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## **Percutaneous Aortic Valve Replacement**

# **The Anatomy of Aortic Root Structures and Postmortem Aortic Valve Stent Implantation**

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# CONTENTS

	<b>Page</b>
<b>1. Introduction</b>	<b>1</b>
1.1. Historical perspective	2
1.2. Recent status	3
1.3. Limitations and Technical Difficulties	4
1.4. Coronary blood flow impairment and anatomic structures of the aortic root	6
<b>2. Materials and Methods</b>	<b>8</b>
2.1. Materials	8
2.2. The method of the heart dissection and examination	8
2.3. Heart dissection and measurement of the diameter of the distal ascending aorta, proximal ascending aorta, STJ and aortic sinus annulus	10
2.4. Determination the relation of valve stent, aortic leaflets and coronary arterial ostia	10
2.5. Determination of the parameters and relation of the aortic leaflets, coronary ostia and STJ after aorta was opened	12
2.6. Results and statistical analysis	16
<b>3. Results</b>	<b>17</b>
3.1. General description of the anatomic findings of the aortic valve, the coronary arteries, and the coronary arterial ostia	17
3.2. Measurement of the aorta, the aortic valve, the coronary arteries, and the coronary arterial ostia	18
3.3. The location, the number, and the shape of coronary ostia in relation to the STJ	24
3.4. The difference between the height of the left and the right aortic leaflet and the height of its corresponding sinus annulus to the ostia	29

3.5.	The findings of the relation among the aortic leaflet, the coronary ostia, and the valve stent before and after valved stent implantation	33
<b>4.</b>	<b>Discussion</b>	<b>41</b>
4.1.	The anatomy of the aortic root structures	42
4.2.	The findings of post mortem aortic valved stent implantation into the aortic position	44
4.3.	Limitations	46
4.4.	Conclusion	47
<b>5.</b>	<b>Summary</b>	<b>48</b>
<b>6.</b>	<b>References</b>	<b>49</b>
<b>7.</b>	<b>Appendix</b>	<b>56</b>
<b>8.</b>	<b>Acknowledgement</b>	<b>61</b>
<b>9.</b>	<b>Curriculum Vitae</b>	<b>62</b>

## **1. Introduction**

Surgical aortic valve replacement has been proven to be the ultimate treatment of symptomatic aortic valve disease with low operative morbidity and mortality in selected patient groups [1]. Traditional surgical approaches require a midline sternotomy and cardiopulmonary bypass with or without cardioplegic arrest. To minimize the invasiveness of operations, a broad spectrum of techniques, including endoscopic and robotic surgery, has been developed and optimized [2, 3, 4].

Despite all the efforts to minimize the invasiveness of operations, trauma associated with such surgical procedures still exist in a large number of patients such as general anesthesia, cosmetic scarring, and co-morbidities associated with ageing, age itself and repeat surgery as independent risk factors for an adverse outcome [2, 5, 6, 7]. All of these factors have led to develop an alternative to open heart operations, and recent reports [6, 8, 9, 18, 23, 24, 25] indicated that percutaneous aortic valve implantation (PAVI) may become an effective and feasible procedure, which could benefit a large patient population.

Percutaneous endovascular therapy has now become a reality. From early balloon valvulotomy for valvular stenosis [10, 11, 13, 14, 15], technologies have been developed to allow percutaneous replacement of pulmonary [23, 32] and aortic valves [24, 25, 33], and repair of regurgitant mitral valves [12, 15, 16] in selected patients.

Following extensive investigations in animals [17, 18, 19], early clinical reports [20, 21, 22, 23, 24, 25, 38] have shown successes in selected patients. As the criteria for patient selection, clinical safety and efficacy trials progressing, the role of these new technologies in patient care strategy will become better understood.

Percutaneous aortic valve implantation is the development of a foldable heart valve that can be mounted on an expandable stent, delivered percutaneously through standard catheter-based techniques and implanted within a diseased aortic valve annulus [8,26,30], after the diseased valve has been dilated [25, 30], or resected [26, 27].

### **1.1. Historical perspective**

Percutaneous valve therapy was initially developed with aortic valve replacement. Such application can be traced back to nearly half a century ago. After Hufnagel and Harvey [28] surgically implanted the first valvular prosthesis in the descending aorta to prevent aortic regurgitation in 1951, Davies H. [29] in 1965 deployed a catheter-mounted unicuspid valve above the aortic valve for relief of the aortic regurgitation into the left ventricle; much effort has been made to develop percutaneous valved stent implantation since then.

Andersen et al [30] initially described the percutaneous valve intervention in a swine model in 1992. These investigators fabricated a stent-mounted bioprosthetic valve and demonstrated that percutaneous implantation of expandable artificial aortic valves in the anesthetized closed-chest pigs by retrograde transluminal catheter technique is feasible. However, complication was associated with restriction of the coronary blood flow in subcoronary implantation. In the same year, Pavcnik [31] reported the implantation of an artificial caged-ball valve in dogs by percutaneous transcatheter approach. Although their results demonstrated that such procedure is feasible, a major difficulty as how to securely position this device in a dynamic environment was encountered, resulting in significant aortic regurgitation.

Since then, several groups [17, 23, 25, 26] have made significant contributions to this development.

## 1.2. Recent status

Although the aortic valve replacement in symptomatic patients with aortic valve disease results in excellent symptom relief and long-term survival in most patients [1,2,4,5]. A growing number of patients are poor surgical (inoperable) candidates due to advanced age, co-morbidities and previous cardiac surgery. Based on our clinical experience, they represent a great management challenge [6, 7]. In the past decades, a number of minimally invasive techniques have been experimentally developed for the aortic valve replacement to overcome the difficulties [4, 17, 18, 19, 32].

Boudjemline and colleagues [9] reported their short term study in lambs in 2002, they implanted a valve stent with trapping native leaflets between the outer nitinol stent and the inner platinum stent into the aortic annulus by retrograde approach. The restriction of coronary ostia, mitral valve insufficiency, and stent migration were encountered.

In 1990s, Lutter and his group [18] began to perform the study of aortic valved stent implantation, and achieved success in animal studies in 2001. A percutaneous stent-based expandable valve was designed by mounting a fresh porcine aortic valve into a self-expandable nitinol stent by suture technique [26]. Although technical difficulties including visualization, deployment, stent migration, and rhythm disturbance were encountered in their studies, subsequent implantation of the valved stent was well tolerated, without significant valve insufficiency. This short term *in vivo* study provided significance that nonsurgical implantation of an aortic valve is feasible.

Based on the contribution of these groups, PAVI have been developed, and experience is accumulating in humans. Bonhoeffer [32] first reported the use of a stent-mounted bioprosthesis for pulmonary valve implantation by a retrograde approach in 2000. This achievement clearly marked the beginning of the era of percutaneous valve replacement therapy in humans. Furthermore, the same group demonstrated the implantation of a biological valve stent into human pulmonary position by antegrade delivery approach,

and reported the possibility of degeneration of the biological prosthesis [23]. Percutaneous aortic valve replacement with a stent-mounted bioprosthetic valve device was initially reported by Cribier et al in 2002 [24]. They published the first human percutaneous aortic valved stent implantation utilizing an antegrade transseptal approach within a stenotic aortic valve. In 2004, by using an antegrade transseptal approach, the same group successfully implanted the valved stent into the stenotic aortic position in eleven end-stage patients without impairing the coronary flow or mitral valve function. Although a successful mid-term therapeutic result was achieved, a mild paravalvular aortic regurgitation was noticed.

Although it is at its early stage with growing experience, all these preliminary studies suggest that percutaneous, and transapical valved stent implantation in the aortic position can be achieved in patients with end-stage calcific aortic stenosis and may become an important therapeutic option for inoperable patients [39].

Despite PAVI hold great promise, and has been proven to be feasible. On the other hand, many technological difficulties and limitations still exist.

### **1.3. Limitations and Technical Difficulties**

Recently published case reports [24, 25] show the technical feasibility of remote access aortic valve implantation. However, severe hindrances to aortic valve implantation remain in percutaneous approaches, including: optimal attachment of the valve into the stent, function preservation of the valved stent, functional anchoring mechanism, appropriate vessel access, suitable visualization method, and potential tools for removal of calcification and native valves [8, 26, 27, 30]. Furthermore, due to the difficulty positioning the stent into the calcified and stenotic aortic annulus, dislodgement and migration of the valved stent, potential complications unique to this procedure include a significant incidence of paravalvular leakage, calcific embolism, stroke, small aortic valve area, and acute heart



failure [8, 24, 25, 31, 38].

In the early stage of PAVI, some experimental percutaneous techniques, placing valved stent in sub- or supra-aortic position showed high complication rates, including the restriction of the coronary blood flow [30, 31] for the infeasibility to implant the aortic valved stent into the aortic annulus.

Lately, most investigators [8, 9, 26, 27, 33, 34, 46] reported the impairment of the coronary blood flow due to the position of the coronary orifice and the close relationship with the aortic leaflets, valved stent, and anterior mitral leaflet during the PAVI. Two potential risks for impaired coronary flow or even complete occlusion of the coronary orifice and consecutive fatal myocardial infarction were considered as: direct occlusion by parts of the valved stent, or obstruction by the native aortic leaflets folded upwards, and being compressed against the coronary ostia.

Up to now, the interest in orthotopic PAVR states accumulating. Physiologically, it is certainly preferable to implant the new valve in the orthotopic aorta, over the native valve, even if it is more technically demanding [35, 36]. To perform a reliable replacement, in cases of severe aortic stenosis the diseased valve has to be predilated, and removed [26, 27]. Quaden [37] firstly reported the endovascular resection of human aortic valves *in situ*. The study showed an AVIC (Aortic Valve Isolation Chamber) system with its advances and drawbacks. The avoidance of embolism and coronary flow impairment caused by the debris were also described in the study.

In 2004, Huber [35] published the feasibility of an acute surgical suture less aortic valve implantation without compromising coronary flow of a properly placed and sized valved stent. Furthermore, he reported the surgical approach, with precise measure of the aortic valve region, especially the coronary sinus dimension, and the analysis of post-deployment coronary flow allows the valved stent implantation of adult size to have adequate

function. Later on, the same group demonstrated the right coronary ostia occlusion during the supra-annularly valved stent deployment via a transapical approach in twelve pigs [39].

Based on the close proximity of the coronary orifice to the aortic valve leaflets, the continuity of the mitral valve annulus and the aortic annulus makes PAVI a major challenge [8, 9, 35]. To avoid the impairment of the coronary flow and paravalvular leakage during an orthotopic PAVI, a basic research concerning the relation between the valved stent and the aortic root anatomic structures (including the coronary arterial ostia, aortic leaflets) is necessary.

#### **1.4. Coronary blood flow impairment and anatomic structures of the aortic root**

Adequate perfusion of the heart depends fundamentally on the right morphological conditions of the left and the right coronary arteries. These arteries have the peculiarity of being the only ones filled during the diastolic phase of cardiac rhythm. Some conditions, such as anatomic integrity of the aortic valve, absence of valvular malformations, and anatomic malformations of the coronary arteries result in a reduction in coronary blood flow to the myocardium [40, 41, 42, 43, 44, 45].

Based on the observation that the impairment of coronary blood flow encountered in PAVI, many investigators supposed that the malfunction of the aortic root structures was due to the valved stent implantation in aorta, particularly in orthotopic position. The stent in the native aortic position may affect the anatomical and physiological integrity of the aortic root, between the coronary ostia and aortic leaflets during cardiac cycle. These mechanical factors indicate that coronary flow can be blocked either directly from the implanted stent, or from the native aortic leaflets immobilized and pushed against the coronary orifices [8, 9, 26, 27, 31, 38]. In 2007, Flecher et al [46] reported that coronary ostia obstruction may occur after PAVR in an in vitro

study. They considered the native leaflets as the main cause of right or left coronary obstruction.

Currently, several studies have been performed to describe the anatomic structures of the aortic root including the coronary ostia and aortic leaflets. In most investigations [40,47,48,49,50], two coronary ostia, one left and one right, located in the two aortic sinuses closer to the pulmonary trunk were described, and the position of the coronary ostia in relation to the sinutubular junction (STJ) and inter-commissural line of aortic leaflets was studied.

Turner [49] reported that from the functional point of view, the typical vertical positioning of the ostia, particularly when both coronary ostia were above the inter-commissural line, seems to confer functional advantages for coronary flow during ventricular systole, and would also prevent the obstruction of the ostia when the aortic valve was opened. Cavalcanti et al [40] described that the left coronary ostium is more medially located in regard to the inter-commissural distance than the right coronary ostium, which is displaced to the right side. Furthermore, Muriago et al [50] added that the more central location of the left coronary ostium is appropriated and justified, because the left coronary artery heads to the space between the pulmonary trunk and the left auricle, branching right after its origin. They also demonstrated that the variations in the position of the coronary ostia in relation to the aortic leaflets and the diameter of the ostia may be involved in the possible reduction in coronary blood flow.

In the current study we observed and measured these aortic root structures (including the aorta, the coronary ostia, and the aortic leaflets) on 40 fresh adult heart specimens. Through the post mortem aortic valved stent implantation, we investigated the relation of coronary ostia, aortic leaflets, and valved stent to find how the PAVI influence the coronary blood flow.

## 2. Materials and Methods

### 2.1. Materials

Between March 2007 and August 2007, 40 post mortem hearts were enrolled and dissected in our study, collected at autopsy in the Department of Pathology of University Hospital of Schleswig-Holstein. All these autopsy material originated from the white adults of both genders (19 men, and 21 women). Those patients died due to different reasons including cardiac surgery and cardiology disease, respiratory disease, trauma, advanced cancer, pulmonary embolism, hemorrhage or embolism of the brain, and so forth. The cadavers were kept in cool place until they were used for autopsy. The general characteristics of the patients at death were listed in table 2. 1.

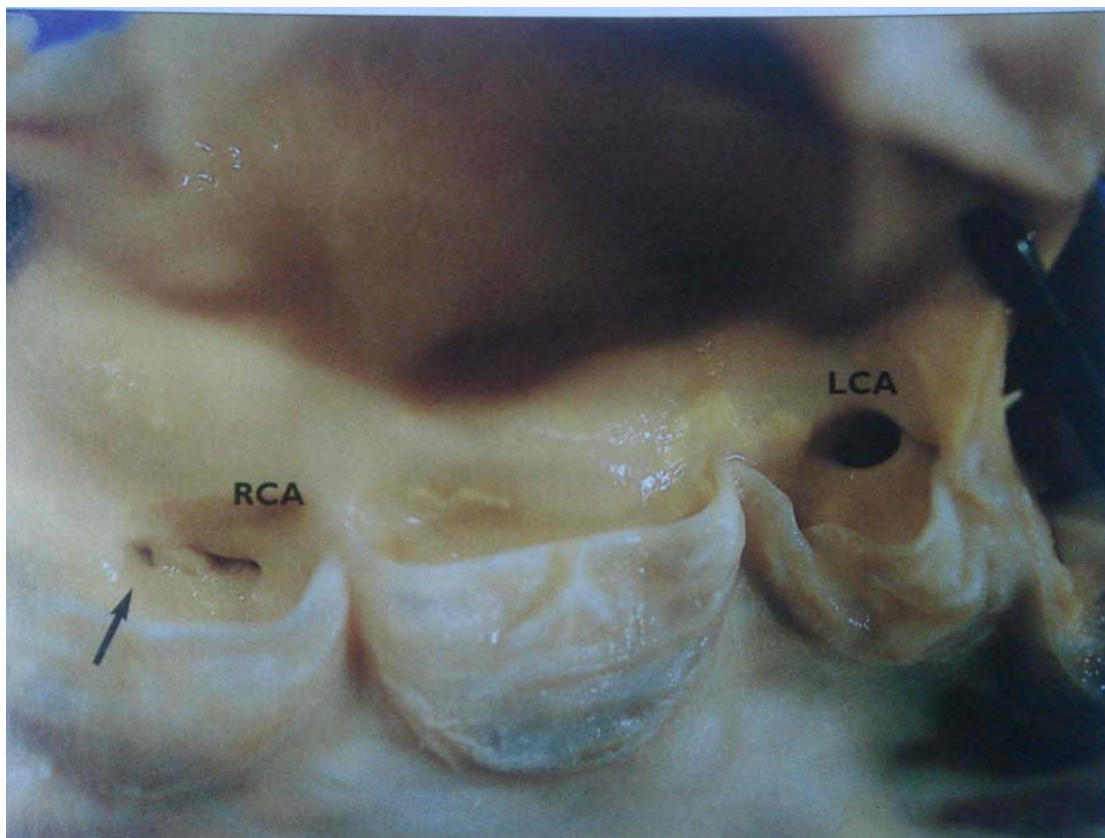
**Tab.2. 1: Patients general characteristics (n=40, male 19; female 21).**

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	40	26.0	96.0	69.7	13.3
Height (cm)	40	122.0	187.0	168.6	10.3
Body Weight (Kg)	40	57.0	124.0	80.6	15.9
Heart Weight (g)	40	264.0	1010.0	453.1	121.2
Body Mass Index (Kg/m <sup>2</sup> )	40	17.9	40.9	27.9	5.1

### 2.2. The method of the heart dissection and examination

All 40 hearts with great vessels were fresh without formalin fixation when they were dissected.

For the dissection methods are learned by personal experience and vary with the individual pathologist. We took the inflow-outflow trans-valvular incisions procedure originally described by Levy, McMillian, and Oppenheimer to dissect these hearts [51, 52, 53]. The aorta was opened between the attachment of left and right aortic leaflet (Fig.2.1). The method taken here is conventional. Each of the four chambers was opened according to the blood flow direction, and allows correlating the morphology with its function as recorded by clinical investigations [50, 54, 55, 56].



**Fig.2.1:** The aorta has been opened to show the outflow tract from the left ventricle. A long incision has been made through the anterior wall of the left ventricle between the left and right leaflets to show the coronary ostia and aortic leaflets. (From: Malcolm D: Cardiovascular Pathology. Third

There is a lack of uniformity in the nomenclature of the leaflets and sinuses of the aortic valve [56]. In this work, the latter of left, right and posterior for description, which advocated by Nomina Anatomica [57] will be

followed.

### **2.3. Heart dissection and measurement of the diameter of the distal ascending aorta, the proximal ascending aorta, the sinutubular junction (STJ), and the aortic sinus annulus**

During the autopsy, the heart were removed and weighted. The origin of the left and right coronary arteries was isolated for measurement of the diameter of root portion of the corresponding arteries. In our study, the distal ascending aorta was reserved for further analysis and measurement. The aortic root including ascending aorta was sectioned sequentially for measuring dimensions as below: first, the ascending aorta was transversally sectioned approximately 1 cm below the arch of aorta and measured the diameter of the distal ascending aorta by using the vernier caliper, circle and aortic valve sizer set (Fig.2.2 and Fig.2.3). Second, we removed the aorta at level of the proximal aorta, just nearly 1 cm above the level of STJ of the aorta, and measured the diameter of the proximal aorta, STJ, and sinus valsalva diameter respectively.



**Fig. 2.2:** Measurement tools: vernier caliper and circle



**Fig. 2.3:** Aortic sizer set (diameter range 19-29mm)

### **2.4. Determination the relation of the valved stent, the aortic leaflets, and the coronary ostia before the aorta was opened**

After the above measurement was performed, a cut across the aorta

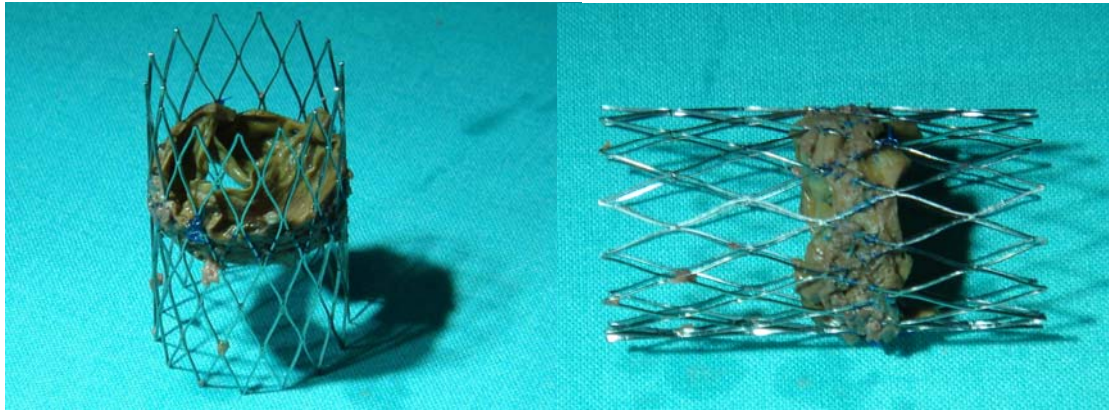
above the aortic annulus (approximately 0.5 cm above the STJ, avoiding the destroy of the coronary ostia which lay above the STJ level) [50] was made to exposure the valve architecture in order to look for abnormalities, and also to show the orifices of the coronary arteries before the aorta was completely opened.

#### **2.4.1. The relation of the valved stent, the aortic leaflets, and the coronary ostia before a complete stent deployment**

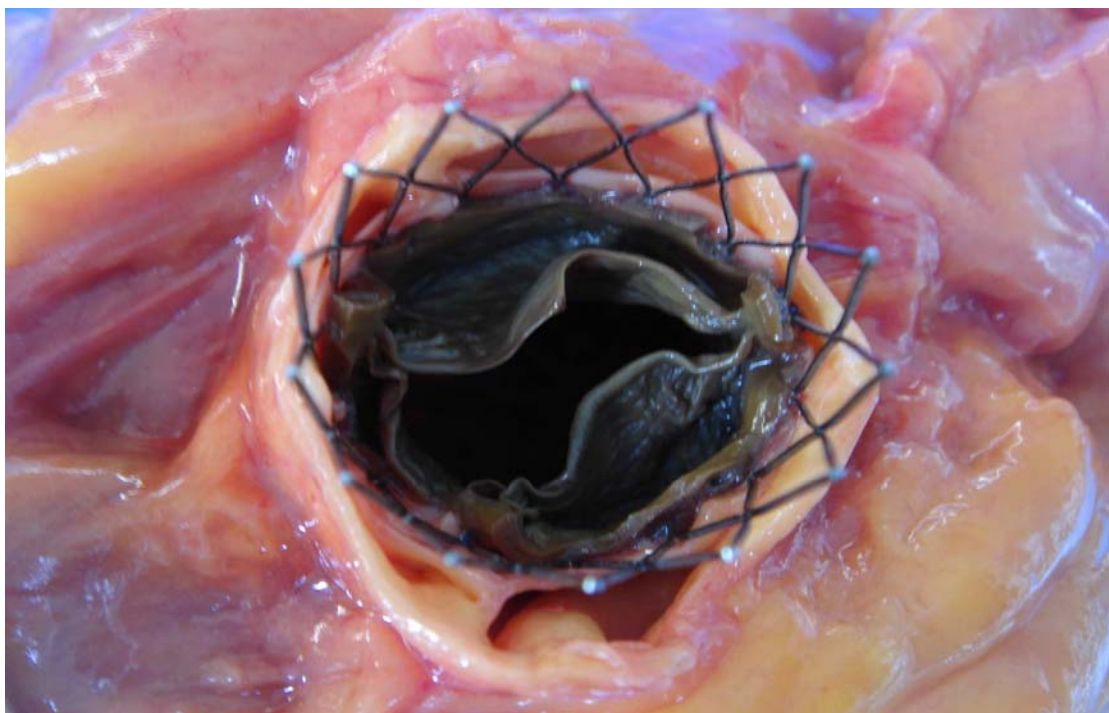
Before stent implantation we put two needles with a green, a blue or a black marker into the left and the right coronary artery ostia. And with the aid of forceps and a small metal stick, we observed the relation between coronary ostia and aortic leaflets, during the process of the leaflets being hold and close to the ostia at different positions, and photographed how the coronary ostia would be covered by the aortic leaflets (fully or partially covered).

#### **2.4.2. The relation of the valve stent, the aortic leaflets, and the coronary ostia after stent implantation**

After taking the pictures of the relation of coronary ostia and aortic leaflets, we implanted the appropriate size of an aortic valve stent. This valved stent is a collapsible and self-expandable nitinol stent (Fig.2.4) [26]. The size of the stent depended on the diameter of the aortic sinus annulus, which was measured before valved stent implantation. Then we observed the relation of the aortic leaflets, the aortic annulus, the coronary ostia, and the valved stent. Photographs documented the coronary ostia coverage and/or possible paravalvular leakage after valved stent implantation (Fig.2.5).



**Fig.2.4** Aortic valved stent (diameter of nitinol stent range from 25-33 mm)



**Fig.2.5** This figure represents the valved stent after implantation into the native aortic annulus. The aortic leaflets were folded upwards close to the aortic wall.

## **2.5. Determination of the parameters and relation of the aortic leaflets, the coronary ostia, and the STJ after the aorta was opened**

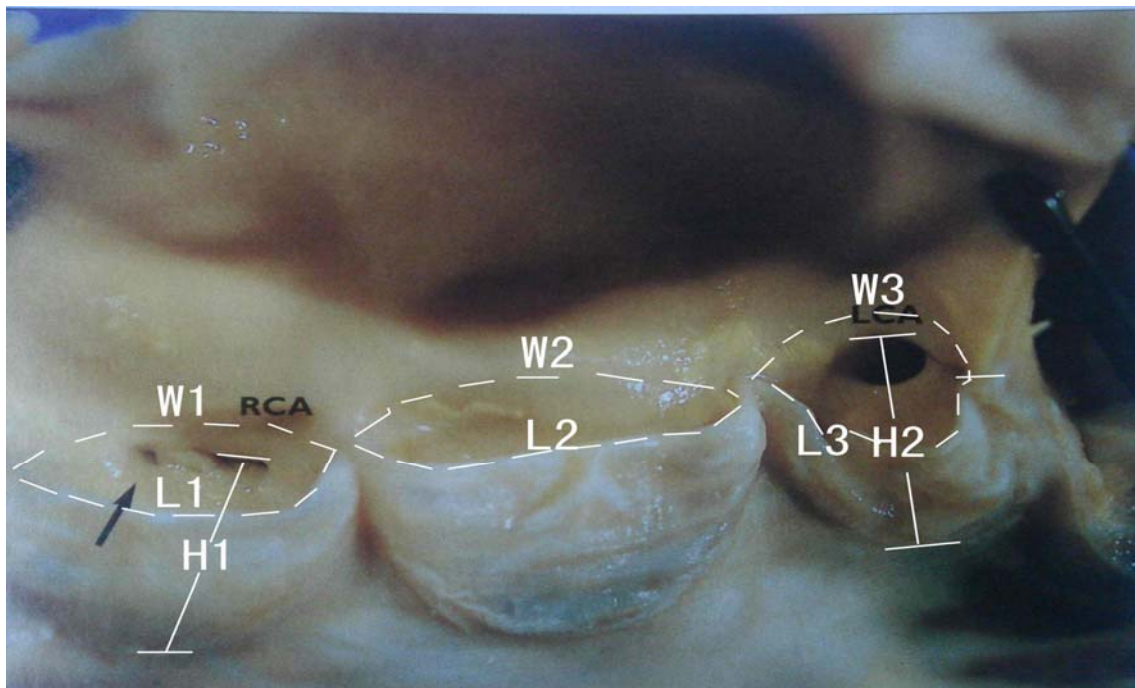
Between the right (anterior) and left (left posterior) aortic leaflets (Fig.2.1), the aorta was opened by a longitudinal incision through its anterior wall [54, 55] to keep the integrity of the coronary ostia and the aortic leaflets. This



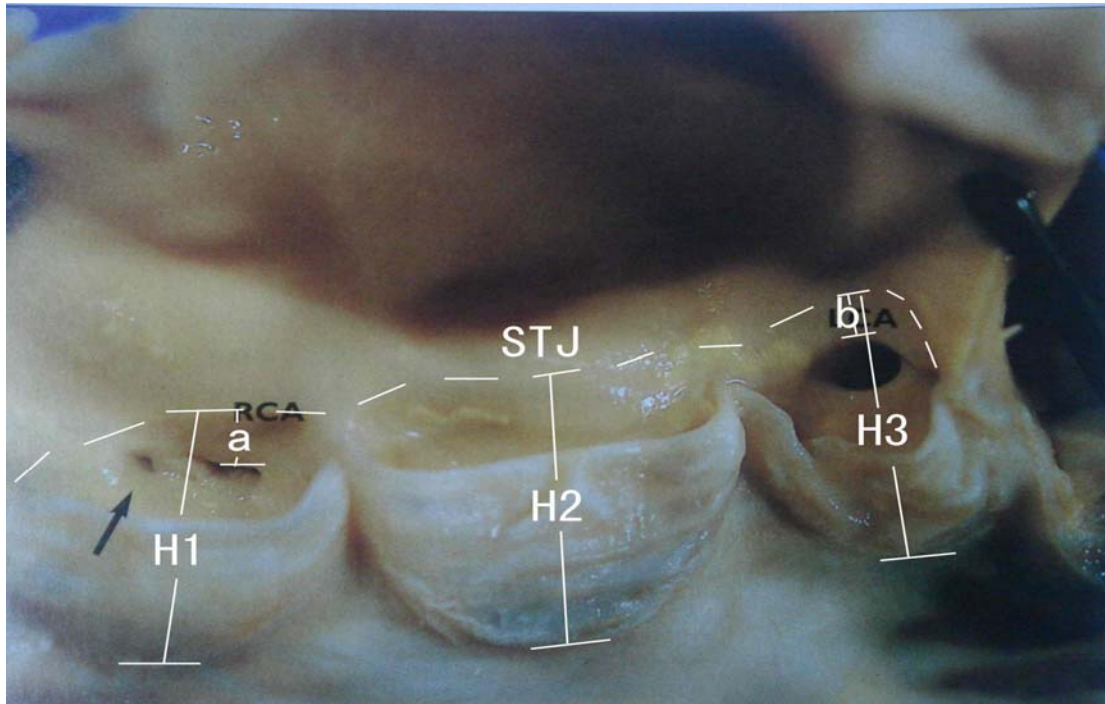
procedure enables the visualization and analysis of the morphology and topography of the aortic root structures (including the left and the right aortic leaflets, and their corresponding coronary ostia). Particularly the position of the zones of apposition between the leaflets, as well as the number and the arrangement of the leaflets, and the position of the coronary ostia in relation to the corresponding aortic sinus and the STJ. In addition, the coronary arteries were sectioned at the level of their origins in the aortic wall.

### 2.5.1. Measurement of the aortic root structures: the aortic leaflets and the coronary ostia

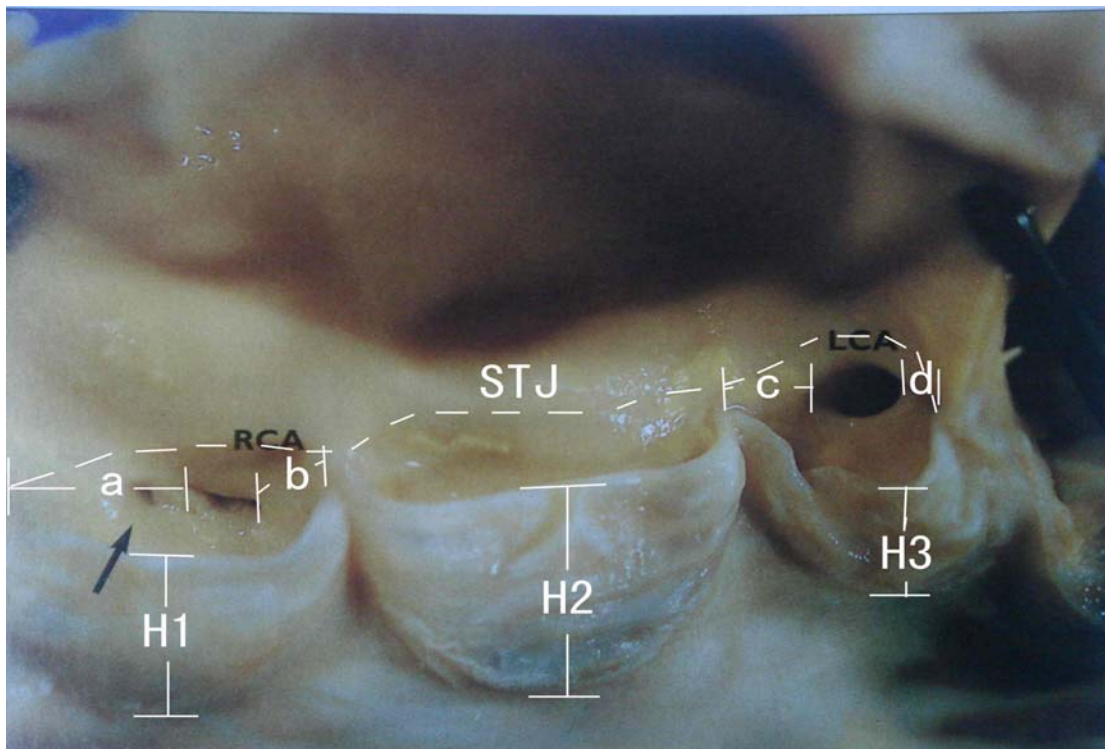
The coronary ostia in relation to the left and the right aortic leaflet were identified and, with the aid of a vernier caliper, the aortic sizer set and a circle, the following measurements were taken (Fig.2.6.1-3):



**Fig.2.6.1:** W1,2,3: the width of the aortic leaflets, and the distance between the two attachments of leaflet at the STJ (sinutubular junction). L1,2,3: The length of the corresponding aortic leaflets. H1,2: The height from the annulus to the corresponding superior margin of the coronary ostia.



**Fig.2.6.2:** H1,2,3: The height of the aortic sinus annulus to the corresponding STJ.  
 a,b: The distance from the superior margin of coronary ostia to the STJ.



**Fig.2.6.3:** H1,2,3: The height of three aortic leaflets from the bottom of sinus annulus to the median region of the free edge of the leaflets. a,b: The distance from the right coronary ostia to the bilateral corresponding attachment of the leaflets. c,d: The distance from the left coronary ostia to the bilateral corresponding attachment of the leaflets.

1. The diameters of the left and right coronary ostia, and the root portion of each coronary artery.
2. The distance from the coronary ostia to the corresponding attachment of the leaflets (left-right commissure, left-posterior commissure and right-posterior commissure).
3. The distance from the aortic sinus annulus to the corresponding superior margin of the coronary ostia, and that from the superior margin of coronary ostia to the STJ.
4. The height of the aortic sinus annulus to the corresponding STJ.
5. The height of three aortic leaflets from the bottom of sinus annulus to the median region of the free edge of the leaflet.
6. The width of the aortic leaflets, and the distance between the two attachments of each leaflet at the STJ (it was measured along the inner wall of the aorta).

#### **2.5.2. Determination of the position of the coronary ostia in relation to the STJ**

In each specimen we observed and recorded the abnormality (malformation), position, number, shape of the coronary ostia, and the presence of an accessory artery. The left and the right coronary ostia in relation to the STJ (inter-commissural line) were observed, and the hearts were grouped according to the following parameters: coronary ostium above the STJ, below the STJ, and at the level of the STJ. The shape of the coronary ostia was described as round, ellipsoidal, and eccentric after the heart was displaced flatly on a table. Then we inspected the accessory coronary artery, its number and diameter of accessory coronary artery were also measured.

### **2.5.3. Determination of the relation of the coronary ostia and the aortic leaflets**

The relation between coronary ostia and aortic leaflets was observed, photographed, and the height difference between the coronary ostia and the aortic leaflets were measured. It was described and categorized as: aortic leaflets covered both ostia; left covered and right not; right covered and left not, and no ostium was covered.

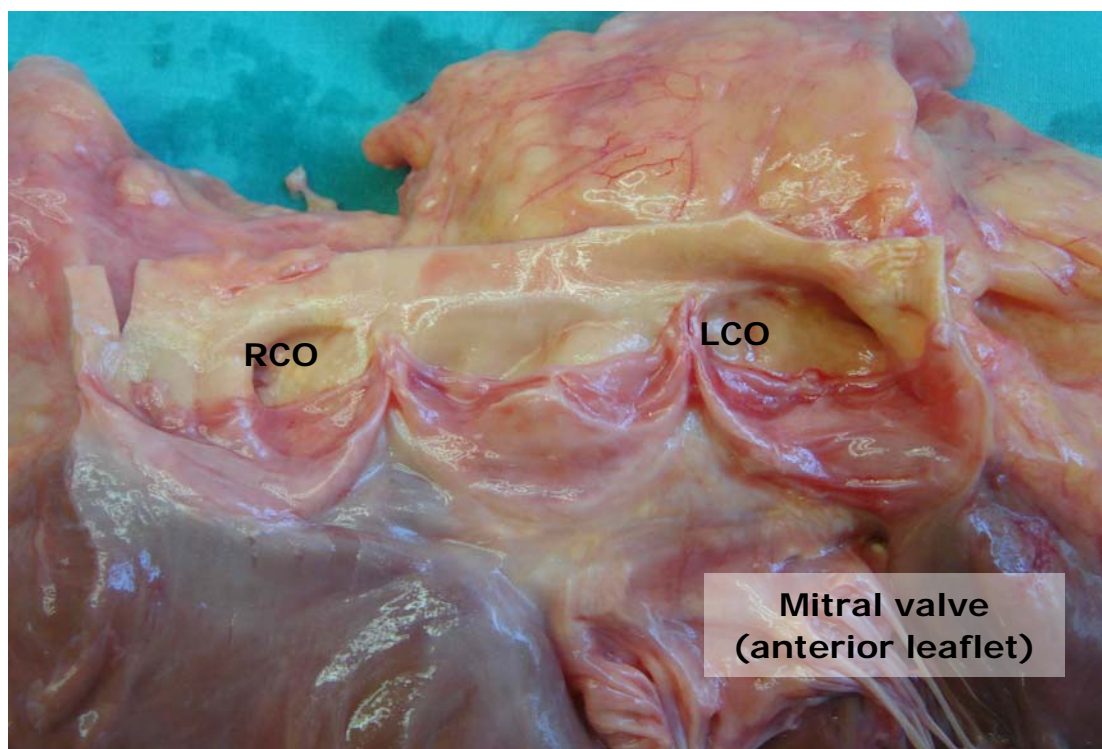
### **2.6. Results and statistical analysis**

The values found in each measurement were listed in tables and the results were presented as Means  $\pm$  SD. Differences between individual groups were statistically analyzed. Continuous variables were compared by use of paired and 2-tailed unpaired Student t test. Categorical variables were presented as frequencies and compared by  $\chi^2$  test. A significant difference was accepted when the p-value was less than 0.05.

### 3. RESULTS

#### 3.1. General description of the anatomic findings of the aortic valve, the coronary arteries, and the coronary ostia

All 40 heart specimens studied in our study, possessed three semi-lunar aortic valves, corresponding sinuses (left, right, and posterior), and three intervening commissures. All aortas had two main coronary ostia (internal luminal diameter > 2 mm). Not all the coronary arteries originated from the appropriated aortic sinuses. The left coronary ostia originated from the left aortic sinus in 34 cases (85%), and in 33 cases (82.5%), the right coronary ostia originated from the right aortic sinus (Fig. 3.1). The accessory coronary opening (<1mm in diameter) was only found in 15 cases (37.5%) in the right aortic sinus (Fig.3.1).



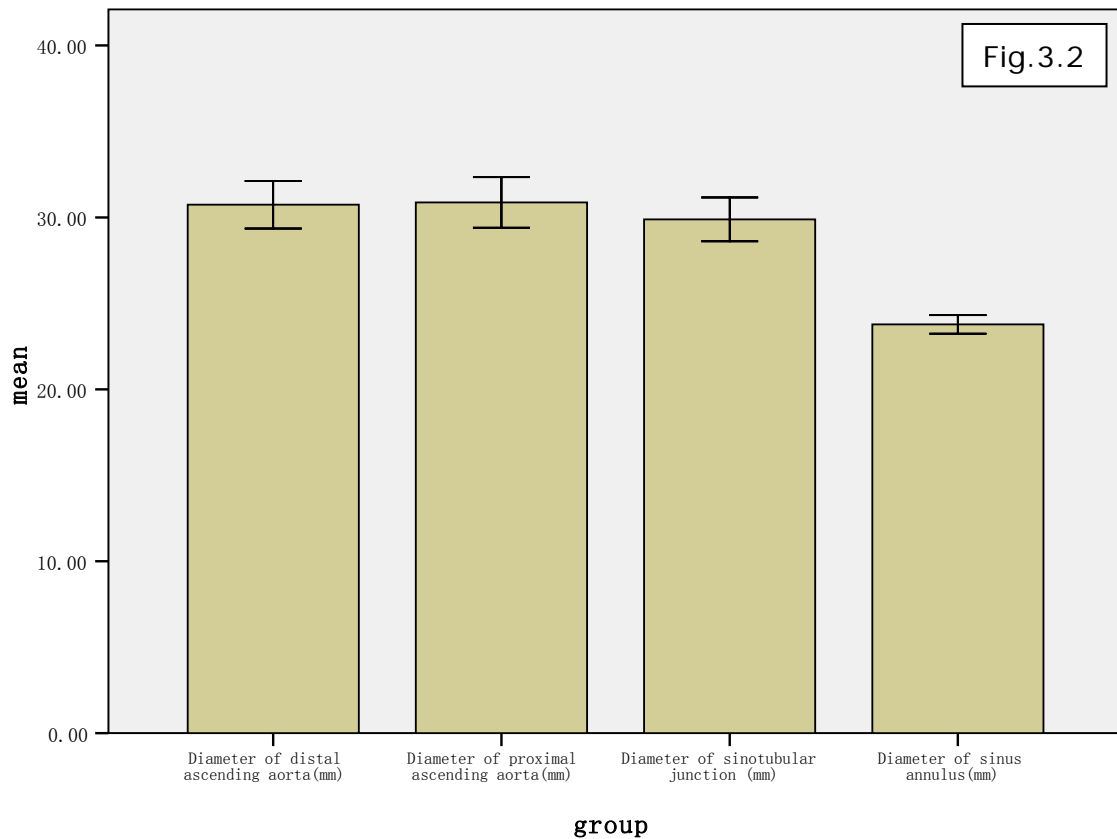
**Fig 3.1:** Diagrammatic representation of the normal aortic valve. The aorta was opened to display the three semi-lunar leaflets enface. The right and left coronary artery ostia (RCO, LCO) resided behind the left and right aortic leaflets, which usually lay below and close to the sinutubular junction

We did not find any arteries taking an epicardial course between the aorta and the pulmonary trunk. Data obtained from the latter heart were not included in the calculation of the means in this study.

### 3.2. Measurement of the aorta, the aortic valves, the coronary arteries, and the coronary ostia

#### 3.2.1. The diameter of the distal ascending aorta, the proximal ascending aorta, the STJ, and the aortic sinus annulus

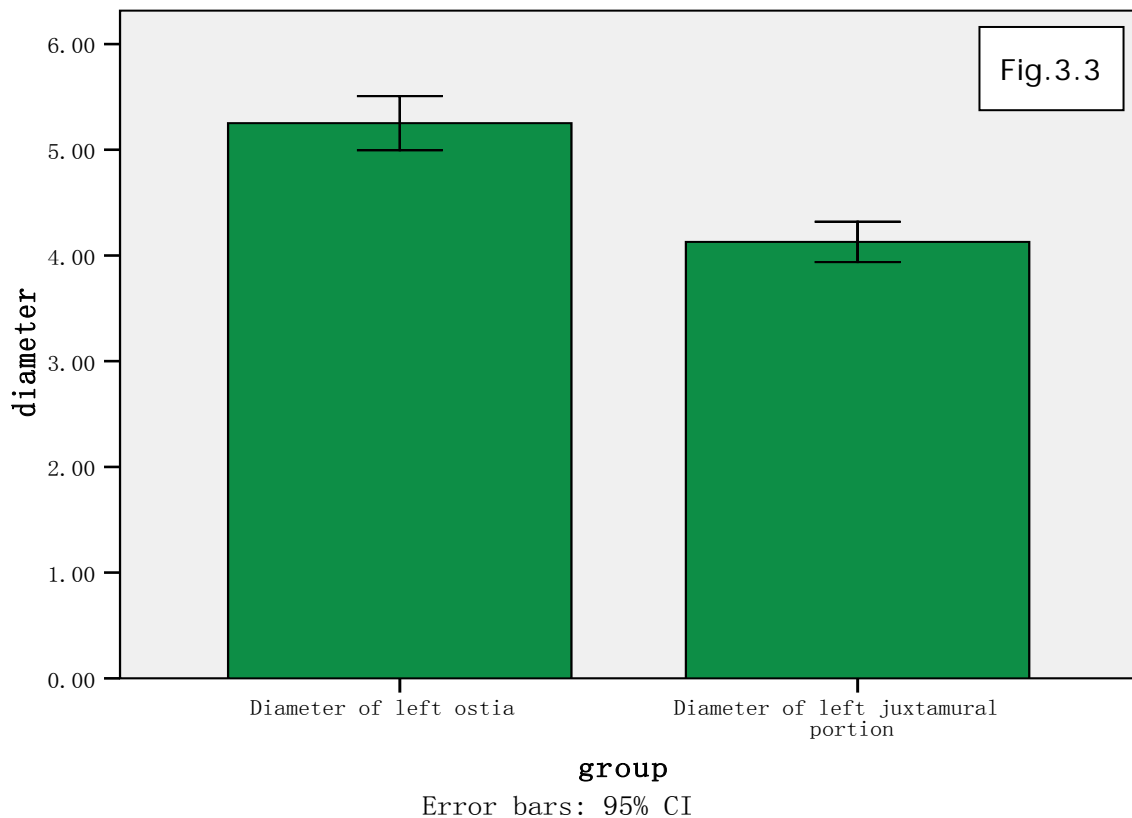
The mean diameter of the distal ascending aorta, the proximal ascending aorta, the STJ, and the aortic sinus annulus measured  $30.70 \pm 4.19$  mm (range 22.20-41.70 mm),  $30.97 \pm 4.45$  mm (range 21.20-41.50 mm),  $29.86 \pm 3.81$  mm (range 20.70-39.70 mm), and  $23.78 \pm 1.69$  mm (range 19.50-27.0 mm), respectively. No significant difference of diameter was found among the group of the distal ascending aorta, the proximal ascending aorta, and the STJ (Fig.3.2).

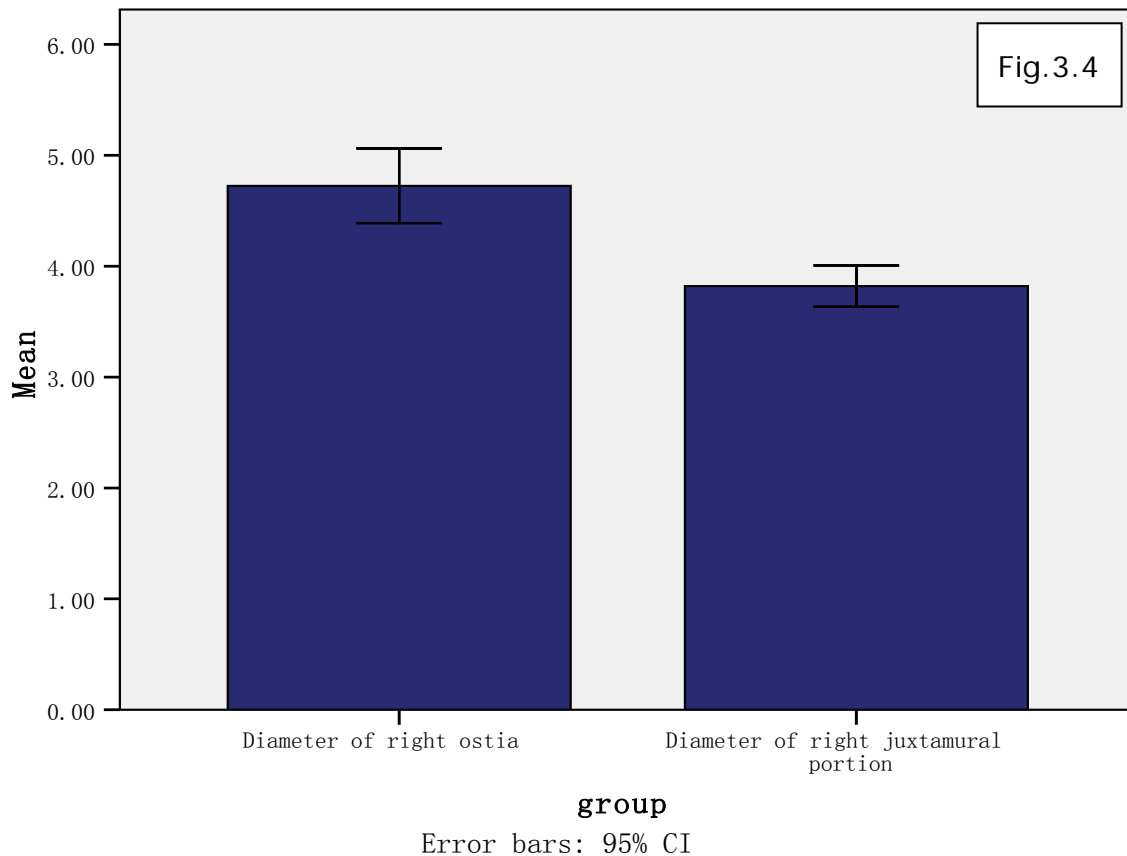


On the other hand, there were significant differences between the group of the aortic sinus annulus, the distal ascending ( $p=0.000$ ), the proximal ascending aorta, and the STJ ( $p=0.000$ ).

### 3.2.2. The diameter of the left and the right coronary ostia, and the root diameters of the respective coronary arteries

The mean diameter of the left coronary ostia and the root of the left coronary artery was  $5.25 \pm 0.80$  mm (range 3.75-7.00 mm) and  $4.12 \pm 0.59$  mm (range 3.0-6.0 mm), respectively. And the mean diameter of the right coronary ostia and the root of the right coronary artery measured  $4.73 \pm 1.05$  mm (range 3.10-8.20 mm) and  $3.82 \pm 0.58$  mm (range 3.0-6.0 mm). There was no significant difference between the left and the right coronary ostia, and same to the left and the right root portion of the coronary artery ( $P > 0.05$ ). By paired samples test, there was significant difference between the diameter of coronary ostia and that of the root of the corresponding coronary artery in the aorta wall ( $P < 0.05$ ). (Fig.3.3, and 3.4).





### 3.2.3. The distance between the left, right coronary ostia, and the inter-commissures of the aortic leaflets

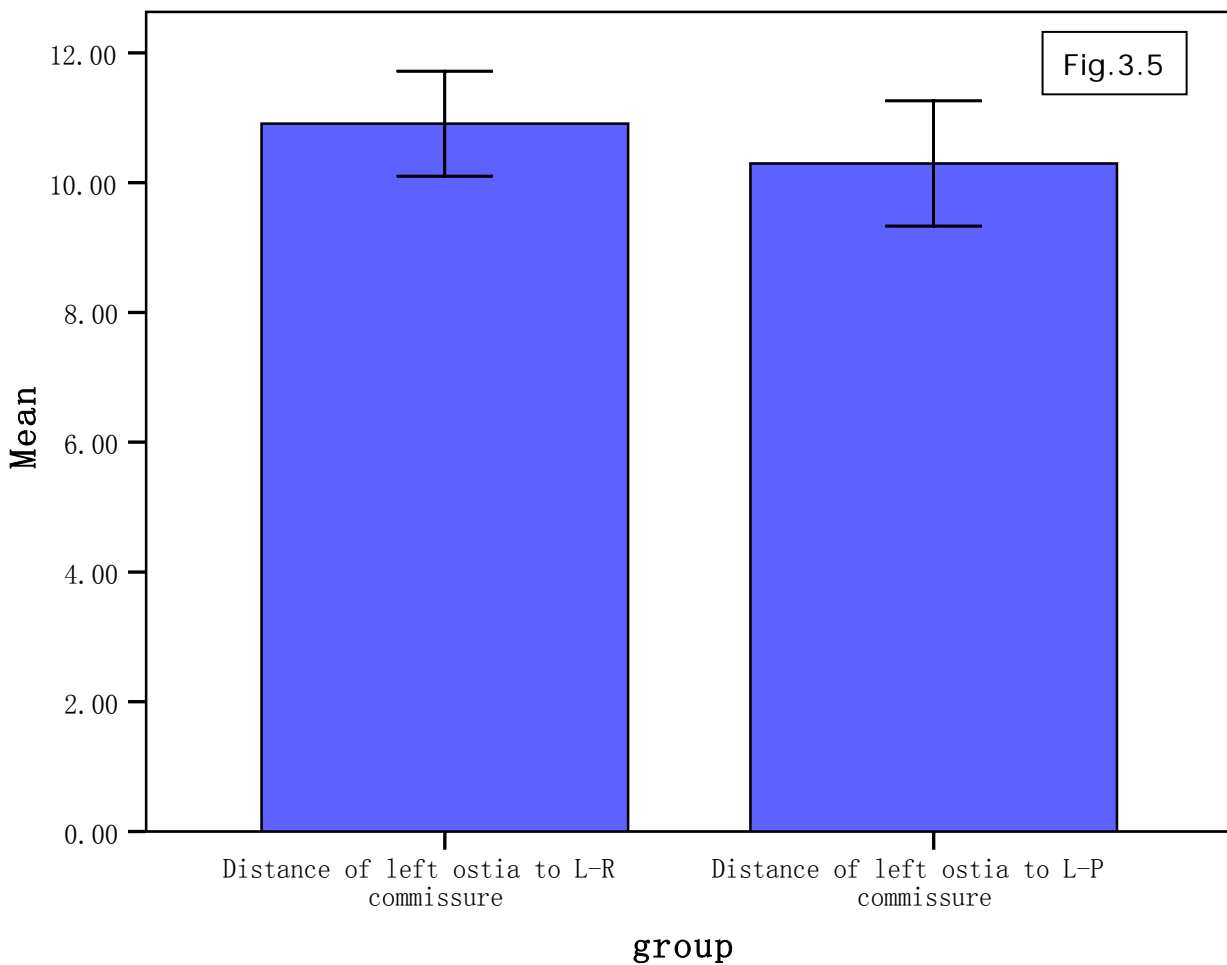
The mean distance from the left coronary ostia to the left –right inter-commissure and the left-posterior inter-commissure was  $10.97 \pm 2.49$  mm (range 5.30-17.0 mm) and  $10.25 \pm 2.95$  mm (range 4.50-18.20 mm). The mean distance from the right coronary ostia to the left–right inter-commissure and the right-posterior inter-commissure was  $13.43 \pm 4.13$  mm (range 5.50-22.70 mm) and  $10.85 \pm 4.79$  mm (range 4.70-30.30 mm). There was no difference between the distance from the left ostia to the commissure of the left-right and the left-posterior leaflet ( $P > 0.05$ ). However, there was a significant difference between the distance from the right ostia to the left-right and the right-posterior inter-commissures ( $P < 0.05$ ). It showed that the left coronary ostia were nearly equally (centrally) distributed in the region of the left aortic sinus, while the clustering of the right ostia were towards the right half of the sinus,

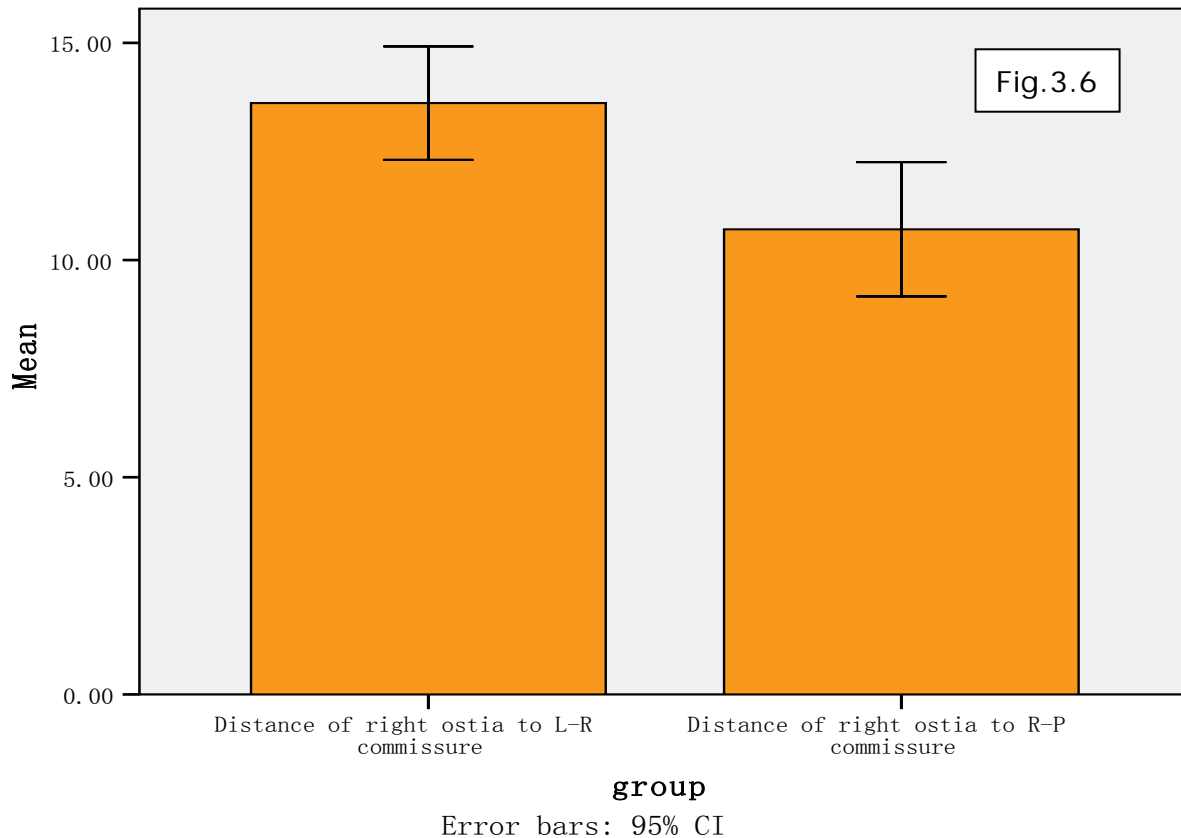


more close to the commissure of the right-posterior leaflet (Tab.3.1, Fig.3.5, 3.6).

**Tab.3.1: Mean values of the distance between the coronary ostia and commissure of the aortic leaflets (mm)**

Coronary ostia	Commissure	Mean distance	Mean point of the intercommissure distance
Left	left-right	10.97±2.49	10.60
	left-posterior	10.25±2.95	
Right	left-right	13.43±4.13	12.14
	right-posterior	10.85±4.79	





### 3.2.4. The length of the left, the right, and the posterior aortic leaflet

The mean length of left, right, and posterior aortic leaflet measured  $28.92 \pm 5.10$  mm (range 19.50-37.70 mm),  $31.22 \pm 6.02$  mm (range 21.20-48.00 mm), and  $30.88 \pm 5.06$  mm (range 23.00-40.50 mm), respectively. There was no significant difference between these groups ( $P > 0.05$ ).

### 3.2.5. The relative length of the left, the right, and the posterior aortic leaflet at the STJ level

The mean length of the left, the right, and the posterior aortic leaflet at the STJ level measured  $24.22 \pm 4.03$  mm (range 17.60-33.50 mm),  $25.75 \pm 3.85$  mm (range 19.70-36.00 mm), and  $25.69 \pm 3.75$  mm (range 18.70-40.20 mm), respectively. There was no significant difference between these groups ( $P > 0.05$ ). Based on the result from 3.2.4 and 3.2.5, it means that all

three aortic leaflets were nearly equally spaced around the aorta.

### **3.2.6. The height of the left, the right, and the posterior aortic sinus annulus to the related STJ level**

The mean height of the left, the right, and the posterior aortic sinus annulus to related STJ level (from the lowest point of aortic sinus annulus to STJ) measured were  $18.52 \pm 2.65$  mm (range 12.70-24.20 mm),  $18.87 \pm 2.55$  mm (range 13.30-23.70 mm),  $18.73 \pm 2.62$  mm (range 13.00-23.50 mm), respectively. There was no significant difference between these groups ( $P > 0.05$ ).

### **3.2.7. The height of the left, the right, and the posterior aortic leaflet**

The mean height of the left, the right, and the posterior aortic leaflet (from the bottom of the aortic valve to the free ridge of the cusp) measured  $16.11 \pm 2.04$  mm (range 10.70-19.80 mm),  $16.36 \pm 2.10$  mm (range 11.80-20.00 mm), and  $16.77 \pm 1.72$  mm (range 12.70-21.50 mm). The difference is insignificant between these groups ( $P > 0.05$ ).

### **3.2.8. The height of the left and the right aortic sinus annulus to its corresponding coronary ostia (to the superior margin of the ostia)**

The mean height of the left aortic sinus annulus to the left coronary artery ostia measured  $16.56 \pm 2.76$  mm (range 10.70-22.20 mm), and that of the right aortic sinus annulus to the right ostia was  $17.22 \pm 3.13$  mm (range 11.30-22.20 mm). There was no significant difference between these two groups ( $P > 0.05$ ).

### **3.2.9. The height of the left and the right coronary artery ostia (from the superior margin of the ostia) to its corresponding STJ level**

The mean height of left coronary artery ostia to the related STJ measured  $1.81 \pm 1.08$  mm (range -2.0-4.70 mm), and the right coronary ostia to STJ

was  $1.78 \pm 1.26$  mm (range -2.20-4.30 mm). There was no significant difference between these groups.

When both ostia lay in the sinus of valsalva (below the STJ level), the mean height of the left ostia to the STJ line measured  $1.85 \pm 0.64$  mm (range 0.5-3.60 mm), and the right coronary ostia to the STJ was  $2.17 \pm 0.94$  mm (range 0.7-4.30 mm). There was a significant difference between the two groups ( $p < 0.05$ ). It means that the right ostia are located at a lower position than the left coronary ostia in the sinus of valsalva.

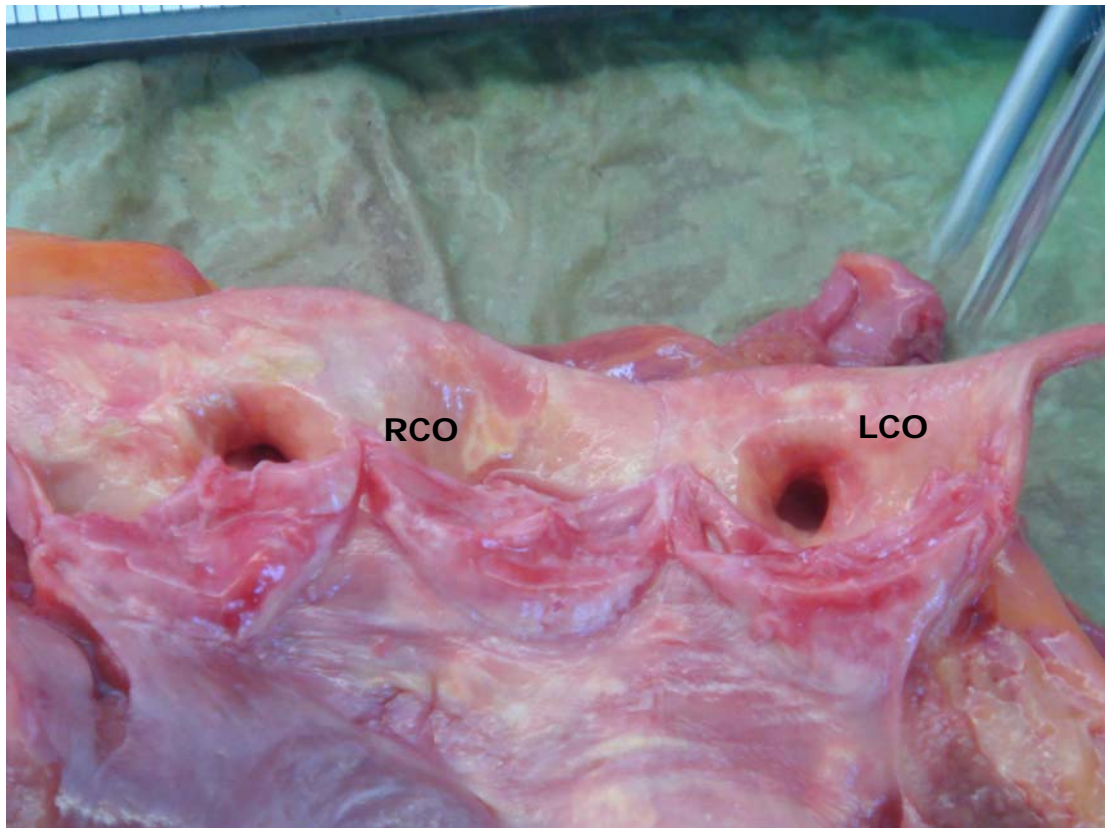
### **3.3. The location, the number, and the shape of the coronary ostia in relation to the STJ**

In our study, the malformation, location, number, and shape of the coronary orifices and the presence of accessory orifices were observed and recorded. The location of the left and the right coronary ostia were measured in relation to the STJ and described as being below, above, and at the level of the STJ. The cases and percentage of coronary ostia in relation to STJ line were listed in table 3.2.

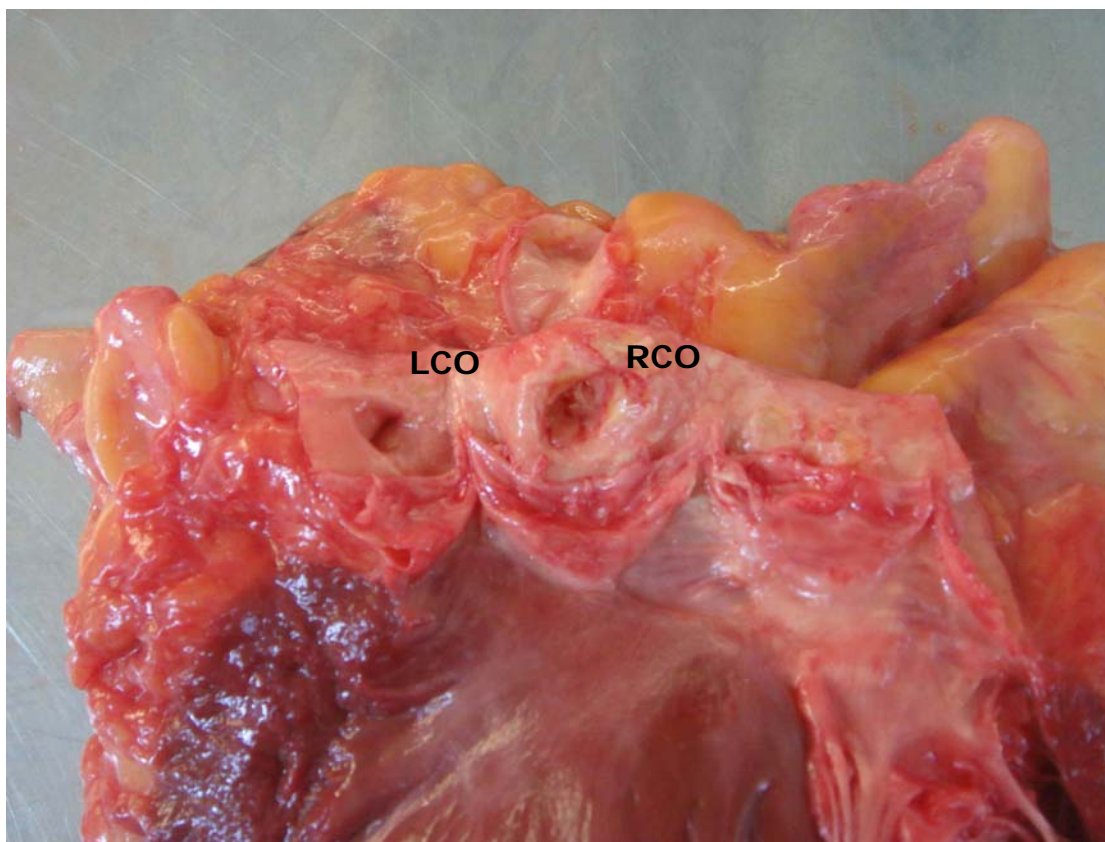
**Tab.3.2: Left and right coronary ostia below, above, or at the STJ level (n=40)**

Location of the coronary ostia with respect to the STJ level		
Coronary ostia	Cases	%
Both below	29	72.5
Both above	1	2.5
Both at level	0	0
Left above, Right below	2	5
Left above ,Right at level	1	2.5
Left below ,Right above	2	5
Left below ,Right at level	3	7.5
Left at level, Right below	2	5
Left at level ,Right above	0	0

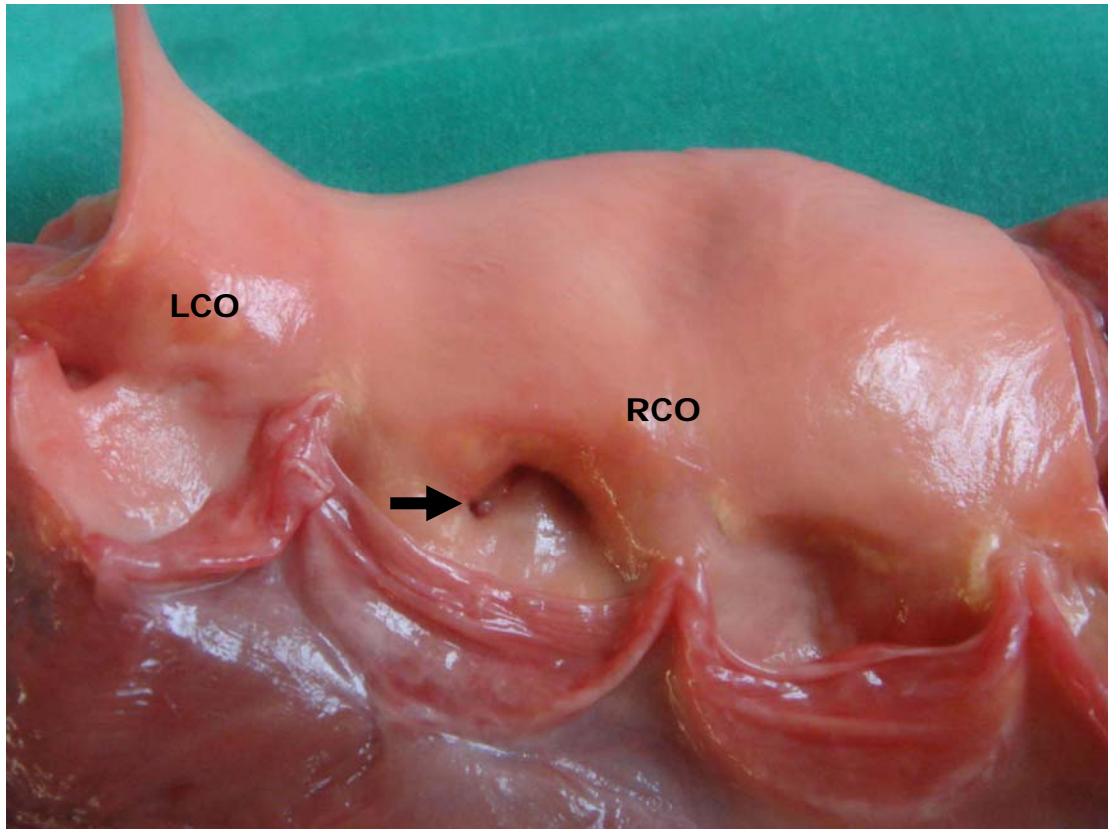
The shape of the coronary ostia was described as round, crescentic, and ellipsoidal. The orifice of the left coronary artery was round in 26 cases (65%), ellipsoidal in 10 cases (25%), and crescentic in 4 cases (10%). The orifice of the right coronary artery was round in 28 cases (70%), ellipsoidal in 9 cases (22.5%), and crescentic in 3 cases (7.5%). Within the right aortic sinus 15 cases (37.5%) had an accessory artery, and 4 cases (10%) had another smaller artery. No additional artery orifice was found in the left aortic sinus. No isolated nourishing artery of the right ventricular infundibulum (conus artery) was observed. The pictures of the position and shape of the coronary ostia were shown below (Fig.3.7; 3.8; 3.9; 3.10; 3.11,3.12).



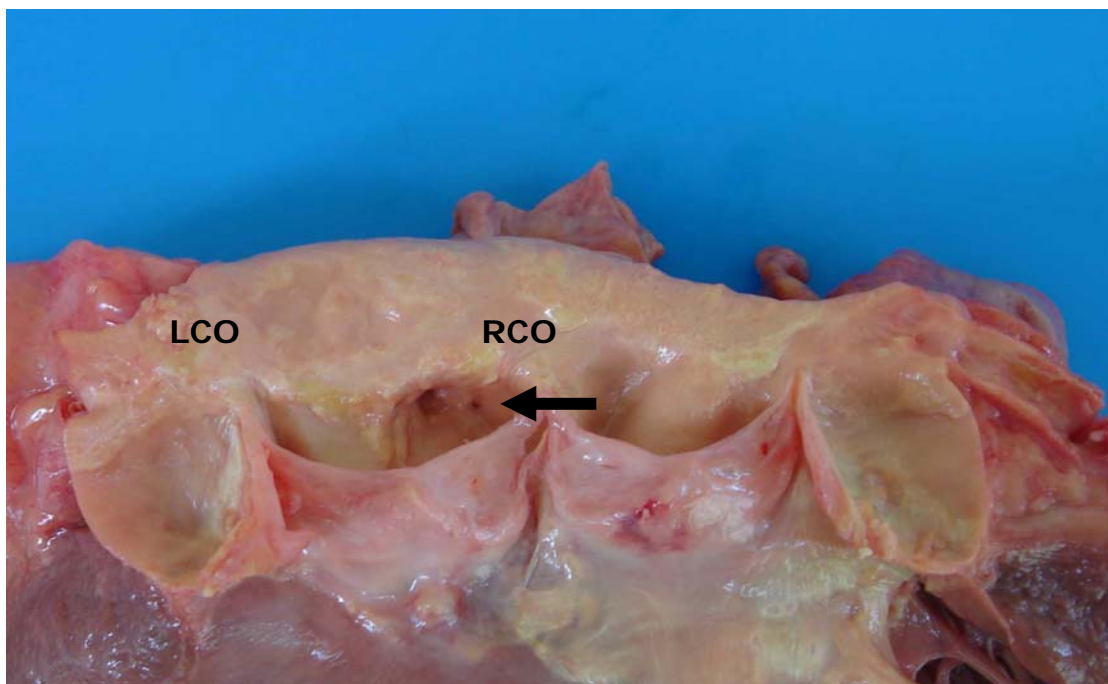
**Fig 3.7:** Both coronary ostia below the sinotubular junction, and the shape were circular.



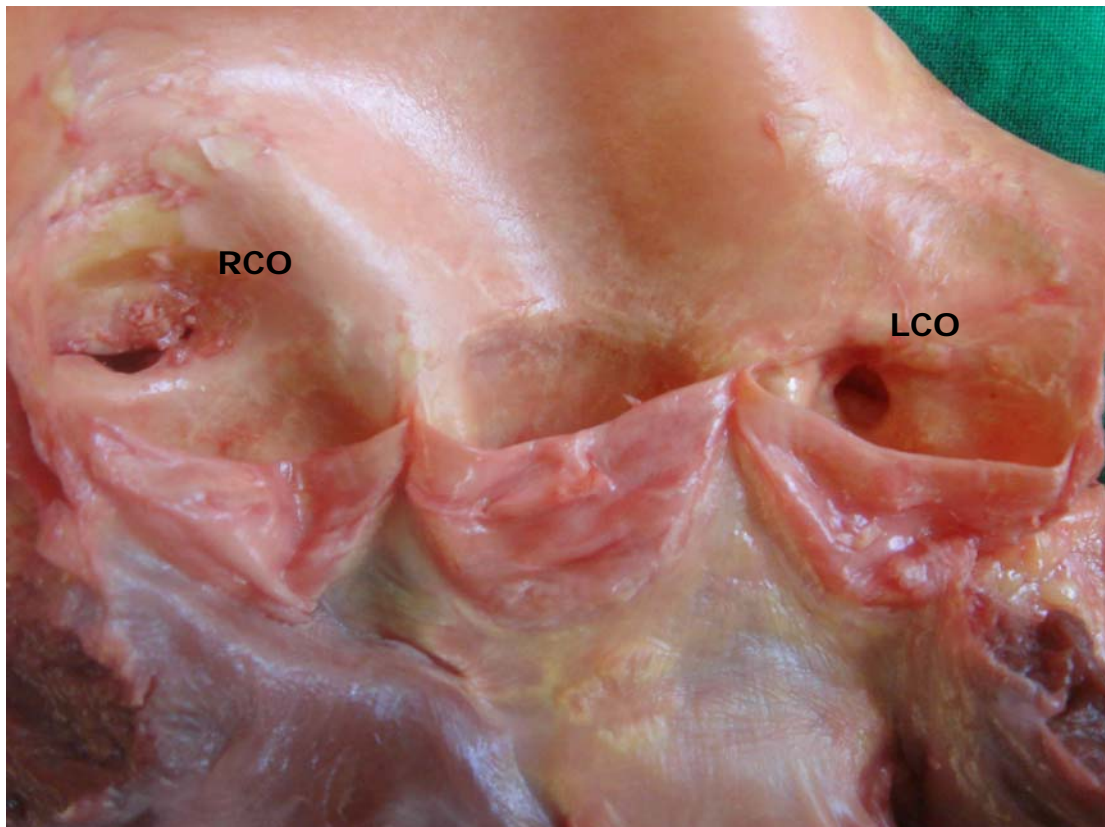
**Fig.3.8:** The left coronary ostium below STJ line, and the right ostium on the STJ line in ellipsoidal shape.



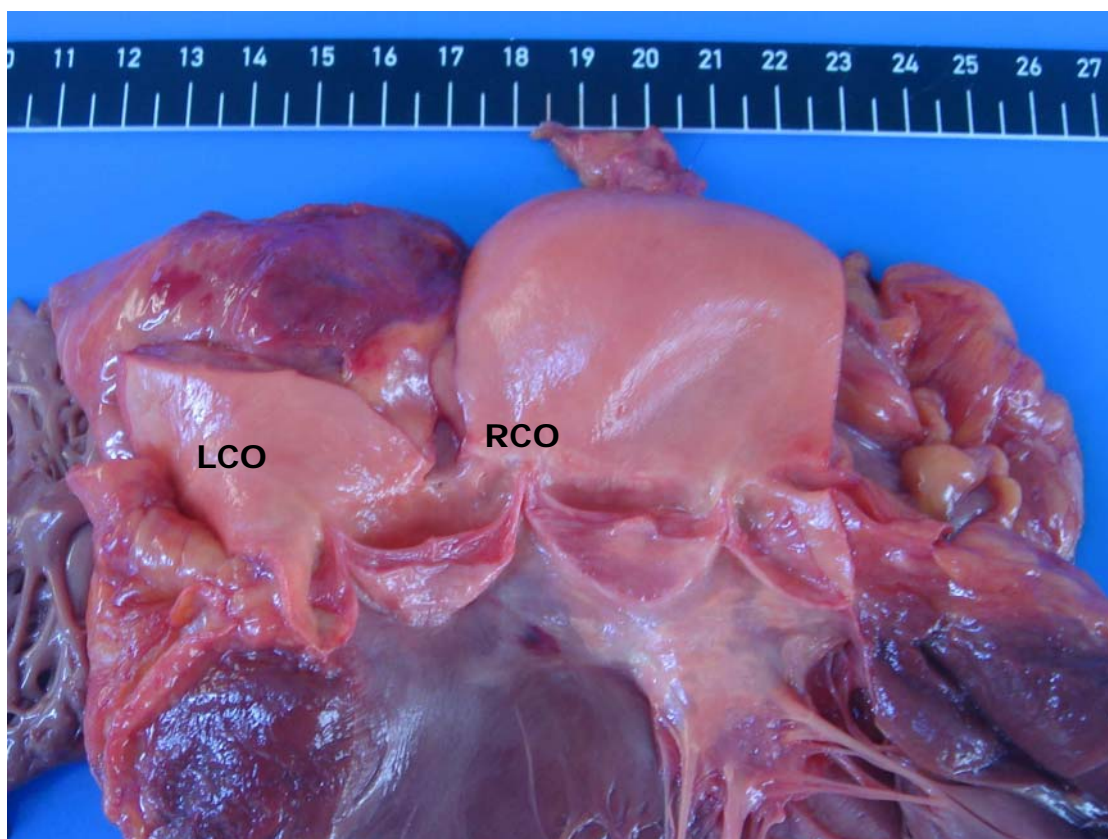
**Fig.3.9:** The left coronary ostium was located at the STJ line, and a crescentic right ostium was below the STJ line. We found an accessory artery (→) within the right aortic sinus, just next to right main artery orifice; the diameter was 0.8 mm.



**Fig.3.10:** The left coronary ostium was located above the STJ line, and the right ostium below the STJ line. An accessory artery (→) within the right aortic sinus, at the left side of right main artery orifice; the diameter was 0.5 mm.



**Fig 3.11:** The left coronary ostium was below the sinotubular junction, round shape. The right ostia above STJ line, crescentic shape.



**Fig 3.12:** The left and right coronary ostia were above the STJ line.



### 3.4. The difference between the height of the left and the right aortic leaflet and the height of its corresponding sinus annulus to the ostia

Both of the height value differences were positive in seven cases (17.5%, four male and three female). Both were negative in eighteen cases (45%, six male and twelve female). There were five cases (12.5%, two male and three female) with positive left value and negative right value. Meanwhile, ten cases (25%, six male and four female) had a right positive value and a left negative value.

Theoretically, if the height of the aortic leaflet is higher than that of the aortic annulus to its corresponding STJ, the difference of the height is positive. This phenomenon might result in covering the coronary ostium by the aortic leaflet. While the height difference is negative, the ostium might not be covered (Tab. 3.3).

**Tab.3.3: The cases and the percentage of the ostia were covered by the leaflet (n=40)**

	Cases	Male	Female
Both ostia covered	7	4 (10%)	3 (7.5%)
Left ostia covered, right not	5	3 (7.5%)	2 (5%)
Right ostia covered, left not	10	6 (15%)	4 (10%)
Both ostia not covered	18	6 (15%)	12 (30%)
Total	40	19 (47.5%)	21 (52.5%)

Totally there were eleven cases (see Tab.3.3), which the coronary ostia were located at or above the STJ. Only one of eleven cases (9.1%), the right coronary ostium was covered by the right leaflet. The other ten of eleven cases (90.9%); the coronary ostia were located at or above the STJ level

and were not covered.

The coronary ostia, which were located in the aortic sinus (below the STJ line), the following ostia were covered: 17 of 29 cases (65.5%) of the right ostia, and 12 of 29 cases (41.3%) of the left ostia.

In our study there was no difference between male (19, 45%) and female (21, 55%). Interestingly, that in the group of one or both ostia was covered by the aortic leaflet, male had 13 (13/19, 68%) cases, while female in 7 (7/21, 33.3%) cases. It had significant difference ( $P < 0.05$ ).

We analyzed the correlation between the height difference (height of each aortic leaflet and height of the aortic sinus annulus to the corresponding superior margin of the ostia) and other factors which we have measured. The statistic results of correlation were shown in table 3.4 and 3.5. Correlation was significant at the 0.05 level (2-tailed).

**Tab.3.4: The correlation of the difference of the height of the left cusp to the height of the left annulus to ostia with other parameters**

Variable	Difference of height of left cusp-height of left annulus to ostia	
	Pearson Correlation	Sig. (2-tailed)
Age	-.273	.089
Height	.147	.365
Body weigh	.092	.571
Body mass index	.144	.377
Heart weight	-.264	.100
Diameter of STJ	.033	.838
Diameter of annulus	.187	.248
Diameter of left ostia	-.238	.139
Distance difference of left ostia to commissure	.347*	.028
Length of left cusp	-.002	.992
Circumference of STJ	.196	.542000
Height of left annulus to ostia	-.701**	.000
Height of left ostia to STJ	.587**	.000
Height of left cusp	.165	.309
Height of left annulus to STJ	-.644**	.000

\*: Correlation is significant at the 0.05 level (2-tailed).

\*\* : Correlation is significant at the 0.01 level (2-tailed).

**Tab.3.5: The correlation of the difference of the height of the right cusp to the height of the right annulus to ostia with other parameters**

Variable	Difference of the height of the right cusp- the height of the right annulus to ostia	
	Pearson Correlation	Sig. (2-tailed)
Age	-.001	.996
Height	.036	.826
Body weigh	.216	.181
Body mass index	.303	.057
Heart weight	-.186	.250
Diameter of STJ	.036	.824
Diameter of annulus	.064	.697
Diameter of right ostia	-.160	.324
Distance difference of rightostia to commissure	-.264	.099
Length of right cusp	-.310	.052
Circumference of STJ	.086	.770
Height of right annulus to ostia	-.650**	.000
	.584**	.000
Height of right ostia to STJ	.112	.493
Height of right cusp	-.514**	.001
Height of right annulus to STJ		

\*: Correlation is significant at the 0.05 level (2-tailed).

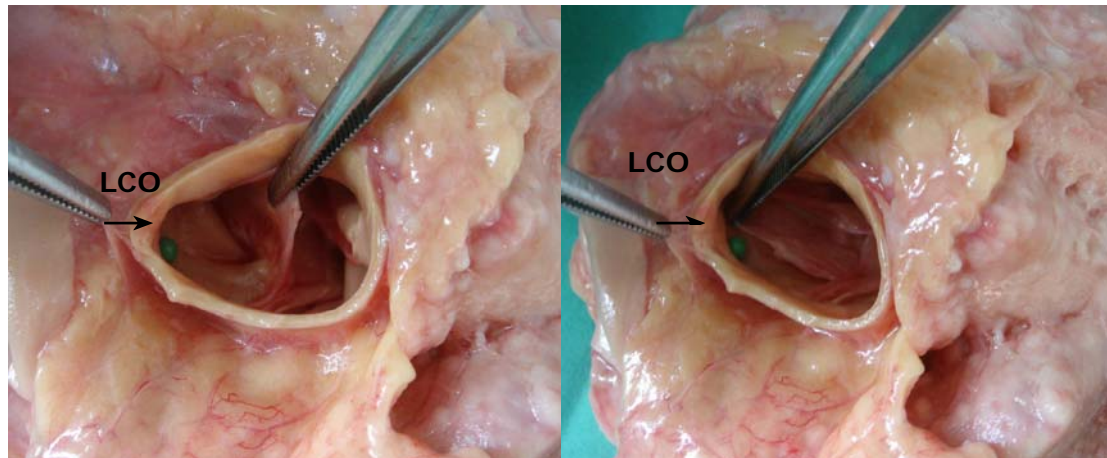
\*\* : Correlation is significant at the 0.01 level (2-tailed).

### **3.5. The findings of the relation among the aortic leaflet, the coronary ostia, and the valve stent before and after valved stent implantation**

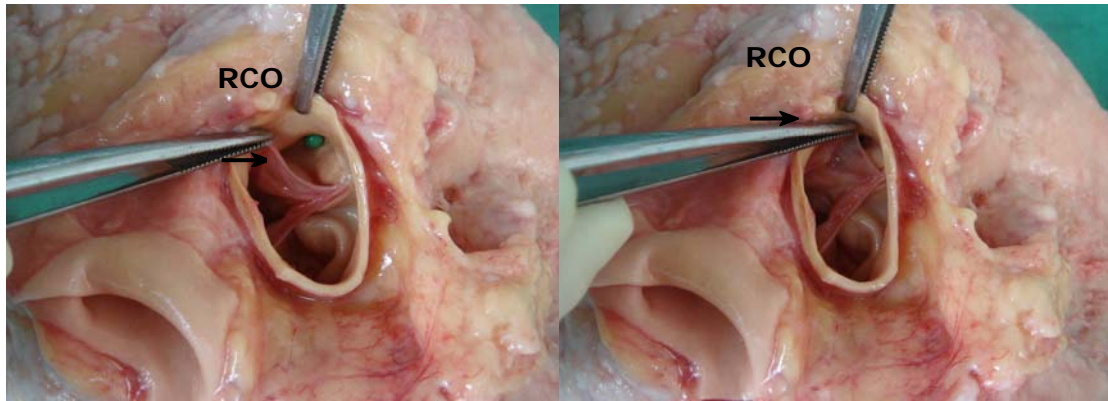
In our study, three steps were undertaken to illustrate the relation of the coronary ostia, the aortic leaflets, and the valve stent. First, the relation between coronary ostia and leaflets were measured before the stent was implanted. Second, we observed the relation among the coronary ostia, leaflets, and stents after the stent implantation in the aortic annulus position. Finally, when the aorta was opened, we inspected if the aortic leaflets would or would not cover the coronary ostia. The results were categorized described and as: both ostia were covered (Fig.3.13); right covered, left not (Fig.3.14); and left covered, right not (Fig.3.15).

#### **3.5.1. Both coronary ostia were covered (Fig.3.13)**

3.5.1(1): Before the stent implantation

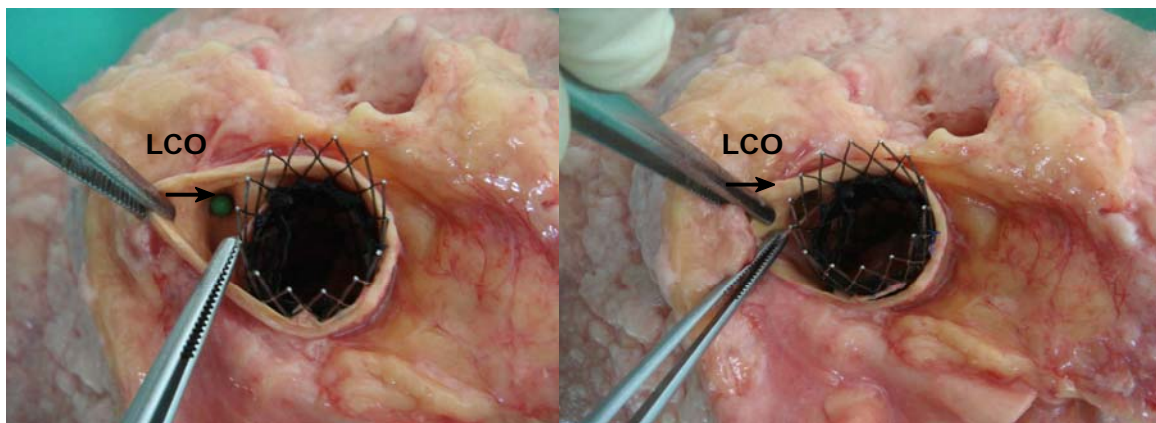


**Fig.3.13 (a):** The left coronary ostium was covered by the left aortic leaflet.

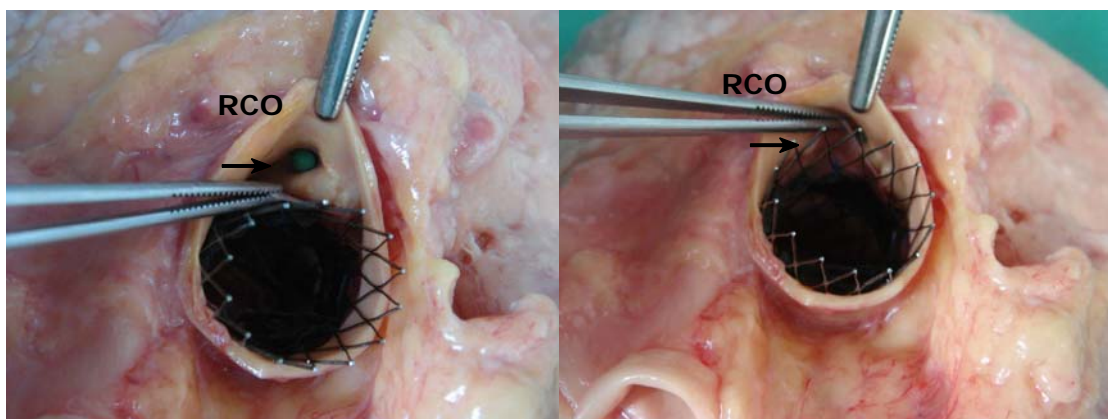


**Fig. 3.13(b):** The right coronary ostium was covered by the right aortic leaflet.

### 3.5.1 (2): After the stent implantation

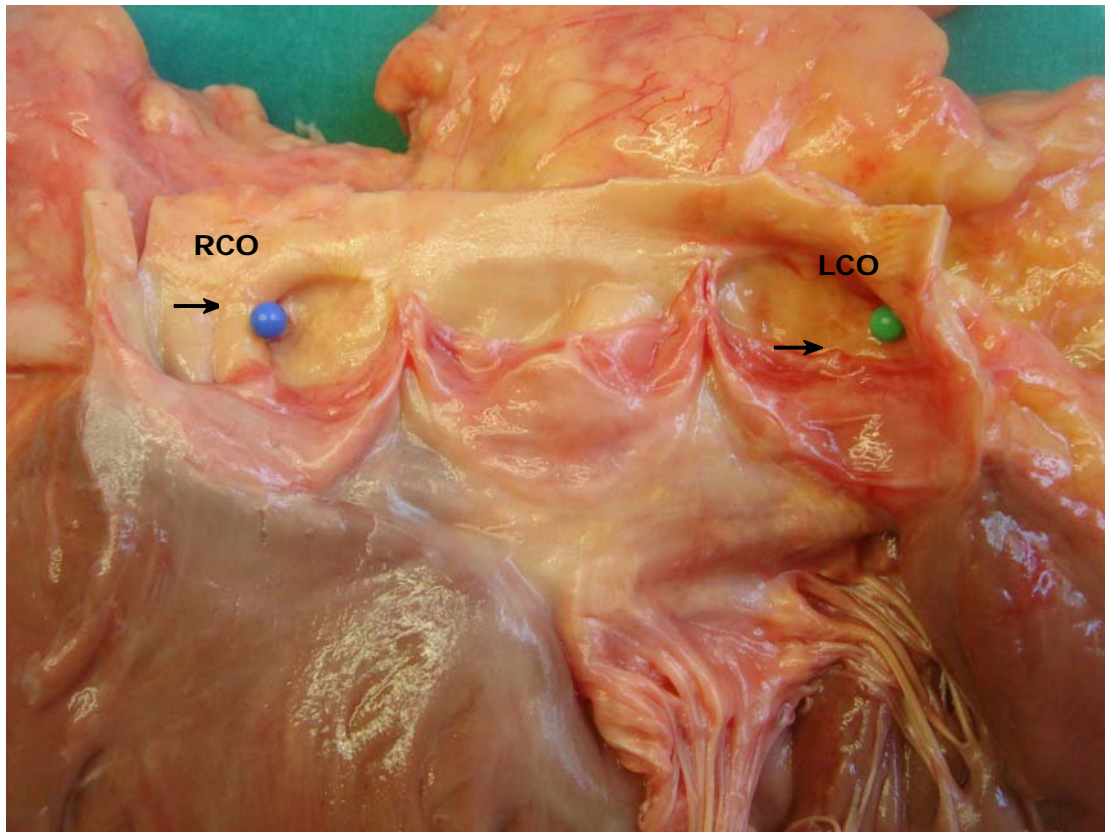


**Fig.3.13(c):** The left coronary ostium was covered by the aortic leaflet after stent implantation.

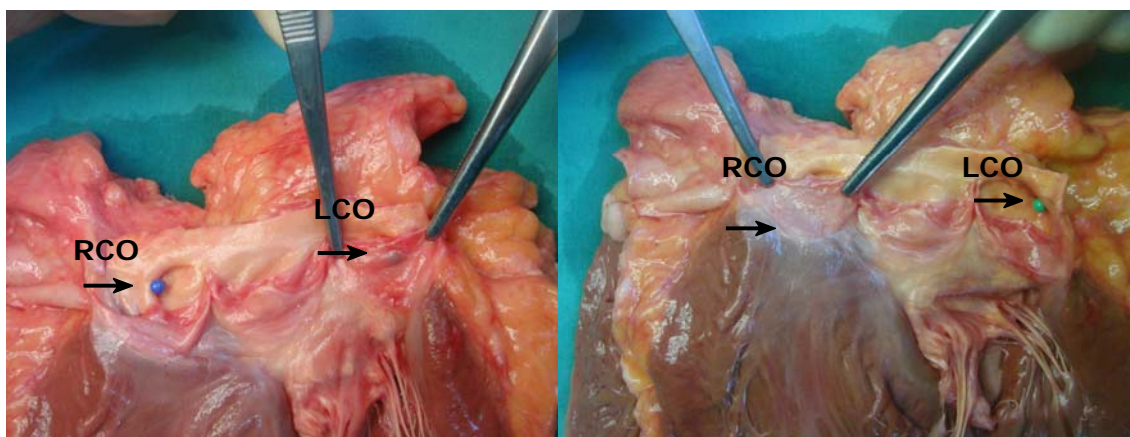


**Fig. 3.13(d):** The right coronary ostium was covered by the leaflet after stent implantation.

**3.5.1(3): After the aorta was opened.**



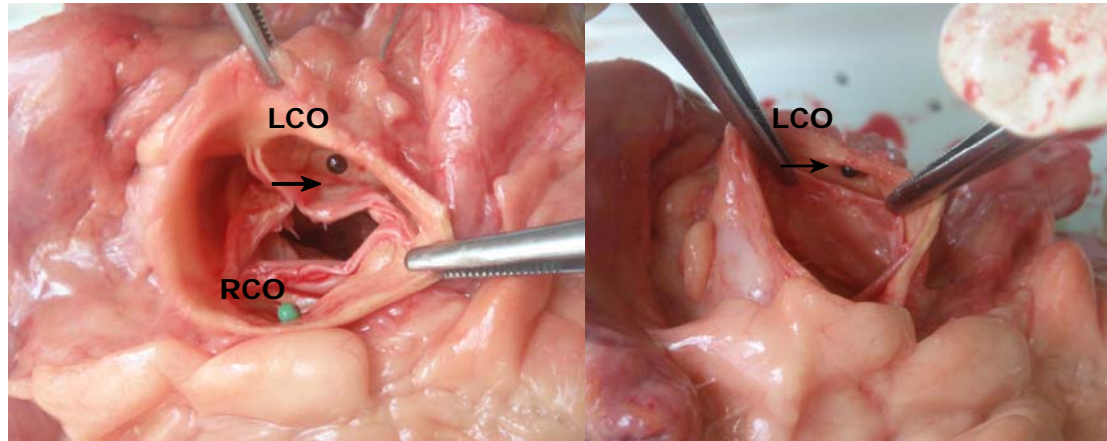
**Fig. 3.13(e):** The aorta was opened by a longitudinal incision through its anterior wall between the commissure of the left and right aortic leaflet. The green needle is in the left ostium, and the blue one in the right ostium.



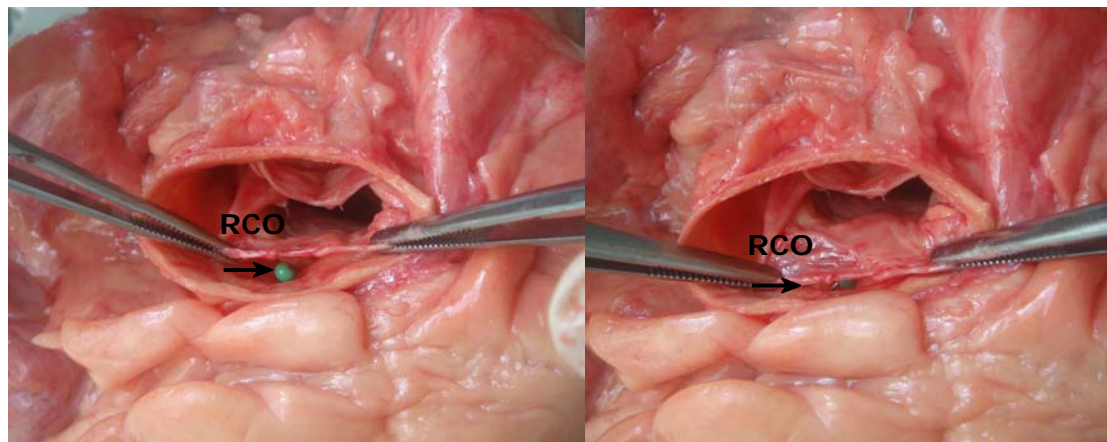
**Fig.3.13 (f, g):** The left and the right ostia were covered by the aortic leaflets when it was tightened by a forceps.

### 3.5.2. Right ostia covered, left not (Fig.3.14)

3.5.2(1): Before the stent implantation



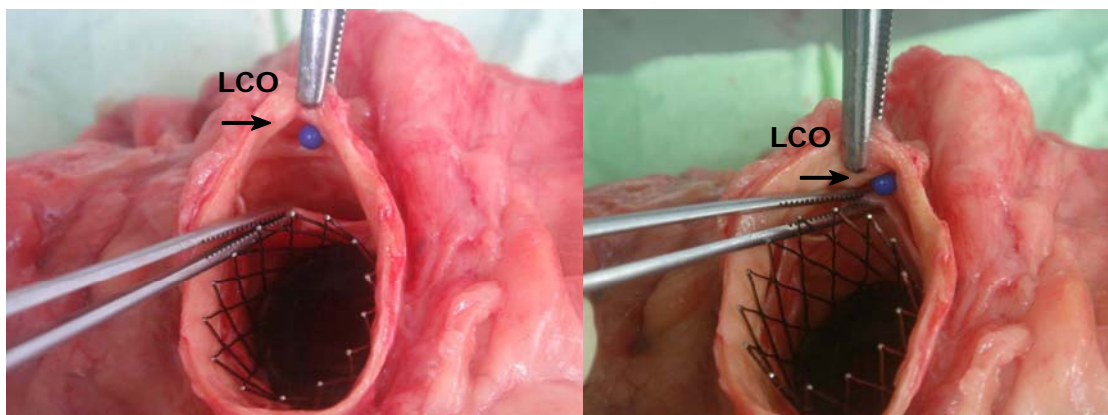
**Fig.3.14 (a):** The left coronary ostia were not covered by the aortic leaflet.



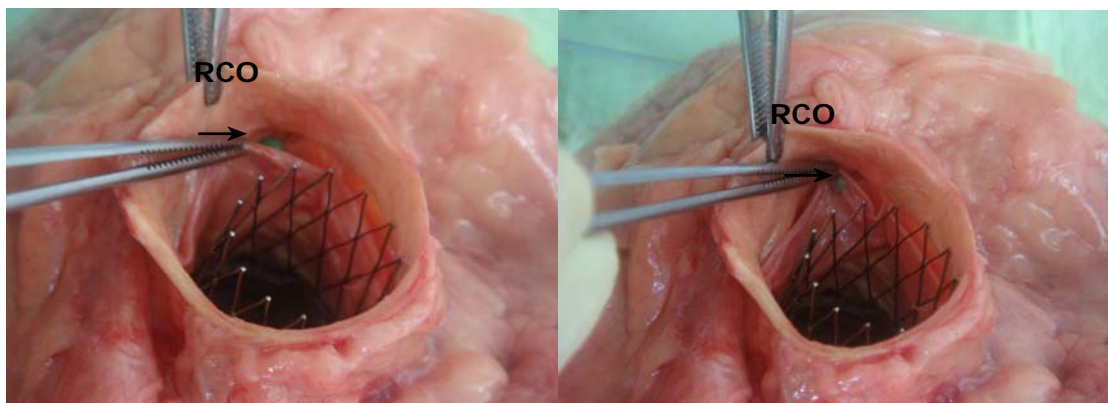
**Fig.3.14 (b):** The right coronary ostia were covered by the right aortic leaflet.



3.5.2(2): After the stent implantation

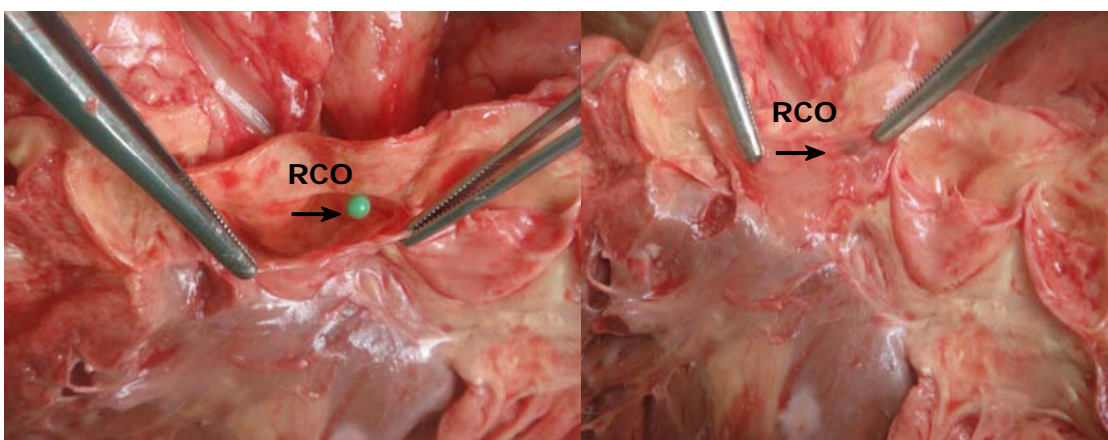


**Fig.3.14(c):** The left coronary ostia were not covered by the aortic leaflet after stent implantation.



**Fig.3.14 (d):** The right coronary ostia were covered by the aortic leaflet after stent implantation.

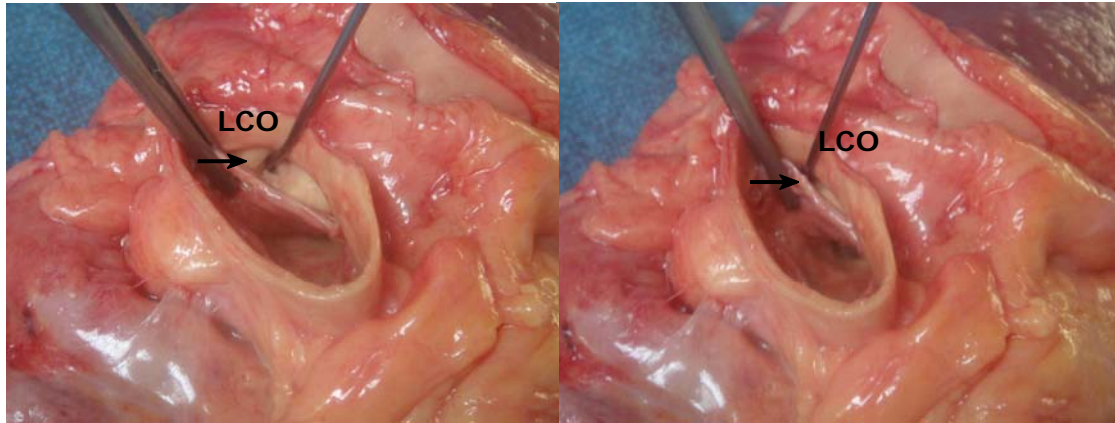
3.5.2(3): After the aorta was opened.



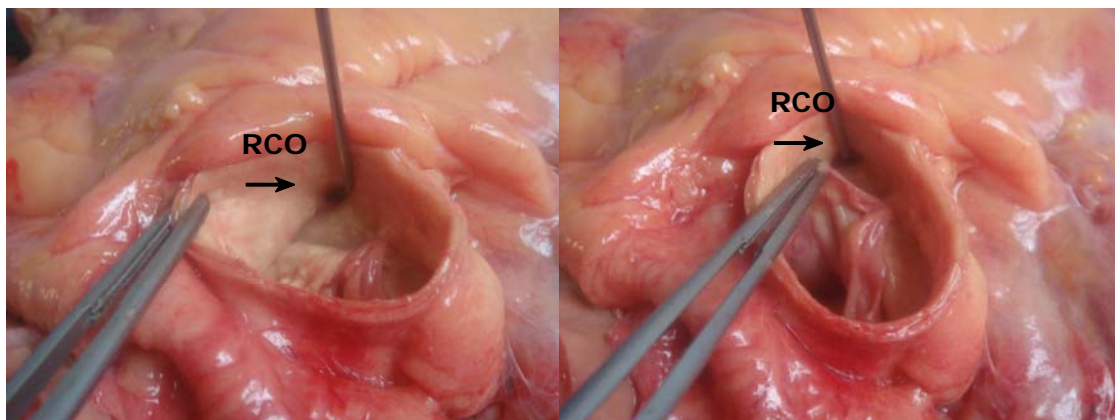
**Fig.3.14 (e, f):** The right ostia (with green needle marked) were covered by the aortic leaflets when it was tightened by a forceps. But the left ostia can't be presented because of the broken of left leaflet.

### 3.5.3. Left ostia covered, right not (Fig.3.15)

3.5.3(1): Before the stent implantation



**Fig.3.15 (a):** The left coronary ostia were covered by the aortic leaflet.



**Fig.3.15 (b):** The right coronary ostia were not covered by the aortic leaflet.

3.5.3(2): After the stent implantation

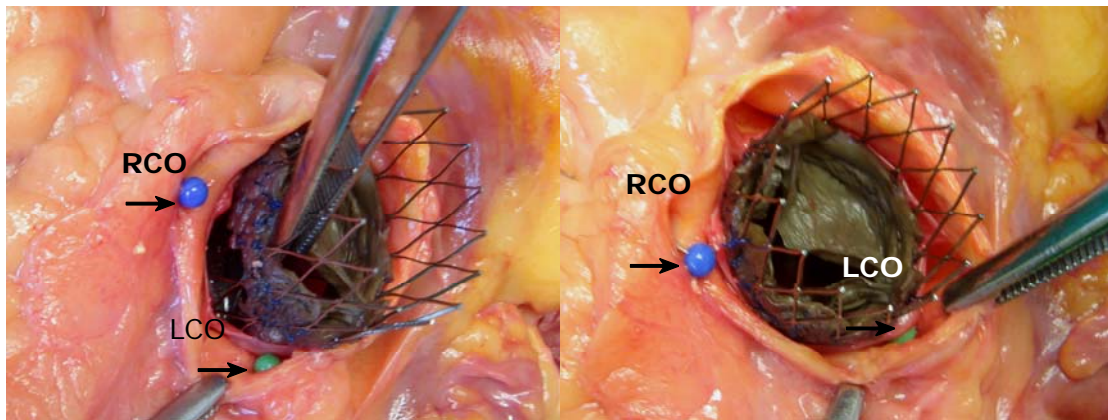
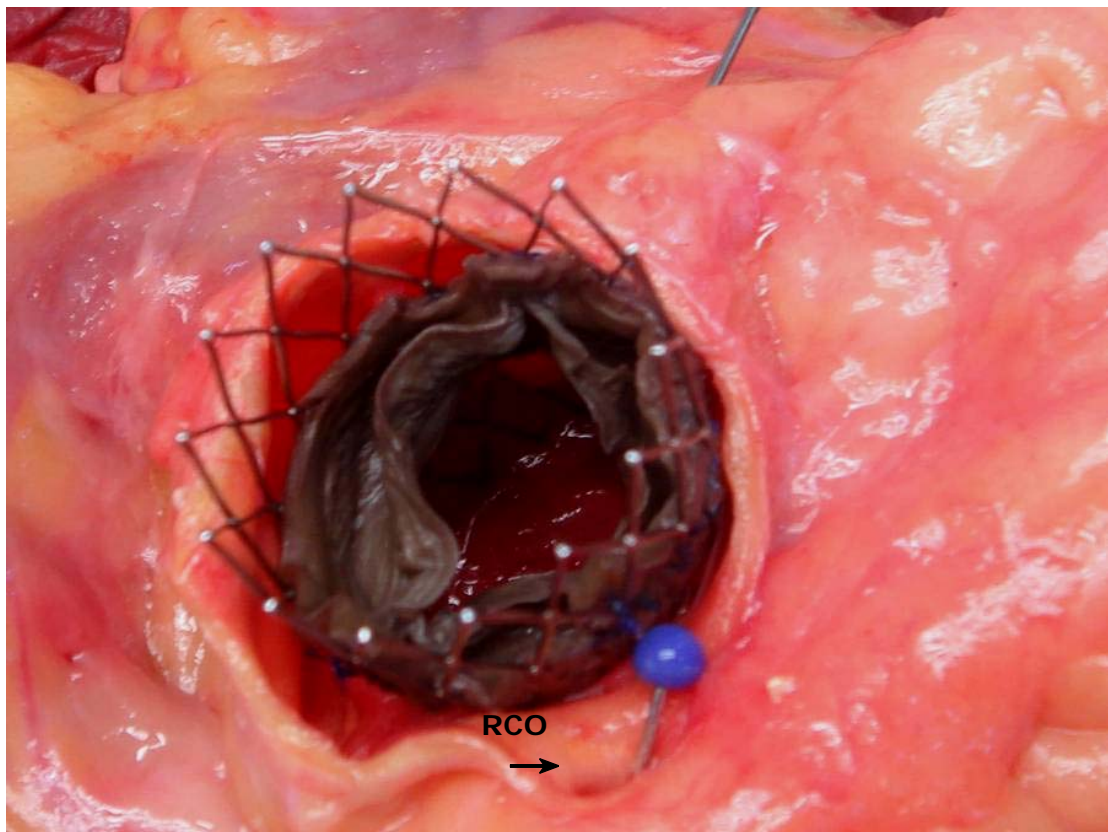


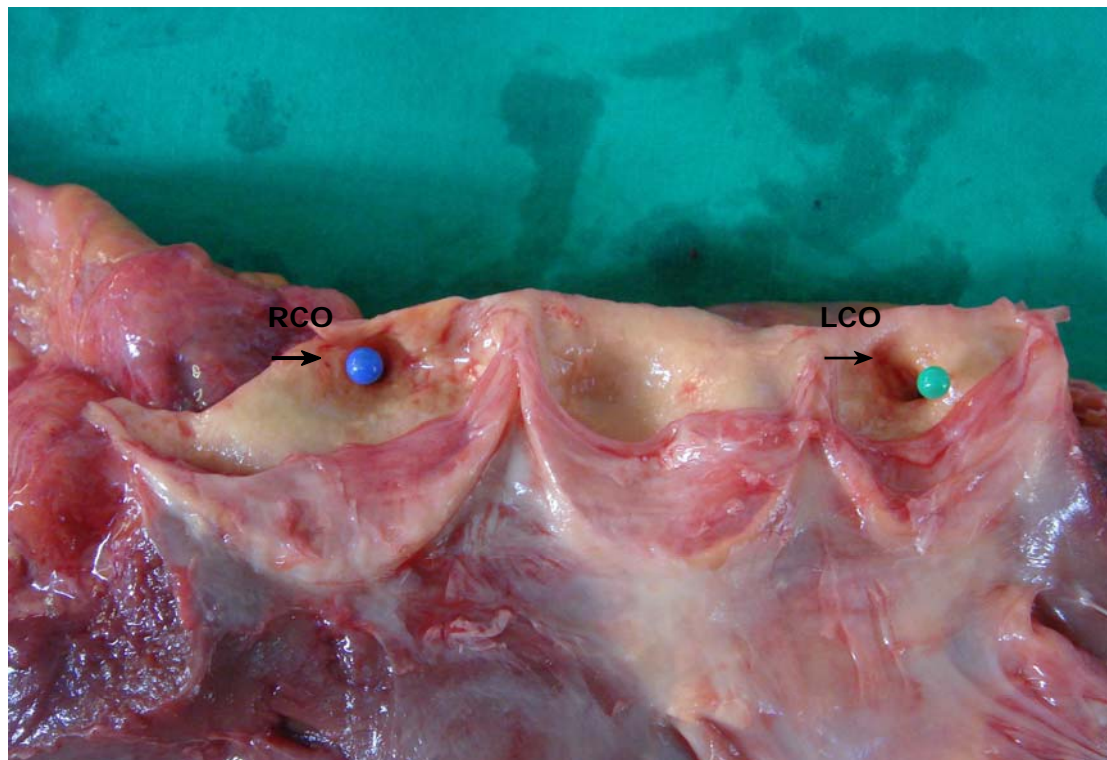
Fig.3.15 (c)

Fig.3.15 (d)

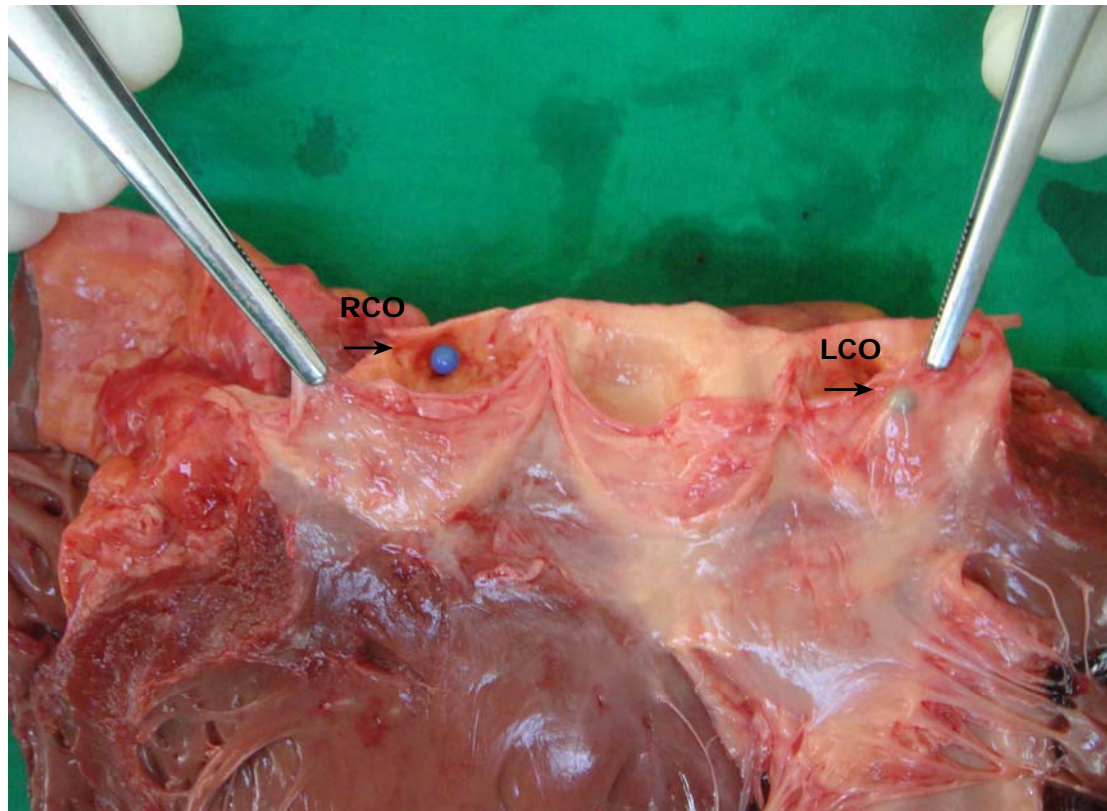


**Fig.3.15 (c, d, e):** The figures illustrated the covered left coronary ostia (green marker), which were by the aortic leaflet after stent implantation, while the right ostia (blue needle marker) were not covered.

3.5.3(3): After the aorta was opened



**Fig.3.15 (f):** The aorta was opened between the left and right aortic leaflet commissure. The green needle is in the left ostium, and the blue one in the right ostium.



**Fig.3.15(g):** The left coronary ostium was covered by the aortic leaflet when it was tightened by a forceps, while the right ostium was not covered.

## 4. DISCUSSION

In elderly patients with declining overall health status or life-threatening co-morbidities, aortic valve replacement is considered either too risky or contraindicate, because of the significant risk of morbidity and mortality [5, 6, 7]. Furthermore, symptomatic patients with severe aortic stenosis managed medically have a poor prognosis [58, 59]. As an alternative, the percutaneous balloon aortic valvuloplasty is palliative and with a certain restenosis [60, 61], although it may result in temporary improvement of valvular function and relief of symptoms.

Given the limited therapeutic options in this subset of patients, there were remarkable developments of percutaneous aortic valve implantation by a retrograde or antegrade approach [24, 25, 30]. However, the technical complexity and risks such as impairment of coronary blood flow and paravalvular leakage, associated with percutaneous and transapical aortic valve replacement appear significantly limit its widespread application [8, 9, 30].

Coronary flow impairment (restriction), as a major issue encountered in PAVR, might be caused by the obstruction of coronary ostia by the native leaflets, which was firstly reported by Andersen in 1992. Late on, many investigators [9, 26, 35] took numerous efforts to study this problem in experimental animal model, however, different conclusion were drawn from these studies. Currently, Flecher et al [46] reported their study results *in vitro*, showed that the deployment of a cylindrical, stented aortic valve can severely affect coronary flow by obstructing the coronary ostia with the native leaflets. During orthotopic PAVI, obstruction of coronary ostia with coronary flow restriction can occur either by direct blocking from the implanted stent, or from the native aortic leaflets immobilized against the coronary orifices [8, 9, 26, 27, 31, 38]. Based on this, we observed and investigated the anatomy of aortic root structures, to elucidate the relation

of aortic root structures and valved stent, and the influence of valved stents on these anatomic structures by post mortem aortic valve stent implantation.

#### **4.1. The anatomy of the aortic root structures**

Our study, which comprised a series of 40 heart specimens, confirms that the three semi-lunar aortic leaflets of all hearts were nearly equally spaced around the aorta, corresponding valsalva sinuses (left, right, and posterior, respectively), and three intervening commissures. And the aorta had two main coronary ostia which arose from the appropriated aortic sinus [47, 49, 50]. Most of the ostia were round shape. The accessory coronary arteries were found in right aortic sinus only. No variation of coronary ostia was found in our case series, which differs from the study of Jatene MB et al [62], in which they reported 1-2% of hearts had both 2 ostia originated from left aortic sinus.

Muriago et al [50] indicated that the coronary orifices are not located in the center of each aortic sinus. On the contrary, both coronary orifices are displaced to the commissure located to the right of the ostia, and close to the level of the free edge of the aortic leaflets. However, in our series, on average, the left coronary ostia cluster near to, albeit not precisely at, the central region of the left sinus curvature; while the right coronary ostia tend to locate a little further laterally, in the right side of the sinus, more close to left-posterior inter-commissure. Our results are in accordance with the studies reported by Cavalcanti et al [40] and Turner and Navaratnam [49].

Regarding the position of the coronary ostia in relation to the STJ, 29 of 40 analyzed hearts (72.5%) had both ostia located in the aortic sinus, and 11 of 40 hearts (27.5%) had one or both ostia above or at the STJ level. Of the 80 ostia, 67/80 ostia (83.7%) were located below the STJ level, only 6/80 ostia

(7.5%) were at its level, and 7/80 ostia (8.8%) above it. These results are similar to the study by Muriago et al [50], in which they reported 3 of 23 hearts (13%), the ostia at or above that level. On the other hand, our results differ from those of Cavalcanti et al [40], which indicated that 34 of 50 studied hearts (68%) had one or both ostia above or at the STJ level, while both ostia were located below the level only in 32% of cases. Moreover, our study also differs from the study by Waller et al [63], who had noted up to three-tenths of coronary orifices arising above the STJ.

Regarding the left and right coronary ostia, our results are significantly different from those by Cavalcanti et al [40], who reported a left coronary ostia were below the STJ in 42%, at or above that level in 58% (18% at level, 40% above level), while the right coronary ostia were below the STJ in 60%, at or above that level in 40% (12% at level, 28% above level) in their studies, respectively. In our case series, the left ostia located were below the STJ in 85% (34/40), at or above the level in 15% (15/40, 5% at level and 10% above the level), while the right coronary ostia were below the level in 82.5% (33/40), at or above the level in 17.5% (7/40, 7.5% at level and 10% above the level), which is similar to the results studied by Muriago et al [50].

In our study, when the coronary ostia were located in the corresponding aortic sinus, most of the left ostia had typical vertical and circumferential positions in relation to the aortic leaflets, sinus and STJ. On the other hand, the right ostia were located more eccentrically at a lower position in its aortic sinus regarding to the left ostia, which almost centrally distributed in a higher position of the aortic sinus. From the functional point of view, Turner [49] described the phenomena as the typical vertical and centrally positioning of the ostia, particularly when both coronary ostia were lying above the STJ level. This might confer functional advantages for coronary

flow during ventricular systole and also prevent the obstruction of the ostia, when the aortic valve was opened.

#### **4.2. The findings of post mortem aortic valved stent implantation into the aortic position**

When the valved stents were properly implanted into the post mortem aortic annulus, we found the native aortic leaflets were obviously folded upwards, pushed and immobilized by the valved stents against the aortic wall. The space of aortic valsalva sinus was narrowed. Most of the coronary ostia were partially or fully covered by its native leaflets. Most of the aortic leaflets and annulus were without severe calcification and stenosis - therefore paravalvular leakages were rarely found.

In 22 of 40 cases (55%) of our post mortem study, one or both coronary ostia were covered by the aortic leaflets after stents implantation (both covered in 7 cases, left in 5 cases, and right in 10 cases). Among them, 21 of 29 cases (72.4%), if both coronary ostia were located below the STJ, the ostia were fully covered by the aortic leaflets. The right ostia were located at the STJ level in 1 of 11 cases (9.1%) and were covered. The remaining 10 cases with one or both ostia located at or above the STJ level did not show any ostia covered. Regarding to the respective ostia, 28 of 67 ostia (41.8%) below the STJ were covered, whereas only 1 of 13 ostia (7.7%) located at or above the STJ level, was covered. That means if the coronary ostia lay below the STJ or in the aortic sinus, there was a higher frequency to be covered by their leaflets if the ostia were located at or above the STJ level. According to our observation, the height of each leaflet and that of the corresponding annulus to the STJ were nearly equal. The different distribution of the ostia in relation to its STJ may result in such contradistinctive outcome.



In total, 28 of 67 ostia (41.8%) were located below the STJ and were fully covered. Connecting the individual ostia, 12 of 34 left ostia (35%) were covered, and 16 of 33 right ostia (48.5%) were covered by its corresponding aortic leaflets. Although there was no significant statistic difference between them, we found that the right coronary ostia were more easily covered by the leaflets. Based on our observation and investigation after the aortas were opened, we considered that the eccentrically distribution of right ostia in aortic sinus and the location in a lower position of the sinus compared to the left ostia might be the possible explanation.

After stent implantation into the aortic annulus, the aortic leaflets were folded upwards and immobilized against the aorta wall, similar to the aortic leaflet position during the measurement after the aorta was opened. According to our observation and measurement of the aortic root structures, the results after implantation demonstrated the relation between the valved stent and the aortic root structures.

Theoretically, the ostium would be covered by its corresponding leaflet if the height of the leaflet is greater than the height of the aortic annulus to the ostium, otherwise the ostium would not be covered. Here, we found the positive correlation among the height difference, the height of leaflets, and distance from the annulus to the ostium. Furthermore, our data suggest the negative correlation between the height difference and the distance of the coronary ostia to the STJ level. It might explain that the ostia which were located below the STJ level had a higher frequency to be covered by its leaflets. This might also support our finding if the ostia were located below the STJ, the right ostia were covered more often than the left one.

To avoid the impairment of coronary flow in the clinical situation, we assess the risk caused by ostia coverage through measuring the aortic root structure by echocardiography [64], CT scan or MRIA techniques before the

orthotopic PAVR or PAVI. Recently, Quaden et al [27] reported the feasibility of endovascular resection of human calcified aortic valves by using a high-pressure water stream scalpel and a thulium:YAG laser. And they firstly performed the endovascular resection of human aortic valves in situ through an Aortic Valve Isolation Chamber (AVIC) system [37], although the capture of debris is required to prevent embolism.

So, to perform a reliable PAVR, resection of the diseased native leaflets before implantation is necessary and feasible. However, resection of none diseased valves is also necessary sometimes because implanting a new style stent to these valves might cover the ostia by crimping the leaflets after implantation of the stent.

### **4.3. Limitations**

In the present study of 40 post mortem hearts, most of the aortic leaflets and annulus tissue were normal or with mild calcification. However, in clinical application of percutaneous aortic valved stent implantation, the candidates have severe aortic stenosis mainly caused by sclerosis and mild to moderate calcification. It is necessary to perform a further study on these cases, which are missing in our study for the reason that a main part of these patients will already be operated on their aortic valve stenosis.

In our study, *in vitro* post mortem aortic valved stent implantation has been performed. It will be more physiological related, if we could study in a dynamic and physiological environment *in vivo*. Regarding this aspect, the implantation in post mortem human anatomy is an essential science.

Performing a study by using a different style of valved stents will be further required. Then, we can compare the options of newly designed valved stents

and resection of the native leaflets before implantation.

It is necessary to find a more feasible imaging method to represent and demonstrate the aortic root structures, the valved stents and their relationship. The difficulty of representation of the relation between the coronary ostia, aortic leaflets, and valved stents were encountered in our study.

#### **4.4. Conclusion**

In conclusion, the current study demonstrated that most of the coronary ostia were located below the STJ level, only very few coronary ostia were at or above the same. The left coronary ostia cluster centrally, and near to the central region of the sinus curvature; while the right coronary ostia tend to locate eccentrically, a lower position, and in the right side of the sinus. Most of the coronary ostia, which were located below the STJ, were covered by its corresponding aortic leaflets; while the ostia were rarely covered by the aortic leaflets when they lay at or above the STJ. The right coronary ostia have a greater frequency to be covered by their aortic leaflets than left ones. The native aortic leaflet is the main cause of obstruction of coronary ostia in post mortem orthotopic aortic valved stent implantation. To perform an orthotopic PAVR, resection of the native leaflets before the implantation might be necessary and new stents have to be designed to prevent coverage of the coronary ostia by crimping the leaflets.

## 5. Summary

**Background:** Previous studies have suggested that the close proximity of the coronary orifice to the aortic valve leaflets made percutaneous and transapical aortic valve implantation a major challenge such as coronary flow impairment. In this study, the aortic root structures were observed and measured in human cadavers.

**Material and Methods:** We assessed the diameter of the distal ascending aorta, the proximal ascending aorta, the STJ, the aortic annulus, the coronary ostia, and the distance of the annulus to the coronary ostia, the coronary ostia to the STJ level, each ostium to its bilateral commissure of the aortic leaflet, the height of the aortic leaflets, and the aortic annulus to the STJ level. Meanwhile, the malformation, location, number, and shape of the coronary artery orifices and the presence of accessory orifices were observed and recorded. During the study, the relation of the coronary ostia, the aortic leaflets, and the valved stent were also investigated through the post mortem aortic valved stent implantation.

**Results:** The results demonstrated that most of the coronary ostia were located below the STJ level, only very few coronary ostia were at or above the same. The left coronary ostia cluster near to the central region of the sinus curvature, while the right coronary ostia tend to locate eccentrically, a lower position, and in the right side of the sinus. Most of the coronary ostia, which were located below the STJ, were covered by its corresponding aortic leaflets; while the ostia were rarely covered by the aortic leaflets if they lay at or above the STJ. The right coronary ostia were more frequently covered by its aortic leaflets than the left ones.

**Conclusion:** To perform an orthotopic PAVR, resection of the native leaflets before implantation of the valved stent might be necessary and new stents have to be designed to prevent coverage of the coronary ostia by crimping the leaflets.

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## 7. Appendix

All the patients' general characteristics including gender, height, body weight, heart weight and main cause of death are list below:

1. Gender: female;                      Age: 75Ys;                      Height: 165cm  
Body Weight: 65kg                      Heart weight: 389g.  
Diagnosis: Post-op CABG, multiple organs failure.
2. Gender: female;                      Age: 85ys;                      Height: 164cm  
Body Weight: 57 kg                      Heart weight: 343 g.  
Diagnosis: advanced lung cancer, multiple organs metastasis.
3. Gender: male;                      Age: 56ys;                      Height: 178cm  
Body Weight: 89kg                      Heart weight: 451 g.  
Diagnosis: unknown, multiple organs failure?
4. Gender: male;                      Age: 53ys;                      Height: 168cm  
Body Weight: 72 kg                      Heart weight: 373g.  
Diagnosis: chronic obstructive pulmonary disease.
5. Gender: male;                      Age: 65ys;                      Height: 165 cm  
Body Weight: 100kg                      Heart weight: 425g.  
Diagnosis: post-op of ECMO.
6. Gender: male;                      Age: 54ys;                      Height: 180 cm  
Body Weight: 67kg                      Heart weight: 480g.  
Diagnosis: sepsis, post-op of femoral artificial joint.
7. Gender: female;                      Age: 88ys;                      Height: 165cm  
Body Weight: 100kg                      Heart weight: 327g.  
Diagnosis: advanced gastric cancer.
8. Gender: female;                      Age: 57ys;                      Height: 160 cm  
Body Weight: 88kg                      Heart weight: 328 g.  
Diagnosis: pulmonary infection.
9. Gender: male;                      Age: 59ys;                      Height: 174cm  
Body Weight: 124 kg                      Heart weight: 505 g.

Diagnosis: trauma.

10. Gender: female; Age: 65ys; Height: 162cm

Body Weight: 63 kg Heart weight: 447g.

Diagnosis: post-op CABG.

11. Gender: female; Age: 87ys; Height: 172 cm

Body Weight: 95 kg Heart weight: 574 g.

Diagnosis: death of age.

12. Gender: female; Age: 82ys; Height: 166cm

Body Weight: 67kg Heart weight: 540g.

Diagnosis: advanced lung cancer.

13. Gender: male; Age: 26ys; Height: 172cm

Body Weight: 57 kg Heart weight: 370g.

Diagnosis: systematic fibrous pneumonia.

14. Gender: female; Age: 84ys; Height: 170cm

Body Weight: 89kg Heart weight: 511g.

Diagnosis: cerebral embolism.

15. Gender: male; Age: 84ys; Height: 178 cm

Body Weight: 93kg Heart weight: 520 g.

Diagnosis: pulmonary infection.

16. Gender: male; Age: 69ys; Height: 176cm

Body Weight: 100 kg Heart weight: 710g.

Diagnosis: chronic pneumonia.

17. Gender: male; Age: 74ys; Height: 178 cm

Body Weight: 89kg Heart weight: 478 g.

Diagnosis: death for ageing.

18. Gender: male; Age: 67ys; Height: 165 cm

Body Weight: 89kg Heart weight: 375g.

Diagnosis: unknown.

19. Gender: female; Age: 76ys; Height: 164 cm

Body Weight: 85kg Heart weight: 430 g.

Diagnosis: chronic multiple organs disease.

20. Gender: female; Age: 71ys; Height: 167 cm

Body Weight: 80 kg Heart weight: 423g.

Diagnosis: coronary heart disease.

21. Gender: male; Age: 73ys; Height: 180cm

Body Weight: 110 kg Heart weight: 1010 g.

Diagnosis: primary hypertension, diabetics, left ventricle embolism.

22. Gender: male; Age: 77ys; Height: 178cm

Body Weight: 98kg Heart weight: 478 g.

Diagnosis: myocardial infarction.

23. Gender: male; Age: 75ys; Height: 172cm

Body Weight: 75 kg Heart weight: 411g.

Diagnosis: diabetics, hypertension.

24. Gender: female; Age: 64ys; Height: 163 cm

Body Weight: 65 kg Heart weight: 402 g.

Diagnosis: advanced breast cancer.

25. Gender: female; Age: 72ys; Height: 161 cm

Body Weight: 75 kg Heart weight: 478 g.

Diagnosis: chronic hepatic failure, post-op pancreatic surgery.

26. Gender: female; Age: 75ys; Height: 122 cm

Body Weight: 78 kg Heart weight: 495g.

Diagnosis: myocardial infarction.

27. Gender: female; Age: 76ys; Height: 166 cm

Body Weight: 78 kg Heart weight: 510g.

Diagnosis: post-op of CABG.

28. Gender: male; Age: 59ys; Height: 174cm

Body Weight: 65 kg Heart weight: 386g.

Diagnosis: pulmonary infective embolism.

29. Gender: male; Age: 67ys; Height: 187cm

Body Weight: 83 kg Heart weight: 415 g.

Diagnosis: arrhythmia, myocardial infarction?

30. Gender: male; Age: 71ys; Height: 175cm

Body Weight: 72kg Heart weight: 452g.

Diagnosis: myocardial infarction.

31. Gender: female; Age: 70ys; Height: 153cm

Body Weight: 60 kg Heart weight: 410g.

Diagnosis: coronary heart disease, post-op of CABG.

32. Gender: female; Age: 77ys; Height: 170 cm

Body Weight: 82 kg Heart weight: 389 g.

Diagnosis: thoracic and abdominal aneurysm.

33. Gender: female; Age: 85ys; Height: 159cm

Body Weight: 82 kg Heart weight: 432g.

Diagnosis: arrhythmia, post-implantation of pacemaker.

34. Gender: male; Age: 65ys; Height: 174cm

Body Weight: 75 kg Heart weight: 463 g.

Diagnosis: advanced cancer.

35. Gender: male; Age: 57ys; Height: 173cm

Body Weight: 80kg Heart weight: 523 g.

Diagnosis: chronic pulmonary infection.

36. Gender: female; Age: 65ys; Height: 168 cm

Body Weight: 86kg Heart weight: 342g.

Diagnosis: chronic renal failure.

37. Gender: male; Age: 63ys; Height: 174 cm

Body Weight: 64kg Heart weight: 412g.

Diagnosis: advanced lung cancer, multiple organs metastasis.

38. Gender: female; Age: 43ys; Height: 170cm

Body Weight: 94 kg Heart weight: 264 g.

Diagnosis: left pulmonary embolism.

39. Gender: female; Age: 96ys; Height: 160cm

Body Weight: 46kg Heart weight: 342g.

Diagnosis: abdominal aneurysm, myocardial infarction.

40. Gender: male; Age: 81ys; Height: 175cm

Body Weight: 86kg Heart weight: 510g.

Diagnosis: chronic colitis, arrhythmia, implantation of pacemaker.



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