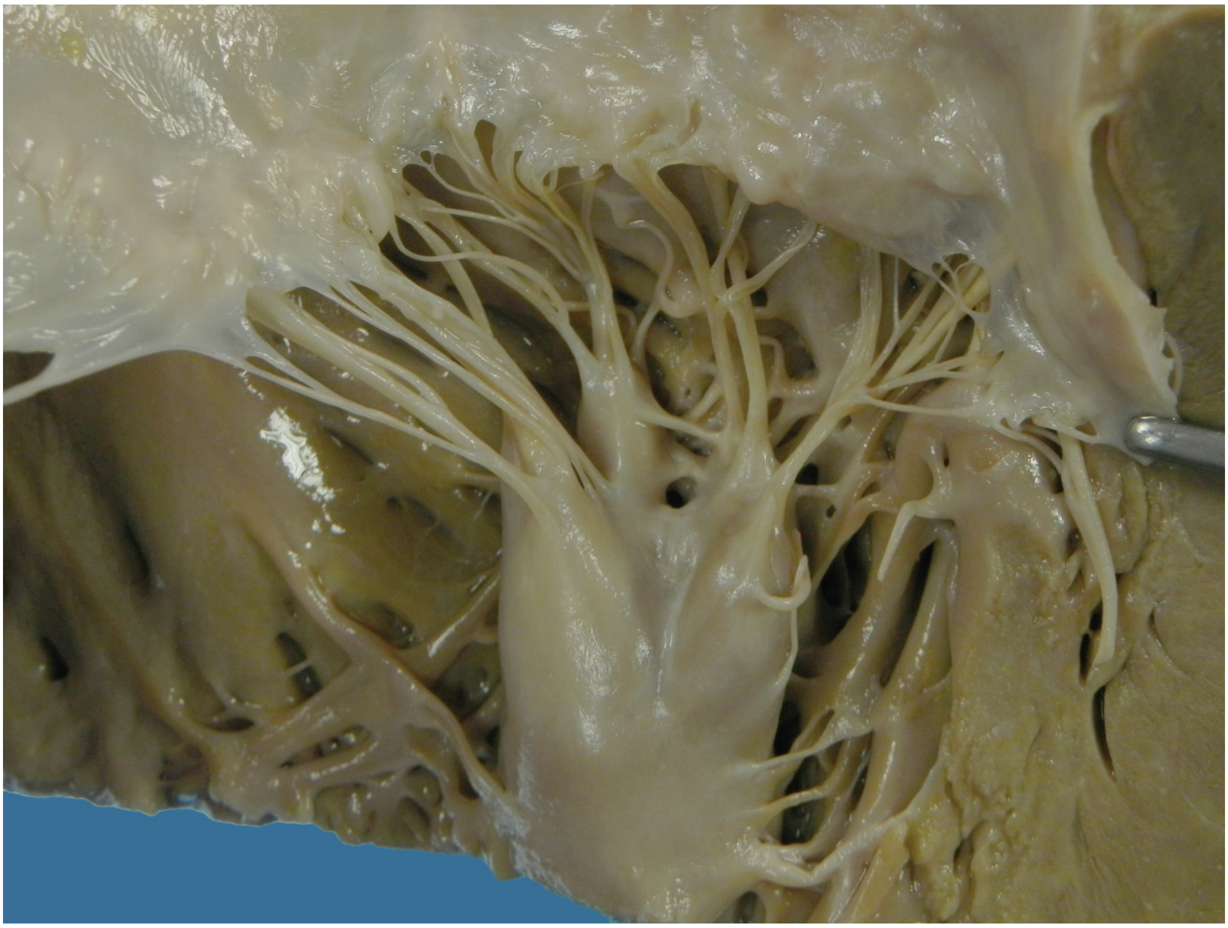


Figure 3.2.9

Macroscopic View opened Mitral Valve

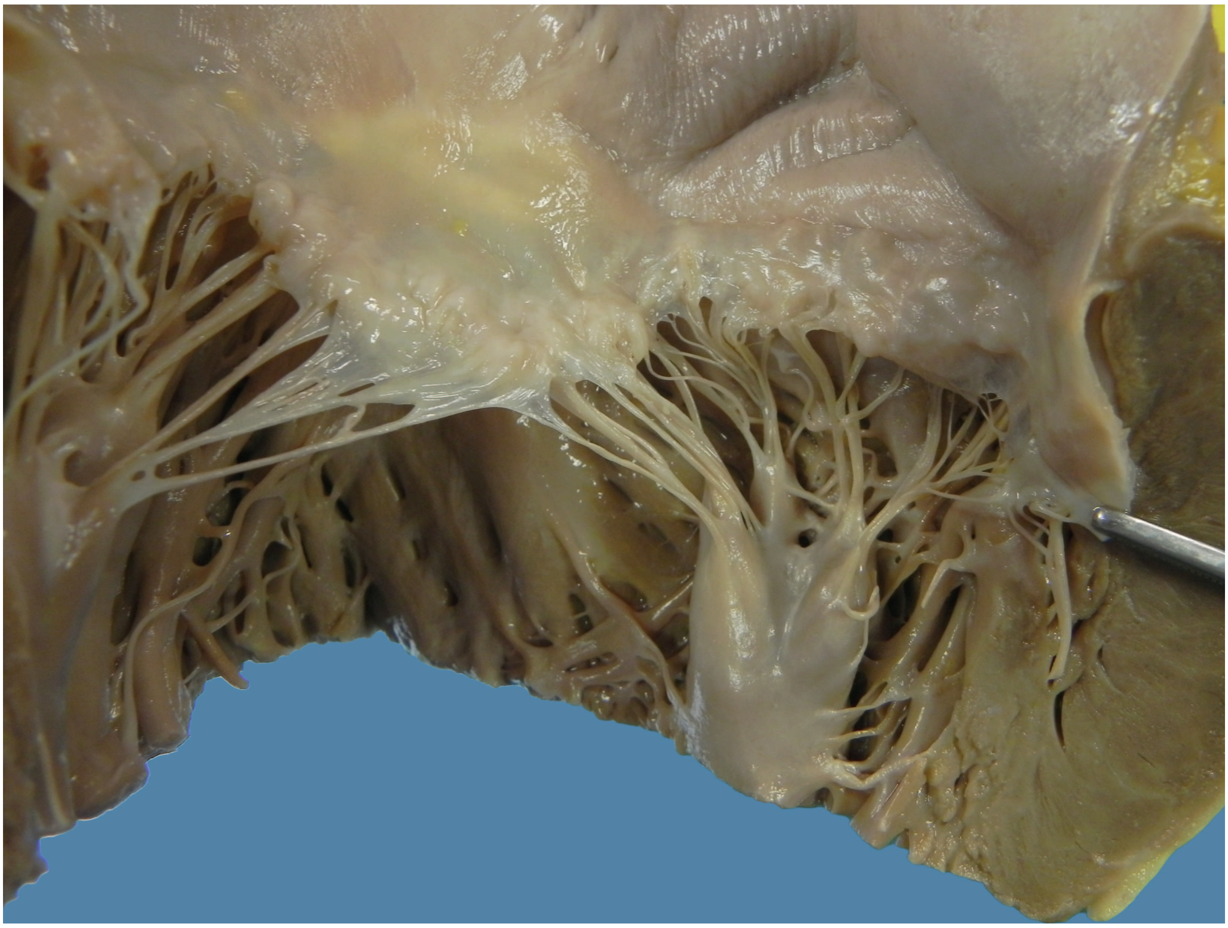


Figure 3.12.10

Macroscopic View opened Mitral Valve

Every specimen was photographed, in a panoramic view and some details.

3.3 Population of the echocardiography study

The echocardiographic evaluations were retrospectically assessed from a database of 706 pts admitted from 2009 to 2012 at the San Raffaele Cardiovascular Department hospital for mitral valve repair, submitted to 3D TOE (Three dimensional Transesophageal Echocardiography) with Philips iE33 technology.

All The trans-oesofageal examinations were collected prospectically in a research protocl study approved by Ethics Committee. Every patients give the agreement to the stusdy protocol with a signature of an informed consent.

It was selected a sample of 268 patients and analyzed 163 examinations, with exclusion of 75 patients considered suboptimal or without 3D analysis with a final total number of good quality examination of 138 pts.

Inclusion criteria:

-Sever mitral regurgitation

-Myxomatousatouse disease

- Posterior leaflet prolapse

-Indication to a mitral valve repair surgery

Esclusion criteria:

-Poor quality of 2D and 3D TOE imaging

- isolated anterior prolapse

-pregnancy

-lack of 3D imaging

-poor 3D acquisition with not possible 3D reconstruction

3.4 Echocardiography Evaluation: 3D technique and reconstruction

Images were acquired using X72t transducers and Trans-oesophageal 3D probe an iE33 imaging platform (Philips, Andover, MA, USA).

Images were stored on DVD support or Tomtec database, and then analyzed online with Q lab System (philips) and offline using Tomtec system.

Two dimensional and three-dimensional transthoracic and trans-oesophageal echocardiographic studies were performed in keeping with guidance from the European Association of Echocardiography.

The severity of MR was classified into mild, moderate, moderate to severe, or severe, using a multiparametric approach as advised by recent guidelines, with color analysis of the jet , regurgitant volume, and vena contracta, pulmonary reverse flow.

Trans-oesophageal echocardiography studies were performed under anaesthetic or conscious sedation, paying particular attention to ensure that systolic blood pressure was maintained throughout the examination.

Two echo experts, recorded a detailed description of each valve using a combination of 2D and 3D imaging .

We systematically assessed the mitral valve, documenting the presence of prolapse or flail and the region affected according to Carpentier's nomenclature.

Two dimensional classical Transthoracic and transoesophagel aquisitions were collected (classical TOE acquisitions: Midesophageal four chamber , two chamber and intercommissural chamber view, transgastric view).

Three-dimensional TOE images were acquired from the mid-oesophagus using the 3D zoom or live 3D function and full volume acquisition.

Care was taken with the depth and gain settings, and sector width was adjusted such that we included the leaflets and annulus in their entirety throughout the cardiac cycle, ensuring frame rates of at least 7 Hz.

We recorded the number and distribution of subcommisure in each patient, starting from the antero-lateral commissure and working across the valve toward the postero-medial commissure.

We classified further the type of lesion seen in the patients with MVP, according to previous descriptions.

Those individuals with thickened, myxomatous leaflets, leaflet billowing and multisegment prolapse we labelled 'Barlow's disease', and those individuals with an isolated segment of prolapse or flail with leaflet thinning were labelled fibro-elastic deficiency.

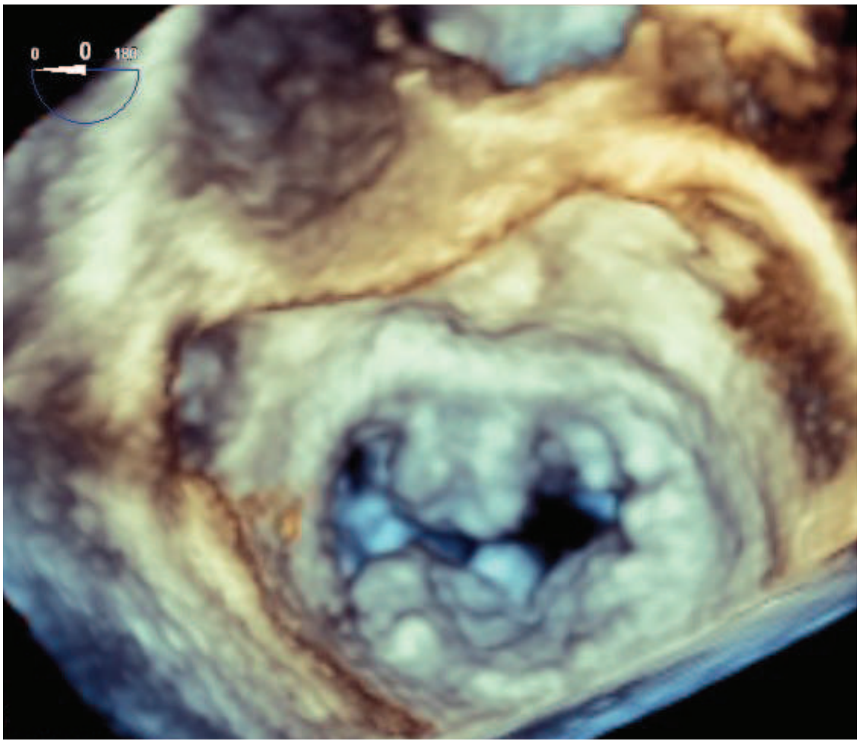


Figure 3.4.1 A

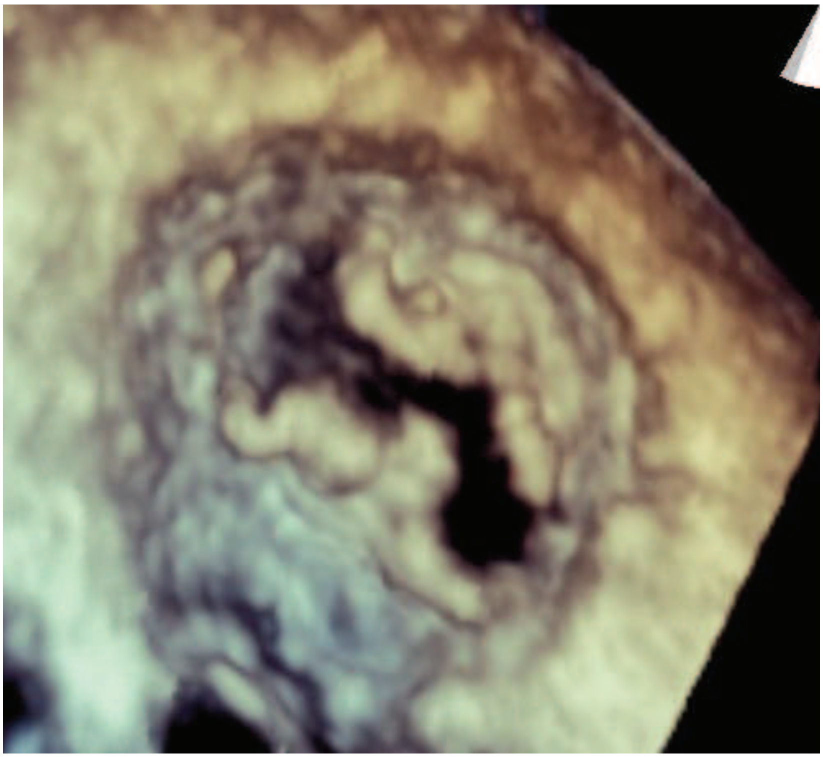


Figure 3.4.1 B

Figures 3.4.1 A and B Pictures of atrial and ventricle side zoom 3D view acquisitions

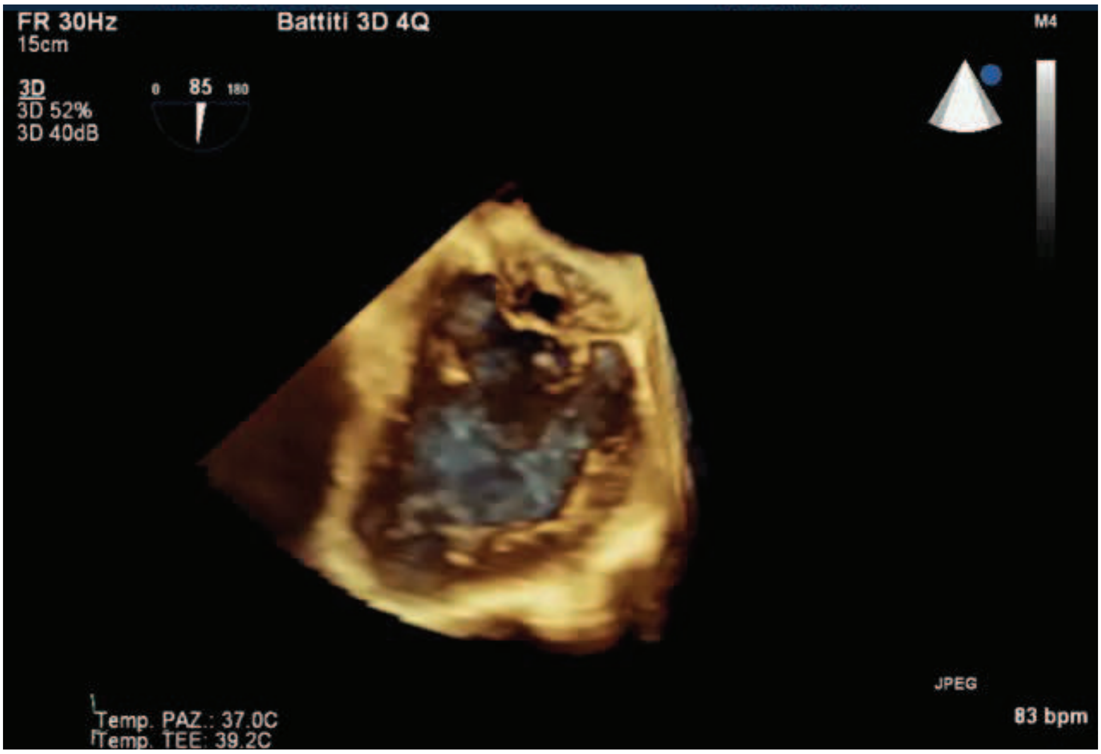


Figure 3.4.2 3D full volume Acquisition

3.5 Echocardiography measurements

Images Protocol of storage and analysis

All the performed examinations have a 2D quantitative standard datas (left ventricle dimension, Ejection Fraction, Grade of mitral regurgitation, atrial dimension, localizzation of eventual annulus or leaflets calcifications).

All the examinations were stored and than analyzed with tomtec system 3 D mitral valve reconstruction.

In the system there are some programs for the valvular 3D imaging reconstruction and analysis.

Analyzing the zoom 3D acquisition, the annulus' circumference was measured, the leaflet scallops' number, the number of subcommissure and incisure.

Eighty eight examinations were excluded for different causes: 1) absence of 3D acquisition, 2) dominant anterior leaflet prolapse with no good evaluation of posterior leaflet anatomy, 3) low quality of 3 D echocardiography acquisition, 4) low quality for analyzable reconstruction, 5) impossibility to take all the measurements.

We measured at the 2D and 3D TOE acquisition:

1) 2D TOE maximun length of anterior leaflet
2) 2D TOE maximum length of posterior leaflet
3) 3D TOE maximun length of anterior leaflet
4) 3D TOE maximun length of posterior leaflet
5) 3D total annular circumference
6) 3D anterior and posterior annulus circumference
7) 2D intercommissural extension or off axis view of the prolapse lesion
8) 3D zoom view intercommissural extension of prolapse leasion

9) Number of subcommissure and incisure
10) Number of posterior leaflet scallops
11) Morphology of posterior leaflet scallops according to the terminology first elicited (monolobato scallop, bilobate or biscllop morphology).
12) Width of every single posterior scallops
13) Localizzation of the prolapse lesion and description of the morphology of the prolapsing scallop
14) We reported also other anatomical characteristics

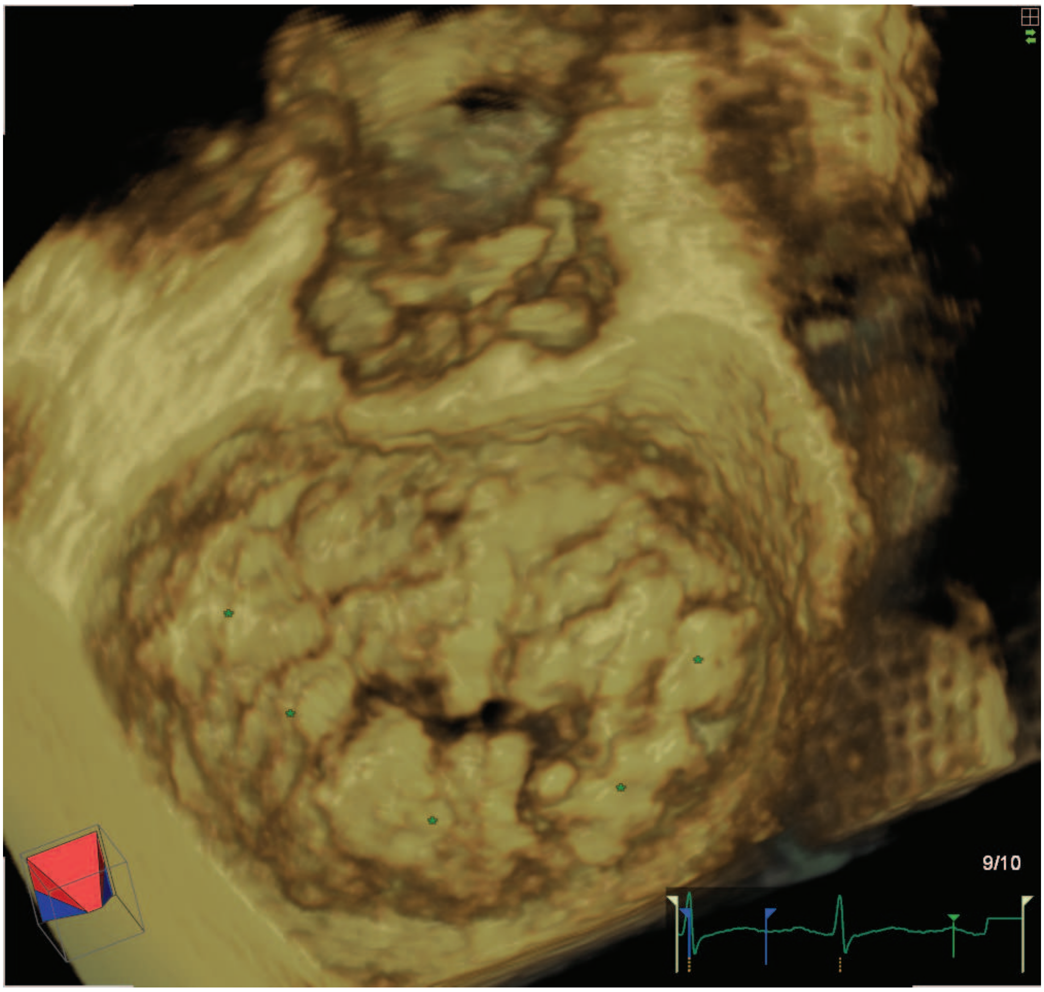


Figure 3.5.1 zoom 3D view reconstruction atrial side telediastolic closed mitral valve leaflets

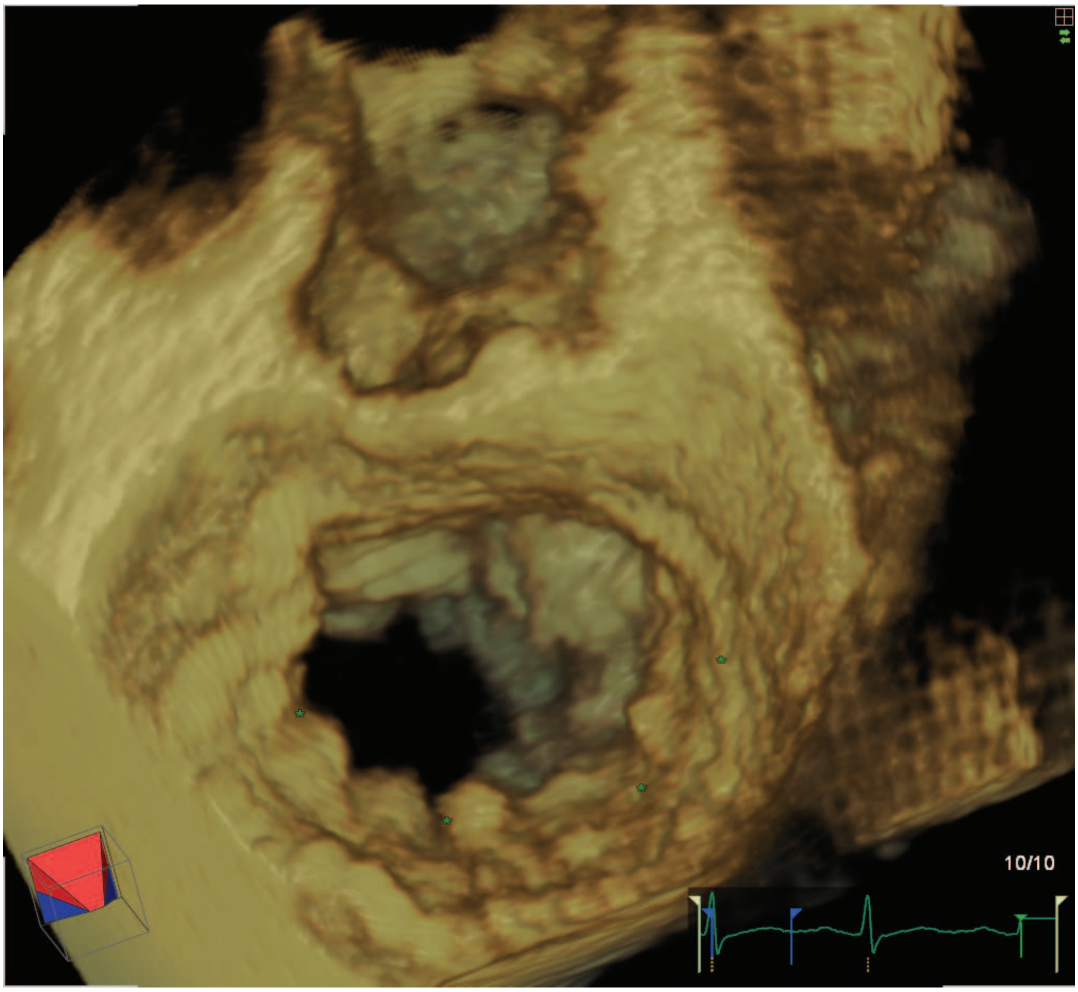


Figure 3.5.2 zoom 3D view reconstruction atrial side telesystolic open mitral valve leaflets

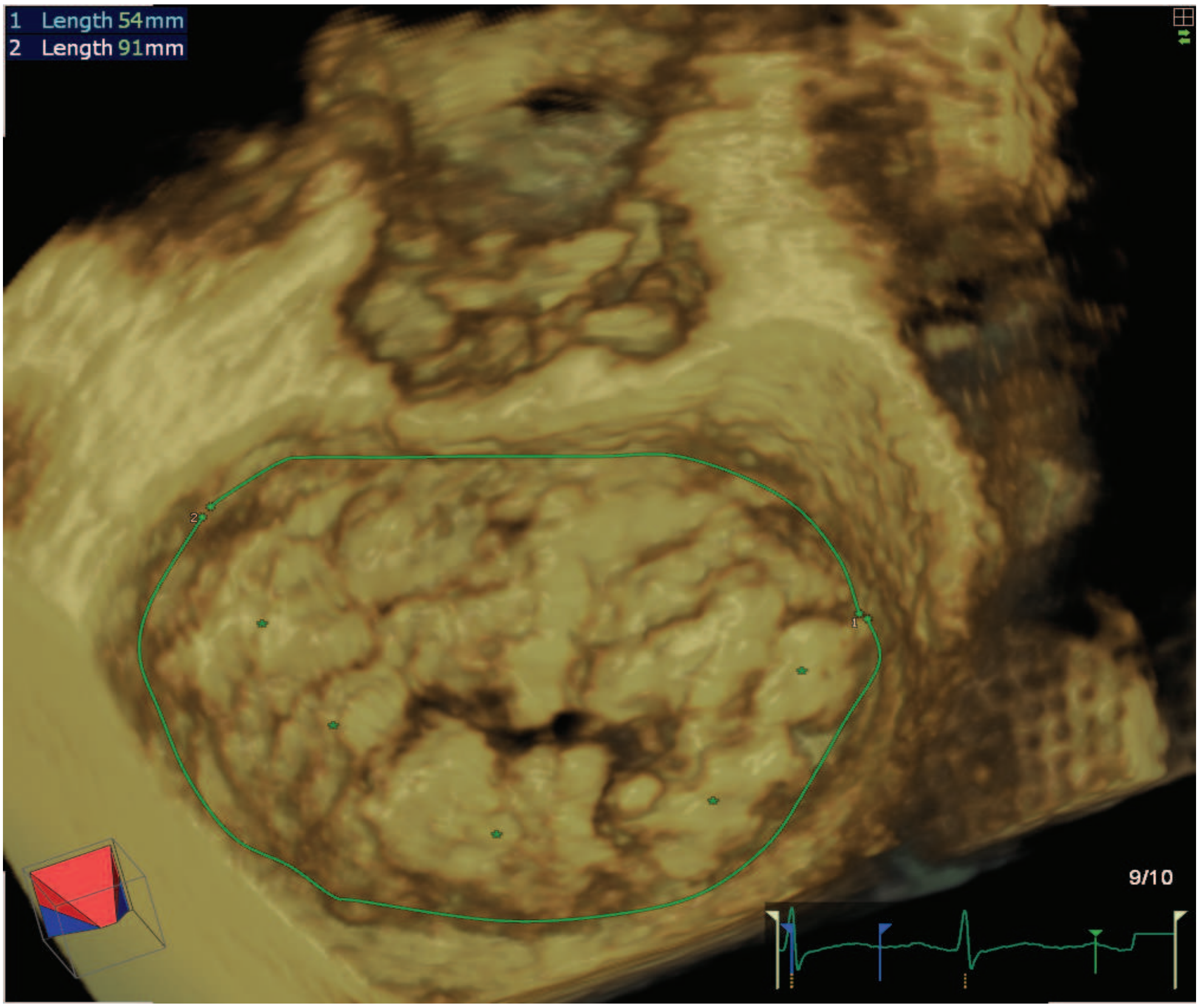
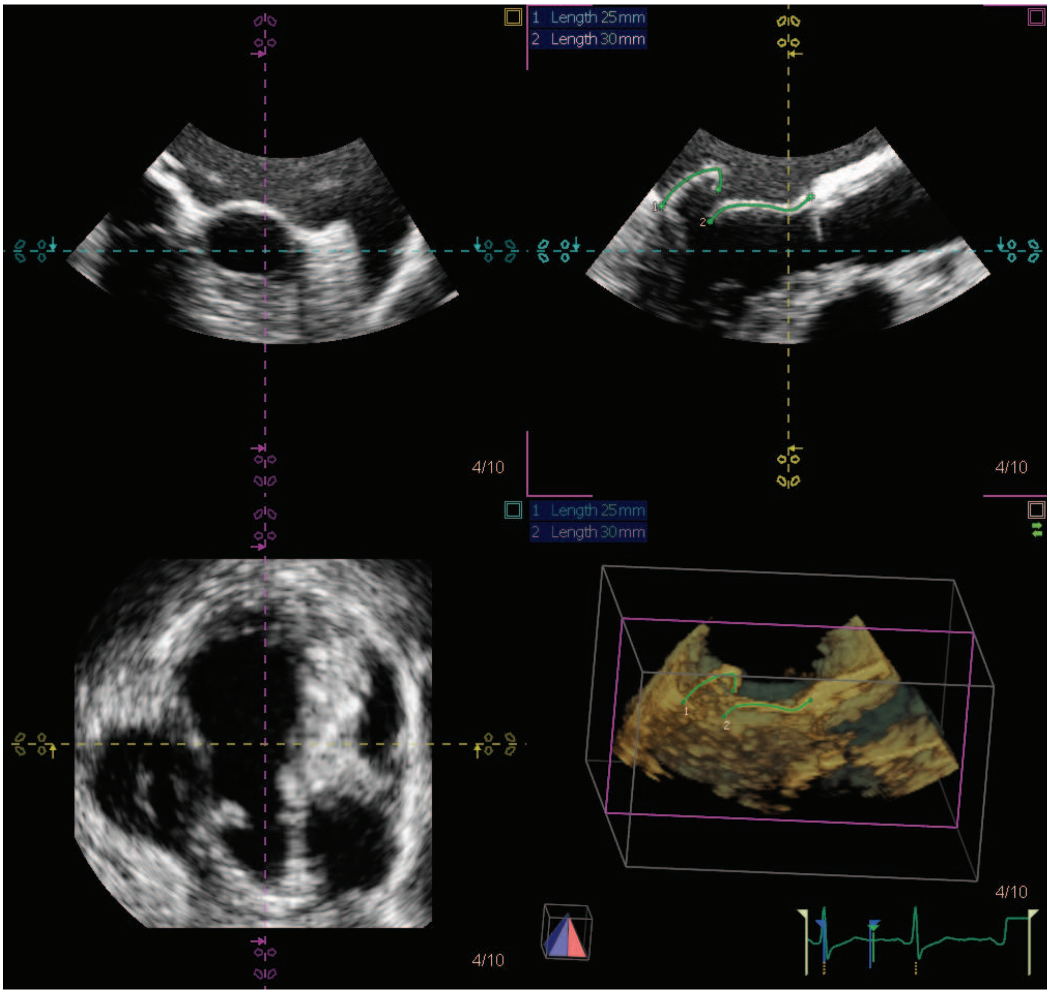


Figure 3.5.3 zoom 3D view reconstruction atrial side with annulus circumference measurement



1 Length 25mm
2 Length 30mm
4/10
4/10
1 Length 25mm
2 Length 30mm
4/10
4/10

Figure 3.5.4 A

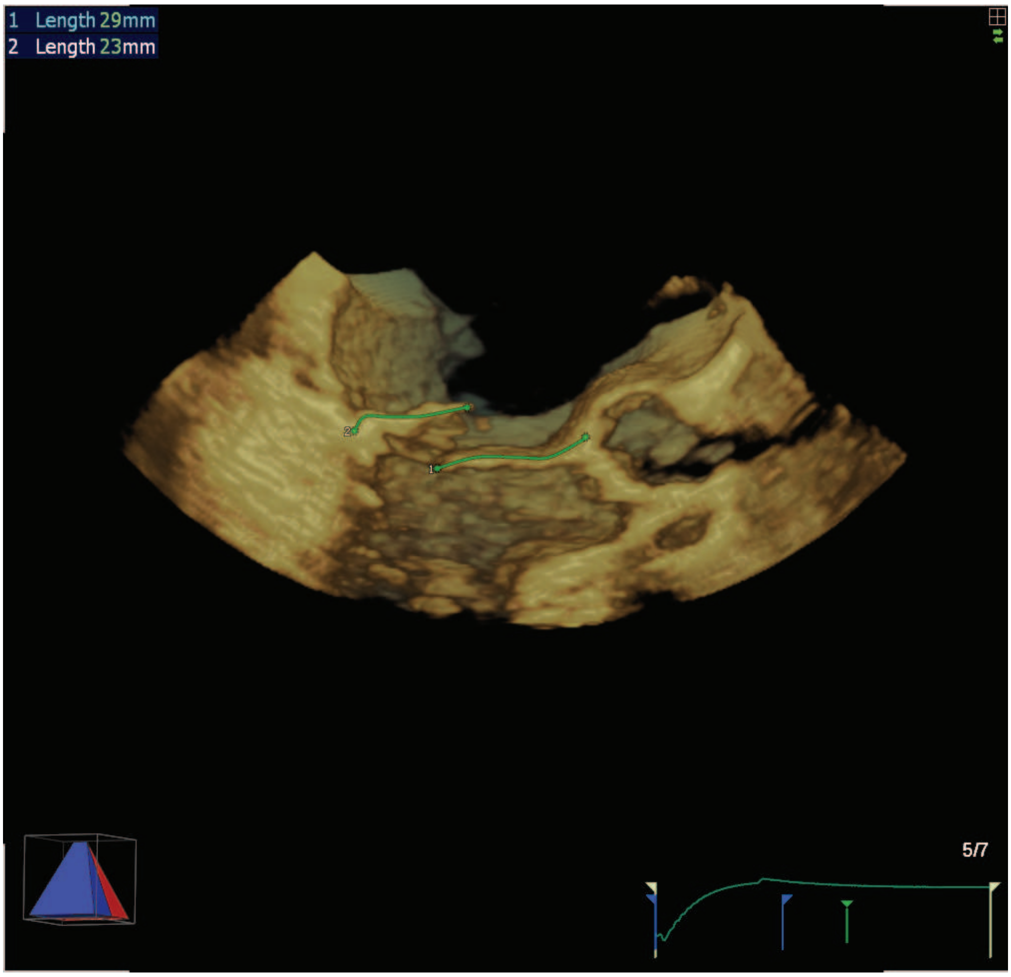


Figure 3.5.4 B

Figures 3.5.4 A and B: 3D long axis view reconstruction for measure of maximal length of anterior and posterior leaflets

Figure 3.5.5 Intercommisural measurement of prolapse lesion extension in 2D and 3D echocardiography: Coincident values 2D vs 3D

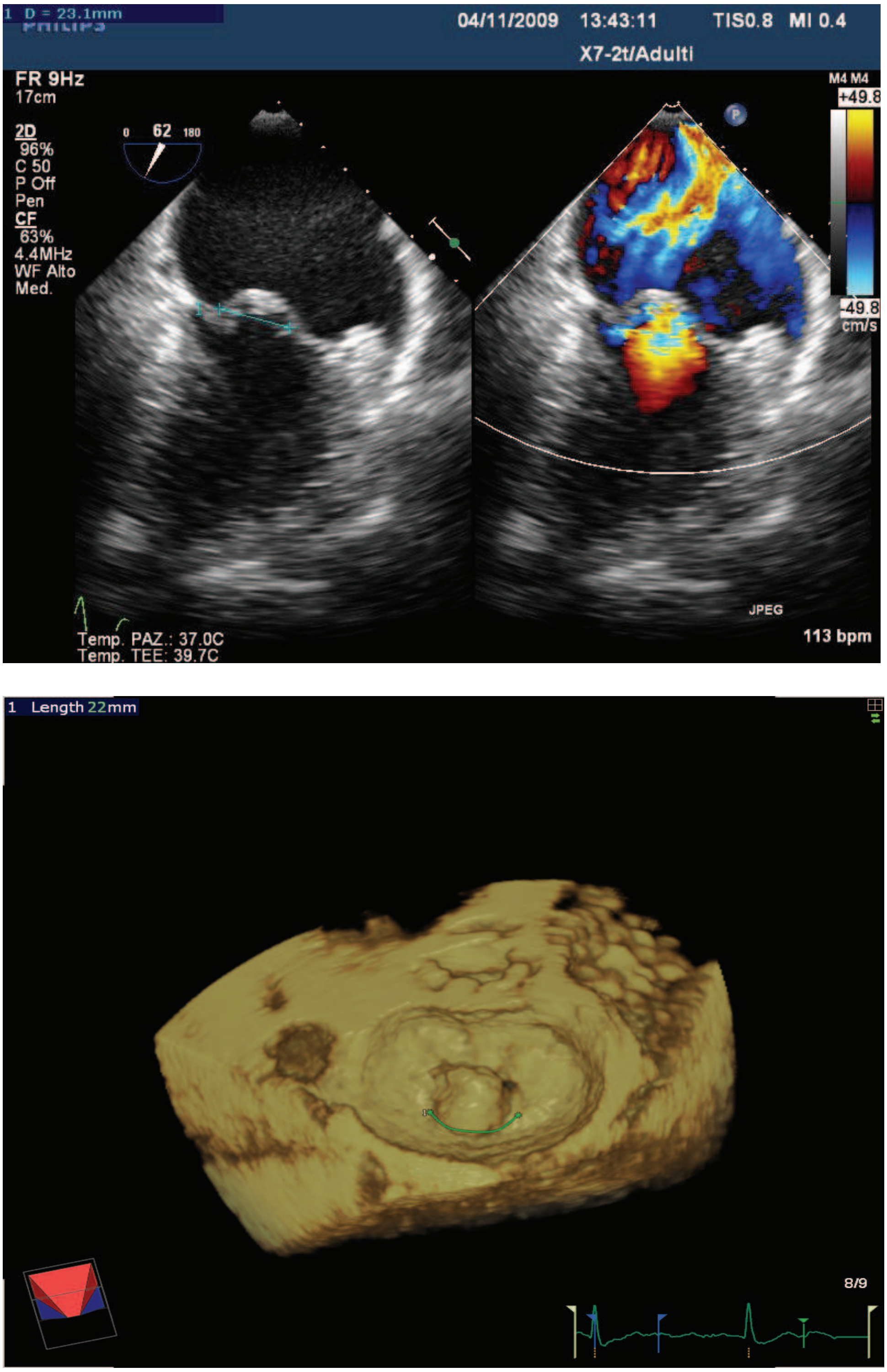
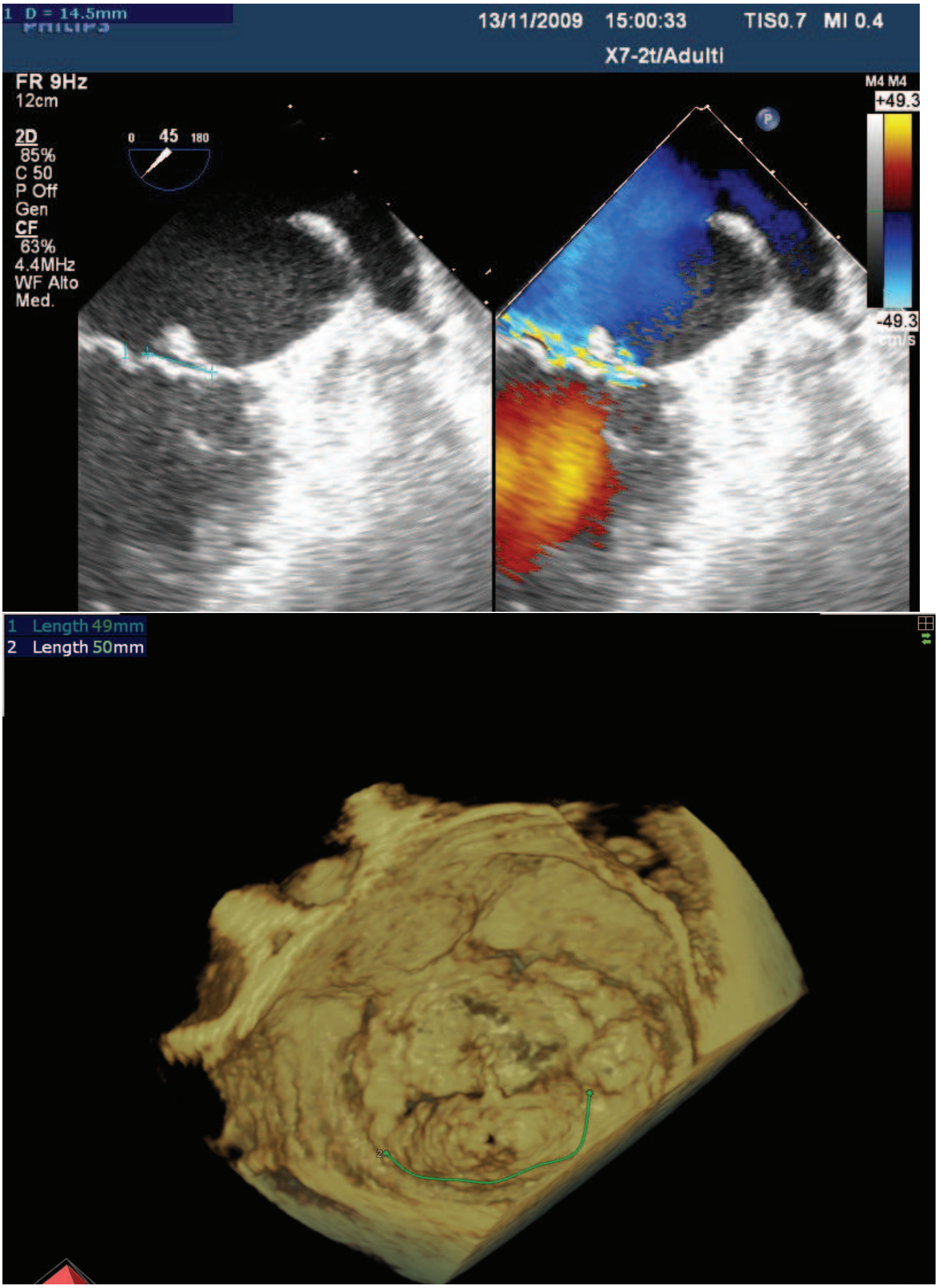


Figure 3.5.6 Intercommisural measurement of prolapse lesion extension in 2D and 3D echocardiography: very different values 2D vs 3D



4. Anatomic Results

We study a population of 30 heart specimens.

There were variability in the number of scallop of posterior leaflet (PL): only 1 sample had 1 scallop (mono-scallop, 3,3%) and another one had 5 scallop (penta scallops 3,3%), 2 samples had 2 scallops (bi-scallop, 6,6%), the major number of PLs had three scallops (63%) and 7 samples had 4 scallops (23%). Mean total annulus circumference was 9,6 ±1,25 cm.

We identified:

1) a sub commissure as an indentation between two leaflets deeper than 50% of the high of the leaflets with fun like chordae as the commissures,

2) Incisure in a scallop with an high less than 50% of the leaflets high and with small marginal chordaes, and an incisure as an indentation without marginal chordae.

In all sample we found: 23 total number of incisure, 4 incisure with chordae fun like and 19 incisure without chordae.

The major number of incisure were on the posterior leaflet (19) and less on anterior (4).

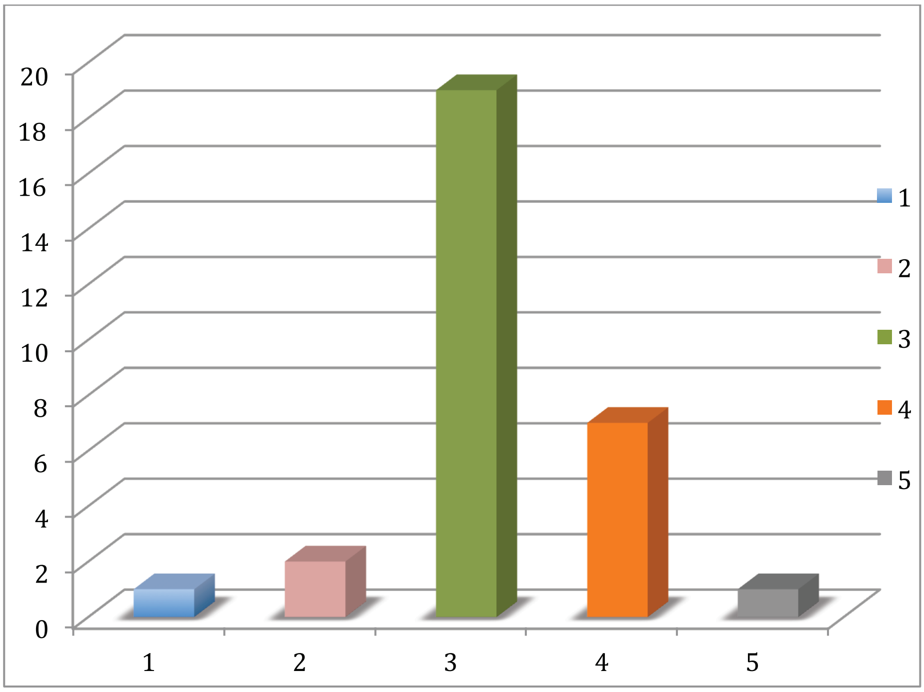
In the PL they were present more frequently in the central scallop P2 (no 9, 47%) and less on P3 ad P1 (no 5 and 3, 26% and 16 %, respectively).

Table 4.1: Demographic Data of necroscopic specimens' Population

Demographic data of 30 Specimens		
Age	**72 mean**	**±15 SD**
Sex	**13 M**	**6F/11 nd**
Post Translplant	**11 Hearts**	**36%**
Mass	**399 mean**	**±96 SD**

Table 4.2: Number of scallop finded in the specimens population

Number of scallop **Posterior Leaflet**	**Number of Specimens**	**%**
1	**1**	**3,3%**
2	**2**	**6,6%**
3	**19**	**63%**
4	**7**	**23%**
5	**1**	**3,3%**



Graphic 4.1: Histogram of the number of posterior leaflet's scallops distribution (rif table 2)

Table 4.3: Dimensions of the leaflets' width and single posterior leaflet's scallops , total and anterior/posterior annulus circumferences

Leaflets	**Width mean**	**SD**
P1	**1,2**	**±0,8**
P2	**1,3**	**±1,1**
P3	**1,14**	**±0,22**
Annulus circumference		
Annulus total	**9,6**	**±1,25**
Annulus anterior	**3,76**	**±0,5**
Annulus posterior	**6**	**±1,35**

Table 4.4: Number of subcommisure, Median high of the commissure and subcommissure and incisure

	Number	Mean	SD
Commissure 1	**30**	**0,77**	**±0,25**
Commissure 2	**30**	**0,7**	**±0,19**
Subcommisure 1 high	**30**	**0,74**	**±0,23**
Subcommisure 2 high	**27**	**0,8**	**±0,23**
Subcommisure 3 high	**7**	**0,8**	**±0,17**
Incisure high	**24**	**1,04**	**±0,22**

Table 4.5: Number of incisure and distribution on the two leaflet anterior/posterior and the single posterior leaflet scallop

	Number	**Percentage**
Incisure tot	**23**	**100%**
I on AML	**4**	**17%**
I on PML	**19**	**83%**
I Without chordae	**19**	**83%**
i with chordae	**4**	**17%**
i onP1	**3**	**16%**
i on P2	**9**	**47%**
i on P3	**5**	**26%**
i on P4-P5	**0**	**0**
i on P monoscallop	**2**	**10%**

Table 4.6: Mean Hgh and SD of the posterior leaflet's scallop and anterior leaflet

Leaflets	high mean	SD	50% mean value
P1	1,2	±0,8	0,6
P2	1,3	±1,1	0,65
P3	1,14	±0,22	0,55
A	2,2	±0,28	1,1

Table 4.7: Morphology of the posterior leaflt in particular of P2 central scallop (total 3 scallop morphology 19)

Leaflets	Number	%
3 scallop	19	63%
Biscallop	7	23%
Monoscallop	10	33%
Bilobato	9	30%

5. Echocardiographic results

From a large database of 706 patients (pts) consecutively admitted to the Cardiovascular Department of San Raffaele Hospital, from January 2008 to December 2012 with a diagnosis of severe mitral regurgitation, we analyzed the first 238 consecutively enroled.

All the patients were studied with pre-operative 2D and 3D Trans-oesophageal echocardiography and submitted to surgical repair of the mitral valve.

I analyzed also the 3D TOE imaging in order to establish the presence of subcommisure and incisure in patients affected by myxomatousatous disease.

All examinations were stored in Tom Tec system and analysed retrospectically with 3D dedicated software. Eighty eight examination were excluded: 1) for low quality of imaging and/or absence of 3D acquisition, 2) left anterior prolapse with no good evaluation of posterior leaflet anatomy. Posterior leaflet prolapse was the most frequent pathology.

In 163 pts I reconstructed with tomtec system the zoom 3D morphology of the mitral valve in order to study the leaflet's characteristics and to establish a clinical correlation with the type of surgical repair.

Results in the total population analyzed

In the all pts analyzed (163) we found the following lesions :

Type of lesions:

46 bileaflet prolapse (28%), 117 posterior leaflet prolapse (72%). Ninety five pts with flail (58%).

Morphology

Type of posterior prolapse:

-P2 involvement 142 pts (87%), other than P2 21 pts (13%)

-P2 monolobate: 45 pts (31%)

-P2 bilobate:48 (33%)

-P2 biscallop: 62 (44%)

-Number of incisure: 61 (on posterior and anterior leaflet).

-Number of pts with 2 subcommisure: 99 (60%).

-Number of pts with >2 subcommisure: 65 (40%).

-Intercommissural extension of the prolapse lesion: 2D evaluation 18,4 mm (±5,5) and 3D evaluation 28,5 mm (±11,12).

The patients were divided in two groups according to the presence of simple (group A :49 pts) and complex surgical repair (group B 114):

Group A (49 pts)

Type of lesion and morphology

15 bileaflet prolapse (30%)

Type of posterior prolapse:

- P2 involvement 39 pts (79%), other than P2 10 pts (20%)
- P2 monolobate: 20 pts (41%)
- P2 bilobate:13 (26%)
- P2 biscallop: 18 (36%)

-Number of psudocleft or incisure: 11(18%, on posterior and anterior leaflet).

-Number of pts with 2 subcommisure: 36 (73%).

-Number of pts with >2 subcommisure: 13 (26%).

-Intercommissural extension of the prolapse lesion: 3D evaluation 25,7 mm

Group B (114 pts):

Type of lesion and morphology

31 bileaflet prolapse (27%)

-Type of posterior prolapse:

-P2 involvement 101 pts (89%), other than P2 13 pts (11%)

-P2 monolobate: 25 pts (22%)

-P2 bilobate: 35 (30%)

-P2 biscallop: 50 (44%)

-Number of incisure: 50 (44%, on posterior and anterior leaflet).

-Number of pts with 2 subcommisure: 63 (55%).

-Number of pts with >2 subcommisure: 51 (45%).

-Intercommissural extension of the prolapse lesion: 3D evaluation 29,5 mm.

Table 5.1: Demographic carachteristic of analyzed patients, total group and divided in A and B groups (according the type of surgery)

	Tot Population	Group A “simple surgery”	Group B “Complex surgery”
Tot number	**163(100%)**	**49 (30%)**	**114 (70%)**
Age	**57± 6,7**	**56± 8,5**	**58± 5,9**
Sex M/F	**122/41**	**35/14**	**87/27**
EF	**62,7± 6,7**	**62,9± 7,22**	**62,64± 6,4**

Table 5 2: type of prolapse in ttotal number of patients

Numb tot pts	*Posterior Prolapse*	*Be-leaflet prol*	*Flail*
163	*113(70%)*	*50 (30%)*	*95 (58%)*

Table 5.3: Number of subcommissure and incisure in total group of patients

2 Subcomm tot	2 Subcomm monolobate	2 subcomm bilobate	3 subcom P2 Biscallop	4 Subcomm	Incisure
98 (60%)	48 (29%)	50 (31%)	62 (44%)	2(2%)	61

Table 5.4: Dimension of intercommissural extension of the prolapse lesion and annulus 2D vs 3D

	Intercommissural ext's Prolapse 2D	Intercommissural ext's Prolapse 3D	Annulus tot	Annulus Ant	Annulus Post
Mean	18,4	28,5	12,4	5	7,4
DS	±5,5	±11,12	± 5,6	± 0,9	± 1,2

Table 5.5: Basal Width of posterior leaflet scallops

Width	P1	P2	P3	Ptot
Mean	1,9	3,2	1,8	7,4
Dev Stand	± 1,2	± 0,9	± 0,54	± 1,2

Table 5.6: Basal length of posterior and anterior leaflets

Length	Post 2D	Post 3D	Ant 2D	Ant 3D
Mean (mm)	20	25	23,4	29
Dev Stand	±4	±5	±10	±4

Table 5.7: Annulus dimension in the total group of patients

	Mean Width	SD
Annulus total	12,4	±1,85
Annulus anterior	5	±0,9
Annulus posterior	7,4	±1,2

Table 5.8 : Morphology of the posterior leaflet in the total group and in the two group dived in Group A Simple MV repair Surgical Technique and group B complex MV repair surgical Technique

Results Morph/surgery	*Surgical repair*	*Simple Techn Group A*	*Complex Techn Group B*
Tot number	***163(100%)***	***49 (30%)***	***114 (70%)***
Bileaflet	***46 (28%)***	***15 (30%) (33%)***	***31 (27%) (67%)***
P2 monol	***45 (31%)***	***20 (41%)***	***25 (22%)***
P2 bilob	***48 (33%)***	***13 (26%) (27%)***	***35 (30%) (73%)***
P2biscallop	***68 (44%)***	***18 (36%) (26%)***	***50 (44%) (73%)***
2 subcomis	***99 (60%)***	***36 (73%) (36%)***	***63 (55%) (64%)***
>2 subcom	***64 (39%)***	***13 (26%) (20%)***	***51 (45%) (80%)***
Incisure	***61***	***11 (22%) (18%)***	***50 (44%) (82%)***
IC 3D ext les	***28,5***	***25,7***	***29,8***

6. Discussions

In the past literature divergent views have been reported regarding the number and morphological description of the mitral leaflets (Anderson &Kanani et al 2007).

There is ambiguity regarding the morphology and the nomenclature of leaflets (Standring et al).

The first innovation of our study is the terminology.

There is a lot of confusion and diatribe in the past literature, between clinicians, surgeons and pathologists.

We believe more correct to limit the use of term “Cleft” to a congenital disease of the mitral valve leaflets according the scientific literature (81-87). The congenital Cleft derives from a cushion fusion defect on the anterior leaflet in the contest of atrio-ventricular septal defect (“AV canal”). Some articles report with same name of “cleft” a rare congenital defect on the posterior leaflet or sometimes more frequently a characterist defect associated to myxomatousatous mitral valve disease.

According to the hypothesis of the Cambridge group’s Study the diastasis (pathological enlargement of the physiological subcommissure) of the subcommisure can be called “Cleft” and is frequently associated to the myxomatous mitral valve disease. In this case the enlargement of the subcommissure produces a pathological regurgitation, and the surgical treatment needs to address also the surgical management of the cleft.

So we introduce a new terminology and call the normal physiological incisure, deep more than 50% of the leaflet high, “SUBCOMMISSURE” and the simple incisure ,deep less than 50% ,“INCISURE”. This nomenclature is supported by the insertion on the subcommissure of tendineae chordae funny like very similar to the commissure ones.

In the heart specimens we found a major prevalence of the morphology with three scallops like Carpentier’s classification. Moreover comparing the anatomic and the echocardiographic results the prevalence of the three scallops posterior leaflt was the same (about 60%).

The posterior leaflet scallops is more wide and long in the myxomatousatous valve than in normal anatomic’s valve examination.

In Western countries the most common etiology of mitral valve pathology is the degenerative disease, affecting around 2% of the population, with a wide spectrum of anatomic lesions, from fibroelastic deficiency (localized prolapse segment, often associated with ruptured chordae), to extensive myxomatous degeneration and Barlow's disease (with multiple valvular segments involved) .

Mitral valve reconstruction is currently the standard treatment for degenerative mitral regurgitation, for the functional mitral incompetence (Ischaemic or dilatative cardiomyopathy) and if there is a favourable anatomy, also in some cases of infective endocarditis and of rheumatic disease.

In the last decades cardiosurgery has developed many techniques for mitral valve repair: quadrangular or triangular resection, ring annuloplasty, artificial chordae replacement, edge-to-edge, sliding plasty, folding plasty, butterfly plasty, chordae transposition etc.

Prolapse of the posterior leaflet (PPL) is the most frequent dysfunction of the mitral valve in the Western world.

Quadrangular resection, first proposed by Alain Carpentier, has progressed to become the gold standard modality to repair posterior leaflet prolapse. Although this "resection technique" is safe, reproducible, and offers favorable long term results, in the last year a lot of different surgical repair technique have developed.

The repair of mitral valve technique are usually classified in simple and complex, based on technical aspect of reproducibility and durability of the procedures.

So we wanted investigate the influence of the mitral valve anatomy on the surgical repair planning. We divided the total population in two group according the type of the repair surgey : Group A "simple surgery" and Group B "complex surgery".

In the group B submitted to a complex surgical repair of the mitral valve prolapse we find a major incidence of pseudocleft or incisure (50/61) and a major incidence of bilobate P2 lesion and biscallop P2 (major incidence also of more than 2 commisure).

In the group A there is a major incidence of monolobate morphology.

An interesting final echocardiophic finding is the significative difference of value of the intercommissural lesion's extension measured with two-dimensional e three-dimensional echocardiography in the total population. When the population was dived based on the complexity of the surgical repair, in the group B I found a major intercommissural extension of the prolapse lesion vs the group A (29,8 mm vs 25,7 mm, mean value).

The three-dimensional echocardiograpy gives a more wide measure of the intercommissural extension of the prolapse more coincident with the real anatomy.

This finding increases the importance of the pre-operative 3D transesophageal echocardiography evaluation before a cardiac surgery mitral valve repair, in order to establishlish a correct surgical planning.

7. Conclusions

We have analyzed throughly the anatomy of the normal leaflets in the anatomic specimens in order to establishlish the incidence of subcommissure and incisure.

It is relevant in the pathological setting of mitral valve incompetence to establish the presence and the role of the subcommisure and incisure, for the choice of an optimal surgical treatment.

The main results of my Phd thesis are:

1° the same prevalence in normal valves and in the myxomatousatous mitral valve diseases of the of three scallop morphology (about 30%);

2° the posterior scallops are more wide and long in the myxomatousatous valve than in normal valve examined, according to the past litterature;

3° The annulus ‘ dimensions are major in the myxomatousaotus disease vs normal mitrla valve

4° in the group B submitted to a complex surgical repair of the mitral valve prolapse I have found a major incidence of incisure (50/61) and a major incidence of bilobate P2 lesion and biscallop P2 (major incidence also of more than 2 commisure);

5° I have found also a significative difference in the evaluation of intercommisural prolapse lesion extension with two dimensional vs three-dimensional- echocardiography, due to the different power of the two imaging technology;

6° In the group B submitted to a complex mitral valve surgery repair there is a major intercommissural extension of the prolapse lesion (29,8 vs 25,7 mm, mean value).

7° in the group A there is a prevalence of three scallops with monolobate morphology of the posterior leaflet (with 2 subcommissure 73%).

My Phd thesis assess that in the analysis of severe myxomatousaotus mitral valve incompetence, is essential to establish with a pre-operative three-dimensional echocardiography the presence of the subcommissure and the incisure, and the intercommissural extension of the prolapse lesion, those elements are important determinants to guide an optimal surgical treatment with mitral valve repair techniques of different complexity.

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Europass curriculum vitae

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2

Work experience

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- October 2006: Postgraduate Cardiology Specialization Catholic University of Rome (50/50 cum laude)
- 2002 July Inscription Physician Regional and National Registry (Teramo).
- 2002 june : Italian National Abilitation(108/110)
- 2001-2002: Research Fellowship Catholic University of Rome Gemelli Hospital
- 2001 : Medical Degree Catholic University of Rome
- 2000-2001 Fellowship internal Medicine
- 1995: Scientific High School leaving qualification (60/60).

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Personal skills and competences

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Stress Test
Transesophageal echocardiography
3D echocardiography
MRI and CT interpretation

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Other language(s)

Self-assessment	**Understanding**		**Speaking**		**Writing**
European level (*)	Listening	Reading	Spoken interaction	Spoken production	
English	**C2**	**C2**	**C2**	C2	
French	**B2**	**B2**	**B1**	B1	

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Social skills and competences

Religion Catholic Teacher 1994, Volleyball Player, Culture no profit association m Festival organization.

Organisational skills and competences

Imaging Service for Cardiosurgery and cardiology department

Technical skills and competences

Cardiological Clinical inpatient and outpatient exeprience
Cardiosurgery clinical managment of patient
Pre-intra e post operative imaging
Echocardiography exeperience (transthoracic, transesophageal, stress test)

Blood pression and EKG Holter, EKG interpretation
Valvular heart disease decision making
Percutaneus Valvulare Treatment Imaging

Computer skills and competences — Good competences in use of windows (execel, world, power point etc) and MAC , SPss , Stata, AVI and JPEg imaging files.

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Annexes

Scientific Publications

1) Rizzello V., Liuzzo G., Trabetti E., G. Di Giannuario, Brugaletta S., Santamaria M., Piro M., Boccanelli A., Pignatti P. F., Biasucci L.M., Crea F. Role of the CD14 C(-260) T promoter polymorphism in determinino the first clinical manifestation of coronary artery disease.

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8) Implantation of a new mitral ring, adjustable during follow-up: a simplified technique.Caradonna E, Testa N, De Filippo CM, Calvo E, Di Giannuario G, Spatuzza P, Rossi M, Alessandrini F.Interact Cardiovasc Thorac Surg. 2012 Oct;15(4):578-9

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2016, 28 th, February, Doctor Giovanna Di Giannuario

Lavori in extensor

1. Autologous bone marrow stem cells transplantation in patients with critical limb ischemia not eligible for revascularization Italian Journal of Vascular and Endovascular Surgery 2011 Giugno;18(2):73-9 Modugno P., De Filippo C. M., Caradonna E., Amatuzio M., Centritto E. M., Sabusco A., **Di Giannuario G.**, Piano S., Giordano G., Storti S., Papini S., Zappacosta B., Sallustio G., Rossi M., Alessandrini F.

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