Role of advanced MRI techniques in comparison of systemic ventricle in atrial switch and congenitally corrected transposition of the great vessels

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Introduction:

Incidence of transposition of great arteries (TGA) is 1 per 3300 live birth according to the center of disease control and prevention **(Parker et al., 2010).**

TGA is subdivided into 2 types; dextro-transposition of great arteries (d-TGA) which is the most common type with an atrio-ventricular concordance and ventriculo- arterial discordance, the other type is levo-transposition of great arteries (l-TGA) with atrio-ventricular and ventriculo-arterial discordance, l-TGA is also known as congenitally corrected transposition of great arteries (cc-TGA) **(Frank et al., 2010)**.

Atrial switch is one of the surgical procedures done for d-TGA by redirecting the deoxygenated blood into the left ventricle which pumps blood into pulmonary artery and redirecting the oxygenated blood through pulmonary baffle to the right ventricle which acts as a systemic ventricle pumping oxygenated blood into the aorta. This procedure is indicated when there is no chance to proceed for arterial switch as the left ventricle is not conditioned to act as a systemic ventricle. Survival is 68% after 39 years while survival free of events like arrhythmias, heart failure and reoperation is 19% only after 39 years **(Cuypers et al., 2014).**

These figures raise questions about the underlying mechanisms of atrial switch complications on the long run, diffuse myocardial fibrosis is considered as a prominent problem **(Plymen et al., 2013)**. Underlying etiology of diffuse systemic ventricle fibrosis is an area of further researches helping to clarify the risk factors which could be the late atrial switch palliation sparing more time for deoxygenated blood to harm the myocardium or the hemodynamic burden on the systemic right ventricle in addition to the exposure to major cardiac surgery with decreased oxygen saturation

Despite being congenitally corrected since birth by having similar circulation as atrial switch patients with right ventricle acting as a systemic ventricle pumping oxygenated blood to aorta, ccTGA patients have high incidence of systemic ventricle failure (up to 34% in case of absent associated other cardiac anomalies and 70% if other anomalies present) and premature death even this cohort without associated cardiac anomalies **(Graham et al., 2000).** This encourages the idea of anatomical repair by doing atrial and arterial switch in the same patient **(Ly 2009).**

Still the gap of knowledge about the different performance of the systemic ventricle in atrial switch and ccTGA patients, is there an effect of the low oxygen saturation before and at the time of surgery in case of atrial switch? which could be the leading point in diffuse myocardial fibrosis in this cohort. What is the effect of the hemodynamic burden on the systemic right ventricle? Is the idea of anatomical repair a wise idea or it leads to more complications (complications of 2 different surgeries together in the same patient)? **(Tweddell 2017).**

Thanks for the advances in cardiac MRI techniques as we can calculate the myocardial fibrosis in a non-invasive manner by combination of T1 mapping and late gadolinium enhancement images, these techniques give an accurate idea about replacement and interstitial myocardial fibrosis. These data will help us to answer the question about systemic ventricle reaction in atrial switch and ccTGA (**Broberg et al., 2010).**

Aim of the Work

This study will compare the systemic ventricle performance in atrial switch and ccTGA patient regarding the presence of interstitial and replacement fibrosis and systemic ventricular function by using the cardiac MRI. We compare the effect of the decreased oxygen and systemic right ventricle hemodynamic stress in atrial switch patients by the effect of only systemic right ventricle stress in ccTGA in presence of myocardial interstitial fibrosis.

Patients and Methods

Patient Selection:

This study will include 15 atrial switch patients and 15 ccTGA patients presenting to the Magdi Yacoub Foundation, Aswan heart center and Ain Shams university hospital.

Inclusion criteria:

- Atrial switch patients.
- ccTGA with oxygen saturation above 90%.

Exclusion Criteria:

Patients found to have one or more of the following criteria will be excluded from the study:

- Patients with contraindication to MRI e.g. cochlear implants or pacemakers.
- Patients with uncontrolled arrhythmias preventing proper MRI imaging.
- Patients with decompensated heart failure and orthopnea which limits the ability to precede for MRI.
- Patient who are claustrophobic.
- Decompensated renal failure.

Methods:

The selected patients will be subjected to the following:

Thorough history taking with stress on:

- Clinical history with special comment on onset of cyanosis, ventricular failure manifestations age of surgery in case of atrial switch.
- Oxygen saturation at time of atrial switch and any surgical problems.
- Previous investigations e.g. echocardiography, MRI or MDCT.
- Previous pacemaker implantation.

Cardiac magnetic resonance imaging (MRI)

Preparation before procedure:

- Explanation of the procedure to parents especially the side effects of the contrast agent including; coldness, warmth, or pain at the injection site, nausea, vomiting, headache, paresthesias, dizziness and itching.
- Parents should be aware of the severe life-threatening anaphylactoid or nonallergic anaphylactic and nephropathic effect.
- Exclusion of any hazards like pacemaker implantation.
- Review kidney function test to avoid nephrogenic systemic fibrosis which may happen in case of contrast administration with acute or chronic renal failure (contrast shouldn't be given in estimated glomerular filtration rate <30 ml/min/1.73 m2).

During procedure:

- Physiological monitoring devices and hearing protection are put in place.

- A high-quality electrocardiogram (ECG) signal is essential for optimum data quality in cardiac-gated sequences.
- The imaging coil should be chosen to maximize the signal-to-noise ratio over the body region to be examined.
- MR compatible equipment should be used to monitor the heart rate, transcutaneous oxygen saturation, blood pressure, expired carbon dioxide and body temperature.
- An appropriately equipped resuscitation cart and emergency management plan for the MR environment should be in place.

Technique of imaging:

- Machine used is 1.5 T scanner (Siemens Magnetom Aera, Siemens Medical Systems, Erlangen, Germany).
- Trufi images which help in assessment of anatomy.
- White blood images which help in assessment of EF, EDV, ESV, EDVI, ESVI, SV, SVI and cardiac out put of both left and right ventricles.
- Injection of gadolinium-based contrast agent (Magnevist, Schering AG, Berlin, Germany, 0.2 mmol/kg).
- Delayed gadolinium enhancement, pre and post contrast T1 mapping in order to calculate the volume of ventricular interstital and replacement fibrosis.

After the procedure:

- Examination is processed on a dedicated work station.
- Serum NT-brain natriuretic peptide (NT-proBNP) is assessed which is correlated to the degree of ventricular impairment if present.

Consent

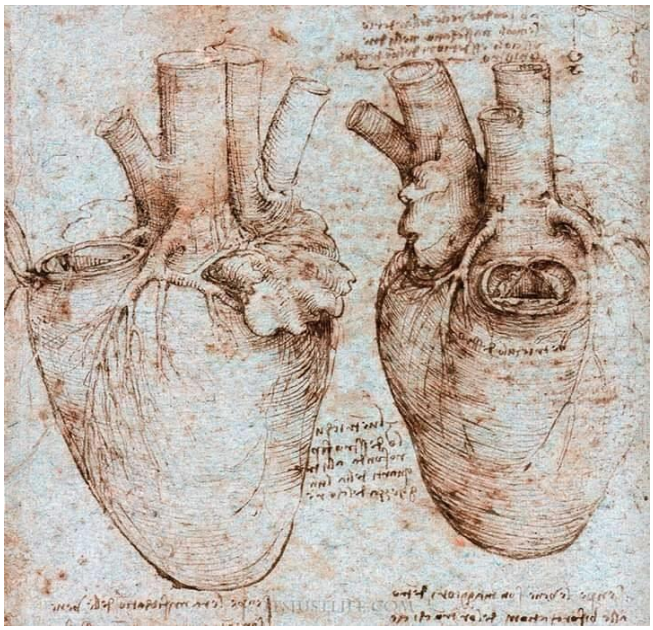
All patients or their relatives will be required to sign a written consent explaining the study. Any inquiries of the patient(s) will be explained thoroughly.

Statistics

All the resulting data will be subjected to adequate statistical analysis, comparison, will be tabulated and then discussed.

Chapter 1

The relevant radiological anatomy



Chapter 1

The relevant radiological anatomy of MRI

Embryology of the heart: *(Yamagishi and Yamagishi., 2014)*

Normal developmental origins of the heart:

The heart is the first organ to develop and be functioning supporting the circulatory system from as early as the 3rd week of intrauterine and it is completed in the 8th week of the intrauterine life.

The heart is derived from 4 main origins

1- The first heart field
2- The second heart field
3- The cardiac neural crest cells
4- The proepicardium

The first heart field formation:

The future cardiac cells originating from the anterior lateral plate mesoderm form a crescent-shaped cardiac precursor in front of a notochord, the cardiac crescent forms bilateral endocardial tubes which then fuse to form the primitive heart tube consisting of an interior layer of endocardial cells and an exterior layer of myocardial cells and containing an extra cellular matrix called the cardiac jelly, the endocardial cushions are formed inside the cardiac jelly.

The primitive heart tube is a beating tube pumping blood from caudal to rostral direction of the embryo.

The first heart field eventually contributes to specific chambers in the future heart which are exclusively the left ventricle and partially all other cardiac parts except for the outflow tract.

The second heart field formation:

It contributes to a large portion of the outflow tract including future right ventricle and atria.

Its contribution to the outflow tract results in its elongation which serves in future proper alignment of the aorta and pulmonary trunk to their corresponding ventricles.

The cardiac neural crest cells:

They originate from the dorsal neural tube then migrate into the outflow tract where they contribute to the conotruncal cushions to give the outflow tract septum, they also migrate to the pharyngeal arches 3, 4, and 6 which give rise to the future great vessels.

The proepicardium

It develops from the coelomic mesothelium overlying the liver bud, it forms the epicardium and coronaries.

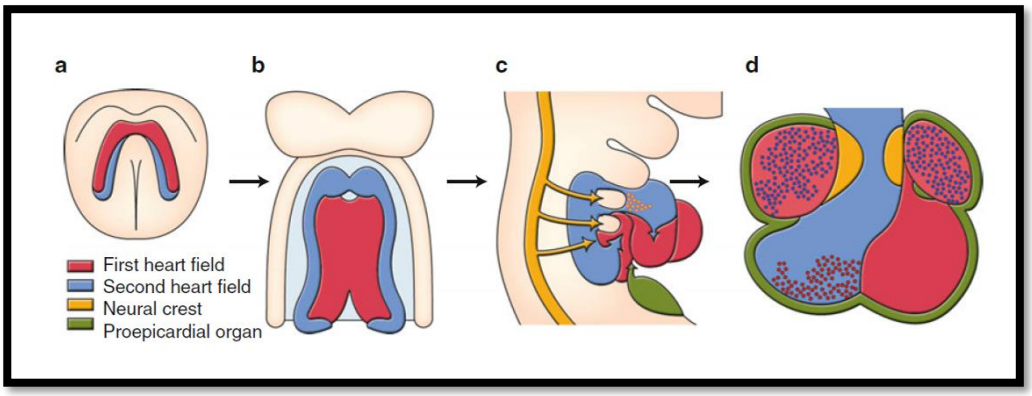


Figure 1: Developmental origins of the heart. a; Cardiac crescent. b; Primitive heart tube. c; Looping heart tube. d; Four chambered heart. Quoted from ***(Yamagishi and Yamagishi 2014)***

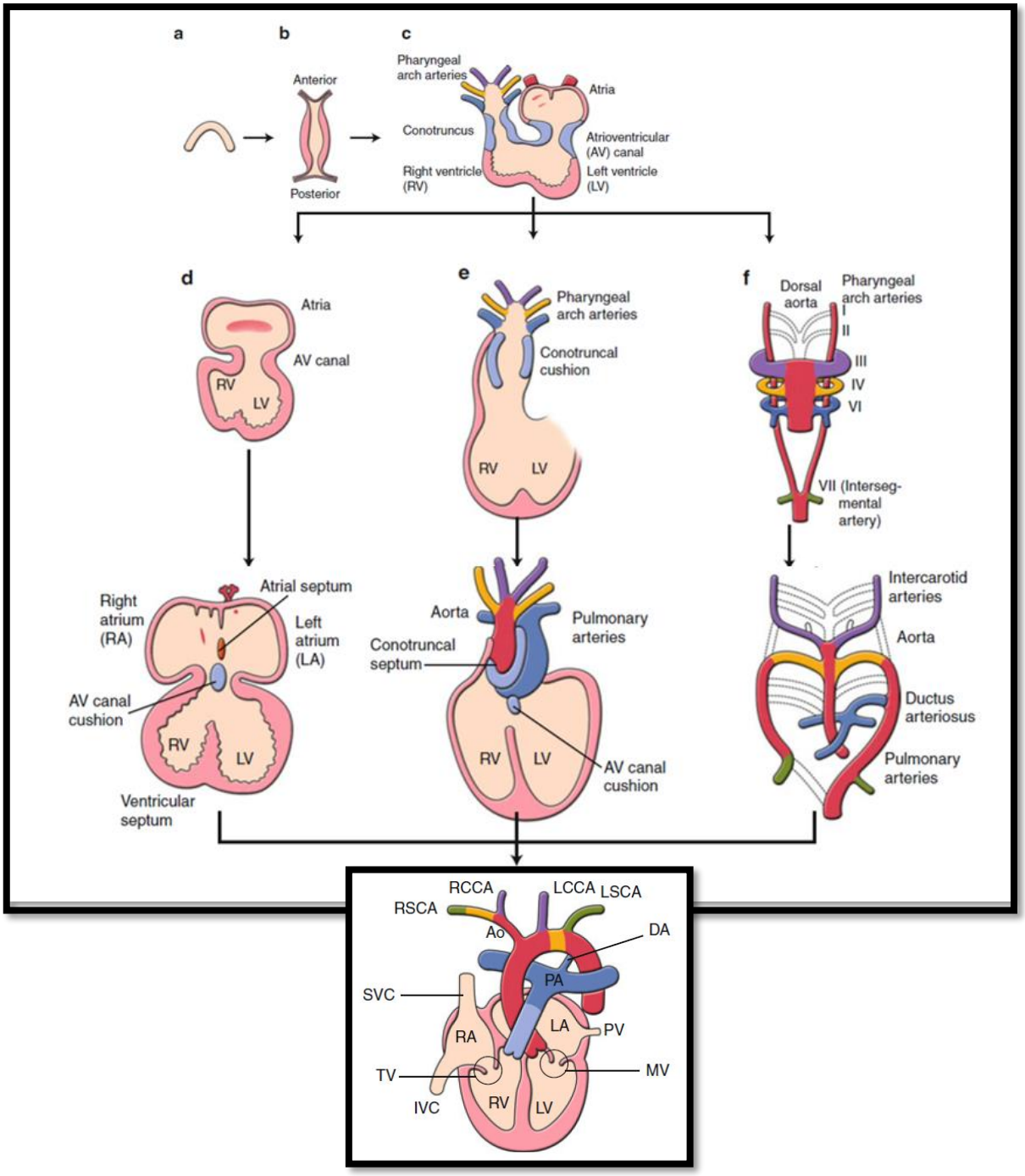


Figure 2: Embryology of the cardiovascular system; a. cardiac crescent. b**.** Primitive heart tube. c**.** Looping. d. Atrio-ventular separation. e. Outflow tract. f**.** Great vessels. Ao; aorta, DA; ductus arteriosus, IVC; inferior vena cava, LCCA; left common carotid artery, LSCA;

left subclavian artery, MV; mitral valve, PA; pulmonary arteries, PV; pulmonary veins, RCCA; right common carotid artery, RSCA; right subclavian artery, SVC; superior vena cava, TV; tricuspid valve. Quoted from ***(Yamagishi and Yamagishi 2014)***

Embryology of the congenital heart diseases: ***(Yamagishi and Yamagishi 2014) and (Lapierre et al., 2010)***

The normal development of the heart results in situs solitus with all the asymmetric internal organs placed on the body where they should be, and the looping of the primitive heart tube happens in a rightward convex direction (dextro loop = d-loop).

The situs of the heart is defined as the relation between the location of the atria and the remaining organs of the body, the position of the heart in the thorax and the orientation of the cardiac apex are not determinative of the situs.

There are three types of situs: ***(Jacobs et al., 2007) and (Lapierre et al., 2010).***

1- Normal situs (situs solitus):
There is normal anatomic arrangement, the right atrium and liver are located on the right side, the left atrium, stomach and spleen are located on the left side.

A right-sided trilobed lung with an early origin of the upper lobe bronchus from the right main bronchus and a left-sided bilobed lung with a more distal origin of the upper lobe bronchus.

The right pulmonary artery lies in front of the right bronchus (eparterial bronchus), the left pulmonary artery crosses above the left bronchus (hyparterial bronchus).

2- Inverted situs (situs inversus): typically, the opposite of normal situs orientation.

3- Situs ambiguous (right or left isomerism):
Also known as heterotaxy, it is subdivided into a right isomerism or asplenia and left isomerism or polysplenia.

Right isomerism shows bilateral early origin of the upper lobe bronchus from the right main bronchus, a large symmetric liver, absence of the

spleen, and total anomaly of the pulmonary venous return to the contralateral atrium.

Left isomerism shows bilateral distal origin of the upper lobe bronchus, an interrupted IVC with azygous continuation, multiple spleens, and pulmonary veins that drain into both the contralateral right atrium and the ipsilateral left atrium.

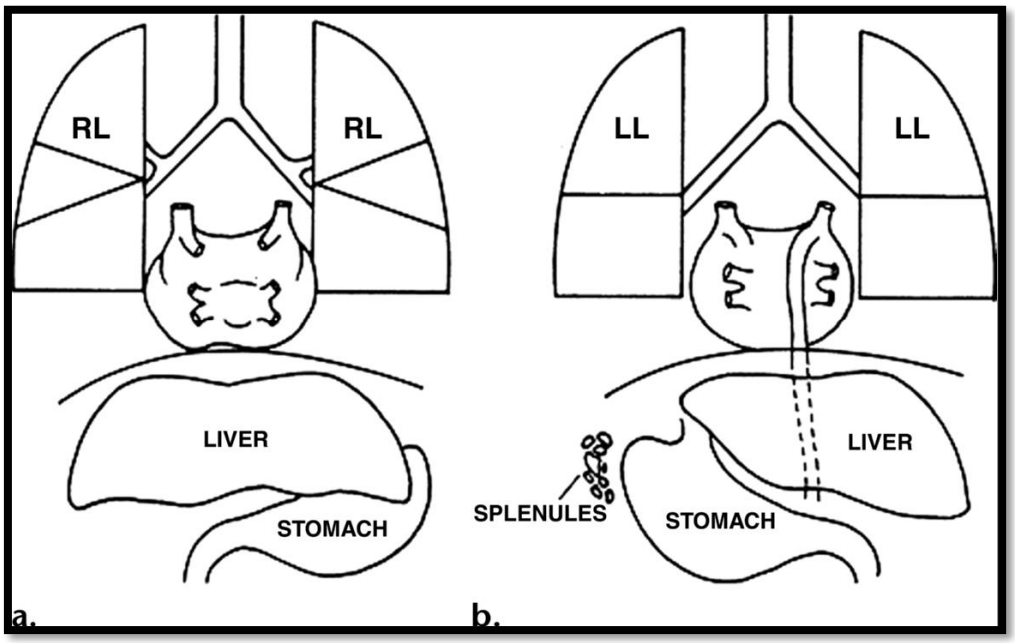


Figure 3: Situs solitus **(a)** and situs inversus **(b)**. LA; left atrium, LL; left lung, RA; right atrium, RL; right lung. Quoted from ***(Winer-Muram and Tonkin., 1989).***

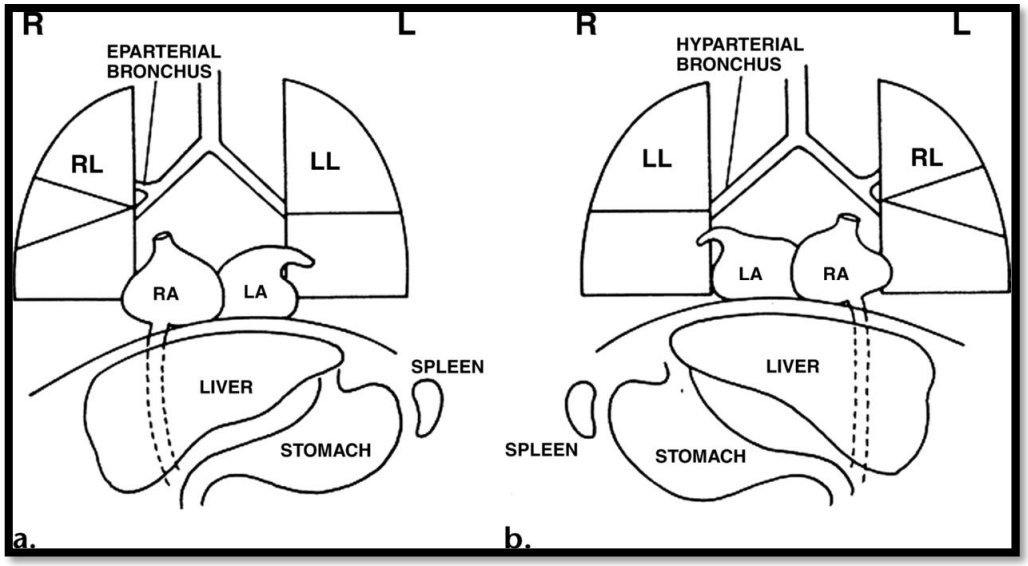


Figure 4: situs ambiguous with right isomerism (asplenia) (a) and left isomerism (polysplenia) (b). LL; left lung, RL; right lung. Quoted from ***(Winer-Muram and Tonkin., 1989).***

Looping of the heart: *(Lapierre et al., 2010)*

The heart tube consists of primitive atria, the left ventricular structure, the bulbus cordis (which will develop into the right ventricle), and the truncus arteriosus (the future great vessels) in caudocephalad arrangement.

The embryonic outflow tract (conotruncus) consists of a distal part (truncus) and a proximal part (conus), at the 4:5 weeks of gestation, two big swellings in the truncal region (right superior and left inferior truncal cushions) and two small swellings in the conal region (right dorsal and left ventral conal cushions) develop in the outflow tract which is divided in a spiral manner leading to proper connection of the great vessels to the corresponding ventricle.

During development, the tube bends over on itself, toward either the right or the left. Normally, the tube folds to the right, forming a d-loop, with consequent orientation of the bulbus cordis to the right of the left ventricle, the cephalic end of the heart tube also bends ventrally, caudally, and slightly to the right. Because of these events, the heart occupies the left thorax. When the tube loops toward the left in case of l-loop, the right ventricle is

oriented to the left of the left ventricle, and rotation of the heart lies into the right thorax which is considered an abnormality.

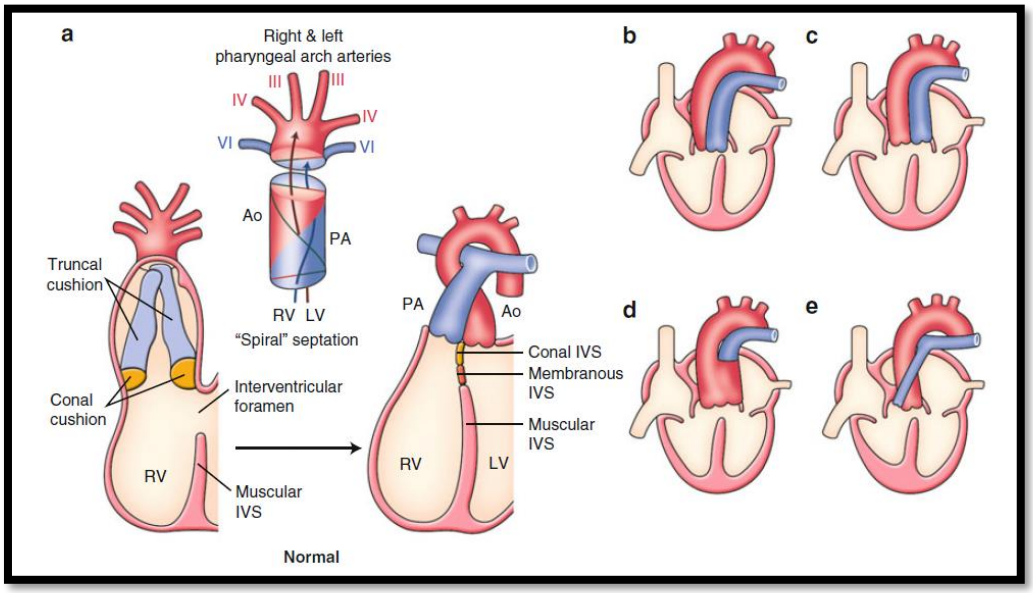


Figure 5: normal septation (a), abnormal septation with the famous conotruncal anomalies (b); Double outlet right ventricle. (c); TGA. (d); Truncus arteriosus. (e) Tetralogy of Fallot. Ao; aorta, IVS; interventricular septum, LV; left ventricle, PA; pulmonary artery, RV; right ventricle. Quoted from ***(Yamagishi and Yamagishi 2014).***

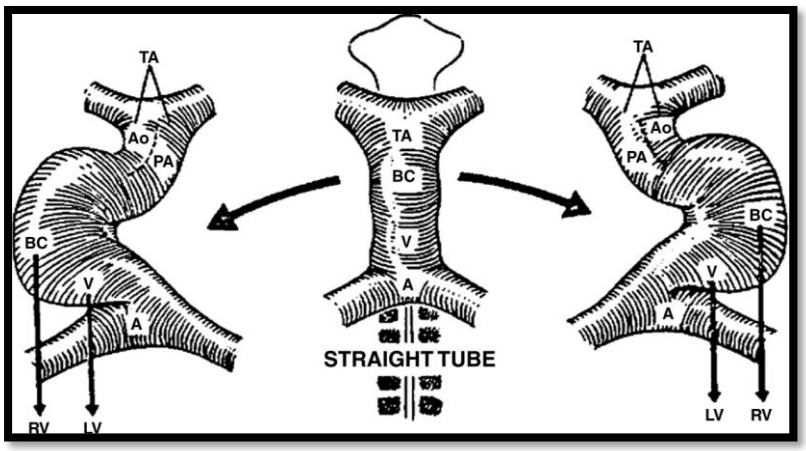


Figure 6: d-loop (left) and l-loop (right) from the primitive cardiac tube (center). A; atria, Ao; aorta, BC; bulbus cordis, LV; left ventricle, PA; pulmonary artery, RV; right ventricle, TA; truncus arteriosus, V; embryonic left ventricle. Quoted from ***(Van Praagh., 1985).***