SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

THIRUVANANTHAPURAM-695011

PROJECT REPORT

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CERTIFICATE

I, Dr.Arun.S.R hereby declare that I have undertaken the work necessary for the project, under the guidance of the faculty, Department of cardiology

Place :Thiruvananthapuram **Signature**
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List of Projects

1) Morphological and clinical Profile of Heterotaxy syndrome in Sree Chitra Tirunal Institute for Medical Science and Technology.

2) Prevalence and predictors of coronary artery disease in Patients Undergoing Repair of Aortic Aneurysms.

STUDY-1

Morphological and clinical Profile of Heterotaxy syndrome in Sree Chitra Tirunal Institute for Medical Sciences and Technology.

INTRODUCTION

In the normal body, the internal organs are arranged in typical patterns on the right and left sides, and are not mirror images of each other. Asymmetry of the thoracic and abdominal organs is the usual or normal situation. The syndrome of visceral heterotaxy includes patients with an unusual degree of symmetry of some of the thoracic and abdominal organs, and the atrial appendages within the heart .

This broad term includes patients with a wide variety of very complex cardiac lesions. Patients with heterotaxy can be stratified into the subsets of asplenia syndrome and polysplenia syndrome, or the subsets of heterotaxy with isomerism of the right atrial appendages and heterotaxy with isomerism of the left atrial appendages

AIM OF THE STUDY

To describe clinical and morphological profile of the cohort of patients with Heterotaxy syndrome .

REVIEW OF LITERATURE:

Heterotaxy results from failure of the developing embryo to establish normal left-right asymmetry. Typical manifestations include abnormal symmetry and malposition of the thoraco-abdominal organs and vessels, complex congenital heart disease and extracardiac defects involving midline-associated structures.

The spleen is almost always affected, and there is syndromic clustering of the malformations corresponding to the type of splenic abnormality present.

Definitions

Although they are bilaterally symmetrical externally, human beings normally display an internal left-right asymmetry whose overall direction is the same in all of them. Malformations result when the process of normal left-right axis specification during embryogenesis is disturbed.

Abnormal sidedness of the heart, lungs, or abdominal viscera is easily recognized in the newborn and is an important clue because of its association with the anomalies .

The term 'situs' is applied to specify the left-right orientation of the asymmetric body structures. 'Situs' literally means site or situation. In anatomy, situs means the pattern of anatomic organization. There are two types of unambiguous situs, being (1) situs solitus, the normal or (2) situs inversus, a mirror image of normal [1] .

The concept of situs applies to the pattern of the viscera as a whole and to each asymmetrical viscus considered singly, such as the lungs, liver, spleen, and gastrointestinal tract. The concept of situs also applies to the heart as a whole and to each of the cardiac segments because each is asymmetrical [1, 2] .

In the so-called heterotaxy syndrome, anomalies of the visceral situs are characterized by an abnormal symmetry of certain viscera and veins (lungs, liver, venae cavae). In addition, there is discordance between the left-right orientation of several organ systems, as well as between the various segments of the heart .

Heterotaxy and heterotaxy syndrome

The term heterotaxy derives from the Greek word ‘heteros’, meaning other, and ‘taxis’, meaning order or arrangement, i.e., ‘other than normal arrangement’ [1] . The Nomenclature Working Group1) offers the following definition for the term “heterotaxy”: “. Heterotaxy is defined as an abnormality where the internal thoracoabdominal organs demonstrate abnormal arrangement across the left-right axis of the body. Heterotaxy” is synonymous with ‘visceral heterotaxy’ and ‘heterotaxy syndrome’

Isomerism

Isomerism in the context of the congenitally malformed heart is defined as a situation where some paired structures on opposite sides of the left-right axis of the body are, in morphologic terms, symmetrical mirror images of each other.

Left Isomerism

Left isomerism in the context of the congenitally malformed heart is defined as a subset of heterotaxy where some paired structures on opposite sides of the left-right axis of the body are symmetrical mirror images of each other, and have the morphology of the normal left-sided structures. The polysplenia syndrome has frequently been described as ‘bilateral leftsidedness’ (left isomerism) [3] because of the duplication of structures normally found on the left side of the body only with absence of the normal right-sided structures .

Right Isomerism

Right isomerism in the context of the congenitally malformed heart is defined as a subset of heterotaxy where some paired structures on opposite sides of the left-right axis of the body are symmetrical mirror images of each other, and have the morphology of the normal right-sided structures.

The asplenia syndrome has often been described as ‘bilateral right-sidedness’ (right isomerism) [3, 4] because of the bilateral presence of organs and structures normally found on the right side with absence of those normally present on the left .

Situs ambiguous

Situs Ambiguus is defined as an abnormality in which there are components of situs solitus and situs inversus in the same person. Situs ambiguus, therefore, can be considered to be present when the thoracic and abdominal organs are positioned in

such a way with respect to each other as to be not clearly lateralised and thus have neither the usual, or normal, nor the mirror-imaged arrangements.

All patients with heterotaxy should also be considered to have “situs ambiguus” and all patients with “situs ambiguus” also have heterotaxy syndrome.[5]

Incidence

It is difficult to calculate precisely the incidence of isomerism due to the potential underestimation of the incidence and prevalence. It seems likely that most cases of right isomerism are recognized in infancy because of the presence of severe forms of cyanotic heart disease. Failure to recognize left isomerism is more likely because of the wider range of associated heart diseases, including mild forms that may not even warrant surgical intervention.

‘The heterotaxy syndrome has an estimated incidence of 1 in 6,000 to 1 in 20,000 live births, or about 1% of all congenital heart defects [3, 4] . However, if abortions and stillbirths are included, heterotaxy syndrome is found more frequently (0.03–1.1% of fetuses) [6,7] .

Interestingly, Asians show a higher prevalence of heterotaxy syndrome compared to Westerners.[8]

Embryologic and Genetic Considerations

Asymmetrical positioning of the visceral organs along the left-right axis occurs very early during gestation. The first organ to move from the symmetrical midline position of origin to a lateral position is the cardiac tube. The embryologic tube forms a rightward loop on embryonic day 23 which is called D-loop (D = *dexter* , Latin). Other organs follow concordantly [9,10] .

At day 35 the stomach starts its 90° rotation, and during the following 1-month period of 270° looping of the small and large intestine, the liver, gallbladder, pancreas and spleen also assume their Characteristic positions [10] . In addition, asymmetric regression of initially paired arteries and veins and the development of left-right asymmetry of paired organs with asymmetric primordia contribute to the development of sidedness [10] .

The complex process of embryonic lateralization is at present only partly understood. The midline is thought to play a critical role in establishing normal left-right asymmetry [11,12] . Cells in the midline, such as notochord cells, may act as

sources of signals that direct left-right asymmetry and function as a barrier to maintain a gradient of left-right signaling molecules [13] .

This gradient is thought to be produced by the dynein arms of the nodal cilia. These have been shown to generate a leftward flow of extra embryonic fluid at the embryonic node which is essential for left-right determination [14, 15] .

Disruption of the midline barrier separating left from right permits mixing of molecules that are normally asymmetrically distributed in early embryos, resulting in abnormal organ sidedness later in development. The importance of the midline in lateralization is supported by the relatively high incidence of midline-associated defects in patients with heterotaxy [16] .

This suggests that this association may result from a coherent or synchronic defect in the primary developmental field rather than representing causally independent malformations [17] .

While the occurrence of heterotaxy with asplenia or polysplenia is usually sporadic, familial cases have been described, and most have been interpreted as demonstrating autosomal recessive transmission [18] . Asplenia, polysplenia and situs inversus totalis may occur in the same family [18,19] .

Recently an increasing number of gene loci have been identified to play a role in the development of sidedness, and lateralization defects appear to be genetically heterogenous.

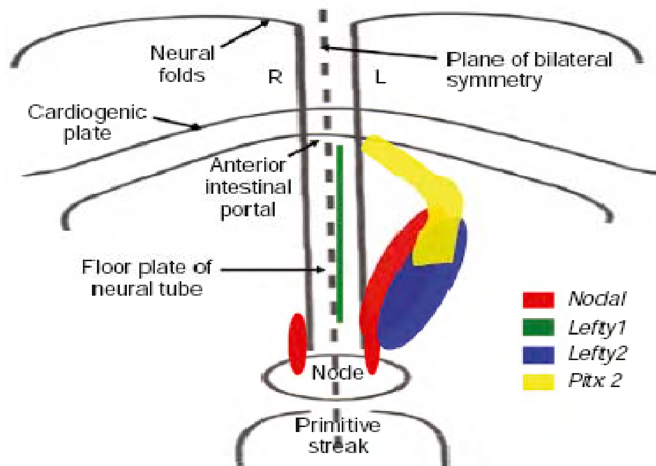
In animals, several genes have been found to exhibit predominant expression patterns along the left side of the developing embryo [20] . These include the TGF-beta family members nodal and lefty-1 and lefty-2 [21] .

A rare X-linked form of heterotaxy has been mapped to the region Xq26 [22,23] . Other cases have been associated with paracentric inversions (involving chromosome 11) [24] , translocations (such as between chromosomes 12 and 13 or chromosomes 11 and 20) [24] , insertions (from chromosome 8q into 7q) [46] , deletions (involving chromosomes 4, 10, 13, and 18) [25] , placental trisomy 16 and with dizygotic, monozygotic or conjoined twinning [26,27]

Environmental factors may also contribute to lateralization defects since heterotaxy has been found in association with diabetes mellitus [26,27] .

MORPHOGENESIS

Cilia in the primitive node create a wave that drives molecules in one specific direction across the cells of the developing embryo



- The wave of molecular material is stopped from crossing the midline by gene *Sonic hedgehog.*
- Midline barrier ->other genes, such as *Lefty,* and *Pitx2,* have their expression confined to the left side of the body. [28]
- Knocking out *Sonic hedgehog* permits the left-forming genes to occupy the right side of the body -> left isomerism
- Knocking out genes such as *Pitx2* produces right isomerism

Abnormalities of the Spleen as Landmark of the Subtypes of Heterotaxy Syndrome

In patients with heterotaxy syndrome, the spleen is almost always affected, although the reason is not understood. Three types of splenic anomalies can be differentiated [1,29,30] :

1) The spleen may be absent (asplenia);
2) It may be composed of a cluster of small splenuli, a large spleen and several small ones, or it may be multilobed (polysplenia).
3) It may be of normal size but located on the right upper quadrant of the abdomen (single, right-sided spleen), while the heart is left-sided and the lungs are solitus, inversus or symmetrical.

In a study of 109 autopsy cases of visceral heterotaxy with congenital heart disease, 58 (53%) had asplenia, 46 (42%) had polysplenia, and 5 (5%) had a single right-sided spleen [1] . In the majority of patients with polysplenia, the multiple spleens are right-sided (64–75% [1, 31]). Rarely, patients with heterotaxy may have a normal left-sided spleen [7] .

The great majority of patients with heterotaxy have complex congenital heart disease. Very rarely, however, the heart may be normal in patients who have visceral heterotaxy [1, 32] . Although the cardiovascular defects in heterotaxic patients show considerable variability, there is also definite syndromic clustering that often corresponds to the type of splenic abnormality present .

This association between the cardiac malformations and the status of the spleen, first described by Polhemus [18] in 1952 and further elaborated upon by Ivemark [33] in 1955, is responsible for the terms 'asplenia' and 'polysplenia syndrome'.

Ivemark [33] first observed and emphasized the association between malformations of the conotruncus and the atrioventricular (AV) canal in patients with asplenia. Because the AV canal and the conotruncus undergo division at about the same time that the splenic primordial appear (30–32 days of gestation), he postulated that it was possible for the same teratogenic factor to adversely affect the formation of the spleen and the division of the AV canal and the conotruncus.

A similar linkage between AV canal defects and conotruncal malformations has not been found for patients with polysplenia. Despite the high incidence of AV canal defects, conal development is usually normal in this group [1] .

While certain associated anatomic features are typical for either the asplenia or the polysplenia syndrome , there sometimes is a certain overlap between groups suggesting that the two syndromes are at least partly etiologically and pathogenetically interrelated [34] .

Malformations in patients with a single, right-sided spleen are similar to those with asplenia [1] .

In addition to these more specific anomalies of the vessels, heart, lung, and liver, many patients with heterotaxy syndrome have further malformations. It is

characteristic that most of these extracardiac anomalies involve midline structures. While the frequency of each of these defects is low, an overall 38% of patients with heterotaxy have a midline- associated anomaly – the frequency of midline defects being about 10–60 times greater than the respective frequency of each lesion in the general population [35)

Extracardiac abnormalities and other associated problems

There is a high incidence of abnormalities of the renal tract, especially biliary atresia, in isomerism. Routine abdominal ultrasound, with a focus on the biliary tree, is warranted even in the absence of jaundice in infants with left isomerism.

Persistent vomiting in the neonatal period should raise suspicion of a upper gastrointestinal obstruction owing to duodenal atresia or compression. Also, late intestinal obstruction might be caused by gastrointestinal malrotation or gastric volvulus.

The state of the spleen should be established in all patients. When congenital absence of the spleen is diagnosed, there is a lifelong risk of overwhelming infection. When septicemia develops in the asplenic patient with congenital cardiac disease, the clinical course is often fulminant.[36,37]

Waldma et al.[38] showed a greater frequency of fulminating and fatal septicemia produced by encapsulated bacteria in patients with asplenia syndrome compared with appropriate controls. It is generally recommended that some form of prophylaxis be given for congenitally asplenic patients. Klebsiella and Escherichia coli are the principle pathogens in patients younger than 6 months of age, whereas Streptococcus pneumoniae (pneumococcus) and Haemophilus influenzae are the predominant pathogens after 6 months.

The Report of the Committee on Infectious Diseases of the American Academy of Pediatrics recommendations includes continuous antibiotic prophylaxis in infants, children, and adults with asplenia syndrome. For antimicrobial prophylaxis, oral penicillin V (125 mg, twice a day, for children younger than 5 years of age and 250 mg, twice a day, for children 5 years of age and older) is recommended. Some experts recommend amoxicillin (20 mg/kg per day).

H. influenzae vaccine (Hib Vax), and hepatitis B vaccine should be given as routinely recommended in infancy. Pneumo-coccal conjugate vaccine is

recommended for routine administration as a four-dose series for all children 23 months and younger (PCV7), and a dose of PS23 is recommended to be given at 24 months and an additional dose 3 to 5 years after the first dose. Quadrivalent meningococcal vaccine is recommended for optimal effect at 2 years of age or older. Routine use of yearly influenza vaccine is also recommended in debilitated cardiac patients.[39]

The electrocardiogram and abnormalities of cardiac rhythm

In some instances of right isomerism, right- and left-sided atrial origin of the P wave is present at different times in the same patient, reflecting activity of bilateral sinus nodes.[40,41] In left isomerism, true sinus rhythm is less common, as might be anticipated from the known hypoplasia of the sinus node in patients with isomeric left appendages.[42] In many patients, progressive slowing of rate has been noted with advanced age, leading to the need for placement of a permanent pacemaker.[43]

Atrioventricular block is exceedingly rare in right isomerism; in contrast, varying degrees of atrioventricular block are common in left isomerism. Overall, complete atrioventricular block is observed in one-tenth of cases with left isomerism

Howell-Jolly bodies

The persistence of Howell-Jolly bodies in the peripheral blood smear is a very useful means of confirming splenic agenesis or hypofunction provided it is remembered that Howell-Jolly bodies can be transiently present in the normal newborn (63). These inclusions are also seen in the late stages of the maturing erythroblast, in megaloblastic and haemolytic anaemias, thalassaemia, leukaemia, and some types of steatorrhoea.

It is important to be aware that even in the presence of splenic tissue from several spleens, splenic function may not be normal. Although the exact amount of splenic tissue necessary for adequate immunologic function is not known, it is generally agreed that the presence of Howell-Jolly bodies in the blood smear is indicative of asplenia or a degree of hyposplenism that represents a risk for overwhelming infections [64] .

Bronchial tree, is a much better guide to the presence of isomerism of the atrial appendages. Bilateral long and hyparterial bronchuses are indicative of left isomerism, and bilateral short and eparterial bronchuses of right isomerism,

respectively. Not all cases with isomeric atrial appendages have bronchial isomerism. Thus, while examination of the penetrated chest radiograph was considered a useful step in the evaluation of the infant or child suspected of having isomeric atrial appendages, it is now rarely used as a diagnostic tool

Most frequently, the suprarenal segment of the inferior caval vein is totally absent. The abdominal segment of the caval vein continues through the azygos venous system to drain to either the right- or the left-sided superior caval vein.In patients with left isomerism, both accessory venous systems are strictly hemiazygos, since the hemiazygos vein is a morphologically left structure. It is simpler, nonetheless, to describe communication via the azygos venous system, and then to account for the right- or left-sided location of the anomalous venous channel.

Although right-sided azygos continuation has been noted in the setting of right isomerism, albeit rarely, continuation through the left-sided azygos veins has been reported only in association with left isomerism, or very rarely, in patients with usual atrial arrangement or mirror-imaged arrangement.

In general, structural cardiac lesions tend to cause less severe hemodynamic compromise in infants with polysplenia, making them less seriously ill than infants with asplenia because of the rarity of pulmonary atresia and total anomalous pulmonary venous connection to a systemic vein in the former group [1, 19] . However, the presence of complete AV block in addition to the structural heart defect will severely aggravate the clinical presentation of patients with polysplenia.

Treatment

Treatment of patients with isomerism should be determined by the nature and severity of the associated cardiac and extracardiac lesions. Most cardiac operations for patients with isomerism are palliative in nature, since normal anatomy is rarely achieved. Not surprisingly, then, mortality rates remain high for patients with heterotaxy syndrome.

Factors that have historically been associated with increased operative risk include abnormalities of the systemic venous connection, a partial or total anomalous pulmonary venous connection, a common atrioventricular valve that is incompetent, and a morphologic right ventricle supporting the systemic circulation.[44,]

Biventricular repair

Patients with left isomerism in general have less severe cardiac malformations than those with right isomerism and, hence, more chance of biventricular repair. Approximately two-thirds of patients with left isomerism have anatomy suitable for biventricular repair. Most commonly, such patients have atrioventricular septal defects, with anomalies of systemic and pulmonary venous return, but with concordant ventriculo-arterial connections. Repair is achieved using standard techniques with appropriate baffling of anomalous venous return.[45]

After biventricular repair, however, it is common to encounter progressive valvar regurgitation, particularly across the left atrio-ventricular valve. This often results in the need for reoperation as does recurrent subaortic stenosis, which is more common in those with left isomerism than in the setting of the usual atrial arrangement.

The anomalies observed in right isomerism are much less amenable to biventricular repair, even when two well balanced ventricles are present. A few reports of biventricular repair for right isomerism do exist.[46,47]

Fontan-type procedure

For almost all patients with right isomerism, and for many with left isomerism, biventricular repair will not be feasible, and all palliative protocols are then staging procedures towards a Fontan-type repair. More complex malformations associated with situs ambiguus, such as common atrium with common inlet single ventricles or unbalanced ventricles, and complex malformations associated with criss-cross AV relationship and severe straddling AV valve have fewer options for successful surgical correction.

Patients with heterotaxy syndrome usually require palliative surgery in the neonatal period. The palliative procedures are diverse and reflect the highly variable anatomy of this syndrome: a systemic-to-pulmonary shunt, banding of the pulmonary trunk, and a neonatal Norwood approach. When anomalies of a pulmonary venous connection or systemic obstruction are present, special efforts must also be directed toward surgical establishment of appropriate venous connections or relief of systemic obstruction.

After a neonatal palliative procedure, most can opt only for surgical palliation directed toward function as a single ventricle such as with bidirectional cavopulmonary shunts, and, finally, modified Fontan procedures.[48] When there is interruption of the inferior caval vein, bidirectional cavopulmonary anastomosis (Kawashima operation)[49] will result in all of the systemic venous return being diverted to the lungs except for that returning from the hepatic veins. It has been widely used in patients with left isomerism and is similar to the completion of a fenestrated Fontan circulation. Moreover, these procedures have many late outcomes such as venovenous collaterals [50] and the development of pulmonary arteriovenous fistulas .[51] Patients with left isomerism seem to be particularly prone to this complication. There is increasing evidence that a hepatic factor may be important in preventing this development. Therefore, a Kawashima operation requires subsequent completion of a Fontan procedure.[52]

Initial reports of the outcomes of the modified Fontan operation for heterotaxy syndrome revealed early mortality of 13% to 80%. These were significantly inferior to those with other single ventricle patterns. Introduction of the extracardiac conduit technique for construction of a Fontan circuit has a particular benefit for this group, since the need for complex intra-atrial baffles and tunnels is obviated. Also, technical advances and modifications of the Fontan operation have led to markedly improved Fontan procedure results in heterotaxy syndrome .[53]

Several reports demonstrated the development of pulmonary arteriovenous fistulas after the Fontan procedure.[52] In these cases, it was closely associated with uneven perfusion of hepatic venous drainage and it excluded hepatic blood flow from the pulmonary circulation, similar to the Kawashima operation. These patients had left isomerism with an interrupted inferior vena cava, and had the conduit position on the contra lateral side to the superior vena cava with azygous drainage. It is essential to design the hepatic venous conduit for achieving balanced perfusion to the lungs bilaterally, and sometimes it is not easy to do so. The reason is that the position of the conduit may be inevitably in the contralateral side of the azygous continuation, if the main mass of ventricle is in the same side of the azygous continuation.

MATERIALS AND METHODS

For identifying the study population ,Searched the medical records,of the Division of Cardiology, Department of Cardiovascular Surgery at the SCTIMST for cases Heterotaxy admitted between between January 2000 and dec2011.

Patients were considered for inclusion in the study after reviewing the charts for these diagnostic features. The diagnoses were made using a variety of investigations. Descriptions of anatomy, cardiac function and dysrhythmias were abstracted from records of surgery, cardiac catheterization with angiography,chest X-ray, echocardiography,ultrasonography and magnetic resonance imaging.

Left atrial isomerism was *confirmed* if there was abdominal situs ambiguous, with or without polysplenia, with bilateral hyparterial bronchi or bilobed lungs or confirmed bilateral left atrial appendage morphology either during surgery or by echo.

A *probable* diagnosis was considered if there was an interrupted inferior caval vein with at least two other features of left isomerism, for example, left atrial rhythm, biliary atresia or congenital heart disease within the spectrum of atrioventricular (AV) septal defects.

Diagnosis of right atrial isomerism was based on plain X-ray films of the chest and abdomen by identifying the position of the liver, stomach and bronchial pattern [54] Echocardiographic or angiographic demonstration of a juxtaposed relation between the aorta and inferior vena cava and the morphology of the atrial appendages was used to support the diagnosis [55,56] When surgical interventions or autopsies made direct visual examination of the atrial morphology possible, the diagnosis was further verified.

RESULTS

There were 57 patients with Heterotaxy admitted during the period from 2000-2011 ,of which 14(24.5%) patients had right isomerism, and 43(75.5%) patients had left isomerism.36 (63%) patients were female and 21(37%) patients were male (M:F-1:1.71). In left and right Isomerism M:F was 1:1.5 and 1:2.5 respectively.

Table 1 Comparison of Clinical features based on diagnosis

		Right Isomerism 24.5% (N-14)	Left Isomerism 75.5% (N-43)	p
Gender	Male	28.6 (4)	39.5 (17)	0.460
	Female	71.4 (10)	60.5 (26)	
SPO2%	<80	57.1 (8)	16.3 (7)	0.006
	80 - 95	42.9 (6)	62.8 (27)	
	>95	0 (0)	20.9 (9)	
Presentation	Cyanotic	85.7 (12)	51.2 (22)	0.022
	Spells	7.1 (1)	7 (3)	0.983
	CHF	0 (0)	16.3 (7)	0.107
	Breathlessness	35.7 (5)	27.9 (12)	0.579
	RECC RTI	28.6 (4)	48.8 (21)	0.184
	Clubbing	35.7 (5)	14 (6)	0.073
	Feeding DIFF	28.6 (4)	23.3 (10)	0.688
Rhythem	EAR	41.7 (5)	83.7 (36)	0.002
	JR	0 (0)	4.7 (2)	
	N	0 (0)	2.3 (1)	
	SR	58.3 (7)	9.3 (4)	
Diagnosed by	Criteria	0 (0)	65.1 (28)	0.000
	Echo	14.3 (2)	16.3 (7)	
	Surgical	78.6 (11)	18.6 (8)	
	MRI	7.1 (1)	0 (0)	
Cardiac position	LC	42.9 (6)	69.8 (30)	0.160
	MC	14.3 (2)	4.7 (2)	
	DC	42.9 (6)	25.6 (11)	
Spleen scan	Not done	85.7 (12)	88.4 (38)	0.124
	Asplenia	14.3 (2)	2.3 (1)	
	Polysplenia	0 (0)	9.3 (4)	

Clinical presentation :Table 1

Most of the right Isomerism patients (92%) were diagnosed before 1 month of age, of whom 23% were diagnosed at birth. In left isomerism 84% were diagnosed at 1st month of life, of which only 7.5 % were detected at birth.

Most of the right Isomerism patients have cyanosis at presentation 85.5%.Where as in left isomerism, cyanosis was present only in 51% of patients at initial presentation .

During admission Most of the right Isomerism patients (57%) have SPO2 of <80% the remaining 43% had SPO2 between 80-95%,none was Acyanotic .Only 16% of LI had SPO2 <80% ,63% had SPO2 80-85% and 21%were acyanotic .

Other presenting symptoms in right isomerism was clubbing 35.7% breathlessness 35.7% feeding difficulty 28.6% recurrent respiratory infection 28.6% and DOE 14.3%

In left isomerism ,after cyanosis most of them 48.8% presented with recurrent respiratory infection .Breathlessness (27.9%) feeding difficulty (23.3%)and clubbing (14%) were other symptoms .

ECG charecteristics_:

In left isomerism 84% of the patients had EAR and SR was noticed in 12%. In left isomerism RVH was seen in 38% BVH in 33% and LVH in 12%.where as 62% of the right Isomerism patients showed RVH.

Chest X-Ray : table 3

In right Isomerism Bilateral right bronchus was noticed in 43% of X-rays .In left isomerism, Bilateral left bronchus was noticed in 53.5% X-rays. In others bronchial pattern was not clear.

Diagnosis of Heterotaxy

In left isomerism, 65% of the patients were diagnosed based on the criteria .In 16% definite Echo diagnosis and in 19% definite surgical diagnosis were present .

In right Isomerism 79 % were surgical diagnosis, 14% had echo diagnosis and one patient was diagnosed by MRI.

Table 2 Comparison Anatomical profile based on diagnosis				
		RI % (N)	LI % (N)	p
Superior venacava	Left SVC (LSVC)	14.3 (2)	11.6 (5)	0.001
	Right SVC (RSVC)	0 (0)	53.5 (23)	
	Bilateral SVC (BLSVC)	85.7 (12)	34.9 (15)	
IVC interruption and continuation as	Nil	78.6 (11)	7 (3)	0.000
	Aygos vein (AZ)	21.4 (3)	72.1 (31)	
	Hemiazygos vein (HA)	0 (0)	20.9 (9)	
Pulmonary vein connection	N	50 (7)	88.4 (38)	0.009
	Partial anomalous pulmonary venous drainage (PAPVC)	21.4 (3)	4.7 (2)	
	Total anomalous pulmonary venous drainage (TAPVC)	28.6 (4)	7 (3)	
Atria	Normal	7.1 (1)	20.9 (9)	0.104
	Patent foramen ovale (PFO)	0 (0)	2.3 (1)	
	Ostium secondum ASD (OSASD)	21.4 (3)	34.9 (15)	
	Ostium primum(OPASD)	35.7 (5)	4.7 (2)	
	Common atrium(CA)	35.7 (5)	27.9 (12)	
	Sinus venosum ASD(SVASD)	0 (0)	4.7 (2)	
	Partial AVCD(PAVCD)	0 (0)	2.3 (1)	
	ASD	0 (0)	2.3 (1)	
Av.valves	N	21.4 (3)	58.1 (25)	0.017
	Common	64.3 (9)	16.3 (7)	0.001
	Rt atresia	0 (0)	4.7 (2)	0.411
	Lt atresia	14.3 (2)	4.7 (2)	0.220
	AV valve regurgitation (AVVR)	21.4 (3)	11.6 (5)	0.359
	CLEFT AML	0 (0)	16.3 (7)	0.107
Pulmonary valve	N	7.1 (1)	44.2 (19)	0.012
	Valvar PS	64.3 (9)	27.9 (12)	0.014
	RV outflow obstruction (RVOTO)	7.1 (1)	7 (3)	0.983
	Pulmonary Arteria	28.6 (4)	18.6 (8)	0.427
Aortic valve	N	100 (14)	97.6 (40)	0.555
	Bicuspid (BAV)	0 (0)	2.4 (1)	
ventricle	Single ventricle	35.7 (5)	14 (6)	0.073
	N	14.3 (2)	51.2 (22)	0.015
	Corrected TGA (CTGA)	0 (0)	4.7 (2)	0.411
	Double outlet Right ventricle (DORV)	42.9 (6)	25.6 (11)	0.220

Single ventricle	Right	14.3 (2)	7(3)	0.517
	Left	14.3 (2)	7 (3)	
	Common ventricles	7.1 (1)	0 (0)	
VSD	Inflow	35.7 (5)	23.3 (10)	0.031
	Sub aortic VSD (SAVSD)	14.3 (2)	32.6 (14)	
	Complete AVCD (CAVCD)	14.3 (2)	0 (0)	
	MUScular-VSD	0 (0)	7 (3)	
	Sub pulmonary VSD (SPVSD)	7.1 (1)	0 (0)	
	No VSD	28.6 (4)	37.2 (16)	
Great vessals	Normal	0 (0)	69.8 (30)	0.000
	Transposition (TGA)	50 (7)	9.3 (4)	
	Sidebyside	14.3 (2)	4.7 (2)	
	L-posed	14.3 (2)	16.3 (7)	
	D-Malposed	21.4 (3)	0 (0)	

Cardiac Morphology

Cardiac position : Levocardia was observed in 70% of the left isomerism , dextrocardia in 25% and mesocardia in 5% of cases .

In right Isomerism levocardia and dextrocardia were in equal numbers (42.9% each) .Mesocardia observed in 14 % of cases .

Systemic venous drainage: B/L superior venacava was present in 86% of right Isomerism patients, where as only 35% of left Isomerism had B/L SVC. Isolated LSVC was present in 14% of right Isomerism and 12% of the left Isomerism.

IVC interruption was noted in 93% of the left isomerism patients with azygous continuation in 72%, remaining 20 % continued as hemiazygous .

Pulmonary venous drainage : PV drainage was abnormal in 50% of the right Isomerism cases .Of these patients PAPVC was noted in 21%,TAPVC in 29%.

PV drainage was normal in 88% of left Isomerism patients .TAPVC was observed in 7%, PAPVC was observed in 2.5% patients each. These differences were statistically significant.

Atria: Common atria was present in 36% of the right Isomerism . The remaining 64% of the right Isomerism had two separate atrias in which 36% had ostium primum ASD and 21% had ostium secundum ASD .

Common atria was noticed in 28% of the left isomerism. In the remaining 72% of left isomerism patients with two separate atria, 35% had ostium secundum ASD . Ostium primum ASD and sinus venosum type ASD was noated in 5% cases each.

AV Valves :

Normal AV valves were noted only in 21.4%of right Isomerism where as 58% of the left isomerism had normal AV valves which was statistically significant. Common AV valves was noted in 64.3% of right Isomerism and 16.3% of left isomerism .It also showed a statistically significant difference in both groups .

Left AV valve atresia was noted in 14.3% of the right Isomerism but it was noticed in only 4.7% of the left isomerism group. Right AV valve atresia(4.7%) and Cleft AML (16.3 %) were noted only in left isomerism Overall 14.3% of right Isomerism and 9.4 % of left isomerism showed AV valve Artesia .

Great vessels

Pulmonary Valve and RV out flow tract were normal in 44.2% of the left isomerism group whereas most of the right Isomerism (93%) had any one of the obstruction (valvar PS 64.3%, pulmonary atresia 28.6%, RVOTO 7%) - which was statistically significant.

Out of the 56% abnormal pulmonary outflow in left isomerism, only 19% had Pulmonary atresia . In the remaining, 28% had valvar PS , and 7% had RVOTO.

Aortic valve was normal in the entire right isomerism group where as bicuspid aortic valve was noted in 2.4% of the left isomerism group.

Great vessel relationship was normal in 70% of the left isomerism but it was abnormal in all of the right isomerism group .Transposition of great arteries were noticed in 50% of the right isomerism group followed by D-malposed great vessels (21%) ,side by side and L-posed great vessels (both 14.%).

Transposition was noticed only in 9% of left isomerism group .Other anomalies were L-posed aorta in 16% and side by side great vessels in 4.7%.

Pulmonary artery hypertension

Pulmonary artery hypertension was noted in 28% of the Isomerism patients' .In left isomerism 34% showed pulmonary hypertension where as only 7% of right Isomerism did so.

Ventricles

Normal ventricles were present in 51% of the left isomerism where as only 14% of right isomerism showed normal ventricles, this difference was statistically significant

Single ventricle was seen in 35.7% of right isomerism out of which single ventricle of LV and RV morphology was present in equal distribution (14.3% each), common ventricle was noted in 7%patients with RI .

Single ventricle was noted in 14% of left isomerism in which LV and RV morphology was present in equal distribution.

36% of right isomerism had inflow VSD, 14% had sub aortic VSD and 7% had sub pulmonic VSD . Complete AV canal defect was noted in another 14% of patients. Pure muscular VSD were not seen in this group.

In left isomerism, sub aortic VSD was noted in 33% of patients, inflow VSD in 23%, and Muscular VSD in 7% of cases.

The difference in incidence of VSD was statistically significant in two groups.

Table 3 Comparison of extracardiac anomelies based on diagnosis

		RAI % (N)	LAI % (N)	p
CXR-bronchus	Not clear	57.1 (8)	46.5 (20)	0.000
	Bilateral left bronchus (BLL)	0	53.5 (23)	
	Bilateral right bronchus (BLR)	43 (6)	0 (0)	
Arch	L	42.9 (6)	72.1 (31)	0.046
	R	57.1 (8)	27.9 (12)	
Extracard				0.794
	Eventration of Diaphragm	0 (0)	2.3 (1)	
	Dysmorphic facies	0 (0)	2.3 (1)	
	Cong porto -systemic shunt	0 (0)	2.3(1)	

	RAI (n-14)	LAI (n-43)
PDA	57% (8)	48%(21)
MAPCAS	36%(5)	12%(5)

Extra cardiac anomalies : (table 3) extra cardiac anomalies were not detected in any patients with right isomerism .In left isomerism, 93% had no extra cardiac anomalies, one patient had eventration of diaphragm, one had dysmorphic facies and another one had congenital Porto-systemic shunt .

Incidence of Right arch was significantly high in right isomerism cohort (57% vs 28%).

Table 4 Comparison of out come based on diagnosis				
		RAI % (n-14)	LAI % (n-43)	p
Type of Surgery	Not done	7.1 (1)	34.8 (15)	0.000
	ICR	0 (0)	44 (18)	
	Central shunt	7.1 (1)	0 (0)	
	Kawashima	21.4 (3)	9.3 (4)	
	BLBDG	42.9 (6)	2.3 (1)	
	PDA ligation	0 (0)	4.7 (2)	
	BT Shunt	7.1 (1)	0 (0)	
	Porta-syste shunt pluging	0 (0)	2.3 (1)	
	Fontan	7.1 (1)	0 (0)	
	Backdout	0 (0)	4.7 (2)	
	BDG	7.1 (1)	0 (0)	
Outcome	Lost follow up	7.1 (1)	2.3 (1)	0.119
	Medical follow up	7.1 (1)	34.9 (15)	
	Post surgical follow up	85.7 (12)	51.2 (22)	
	expired	0 (0)	9.3 (4)	
	Waiting for surgery	0 (0)	2.3 (1)	

Table 5 :Types of surgery done in ICR group of Left isomerism

ICR	LI(n-43)
Atrial septation	9.3%(4)
VSD repair +Atrial septation	6.9% (3)
ASD+ VSD closure	4.6% (2)
ASD+PDA interruption	4.6%(2)
ASD closure	2.3%(1)
PDA interruption	4.6%(2)
VSD closure	4.6%(2)
VSD closure+TAPVC repair	2.3%(1)
Cor triatriatum excision	2.3%(1)

Outcome : None of the right isomerism underwent ICR .In these group 93% of patients under went palliative procedures in the form of Bidirectional glen shunt (50%) ,Kawashima (21%),BT shunt (7%),Fontan (7%) and Central shunt (7%).

In left isomerism, 44% of patients underwent ICR . Kawashima was done in 9%,BDG and porto- systemic shunt plugging in one patient each.

In those Left Isomerism patients under gone ICR, Atrial septation was done in 9.3%, VSD repair +Atrial septation in 6.9%. ASD+ VSD closure, ASD+PDA interruption, VSD closure and PDA interruption in 4.6% patients each. ASD closure, VSD closure+TAPVC repair and Cor triatriatum excision done in 2.3% of patients each.(table 5)

Four patients in left isomerism group expired .Out of which three expired due to post-op sepsis and one due to spell- cardiac arrest.

DISCUSSION

In our study we observed female predominance in both left and right Isomerism which is in contrast to the observation of male predominance in right Isomerism[1, 19] and equal distribution in left Isomerism[1, 34]. But there are conflicting results in various studies and the exact gender distribution can be made out only by including those of aborted and still birth fetuses. Therefore, gender cannot be used reliably to predict cardiac or splenic state in infants with suspected isomerism.

Because of the serious nature of associated cardiac anomalies the patients with right Isomerism were symptomatic early in neonatal life and in fact a significant percentage were diagnosed at birth . Nearly all patients with right isomerism have stenosis or atresia of the pulmonary outflow tract with a large ventricular septal defect or single ventricle, so cyanosis is almost universal and severity of cyanosis was more in right Isomerism.

In general, structural cardiac lesions tend to cause less severe hemodynamic compromise in infants with left isomerism, making them less seriously ill less cyanotic and the initial diagnosis was relatively delayed ,than infants with right isomerism .This may be due to the rarity of pulmonary atresia and total anomalous pulmonary venous connection to a systemic vein in the former group.

However, many infants with complex disease and isomeric left appendages present with cardiac failure owing to left-to-right shunting without pulmonary obstruction.

We have observed that P wave axis often helpful in determining atrial situs in patients with Right Isomerism .In right Isomerism most of the patients are having sinus rhythem reflecting normal sinus activity in most of these patients .

In Left Isomerism ,rhythm disorders are characteristic. Ectopic rhythms – such as nodal or coronary sinus rhythms – with varying pacemakers are common, making the P wave axis an unreliable parameter for the determination of atrial situs in this group [1] .

The consistent electrocardiographic abnormality - ectopic atrial rhythem was found in most cases of Left Isomerism .This might be due to hypoplasia of the sinus node in patients with isomeric left appendages.

Even though high incidence of Atrioventricular blocks,and complete heart blocks in left isomerism patients were described in the various literature, our study did not showed Atroventricular blocks .This may be due to the early presentation of patients . Progressive AV blocks may develop as the child grows.

According to literature the presence of eparterial or hyparterial bronchi which are a clue to bronchopulmonary isomerism is difficult to ascertain from the conventional radiograph is (60,61).In our study , since all of the patients are having large number of Chest X-rays and some of them are over penetrated films, branching pattern was able to distinguish in approximately half of the patients. So careful evaluation of Chest X-rays gives important clue regarding the type of the patients we are handling .

In the current study peripheral smear examination for Howell-Jolly bodies are done in only one case, suggesting the under utilization of this useful investigation . Since the presence of Howell-Jolly bodies in the blood smear is an indicative of asplenia or a degree of hyposplenism that represents a risk for overwhelming infections it is advisable to do peripheral smear examination in all suspected cases of Heterotaxy syndrome .

A splenic scan and ultrasound can be very helpful in diagnosing the presence of one or multiple small spleens [1, 19] .But in our patients these modalities were significantly underutilized.

An unusual position of the heart should always alert to the presence of isomerism. In our study the heart was left-sided in 63%, right-sided in 30%, with 7% showing a midline arrangement. The location of the heart, and the position of its apex, however, failed to discriminate between right and left isomerism.

Normal right sided SVC was present in most of the left isomerism, where as the incidence of Bilateral SVC and isolated left SVC was significantly high in right isomerism .So it may be a clue to the more severe Right isomerism.

IVC interruption was noted in all except three patients of left isomerism .So Presence of IVC interruption with left sided venous channel continuation gives a definite diagnosis of left isomerism in a case of suspected Heterotaxy syndrome .

In our study pulmonary venous drainage was abnormal in 50% cases of right isomerism .Even though the pulmonary connection is always anatomically abnormal in right isomerism (because the pectinate muscle does not extend up to crest in left atrium;) they can drain to the left sided chamber. The significantly high incidence of pulmonary venous anomaly makes right isomerism a more severe form of heart disease than left isomerism.

Common atria was detected in a significant number of cases of right and left isomerism(36% vs 28%). .Though there was high incidence of common atrium and ASDs were present in both groups , there are no significant difference between left and right isomerism with respect to incidence of common atrium .

In our study, Irrespective of the presence of biventricular or univentricular atrioventricular connections, most hearts with right isomerism have a common atrioventricular junction guarded by a common valve. The high incidence of Common AV valve may be one of the reasons which make right isomerism a more severe disease with bad operative outcome.

Though other valve abnormalities like right, left AV valve Artesia and cleft AML were present in isomeric patients, they did not showed significant clustering to a particular group.

Pulmonary out flow was abnormal in all except one patient in right isomerism group. Atresias are the most common anomaly of outflow tract with the majority of valvar pulmonary atresia followed by pulmonary artery atresias. The incidence of abnormal pulmonary outflow and valvar pulmonary atresias were significantly higher in right isomerism comparing left isomerism, which makes the former a more severe form of heart disease.

Univentricular atrioventricular connections, typically with double inlet via a common atrioventricular valve, are significantly more frequent in hearts with right rather than left isomerism. In about 40% of such instances, the univentricular connection will be to a morphologically right ventricle, another 40% of hearts will

have double inlet to a morphologically left ventricle and the remaining 20% to an indeterminate single ventricle.

Thus, in isomerism, any type of univentricular atrioventricular connection along with any possible ventricular morphology must be anticipated. In comparing with right Isomerism, fewer hearts with left isomerism have univentricular atrioventricular connections, but the same variability must be expected.

In heterodoxy, the ventricular septum in the majority of hearts with biventricular atrioventricular connections is deformed in the anticipated fashion. In those with left isomerism, however, the ventricular septum is more frequently Intact. The significantly high incidence of AV canal defect and inflow VSD in right isomerism will help to differentiate right isomerism from left.

Analysis of the ventriculo-arterial junctions as a whole shows significant differences between the two isomeric arrangements. Transposition of great vessels are commoner with right isomerism, while concordant ventriculo-arterial connections are more frequent in left isomerism.

On analyzing the outcome, as we expected none of the right isomerism underwent ICR .This indicates the more complex anatomy of this group which is not amenable to complete correction.

In left isomerism, a good number of patients (44%) underwent ICR indicating less severe cardiac anomalies in this group.

In those left Isomerism patients who under went ICR ,Atrial septation was done in 9.3%, VSD repair +Atrial septation in 6.9% ASD+ VSD closure ,ASD+PDA interruption , VSD closure and PDA interruption in 4.6% each . ASD closure, VSD closure+TAPVC repair and Cor triatriatum excision done in 2.3% each.(table 5)

4 patients in left isomerism group expired .out of which 3 expired due to post-op sepsis and one due to spell- cardiac arrest.

SUMMARY

The diagnosis of right isomerism can be established on the basis of:

1) Howell-Jolly bodies in the blood smear,
2) Absence of splenic tissue on ultrasound/splenic scan.
3) IpsilatIral position of hepatic veins and the descending aorta and ,
4) complex congenital heart disease with the constellation of total anomalous pulmonary venous connection to a systemic vein,B/L SVC common AV canal, double-outlet right ventricle, single ventricle or transposition of the great arteries with bilateral or subaortic conus, and subvalvar and valvar pulmonary stenosis or atresia.
5) Detection of bilateral short eparterial bronchus on X-rays.

The diagnosis of left isomerism can be established on the basis of

1) The presence of multiple spleens or a multilobe spleen on ultrasound/splenic scan,
2) An interrupted inferior vena cava with uni- or bilateral azygos extension to the ipsilateral superior vena cava,
3) Characteristic heart defects including total or partial anomalous pulmonary venous drainage to the right atrium , complete or partial common AV canal, normally related great arteries
4) Rhythm disturbances.
5) Detection of bilateral long hyparterial bronchus on x-rays .

CONCLUSION

The prognosis of patients with complex cardiac lesions and heterotaxy is poor. The 1-year mortality is >85% for patients with right isomerism and >50% for patients with left isomerism.[72]

Isomerism is a fundamental disorder of lateralization, and is often associated with important extracardiac anomalies. A careful evaluation of all systems is mandatory prior to referral for cardiac surgery.

The presence of a symmetrical liver or a right-sided stomach and dextrocardia in the chest X-ray should alert the physician to the presence of heterotaxy. In the great majority of patients, visceral heterotaxy is associated with complex congenital heart disease which shows syndromic clustering corresponding to the type of splenic abnormality present.

REFERENCES

1	Van Praagh S, Santini F, Sanders SP: Cardiac malpositions with special emphasis on visceral heterotaxy (asplenia and polysplenia syndromes); in Fyler D (ed): Nadas' Pediatric Cardiology. Philadelphia, Hanley & Belfus Inc/ Mosby, 1992, pp 589–608.
2	Van Praagh R: The importance of segmental situs in the diagnosis of congenital heart disease. Semin Roentgenol 1985; 20: 254–271.
3	Moller JH, Nakib A, Anderson RC, Edwards JE: Congenital cardiac disease associated with polysplenia. A developmental complex of bilateral 'left-sidedness'. Circulation 1967; 36: 789–799.
4	Van Mierop LHS, Gessner IH, Schiebler GL: Asplenia and polysplenia syndromes. Birth Defects 1972; 8: 36–44.
5	Heterotaxy Syndrome – Asplenia and Polysplenia as Indicators of Visceral Malposition and Complex Congenital Heart Disease Ulrike Bartram Johannes Wirbelauer Christian P. Speer Biol Neonate 2005;88:278–290
6	Atkinson DE, Drant S: Diagnosis of heterotaxy syndrome by fetal echocardiography. Am J Cardiol 1998; 82: 1147–1149.
7	Lin AE, Ticho BS, Houde K, Westgate MN Holmes LB: Heterotaxy: Associated conditions and hospital-based prevalence in newborns. Genet Med 2000; 2: 157–172.
8	Kim SJ, Kim WH, Lim HG, Lee JY. *Outcome of 200 patients after an extracardiac Fontan procedure. J Thorac Cardiovasc Surg 2008; 136:108-16.*
9	Brueckner M, McGrath J, D'Eustachio P, Horwich AL: Establishment of left-right asymmetry in vertebrates: Genetic distinct steps are involved. Ciba Found Symp 1991; 162: 202– 212.
10	Kosaki K, Casey B: Genetics of human leftright axis malformations. Cell Dev Biol 1998; 9: 89–99.
11	Danos MC, Yost HJ: Role of notochord in specifi cation of cardiac left-right orientation in zebrafi sh and *Xenopus* . Dev Biol 1996; 177: 96–103.
12	Lohr JL, Danos MC, Yost HJ: Left-right asymmetry of a nodal-related gene is regulated by dorsoanterior midline structures during *Xenopus* development. Dev 1997; 124: 1465–1472.
13	Yost HJ: Left-right development in *Xenopus* and zebrafi sh. Semin Cell Dev Biol 1998; 9: 61–66.
14	Afzelius BA: Asymmetry of cilia and of mice and men. Int J Dev Biol 1999; 43: 283–286.
15	Nonaka S, Tanaka Y, Okada Y, Takeda S, Harada A, Kanai Y, Kido M, Hirokawa N: Randomization of left-right asymmetry due to loss of nodal cilia generating leftward fl ow of extraembryonic fl uid in mice lacking KIF3B motor protein. Cell 1998; 95: 829–837.
16	Ticho BS, Goldstein AM, Van Praagh R: Extracardiac anomalies in the heterotaxy syndromes with focus on anomalies of midline-associated structures. Am J Cardiol 2000; 85: 729–734.

17	Noack F, Sayk F, Ressel A, Berg C, Gembruch U, Reusche E: Ivemark syndrome with agenesis of the corpus callosum: A case report with a review of the literature. Prenat Diagn 2002; 22: 1011–1015.
18	21 Polhemus D, Schafer WB: Congenital absence of the spleen: Syndrome with atrioventricularis and situs inversus. Pediatrics 1952; 9: 696– 708.
19	22 Rose V, Izukawa T, Moës CAF: Syndromes of asplenia and polysplenia. A review of cardiac and non-cardiac malformations in 60 cases with special reference to diagnosis and prognosis. Br Heart J 1975; 37: 840–852.
20	24 Casey B: Two rights make a wrong: Human left-right malformations. Hum Mol Genet 1998; 7: 1565–1571.
21	25 Lowe LA, Supp DM, Sampath K, Yokoyama T, Wright CV, Potter S, Overbeck P, Kuehn MR: Conserved left-right asymmetry of nodal expression and alterations in murine situs inversus. Nature 1996; 381: 158–161.
22	40 Casey B, Devoto M, Jones KL, Ballabio A: Mapping a gene for familial situs abnormalities to human chromosome Xq24–q27.1. Nat Genet 1993; 5: 403–407.
23	41 Ferrero GB, Gebbia M, Pilia G, Witte D, Peier A, Hopkin RJ, Craigen WJ, Shaffer LG, Schlessinger D, Ballabio A, Casey B: A submicroscopic deletion in Xq26 associated with familial situs ambiguous. Am J Hum Genet 1997; 61: 395–401.
24	42 Iida A, Emi M, Matsuoka R, Hiratsuka E, Okui K, Ohashi H, Inazawa J, Fukushima Y, Imai T, Nakamura Y: Identifi cation of a gene disrupted by inv(11)(q13.5;q25) in a patient with left-right axis malformation. Hum Genet 2000; 106: 277–287.
25	49 Splitt MP, Burn J, Goodship J: Defects in the determination of left-right asymmetry. J Med Genet 1996; 33: 498–503.
26	50 Burn J: Disturbance of morphological laterality in humans. Ciba Found Symp 1991; 162: 282–296.
27	52 Kosaki K, Bassi MT, Kosaki R, Lewin M, Belmont J, Schauer G, Casey B: Characterization and mutation analysis of human LEFTY A and LEFTY B, homologues of murine genes implicated in left-right axis development. Am J Hum Genet 1999; 64: 712–721.
28	25.LA, Supp DM, Sampath K, Yokoyama T, Wright CV, Potter S, Overbeck P, Kuehn MR: Conserved left-right asymmetry of nodal *expression and alterations in murine situs inversus. Nature 1996; 381: 158–161.*
29	55 Van Praagh S, Kakou-Guikahue M, Kim HS, Becker J, Alday L, Van Praagh R: Atrial situs in patients with heterotaxy and congenital heart disease: Conclusions based on fi ndings in 104 postmortem cases. Coeur 1988; 19: 484– 502.
30	Van Praagh S, Kreutzer J, Alday L, Van Praagh R: Systemic and pulmonary venous connections in visceral heterotaxy, with emphasis on the diagnosis of atrial situs: A study of 109 postmortem cases; in Clark E, Takao A (eds): Developmental Cardiology: Morphogenesis and Function. Mt Kisco/NY, Futura, 1990, pp 671–721.
31	Gayer G, Apter S, Jonas T, Amitai M, Zissin R, Sella T, Weiss P, Hertz M: Polysplenia syndrome detected in adulthood: Report of eight cases and

	review of the literature. Abdom Imaging 1999; 24: 178–184.
32	57 Gayer G, Apter S, Jonas T, Amitai M, Zissin R, Sella T, Weiss P, Hertz M: Polysplenia syndrome detected in adulthood: Report of eight cases and review of the literature. Abdom Imaging 1999; 24: 178–184.
33	Ivemark BI: Implications of agenesis of the spleen on the pathogenesis of conotruncus anomalies in childhood. Acta Paediatr Scand Suppl 1955; 44: 1–116.
34	60 Aylsworth AS: Clinical aspects of defects in the determination of laterality. Am J Med Genet 2001; 101: 345–355.
35	Khoury MJ, Cordero JF, Mulinare J, Opitz JM: Selected midline defect associations: A population study. Pediatrics 1989; 84: 266– 272.
36	Dyke MP, Martin RP, Berry PJ. *Septicaemia and adrenal haemorrhage in congenital asplenia. Arch Dis Child 1991;66:636-7.*
37	Murdoch IA, Anjos RD, Mitchell A. *Fatal pneumococcal septicaemia associated with asplenia and isomerism of the right atrial appendages. Br Heart J 1991;65:102-3.*
38	Waldman JD, Rosenthal A, Smith AL, Shurin S, Nadas AS. *Sepsis and congenital asplenia. J Pediatr 1977;90:555-9.*
39	Technical Report: Prevention of Pneumococcal Infections, Including the Use of Pneumococcal Conjugate and Polysaccharide Vaccines and Antibiotic ProphylaxisGary D. Overturf, the Committee on Infectious Diseases, Committee on InfectiousDiseases, *Pediatrics* 2000;106;367
40	Blieden LC, Moller JH. *Analysis of the P wave in congenital cardiac malformations associated with splenic anomalies. Am Heart J 1973; 85:439-44.*
41	Wren C, Macartney FJ, Deanfield JE. *Cardiac rhythm in atrial isomerism. Am J Cardiol 1987;59:1156-8.*
42	Dickinson DF, Wilkinson JL, Anderson KR, Smith A, Ho SY, Anderson RH. *The cardiac conduction system in situs ambiguus. Circulation 1979;59:879-85.*
43	Frogoudaki A, Sutton R, Gatzoulis MA. *Pacing for adult patients with left atrial isomerism: efficacy and technical considerations. Europace 2003;5:189-93.*
44	Humes RA, Feldt RH, Porter CJ, Julsrud PR, Puga FJ, Danielson GK. *The modified Fontan operation for asplenia and polysplenia syndromes. J Thorac Cardiovasc Surg 1988;96:212-8.*
45	Uemura H, Yagihara T, Kawahira Y, Yoshikawa Y. *Anatomic biventricular repair by intraatrial and intraventricular re-routing in patients with left isomerism. Cardiol Young 2001;11:12-6.*
46	Kawashima Y, Matsuda H, Naito Y, Yagihara T, Kadoba K, Matsuki O. *Biventricular repair of cardiac isomerism with common atrioventricular canal with the aid of an endocardial cushion prosthesis. J Th-orac Cardiovasc Surg 1993;106:248-53; discussion 253-4.*
47	Koh M, Yagihara T, Uemura H, et al. *Biventricular repair for right at-rial isomerism. Ann Thorac Surg 2006;81:1808-16; discussion 1816.*
48	Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. *Moss and Adams' He-art Disease in Infants, Children, and Adolescents. 7th ed. Philadelphia:*

	Lippincott William & Wikins;2008.
49	Kawashima Y, Kitamura S, Matsuda H, Shimazaki Y, Nakano S, Hirose H. *Total cavopulmonary shunt operation in complex cardiac anomalies: a new operation. J Thorac Cardiovasc Surg 1984;87:74-81.*
50	Stümper O, Wright JG, Sadiq M, De Giovanni JV. *Late systemic desaturation after total cavopulmonary shunt operations. Br Heart J 1995;74:282-6.*
51	Kim SJ, Bae EJ, Cho DJ, et al. *Development of pulmonary arteriovenous fistulas after bidirectional cavopulmonary shunt. Ann Thorac Surg 2000;70:1918-22.*
52	Kim SJ, Bae EJ, Lee JY, Lim HG, Lee C, Lee CH. *Inclusion of hepa-tic venous drainage in patients with pulmonary arteriovenous fistulas. Ann Thorac Surg 2009;87:548-53*
53	Kim SJ, Kim WH, Lim HG, Lee CH, Lee JY. *Improving results of the Fontan procedure in patients with heterotaxy syndrome. Ann Thorac Surg 2006;82:1245-51.*
54	21) Koh M, Yagihara T, Uemura H, et al. *Biventricular repair for right at-rial isomerism. Ann Thorac Surg 2006;81:1808-16; discussion 1816.*
55	22) Lim HG, Bacha EA, Marx GR, et al. *Biventricular repair in patients with heterotaxy syndrome. J Thorac Cardiovasc Surg 2009;137:371-9.*
56	23) Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. *Moss and Adams' He-art Disease in Infants, Children, and Adolescents. 7th ed. Philadelphia: Lippincott William & Wikins;2008.*
57	Walsh EP, Saul JP: Cardiac arrhythmias; in Fyler D (ed): Nadas' Pediatric Cardiology. Philadelphia, Hanley & Belfus Inc/Mosby, 1992, pp 377–433.
58	Momma, K., and Linde, L. M. (1970). Cardiac rhythms in dextrocardia. American Journal of Cardiology, 25, 420.
59	van der Horst, R. L., and Gotsman, M. S. (I972). Abnormalities of atrial depolarization in infradiaphragmatic interruption of inferior vena cava. British Heart Journal, 34, 295.
60	Landing, B. H., Lawrence, T. K., Payne, V. C., Jr., and Wells, T. R. (I97i). Bronchial anatomy in syndromes with abnormal visceral sitUs, abnormal spleen and congenital heart disease. American Journal of Cardiology, 28, 456.
61	Applegate KE, Goske MJ, Pierce G, Murphy D: Situs revisited: Imaging of the heterotaxy syndrome. Radiographics 1999; 19: 837–852.
62	Van Mierop LHS, Gessner IH, Schiebler GL: Asplenia and polysplenia syndromes. Birth Defects 1972; 8: 36–44.
63	Padmanabhan, J., Risemberg, H. M., and Rowe, R. D. (I973). Howell-Jolly bodies in the peripheral blood of full-term and premature neonates. Johns Hopkins Medical Journal, 132, 146.
64	Bridgen ML: Detection, education and management of the asplenic or hyposplenic patient. Am Fam Physician 2001; 63: 499–506.
65	42 Iida A, Emi M, Matsuoka R, Hiratsuka E, Okui K, Ohashi H, Inazawa J, Fukushima Y, Imai T, Nakamura Y: Identifi cation of a gene disrupted by inv(11)(q13.5;q25) in a patient with left-right axis malformation. Hum Genet 2000; 106: 277–287.

66	Van Praagh, R., Van Praagh. S., Vlad, P., and Keith, J. D. (I964). Anatomic types of congenital dextrocardia, diagnostic and embryologic implications. American J7ournal of Cardiology, 13, 5I0.
67	Phoon CK, Villegas MD, Ursell PC, Silverman NH: Left atrial isomerism detected in fetal life. Am J Cardiol 1996; 77: 1083–1088
66	Geva T, Vick GW 3rd, Wendt RE, Rokey R: Role of spin echo and cine magnetic resonance imaging in presurgical planning of heterotaxy syndrome. Comparison with echocardiography and catheterization. Circulation 1994; 90: 348–356.
67	Ivemark, B. I. (I955). Implications of agenesis of the spleen on the pathogenesis of conotruncus anomalies in childhood: analysis of the heart malformations in splenic agenesis syndrome, with fourteen new cases. Acta Paediatrica, 44, Suppl. 104, I.
68	Freedom, R. M. (I972). The asplenia syndrome: a review of significant extracardiac structural anomalies in 29 necropsied patients. Journal of Pediatrics, 8i, I130.
69	Sapire DW, Ho SY, Anderson RH, Rigby ML. Diagnosis and significance of atrial isomerism. Am J Cardiol 1986;58:342– 6.
70	29 Morgan D, Turnpenny L, Goodship J, Dai W, Majumder K, Matthews L, Gardner A, Schuster G, Vien L, Harrison W, Elder FFB: Inversin, a novel gene in the vertebrate left-right axis pathway, is partially deleted in the inv mouse. Nat Genet 1998; 20: 149–156.
71	Chandra RS: Biliary atresia and other structural anomalies in the congenital polysplenia syndrome. J Pediatr 1974; 85: 649–655.
72	Bartz PJ, Driscoll DJ, Dearani JA, et al. *Early and late results of the modified fontan operation for heterotaxy syndrome 30 years of experience in 142 patients. J Am Coll Cardiol 2006;48:2301-5.*

STUDY-2

Prevalence and predictors of coronary artery disease in Patients Undergoing Repair of Aortic Aneurysms.

INTRODUCTION

Cardiac complications constitute the principal cause of early and late morbidity and mortality after the surgical treatment of abdominal aortic aneurysm (AAA). The importance of preoperative evaluation of the coronary artery and a required myocardial revascularization has been emphasized for the improvement of early, and late survival after AAA repair.[1]

When significant coronary artery disease (CAD) is present in patients scheduled for AAA repair, treatment of CAD will be selected from percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), or medical treatment on the basis of the severity of coronary artery lesions and ischemic symptoms. There have been many reports demonstrating the incidence of CAD in AAA, and the reported incidence ranged from 40 to 60%.[2,3]

The preoperative cardiovascular assessment for elective surgery of AAA remains controversial. According to the 2007 guidelines of the American College of Cardiology (ACC) and American Heart Association (AHA), routine screening of the cardiovascular system, even for vascular surgery, is not recommended.[4] However, this does not mean that these patients would not need any screening for cardiovascular disease (CVD) after the operation because these patients usually have more risks of CVD and early detection could change the subsequent management that may improve life expectancy in patients undergoing AAA repair.

AIM OF THE STUDY

1) To find out the incidence of significant coronary artery disease in patients with aortic aneurysm who required surgery .
2) To find out the predictors of concomitant coronary artery disease in patients with aortic aneurysm.
3) To review preoperative coronary evaluation and the choice of treatment.

Exclusion criteria : Patients who underwent emergency surgery due to complication

REVIEW OF LITERATURE

The aorta has a complex intrinsic biology and sophisticated mechanical properties involving intrinsic relaxation and contraction that interact with left ventricular ejection to enhance hemodynamic function.

The major conductance vessel of the body, the aorta is an elastic artery with a trilaminar wall: the tunica intima, tunica media, and tunica adventitia. The predominance of elastic fibers in the aortic wall and their arrangement as circumferential lamellae distinguish this elastic artery from the smaller muscular arteries. A lamellar unit comprises two concentric elastic lamellae and the smooth muscle cells, collagen, and ground substance contained within. The thoracic aorta incorporates 35 to 56 lamellar units and the abdominal aorta about 28 units.[5]

The ascending aorta is approximately 3 cm in diameter, depending on age, gender, and body surface area. The diameter of the aortic arch is similar. Descending in the posterior mediastinum, the thoracic aorta tapers slightly to about 2 to 2.3 cm. The abdominal aorta narrows to 1.7 to 1.9 cm in its distal portion. The aortas of males are larger than those of females, and aortic root dimension increases with age, height, and weight. The gender difference in aortic root dimension is not entirely explained by body surface area.[5]

Changes with Age and Disease

Each of the four components of the aortic wall—elastic tissue, collagen fibers, smooth muscle cells, and mucoid ground substance—changes with age. Elastic fibers fragment, collagen becomes more prominent at the expense of smooth muscle cells, and glycosaminoglycans accumulate. As a result, the aorta becomes less distensible; reducing its capacity to absorb the forces derived form left ventricular contraction. [7] Weakening of the aortic wall leads to dilatation of the lumen, as well as elongation and uncoiling of the aortic arch, collectively producing ectasia.

The combination of inherited, degenerative, mechanical, and hemodynamic factors adversely affects the medial layer of the aortic wall, leading to dilatation and setting the stage for the catastrophes of aortic dissection or rupture.

Definitions and Categories

The aorta can be affected by a variety of pathologic processes leading to aneurysm, dissection, or ischemic syndromes. The term aneurysm—derived from the Greek aneurysma, referring to dilatation—is distinguished from ectasia, which refers to the modest generalized dilatation and elongation of the aorta that occurs with aging.[8]

The criterion for definition of small aneurysms is controversial. Although the size of the normal aorta varies with gender and body size, most would agree that maximum diameter of the thoracic aorta should not exceed 4 cm. For the abdominal aorta, which normally has a smaller diameter than the thoracic segments, it has been suggested that the term aneurysm be restricted to situations where the diameter exceeds 3 cm.[9] Another proposed definition depends on the affected segment having a diameter more than 1.5 to 2 times normal.[10]

Aneurysm formation can be considerably more widespread along the length of the aorta than obstructive atherosclerotic disease, potentially affecting almost the entire vessel, whereas obstruction tends to involve only the abdominal portion of the aorta, when the iliac arteries are commonly affected as well.

Over the course of normal aging, degenerative changes occur throughout most of the length of the aorta, leading to a mild form of what is termed cystic medial necrosis. Although essentially a normal physiologic process of aging, cystic medial necrosis develops more rapidly in patients with bicuspid aortic valve, during pregnancy, and very markedly in the Marfan syndrome.

Cystic medial necrosis is the most common cause of ascending aortic aneurysm, and although this type of aortic pathology is typical of patients with the Marfan syndrome, it may also occur in the absence of any clinical Marfan stigmata.

Ascending Aortic Aneurysms

Ascending aortic aneurysms occur more frequently in men than in women, are typically fusiform, and extend into the aortic arch. Consequently, aneurysms of the aortic arch are often contiguous with aneurysms in the ascending aorta. Ascending aortic aneurysms are divisible into three categories according to the pattern of involvement of the aortic root, with direct implications for surgical treatment. The

most common type is supracoronary aneurysm, others were annuloaortic ectasia, and tubular type of ascending aortic aneurysm.

Descending Thoracic Aortic Aneurysms

In contrast to the ascending aorta, the majority of aneurysms of the descending thoracic aorta are atherosclerotic.[12] These are typically fusiform, may extend to the level of the abdominal aorta, and often begin distal to the origin of the left subclavian artery. Descending thoracic aneurysms may also develop in patients with aortic coarcation.

Abdominal Aortic Aneurysms

In more than 90 percent of cases, the superior margins of abdominal aneurysms are distal to the renal arteries. Atherosclerosis has been held responsible for the majority, although some authors suggest that atherosclerosis may be a secondary phenomenon in aneurysmal disease.

Thoracoabdominal Aortic Aneurysms

As suggested by the nomenclature, thoracoabdominal aortic aneurysms have features of both thoracic and abdominal aortic aneurysms. Although they constitute only approximately 3 percent of all aortic aneurysms, thoracoabdominal aneurysms are considered as a separate class because of the diffuse and extensive aortic involvement in the disease process (usually atherosclerosis) and special considerations for surgical repair, which may entail reimplantation of the origins of visceral arteries.

Epidemiology of Aneurysmal Disease

Aortic aneurysmal disease is the 17th most common cause of death in all individuals and the 15th most common in individuals older than 65 years of age. Abdominal aortic aneurysm affects approximately 5 percent of individuals older than age 65 years, and the prevalence is considerably higher in men than women.[14]

The annual incidence of ruptured abdominal aortic aneurysm is approximately 10 per 100,000 population, and is similar in men and women. However, age at diagnosis is a decade higher in women.[15] For men in their sixties, the rate rises to approximately 50 per 100,000, and for those in their seventies, the rate exceeds 1 in 1000 men suffering rupture of abdominal aortic aneurysm each year.

The incidence of thoracic aortic aneurysm is also approximately 10 per 100,000 population, and is similar in women and men, but the age at diagnosis is a decade higher in women (seventies). The yearly incidence of rupture or dissection of an existing thoracic aortic aneurysm is approximately 7 percent, divided equally between rupture and dissection. A curious and as yet unexplained finding is that 79 percent of thoracic aortic aneurysm ruptures occur in women.[15]

Natural History, Prognosis, and Clinical Decision-Making

Thoracic aortic aneurysm is associated with approximately 50% mortality over 5 years, but not all deaths in these cohorts are directly attributable to aneurysm. On average, aneurysms of the aorta expand at a rate of about 0.1 cm annually, the descending aorta enlarging somewhat more rapidly than the ascending aorta. Such aneurysms usually develop over decades, so imaging is seldom necessary more often than once a year, and often only every 2 or 3 years, depending on the initial diameter and other factors.

Concomitant Coronary Artery Disease

The most important risk factor for cardiac events and death in patients undergoing aneurysm surgery is coronary artery disease. Because operative mortality is related mainly to myocardial ischemia, it has been suggested that coronary revascularization be performed in selected patients prior to abdominal aortic aneurysm resection.[17,18]

No well-designed studies are available, however, comparing the outcome of serial myocardial revascularization and abdominal or thoracic aortic aneurysm repair with aneurysm surgery alone. Even so, an effort should be made to identify preoperatively those patients at highest cardiac risk using noninvasive diagnostic methods. Findings of extensive myocardial ischemia may prompt angiography to define the coronary patho anatomy and LV function.

Thereafter, decisions regarding coronary revascularization must be based on symptoms, angiographic findings, and other elements of risk. One anticipates a survival advantage imparted by surgical revascularization in patients with left main coronary artery disease or stenosis greater than 70 percent involving each of the three major coronary arteries in patients with substantial zones of ischemia. In those with severe discrete proximal stenosis of a first-order coronary artery and either

symptomatic or extensive ischemia or reversible left ventricular dysfunction amenable to catheter-based myocardial revascularization, clinical decision making must balance the long-term advantages of drug-eluting intracoronary stents against the need for potent platelet inhibitor therapy that may be difficult to administer in the days prior to and following aortic aneurysmectomy.

Furthermore, in patients soon to undergo aortic reconstructive surgery, coronary balloon angioplasty or bare-metal stenting may be preferred, even though the potential for coronary restenosis may later require a second revascularization procedure ..

ASSESSING OPERATIVE RISK.

Because patients with abdominal aortic aneurysms , almost all cases have atherosclerosis and their high likelihood of concomitant coronary, renal, and cerebrovascular arterial disease significantly increases the risk of major vascular surgery.

One-half of all perioperative deaths from aneurysm repair result from myocardial infarction. In addition, in one study, routine coronary arteriography in patients undergoing aneurysm repair revealed severe revascularizable coronary artery disease in 18 percent of all patients, including an 8 percent incidence in patients without prior symptoms of coronary ischemia.[19] Among those with angiographically significant coronary artery disease, about one-half have multivessel disease.

Several studies have demonstrated that cardiac scintigraphy is an effective means of identifying patients at highest risk for perioperative ischemic events. Patients with reversible perfusion defects in multiple segments of myocardium are at highest risk, and it is in this subgroup that coronary angiography is likely to be most helpful. Although exercise scintigraphy is also a useful screening method, many patients with vascular disease fail to achieve an adequate heart rate because of limited exercise capacity. Other useful techniques for preoperative evaluation of myocardial ischemia include dobutamine stress echocardiography and electrocardiographic exercise testing in patients with a normal baseline electrocardiogram and adequate exercise tolerance.

Selective preoperative evaluation to identify the presence and severity of coronary artery disease in patients with clinical markers of coronary artery disease has been widely advocated, and some investigators further suggest screening those with strong cardiac risk factors despite the absence of clinical evidence of coronary artery disease.

Although patients found to have significant revascularisable coronary artery disease are presumed to benefit from preoperative coronary revascularization with selective coronary artery bypass surgery or angioplasty, this conclusion remains unproved. Data available from nonrandomized studies demonstrate lower mortality for those who have undergone coronary bypass surgery. Furthermore, a randomized study demonstrated that the long-term outcome of patients with combined peripheral vascular disease and high-risk coronary artery disease is improved by coronary artery revascularization in patients with three-vessel coronary disease. As is the case for coronary artery bypass surgery, no data are yet available to confirm that preoperative percutaneous coronary revascularization for significant coronary stenoses decreases the risk from major vascular surgery.

In addition to preoperative screening and potential coronary revascularization, the use of perioperative invasive hemodynamic monitoring and careful perioperative surveillance for evidence of ischemia may further reduce operative risk secondary to cardiac ischemic events.

Coronary revascularization

Coronary revascularization has been suggested as a means of reducing perioperative risk surrounding noncardiac surgery. Previous retrospective evidence indicates that prior successful preoperative revascularization may decrease postoperative cardiac risk twofold to fourfold in patients undergoing elective vascular surgery. The strongest evidence comes from the Coronary Artery Surgery Study (CASS) Registry, which enrolled patients from 1978 to 1981. The operative mortality for patients with CABG before noncardiac surgery was 0.9 percent but was significantly higher (2.4 percent) in patients without prior CABG. However, there was a 1.4 percent mortality rate associated with the CABG procedure itself.

Eagle and colleagues[20] reported a long-term analysis of patients entered into CASS and assigned to medical or surgical therapy for coronary artery disease for

more than 10 years who subsequently underwent 3368 noncardiac operations in the years following assignment of coronary treatment. Intermediate-risk surgery such as abdominal, thoracic, or carotid endarterectomy was associated with a combined morbidity and mortality of 1 to 5 percent with a small but significant improvement in outcome in patients who had undergone prior revascularization. The most significant improvement in outcome was in patients undergoing major vascular surgery such as abdominal or lower extremity revascularization. However, this observational study did not randomize patients and was undertaken in the 1970s and 1980s before significant advances in medical, surgical, and percutaneous coronary strategies.[20]

Landesberg and colleagues[21] reported retrospectively reviewed long-term outcome in 578 major vascular procedures. By multivariate analysis, age, type of vascular surgery, presence of diabetes, previous MI, and moderate-severe ischemia on preoperative perfusion imaging independently predicted mortality, and preoperative coronary revascularization predicted improved survival. Long-term survival after major vascular surgery significantly improved if patients with moderate to severe ischemia on preopera-tive perfusion imaging underwent selective coronary revascularization.

Several cohort studies have examined the benefit of percutaneous coronary intervention (PCI) before noncardiac surgery. Posner and colleagues used an administrative data set of patients who underwent PCI and noncardiac surgery in Washington State.[22] They matched patients with coronary disease undergoing noncardiac surgery with and without prior PCI and looked at cardiac complications. In this nonrandomized design, they noted a significantly lower rate of 30-day cardiac complications in patients who underwent PCI at least 90 days before the noncardiac surgery. Importantly, PCI within 90 days of noncardiac surgery did not improve outcome. Moreover, the advent of drug-eluting stents that involve prolonged antiplatelet therapy may promote operative bleeding complications or increase subacute stent thrombosis if antiplatelet treatment stops perioperatively.

Poldermans and colleagues[23] randomized patients at intermediate risk to *testing and interventions / no testing* demonstrated no difference in 30-day cardiac events. Given the results of the older cohort series, further research is necessary to

define the value of prophylactic coronary artery revascularization in the highest-risk patients.

The DECREASE II trial39 was designed to evaluate the utility of cardiac testing in patients undergoing major vascular surgery with intermediate cardiac risk. This study confirms that **extensive cardiac ischemia** is a risk factor for perioperative cardiac events, but it was too small to assess the effect of revascularization.

The DECREASE-V pilot study40 identified a high-risk cohort of patients scheduled for vascular surgery who were randomized to best medical therapy and revascularization or best medical therapy alone before vascular surgery. There was no difference in the combined outcomes of death or MI at 30 days or 1 year between the revascularization and medical therapy groups, although there was a high incidence of cardiac events in this high-risk cohort.

Several randomized trials now address the value of both CABG and PCI in a subset of patients. McFalls and colleagues[24] reported the results of a multicenter randomized trial in the Veterans Administration Health System in which patients with documented CAD on coronary angiography, excluding those with left main disease or severely depressed ejection fraction (<20 percent), were randomized before elective major vascular surgery to CABG (59 percent) or PCI (41 percent) versus routine medical therapy. At 2.7 years after randomization, mortality in the revascularization group was not significantly different (22 percent) compared with the no-revascularization group (23 percent). Within 30 days after the vascular operation, a postoperative MI, defined by elevated troponin levels, occurred in 12 percent of the revascularization group and 14 percent of the no-revascularization group ($p = 0.37$). The authors suggested that coronary revascularization is not indicated in patients with stable CAD and further support the lack of efficacy of PCI or CABG for single- or double-vessel disease before noncardiac surgery. In a reanalysis of the data, the completeness of the revascularization affects the rate of perioperative MI with CABG being more effective than PCI.[25]

One issue in interpreting the results is that length of time between the coronary revascularization and noncardiac surgery most likely affects its protective effect and potential risks. Back and colleagues[26] concluded that previous coronary revascularization (CABG, >5 years; PTCA, >2 years) may provide only modest

protection against adverse cardiac events and mortality following major arterial reconstruction.

PCI using coronary stenting poses several special issues. Kaluza and colleagues[27] reported the outcome in 40 patients who underwent prophylactic coronary stent placement less than 6 weeks before major noncardiac surgery requiring a general anesthesia. They reported 7 MIs, 11 major bleeding episodes, and 8 deaths. All deaths and MIs, as well as 8 of 11 bleeding episodes, occurred in patients subjected to surgery fewer than 14 days after stenting. Four patients expired after undergoing surgery 1 day after stenting.

Wilson and colleagues[28] reported on 207 patients who underwent noncardiac surgery within 2 months of stent placement. A total of 8 patients died or suffered an MI, and all 8 were among the 168 patients undergoing surgery 6 weeks after stent placement. Vincenzi and colleagues[29] studied 103 patients and reported that the risk of a perioperative cardiac event was 2.11-fold greater in patients with recent stents (<35 days before surgery) as compared with PCI more than 90 days before surgery.[29]

On the basis of the accumulating data, elective noncardiac surgery after PCI, with or without stent placement, should be delayed for 4 to 6 weeks.

Drug eluting stents may represent an even greater problem during the perioperative period on the basis of a series of recent analyses. Data is emerging that suggest that the risk of thrombosis continues for at least 1 year after insertion. [30] Nasser and colleagues described two patients with in-stent thrombosis occurring 4 and 21 months after implantation of sirolimus-eluting stents.[31] A science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association was published in 2007 that stresses the importance of 12 months of dual antiplatelet therapy after placement of a drug-eluting stent.[32] It also recommends postponing elective surgery for 1 year, and, if surgery cannot be deferred, considering the continuation of aspirin during the perioperative period in high-risk patients with drug-eluting stents.

Review of the literature suggests that PCI before noncardiac surgery is of no value in preventing perioperative cardiac events, except in those patients in whom PCI is independently indicated for an acute coronary syndrome.[4]

Rapid endothelialization of bare-metal stents makes late thrombosis rare, and thienopyridines are rarely needed for more than 4 weeks after implantation of baremetal stents. For this reason, delaying surgery 4 to 6 weeks after bare-metal stent placement allows proper thienopyridine use to reduce the risk of coronary stent thrombosis; then, after the thienopyridine has been discontinued, the noncardiac surgery can be performed.

In the setting of noncardiac surgery in patients who have recently received a bare-metal stent, the risk of stopping dual-antiplatelet agents prematurely (within 4 weeks of implantation) is significant compared with the risk of major bleeding from most commonly performed surgeries.

There is little evidence to show how long a more distant PCI (ie, months to years before noncardiac surgery) protects against perioperative MI or death. [4]

MATERIALS AND METHODS

Study Population: Patient medical records and imaging study results were retrospectively reviewed for 53 consecutive patients who were evaluated for elective graft replacement for Aortic aneurysm from January 2009to january 2012 at the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST)Trivandrum.

Methods : The baseline clinical characteristics (physical examination, smoking habit, familial vascular history, cardiovascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, and standardized noninvasive screening test were evaluated using hospital records.

A patient was diagnosed as having "significant stenosis" when CAG demonstrated the stenosis 70% in at least one major coronary artery or in its main branch. In addition to CAG, all patients underwent a standard electrocardiogram and echocardiography for the assessment of myocardial ischemia and viability. Clinical symptoms related to myocardial ischemia were also checked carefully in the patient's record and history.

When the patient presented with significant CAD showing myocardial ischemia, the treatment option for the CAD was determined by the standard guidelines. When CABG was indicated for a patient with significant CAD, the patient underwent either CABG as the first operation followed by AAA repair or a combined CABG and AAA repair simultaneously.

Isolated CABG was performed with the use of standard cardiopulmonary bypass (CPB) In the case of combined CABG and AAA repair, CABGwas performed first and the sternotomy incision was extended to the pubic symphysis. Abdominal aortic surgery was carried out after the patient was weaned off CPB.

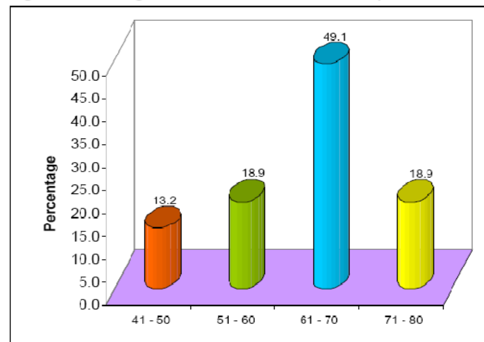
Statistical analysis: All continuous variables are presented as the mean standard error (SEM). Univariate analysis was conducted with Student's t-test for comparisons of continuous variables, and the chi-square test for dichotomous variables. All analyses were performed with SPSS software (SPSS Inc., Chicago, IL). Difference was considered significant at $p<0.05$.

RESULTS

This study included 53 patients (90.6% male and 9.4% female with M:F 9.6: 1) who underwent coronary angiogram prior to Aneurysm surgery .

Most of the patients are between 61-70yrs (49%) with mean age of 62.5+/- 9.6 yrs

Fig. Percentage distribution of the sample according to age



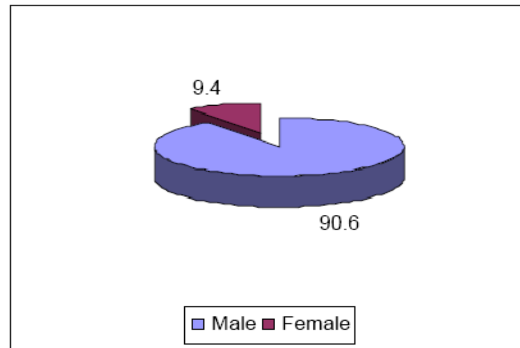


Table 1 Percentage distribution of risk factors

Risk factors	Count	Percent
Nil	8	15.1
Hypertension(HT)	30	56.6
Diabetes (DM)	17	32.1
Dyslipidemia(DLP)	8	15.1
Smoking(SM)	31	58.5

Majority of patients (84.9%) patients were having one or more risk factors . Most of them are smokers (58.5%) followed by hypertension (56.6%) Diabetes (32.1%) and DLP (15.1%). Only 15.1% of the patients were with out major risk factors .

Most of the patients are having normal body mass index (71.7 %). Over weight was noticed in 15.1 % and none were obese .

Abdominal pain (58.8 %) was the most common presenting complaint followed by back ache (20.8%) dyspnea (17 %) chest pain (17%) and leg pain (7.9%) . In 13.1 % of patients aneurysm was detected during evaluation of other diseases.

Table 2 Percentage distribution of the sample according to history of CAD

History of CAD	Count	Percent
Nil	41	77.3
Acute coronarysyndrome (ACS)	1	1.8
Non ST elevation MI (NSTEMI)	5	9.4
Anterior wall MI (AWMI)	3	5.5
Coronary artery bypass graft(CABG)	3	5.5

Majority (77.3 %) of the patients didn’t give prior history of coronary artery disease . previous history of Non ST elevation MI was present in 9.4 % , about 5.5 % of patients had history of Anterior Wall MI and history of CABG was present in 5.5% patients .

Table 3 Incidence of Coronary artery disease in various types of aortic aneurysm

Types of Aortic aneurysm	**Incidence of CAD**			
	Yes		**No**	
	Count	**Percent**	**Count**	**Percent**
Infra renal abdominal aortic aneurysm (IRAAA)	**16**	**55.2**	**13**	**44.8**
Juxta renal abdominal aortic aneurysm (JRAAA)	**3**	**50.0**	**3**	**50.0**
Thoraco abdominal aortic aneurysm (TAAA)	**3**	**30.0**	**7**	**70.0**
Supra renal abdominal aortic aneurysm (SRAAA)	**0**	**0.0**	**1**	**100.0**
Ascending aortic aneurysm (ASAOA)	**1**	**25.0**	**3**	**75.0**
Descending thorasic aortic aneurysm (DTAA)	**0**	**0.0**	**1**	**100.0**
Arch aneurysm	**1**	**100.0**	**0**	**0.0**
Aneurysm involving ascending ,arch and descending aorta	**0**	**0.0**	**1**	**100.0**

Of the 53 elective cases of aortic aneurysm who underwent coronary angiogram 24 (45%) had significant coronary artery disease. Out of this significant coronary artery disease patients, majority had single vessel disease followed by two vessel and three vessel disease.

Incidence of coronary artery disease was significantly high in abdominal aortic aneurysm patients (53%) followed by Thoraco-abdominal aortic aneurysm(30%).The incidence of coronary artery disease was negligible in other group of aortic aneurysm.

Preoperative clinical characteristics that did not show any statistical difference between the groups with and without CAD were: age, 64.7 +/-9.7 vs 60.8. ±9.3 yrs ; BMI 22.6+/-3 vs 21.3+/-4.9 , Gender (p 0.33) and smoking (p0.98) .

Preoperative clinical characteristics that showed significant statistical difference between the two groups were: The incidence of **Hypertension** 63.3% vs 34.7% , **Dyslipidemia** 87.5% vs 12.5% and **diabetes** 64.7% vs 35.3% .

Table 4 distribution according to type of revascularisation

Revascularisation	Count	Percent
Nil	42	79.2
CABG	4	7.5
Combined CABG+aneurysm Surgery	1	1.9
PTCA	6	11.3

Of all patients with CAD, 20.8% underwent coronary revascularization before or during aortic surgery. Of this 11.3 % patients underwent percutaneous coronary revascularization , 7.5% undergone coronary artery bypass graft prior to surgery and one patient underwent simultaneous CABG and aneurysm surgery

Table 5 Percentage distribution of cause of death

Cause of death	%(n)	CAD status	Revascularization status
Cardiac arrest	16.7%(1)	SVD	Combined CABG+SX
Intraop Hemorrage	16.7%(1)	Normal coronaries	0
Intraop Mycocordial failure	16.7%(1)	SVD	PTCA
Mods - Sepsis	16.7%(1)	Normal coronaries	0
Renal failure	33.3%(2)	Normal coronaries 2VD	0 CABG

Most of the death (66.7% , n-4) are due to complication of sepsis ,Renal failure and hemorrhage .Only 33.4 %(n-2) were due to myocardial failure or cardiac arrest.

Patient who sustained intra operative myocardial failure had history of single vessel coronary artery disease on pre operative coronary angiogram and underwent percutaneous bare metal stent implantation prior to surgery.

The other patient who sustained cardiac arrest intra operatively had single vessel disease and underwent combined CABG and aortic surgery.

Table 6 Percentage distribution of outcome

	Post op MI	EXPIRED	SURVIVED
Coronary artery disease(CAD)	1 (4.8)	3 (14.3)	17 (81)
NO CAD	0 (0)	3 (10.7)	25 (89.3)

In our study most of the patients with coronary artery disease (81%) underwent surgery uneventfully.Post operative MI was observed in only 4.8% of cases .14.3% of patients expired in the coronary artery disease group. In those patients with out coronary artery disease 89.3% of cases survived after surgery .10% of patients in this group expired .

In those patients underwent revascularization 70% underwent surgery uneventfully 30 % of patients expired in this group. In CAD patients without revascularization 92.3% survived the surgery where as 7.7% expired perioperatively .

Table 7 Percentage distribution of outcome

	EXP	survived
Revascularisation status		
Nil	3 (7.7)	36 (92.3)
CABG	1 (25)	3 (75)
Combined CABG+aneurysm Surgery	1 (100)	0 (0)
PTCA	1 (20)	4 (80)

The mortality in patients who underwent CABG and PTCA prior to surgery was 25% and 20% respectively. But the only one patient who underwent combined surgery of CABG and Aortic surgery expired intra operatively due to cardiac arrest.

DISCUSSION

In our study the 53 patients who underwent Coronary angiogram (CAG) prior to Aneurysm surgery out of which 90.6% were male and 9.4% were female .It shows a trend towards increased incidence of Aortic aneurysm in male gender.

Most of the population – based studies [33,34] showed a trend towards a higher male prevalence among AAA cases . Poon et al.[35] exclusively detected AAA in male CAD patients when using the common AAA definition "infrarenal aortic diameter ≥ 30 mm". Our study also tallies the previous study results .

The age distribution in our study was from 41 yrs to 80 yrs out of which most of the patients were aged between 61-71 (49.1%), least number of patients was found in the 41-50 yrs group (13.2%) It shows a significant relation exists between age and incidence of Aortic aneurysm.In a meta analysis Nine studies only seven find an association [33,35]. Age was associated with AAA by multivariate analysis after adjustment for other known risk factors in 4 studies . In Nemati et al., ROC curve analysis showed that age of patients with CAD (67 years) predicted the presence of AAA with a sensitivity and specificity of 75% and 80%, respectively [34]

The result in our study supports the guidelines that favor one time AAA screening for male patients of 65 years or older in the general population. The low prevalence of aortic aneurysm in younger group of our study population supports the previous belief of only the AAA that are vulnerable to rupture benefitted from screening at an earlier age [36]

In our study 84.9% of the patients are having one or more risk factors . Most of them are smokers (58.5%) and Only 15.1% of the patients were without major risk factors.

In population – based studies, smoking may be more strongly associated with AAA than with CAD (3 fold) or with cerebrovascular disease (5 fold) [37] . It also was strongly associated with AAA progression and rupture.

The duration of smoking is more important than the current or past smoking in AAA , as the risk of AAA after cessation of smoking was not statistically different from the risk of current smokers [38] This relative slow decline in risk differs strongly

between AAA and CAD. Cessation of smoking is strongly advisable in our study population as it can definitely alter the cardiovascular morbidity and mortality.

Incidence of Diabetes was 32.1% in our study population .Meta analysis of 7 studies on AAA prevalence in CAD patients, Five studies reported no association. So DM, a strong coronary atherosclerosis risk factor, may therefore lack an association with AAA prevalence in CAD patients.[39]

Incidence of hypertension was 56.6% in the study population Seven papers on AAA prevalence in CAD patients evaluated the association between AAA and arterial hypertension. Only two confirmed a significant association [40,41]. Arterial hypertension seems to be more positively associated with coronary heart disease and cerebrovascular disease than with aneurysm formation. These findings indicate that a history of hypertension should not be held as a significant risk factor for AAA among CAD patients.

Incidence of dyslipidemia was 15.1% in our study population .Few studies did evaluate the association between serum lipoproteins levels or history of dyslipidemia and AAA prevalence [33,40,41] None found a statistically significant association. Moreover, in view of current guidelines on atherosclerosis treatment, one cannot construct a study on association between basal lipid profile and AAA prevalence in CAD patients without lipid modifying therapy prescription.

Our study doesn't support any association between obesity and abdominal aortic aneurysm , as majority of patients are having normal BMI .Overweight was noted in 15% and none were obese. As far as obesity is concerned, previous studies reported the lack of association between AAA and BMI in CAD patients [33,40]. A potential association between obesity and AAA or infrarenal aortic diameter in CAD patients requires evaluation by further studies.

Our study support the fact that , in a CAD population, all evaluated potential AAA risk factors are also well – known CAD risk factors. Among these, only age , male gender and smoking seem to have a specific impact on AAA prevalence among CAD patients.

Even though 79.1% of the patients didn't give any history of coronary artery disease,after angiography 52.7% of patients with Abdominal aortic aneurysm showed significant coronary artery disease .It shows that a significant proportion of Aortic

aneurysm patients are having concomitant silent myocardial ischemia .This may be due to the common etiology of atherosclerosis in both diseases. These results were comparable to the previous studies which has been reported a high incidence of coronary artery disease (approximately 50%) in abdominal aortic aneurysm [19,42,43].

The high incidence of coronary artery disease in abdominal aortic aneurysm than the general population, (< 60yrs -2.5% and > 70yrs - >10%. [44]) may be due to the common risk factors contributing development of coronary artery disease and abdominal aortic aneurysm.

Thoraco abdominal aneurysm also showed a high prevalence of coronary artery disease .But in other types the incidence of CAD was negligible, as atherosclerosis doesn't play a role in aneurysm formation .

Table 8 Comparison of selected variables based on incidence of CAD

		Incidence of CAD				χ^2	**p**
		Yes		**No**			
		Count	**Percent**	**Count**	**Percent**		
Sex	**Male**	**23**	**47.9**	**25**	**52.1**	**1.42**	**0.233**
	Female	**1**	**20.0**	**4**	**80.0**		
Risk factors	**Nil**	**2**	**25.0**	**6**	**75.0**	**1.56**	**0.211**
	HT	**19**	**63.3**	**11**	**36.7**	**9.09****	**0.003**
	DM	**11**	**64.7**	**6**	**35.3**	**3.81**	**0.051**
	DLP	**7**	**87.5**	**1**	**12.5**	**6.78****	**0.009**
	Smocking	**14**	**45.2**	**17**	**54.8**	**0**	**0.983**

Table 9 Comparison of selected variables based on incidence of CAD

	Incidence of CAD						**t**	**p**
	Yes			**No**				
	Mean	**SD**	**N**	**Mean**	**SD**	**N**		
Age	**64.7**	**9.7**	**24**	**60.8**	**9.3**	**29**	**1.5**	**0.140**
BMI	**22.6**	**3.0**	**24**	**21.3**	**4.9**	**29**	**1.1**	**0.277**

Eventhough age, male gender and smoking are significant risk factors for development of aortic aneurysm, in our study they were non-significantly distributed in patients with/without concomitant coronary artery disease.

As most of the patients in this study group had normal body mass index , no significant difference was noted between two groups .Further large scale studies are needed to find out the association of obesity and concomitant coronary artery disease in the setting of aortic aneurysm.

Even though only 15% of our study population had dyslipidemia, a considerable number of patients with significant coronary artery disease had dyslipidemia (p-0.009). This suggest that ,its presence in abdominal aortic aneurysm (AAA) may indicate co-existing coronary artery disease.

Similar association was found in hypertension(p0.003) and diabetes mellitus(p0.051) Because silent myocardial ischemia correlates with serious or fatal cardiac events, routine screening to assess significant coronary artery disease should be performed for patients with AAA having dyslipidemia ,hypertension and diabetic mellitus.

The incidence of post operative death were numerically more in the coronary artery disease group .but its significance could not be assessed assess as the number of cases were small in both groups.

Table 10 Outcome against revascularization status

REVASCULARISED	EXP	survived	P
No	3 (7.7)	36 (92.3)	0.055
Yes	3 (30)	7 (70)	

There was no statistically significant difference in death in both revascularised and non- revascularised group. This result was supported by a multicenter randomized trial in the Veterans Administration Health System by McFalls and colleagues[24] In which patients with documented CAD on coronary angiography were randomized before elective major vascular surgery to CABG or PCI versus routine medical therapy. At 2.7 years after randomization, mortality in the revascularization group was not significantly different (22 percent) compared with the no-revascularization group (23 percent).

Since the number of patients were small in our study , it was not possible to demonstrate which method of revascularization (CABG vs PTCA) is better regarding survival and peri operative cardiac events . A randomized trial suggested that since

CABG offers more complete revascularization , the rate of perioperative MI with CABG was significantly lower than PCI.[45]

In our study, combined surgery showed a high mortality -indicating elective revascularization is better whenever indicated rather than combining both CABG and aortic surgery .This high mortality may be due to the additional pump time required for the combined procedure.

There was one case of Post operative Myocardial infarction in an asymptomatic patient who was detected to have two vessel disease on pre operative evaluation who didn't undergo revascularization in view of asymptomatic CAD status .But the significance of this is difficult to assess due to inadequate sample size. McFalls and colleagues[24] in their randomized study reported that the incidence post operative MI was not different in revascularization group and no-revascularization group (p = 0.37), and suggested that coronary revascularization is not indicated in patients with stable CAD.

Limitations

The main limitation of this study were

1) Small population in a single center.
2) It was a retrospective study

CONCLUSIONS

This study confirmed a high prevalence of coexistent silent myocardial ischemia in abdominal aortic aneurysm. Our study support the fact that, potential AAA risk factors are also well – known CAD risk factors. Among these, only age, male gender and smoking seem to have a specific impact on AAA prevalence among CAD patients.

Different predictors existed among different coexistent silent myocardial ischemia in abdominal aortic aneurysm. These include Dyslipidemia, hypertension and diabetes mellitus. Thus, AAA patients, especially with Dyslipidemia ,hypertension and diabetes mellitus, should be considered for further evaluation for CAD .

REFERANCES

1)	Bayazit M, Gol MK, Battaloglu B, Tokmakoglu H, Tasdemir O, Bayazit K. Routine coronary arteriography before abdominal aortic aneurysm repair. *Am J Surg* 1995; **170**: 246–50.
2)	Hollier LH, Plate G, O'Brien PC, et al. Late survival after abdominal aortic aneurysm repair: influence of coronary artery disease. *J Vasc Surg* 1984; **1**: 290–9.
3)	Golden MA, Whittemore AD, Donaldson MC, Mannick JA. Selective evaluation and management of coronary artery disease in patients undergoing repair of abdominal aortic aneurysms. A 16-year experience. *Ann Surg* 1990; **212**: 415–20
4)	Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: Circulation. 2007;116:e418-499.
5)	Glagov S, Wolinsky H. New concepts of the relation of structure to function in the arterial wall. *Proc lnst Med Chicago.* 1968;27:106. [PMID: 5743251]
6)	Caro CG. *The Mechanics of the Circulation,* New York: Oxford University Press; 1978.
7)	Avolio AP et al, Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation.* 1983;68:50–58. [PMID: 6851054]
8)	Becker AE. Medionecrosis aortae. *Pathol Microbiol.*1975;43:124.
9)	Weintraub AM, Gomes MN. Clinical manifestations of abdominal aortic aneurysm and thoracoabdominal aneurysm. In: Lindsay J Jr, Hurst JW, eds. *The Aorta.* New York: Grune & Stratton; 1979:131–168.
10	Crawford ES, Hess KR. Abdominal aortic aneurysm (editorial). *N Engl J Med.* 1989;321:1040–1042. [PMID: 2674718]
11	Becker AE. Medionecrosis aortae. *Pathol MicrobioI.* 1975;43:124. [PMID: 1228573]
12	Dillon ML, Young WG, Sealy WC. Aneurysms of the descending thoracic aorta. *Ann Thorac Surg.* 1967;3;430–438.
13	Crawford ES, Coselli JS. Thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg.* 1991;3:302.
14	Health Services/Technology Assessment Text (HSTAT). Guide to Clinical Preventative Services, 3rd Ed. Evidence Syntheses, formerly Systematic Evidence Reviews. National Library of Medicine and NCBI. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
15	Acosta S, Ogren M, Bengtsson H, Bergqvist D, Lindblad B, Zdanowski Z. Increasing incidence of ruptured abdominal aortic aneurysm: a population-based study. *J Vasc Surg*. 2006;44:237–243. [PMID: 16890847]
16	Barrat-Boyes BG. Symptomatology and prognosis of abdominal aortic aneurysm. *Lancet.* 1957;2:716–720.
17	Hertzer NR, et al. Coronary artery disease in peripheral vascular patients. *Ann Surg*. 1984;199:223–233. [PMID: 6696538]
18	McCollum CH, et al. Myocardial revascularization prior to subsequent major surgery in patients with coronary artery disease. *Surgery.* 1977; 81:302–304. [PMID: 841465]
19	Kioka Y, Tanabe A, Kotani Y, et al: Review of coronary artery disease in patients with infrarenal abdominal aortic aneurysm. *Circ J* 2002; 66:1110-1112.
20	Eagle KA, Rihal CS, Mickel MC, et al: Cardiac risk of noncardiac surgery: Influence of coronary disease and type of surgery in 3368 operations. CASS Investigators and University of Michigan Heart Care Program. Coronary Artery Surgery Study. *Circulation* 1997; 96:1882
21	Landesberg G, Mosseri M, Wolf YG, et al: Preoperative thallium scanning, selective coronary revascularization, and long-term survival after major vascular surgery. *Circulation* 2003; 108:177.

22	Posner KL, Van Norman GA, Chan V: Adverse cardiac outcomes after noncardiac surgery in patients with prior percutaneous transluminal coronary angioplasty. *Anesth Analg* 1999; 89:553.
23	Poldermans D, Bax JJ, Schouten O, et al: Should major vascular surgery be delayed because of preoperative cardiac testing in intermediate-risk patients receiving beta-blocker therapy with tight heart rate control?. *J Am Coll Cardiol* 2006; 48:964.
24	McFalls EO, Ward HB, Moritz TE, et al: Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med* 2004; 351:2795.
25	Ward HB, et al: CABG is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery. *Ann Thorac Surg* 2006; 82:795.discussion 1,
26	Back MR, Stordahl N, Cuthbertson D, et al: Limitations in the cardiac risk reduction provided by coronary revascularization prior to elective vascular surgery. *J Vasc Surg* 2002; 36:526.
27	Kaluza GL, Joseph J, Lee JR, et al: Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol* 2000; 35:1288.
28	Wilson SH, Fasseas P, Orford JL, et al: Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol* 2003; 42:234
29	Vicenzi MN, Meislitzer T, Heitzinger B, et al: Coronary artery stenting and non-cardiac surgery—a prospective outcome study. *Br J Anaesth* 2006; 96:686.
30	Moreno R, Fernandez C, Calvo L, et al: Meta-analysis comparing the effect of drug-eluting versus bare metal stents on risk of acute myocardial infarction during follow-up. *Am J Cardiol* 2007; 99:621.
31	Nasser M, Kapeliovich M, Markiewicz W: Late thrombosis of sirolimus-eluting stents following noncardiac surgery. *Catheter Cardiovasc Interv* 2005; 65:516.
32	Grines C, et al: Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: A science advisory from the AHA, ACC , *J Am Coll Cardiol* 2007; 49:734.
33	Dupont, A.,B. et al Frequency of abdominal aortic aneurysm in patients undergoing coronary artery bypass grafting. *Am J Cardiol.*, Vol. 105, No. 11, (Jun 2010), pp. 1545
34	Nemati, M., Shakeri, A., Dehghan R. & Ghaffari S. (2009). Prevalence of abdominal aortic aneurysm in patients with coronary artery disease. *J. Cardiovasc Thorac res.*, Vol. 1, No. 1, (2009), pp. (1-4),
35	Poon, JT., Cheng, SW., Wong, JS. & Ting, AC. (2010). Prevalence of abdominal aortic aneurysm in Chinese patients with severe coronary artery disease. *ANZ J Surg.* ,Vol. 80, No. 9, (Sep 2010), pp. (630-3)
36	Ferket, BS., Grootenboer, N., Colkesen, EB., Visser, JJ., van Sambeek, MR., Spronk, S., Steyerberg, EW. & Hunink, MG. (2011). Systematic review of guidelines on abdominal aortic aneurysm screening. *J Vasc Surg.*, (Feb 2011)
37	Lederle, FA., Nelson, DB. & Joseph, AM. (2003). Smokers' relative risk for aortic aneurysm compared with other smoking-related diseases: a systematic review. *J Vasc Surg.*, Vol. 38, No. 2, (Aug 2003), pp. (329-34),
38	Singh, K., Bønaa, KH., Jacobsen, BK., Bjørk, L. & Solberg, S. (2001). Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study. *Am J Epidemiol.*, Vol. 154, No. 3, (Aug 2001), pp. (236-44), ISSN 0002-9262
39	Abdominal Aortic Aneurysm in Patients with Coronary Artery Disease: A Review Article Ahmed Elkalioubie, Brigitte Jude and Annabelle Dupont*EA 2693, Medicine Faculty, Lille 2 University France*
40	Monney, P., Hayoz, D., Tinguely, F., Cornuz, J., Haesler, E., Mueller, XM., von Segesser, LK. & Tevaearai, HT. (2004). High prevalence of unsuspected abdominal aorticaneurysms in patients

	hospitalised for surgical coronary revascularisation. *Eur J Cardiothorac Surg*. Vol. 25, No. 1, (Jan 2004), pp. (65-8),
41	Shirani, S., Shakiba, M., Soleymanzadeh, M., Bakhshandeh, H. & Esfandbod, M. (2009). Ultrasonographic screening for abdominal aortic aneurysms in Iranian candidates for coronary artery bypass graft surgery. *Arch Iran Med*., Vol. 12, No. 4, (Jul 2009), pp. (383-8)
42	19. Hertzer NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. Ann Surg. 1984;199(2):223-233.
43	Lachapelle K, Graham AM, Symes JF. Does the clinical evaluation of the cardiac status predict outcome in patients with abdominal aortic aneurysms? J Vasc Surg. 1992;15:964-970; discussion 970-971.
44	Fleg JL, Gerstenblith G, Zonderman AB, et al. Prevalence and prognostic significance of exercise-induced silent myocardial ischemia detected by thallium scintigraphy and electrocardiography in asymptomatic volunteers. Circulation. 1990;81(2):428-436.
45	Ward HB, Kelly RF, Thottapurathu L, et al: Coronary artery bypass grafting is superior to percutaneous coronary intervention in prevention of perioperative myocardial infarctions during subsequent vascular surgery. *Ann Thorac Surg* 2006; 82:795.discussion 1