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## Editorial

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## Treatment of Cardiac Hemochromatosis

**Wilbert S. Aronow\***

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Treatment of iron-overload states is important to prevent or reverse cardiac dysfunction.<sup>1-5</sup> Removal of excess iron from the tissues in these patients reduces generation of free radicals, decreasing organ damage.<sup>6,7</sup> Removal of excess iron stores includes therapeutic phlebotomy and iron-chelating agents. Management of the disease causing iron overload and dietary management are also important in treating cardiac hemochromatosis. Dietary management includes avoidance of medicinal iron, mineral supplements, excess vitamin C, and uncooked seafoods.<sup>5</sup> Congestive heart failure should be treated with guideline-directed medical therapy for heart failure.<sup>8</sup>

Therapeutic phlebotomy is the treatment of choice in non-anemic patients with cardiac hemochromatosis. Phlebotomy should be initiated in men with serum ferritin levels of 300 µg/L or more and in women with serum ferritin levels of 200 µg/L or more, regardless of presence or absence of symptoms.<sup>5</sup> Phlebotomy should remove 1 unit of blood (450-500 mL) weekly until the serum ferritin level is 10 to 20 µg/L and maintenance of the serum ferritin level at 50 µg/L or lower thereafter by periodic removal of blood.<sup>5</sup> Each unit of blood removed depletes 200-250 mg of iron from the blood, which mobilizes an equal amount of iron stored in the tissues to form hemoglobin.<sup>9</sup> Patients with ferroportin mutation-associated iron overload may not tolerate a more aggressive schedule.<sup>10</sup> Serum ferritin is measured every month until it reaches 200 ng/mL and once in 1 to 2 weeks after. Hemoglobin and hematocrit should be measured before each phlebotomy. Phlebotomy should not be performed if the hematocrit falls below 80% of the previous value.<sup>11</sup> After reaching a target ferritin level less than 50 ng/mL and transferrin saturation below 30%, the frequency of phlebotomy is decreased. The frequency of maintenance phlebotomy varies once every few months to few years depending on the iron reaccumulation rate.<sup>12</sup> Adequate hydration is recommended before and after phlebotomy to prevent volume depletion. Phlebotomy reduces myocardial iron content and improves left ventricular diameter, left ventricular fractional shortening, left ventricular ejection fraction, left ventricular mass, and left atrial dimension in patients with cardiac hemochromatosis.<sup>13-15</sup>

Medical therapy to treat congestive heart failure from cardiomyopathy and serious cardiac arrhythmias in patients with cardiac hemochromatosis must be used until phlebotomy possibly combined with iron chelation therapy reduces the excess myocardial iron content.<sup>5</sup> Complete atrioventricular block caused by iron deposition may need implantation of a permanent pacemaker.<sup>16</sup>

Phlebotomy is not a treatment option in patients with anemia (secondary iron-overload disorders) nor in patients with severe congestive heart failure.<sup>17</sup> In these patients, the treatment of choice is iron chelation therapy.<sup>18</sup> Iron chelating agents increase the iron excretion rate by binding to the iron in plasma and tissues, depleting the body of excess iron.<sup>19</sup> Serum ferritin levels should be monitored periodically. When the serum ferritin level falls below 1000 ng/mL, iron chelation therapy should not be given.<sup>20</sup> Deferoxamine, deferiprone, and deferasirox are the 3 iron-chelating drugs approved by the United States Food and Drug administration for therapy of chronic secondary iron overload.

End-stage cardiomyopathy caused by hereditary hemochromatosis was successfully

treated with erythrocytapheresis in combination with left ventricular assist device support.<sup>21</sup>

Cardiac transplantation is a therapeutic option for patients with cardiac hemochromatosis with severe congestive heart failure refractory to optimal medical therapy and cardiac resynchronization therapy.<sup>8,22</sup>

#### CONFLICTS OF INTEREST

The author has no conflicts of interest.

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## Research

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## A Clinical Application of the "Brody Effect"

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### ABSTRACT

Brody described the importance of differences in resistivity between blood in the left ventricular lumen and the myocardium, and the distance between the primary dipole in the myocardium and the image dipole in the lumen. The image dipole existing in the ventricular lumen influences the ECG voltages recorded from leads either radial or tangential to the left ventricular mass. The intensity of the image dipole and the magnitude of the effect on the body surface ECG are proportional to the differences in resistivity and the distance between primary and image dipoles. Tacrolimus, a commonly-used immunosuppressant, decreases left ventricular lumen and thickens the left ventricular free-wall tremendously; thus, although left ventricular myocardial mass does not change, ECG voltages in leads facing the left ventricular free-wall should decrease monumentally. The hypothesis of this study is that ECG voltages in lead aVF facing the left ventricular free-wall and oriented radially from its mass would decrease proportional with the decrease in luminal radius and thickening of the free-wall. ECG's and 2D-directed M-mode ECHO's of the left ventricle were recorded from dogs before and after receiving tacrolimus and developing drastic reductions in left ventricular luminal volumes. R waves in lead aVF determined by the radial spread of depolarization from subendocardium to subepicardium of the left ventricular free-wall decreased precipitously as the ratio of luminal radius to wall thickness decreased. The hypothesis that ECG voltages would decrease as luminal volume decreases and the wall thickens was accepted. This study demonstrates that factors other than wall mass must be considered in electrocardiology.

**KEYWORDS:** Brody Effect; ECG voltages; Echocardiography.

### INTRODUCTION

The Electrocardiogram (ECG) is the best method for studying the rate and rhythm of the heart, it is also useful for detecting left ventricular hypertrophy in humans, and possibly so in dogs. In 1956, Brody described the effect of intracardiac blood volume on body surface potentials.<sup>1</sup> The powerful influence of the intracavitary blood mass on the heart-lead relationship increases the validity. The analysis of the inhomogeneity problem leads to a theoretically correct but eliminating inhomogeneity effects need to be evaluated clinically for the use of the methods. The relationship between QRS amplitude and left ventricular mass was evaluated in early stages of left ventricular hypertrophy. A decrease in QRSmax and the specific potential of myocardium was observed in both models of experimental left ventricular hypertrophy. The changes in electrogenetic properties of myocardium have been shown in the early stage of developing left ventricular hypertrophy. The changes of nonspatial determinants influence the resultant QRS voltage in terms of the solid angle theory.<sup>2</sup> Tacrolimus (FK506) is an immunosuppressive macrolide antibiotic that is used to minimize transplant rejections having strong effects on the heart.<sup>3,4</sup> Tacrolimus leads an increase in end-diastolic wall thickness and a decrease in left ventricular end-diastolic volume in dogs.<sup>3</sup>

Pattern of left ventricular hypertrophy is an R wave – greater than normal in amplitude

and longer than normal in duration – in a lead whose electrical axis (lead aVF) is normal to the epicardium of the hypertrophied left ventricular free-wall. The hypothesis of this study is that ECG voltages in lead aVF facing the left ventricular free-wall and oriented radially from its mass would decrease proportional with the decrease in luminal radius and thickening of the free-wall. ECG's and 2D-directed M-mode ECHO's of the left ventricle were recorded from dogs before and after receiving 0.1 mg/kg tacrolimus and developing drastic reductions in left ventricular luminal volumes.

## MATERIALS AND METHODS

All animals received humane care in accordance with guidelines of the American Physiological Society and The Ohio State University. Ten, healthy dogs of either sex weighing between 10 and 14 kg were anesthetized with morphine-chloralose. Electrodes forming ECG lead aVF were placed, and lead aVF was recorded on a data acquisition system. Dimensions of the left ventricular and left atrial lumena were measured from two-dimension directed mode echocardiograms. After baseline measurements of echocardiograms and electrocardiograms were obtained, dogs were given IV 0.1 mg/kg tacrolimus, and recordings were obtained 15 minutes later. Peak voltages of P waves and R waves in lead aVF were measured, and left ventricular internal dimensions and free-wall thicknesses were measured from the M-mode obtained just below the position of the mitral valves. The ratios of left ventricular lumena, thicknesses of the

left ventricular free-walls, and of P and R wave heights before and after tacrolimus were calculated. Ratios of values measured or calculated were compared by one-tailed Student's t requiring a  $p < 0.05$  for significance.

## RESULTS

Table 1 shows values for all measures of ECG and echocardiography. All dogs given tacrolimus remained in sinus rhythm but all developed sinus tachycardia. Mean heart rate before tacrolimus was 78 (SEM 4.3) beats/minute and after tacrolimus was 158 (SEM 9.5) beats/minute ( $p < 0.0001$ ). The R wave decreased ( $p < 0.001$ ) from 2.29 (SEM 0.193) mV to 1.48 (SEM 0.163) mV, a difference of 0.81 mV. The height of the P wave increased ( $p < 0.001$ ) from 0.148 (SEM 0.024) mV to 0.392 (SEM 0.025) mV, a difference of 0.244 mV. The thickness of the left ventricular free-wall increased ( $p < 0.001$ ) from 0.655 cm to 0.92 cm, a difference of 0.265 cm. The original ECG recording has been shown in Figure 1. 2D echocardiography of the heart has been shown in Figure 2. A remarkable thickening of the myocardium was seen after tacrolimus administration. The calculation of the amplitudes for the clinical application of Brody Effect has been shown in Figure 3.

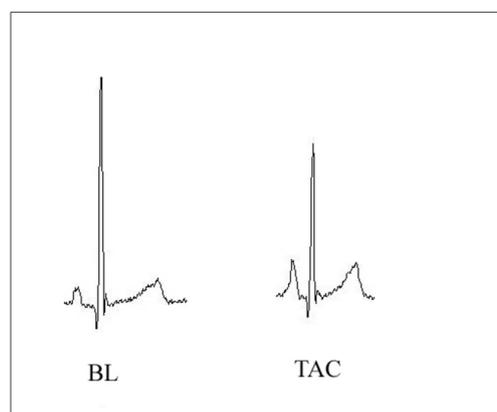
## DISCUSSION

Conventional assessment of left ventricular hypertrophy using the electrocardiogram have relied on assessing

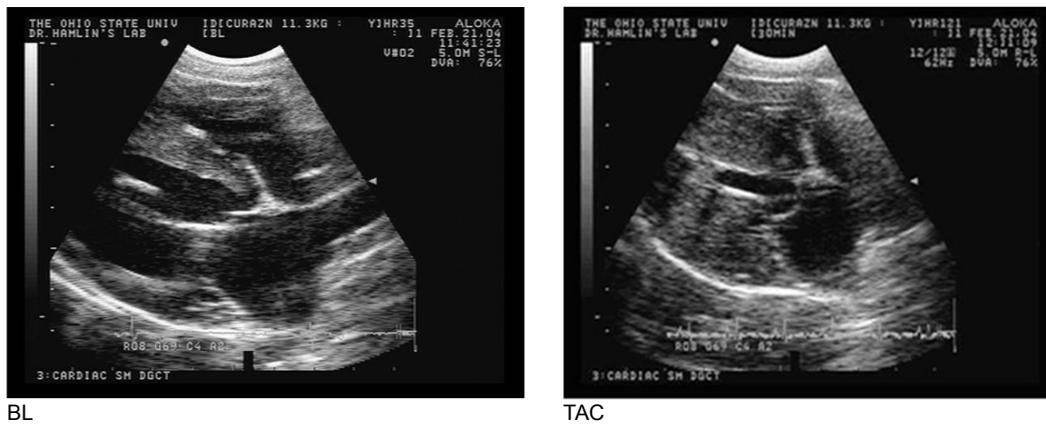
	Baseline	Tacrolimus	Difference	Ratio	T-test (P)
HR (bpm)	78.11±4.35	158.35±9.5	80.24	2.03	=0.021
P aVF (mV)	0.148±0.024	0.392±0.025	0.244	2.6	<0.001
R aVF (mV)	2.29±0.193	1.48±0.163	0.81	0.6	<0.001
LVEDDi (cm)	2.85±0.155	2.06±0.235	0.79	0.7	=0.032
LVEDWT(cm)	0.655±0.045	0.92±0.059	0.265	1.4	=0.012
LAA-d (cm <sup>2</sup> )	7.18±0.67	4.17±0.286	3.01	0.6	=0.014
LAA-s (cm <sup>2</sup> )	5.13±0.65	2.49±0.39	2.64	0.5	=0.024

±: SEM, HR: Heart rate, LVEDDi: Left ventricular end-diastolic diameter, LVEDWT: Left ventricular end-diastolic wall thickness, LAA-d: Left atrial area in diastole and LAA-s: Left atrial area in systole.

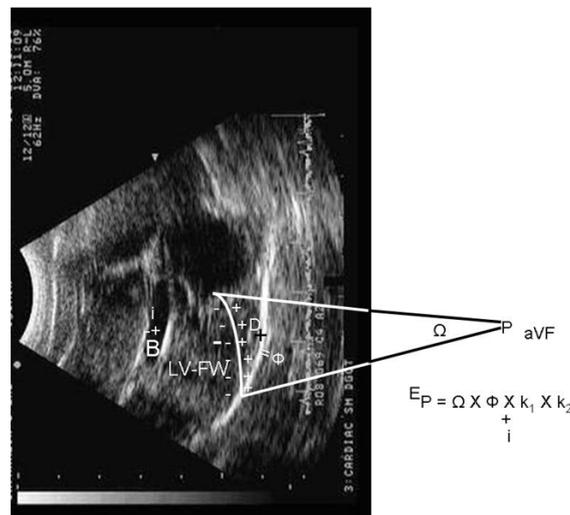
**Table 1:** Values for all measures of ECG and echocardiography.



**Figure 1:** Electrocardiographic recordings before (BL) and after 1 mg/kg Tacrolimus (TAC). Note the decrease in R wave and the increase in P wave after tacrolimus administration.



**Figure 2:** 2D echocardiography of the heart before (BL) and after 1 mg/kg Tacrolimus (TAC). Note the thickening of the myocardium after tacrolimus administration.



**Figure 3:** The calculation of the amplitudes for the clinical application of Brody Effect over lead aVF, ECG.

changes in the amplitude and/or duration of the QRS complex of the ECG to quantify LV mass. ECG measures of LV mass have typically been validated by imaging such as echocardiography.<sup>5</sup> Decreases in R-wave amplitude were evaluated in myocardial ischemic infarction in previous reports.<sup>6</sup> For further investigation of the effects on the amplitudes, this study evaluates amplitude and the blood volume of the heart when myocardial mass is stable. The amplitude of the R wave may be predicted by the solid angle concept (Figure 3). This necessitates constructing radii from the open ends of a boundary between resting (positive) and depolarized (negative) myocardium, to the electrodes on the body surface. The voltage generated at this electrode may be approximated by the solid angle ( $\Omega$ ) subtended, on a sphere of unit radius, by an infinite number of radii from the perimeter of the boundary between depolarized and resting myocardium to the point on the torso surface. The amplitude may be defined quantitatively as the magnitude of the solid angle, times the strength of the unit dipole ( $\Phi$ ), an infinite number of which produce the boundary, times a constant of resistivity of the medium between the heart and the electrodes, times a geometrical constant (for which there is no intuitive explanation).

In 1956 Brody described the effect of intracardiac blood volume on body surface potentials.<sup>1</sup> He demonstrated that a body surface potential, at point aVF produced by a wave of depolarization resolved to a single dipole (P) traversing the myocardium normal to its epicardial surface, would have a magnitude greater than might be expected from the single (primary) dipole, because an image (i) dipole exists in the volume of blood within the left ventricle. The magnitude of the image dipole and its contribution to the voltage on the body surface depends upon how large the primary dipole is, the distance (x) between the P and i, and the differences in resistivity between the myocardium ( $\sigma$ ) and blood ( $\sigma$ ) containing the two dipoles. When the wave of depolarization travels through the myocardium tangentially to the volume of blood (B), the image dipole actually detracts from the voltage recorded from a lead towards which the boundary is traveling.

Since the R-wave of lead aVF ECG is produced by radial spread in an endocardial to epicardial direction through the left ventricle, and the P wave is produced by tangential spread through the atria, if both ventricle and atria become smaller and

therefore have thicker walls, the voltages of the R wave should be decreased and that of the P wave should be increased due to a decreased image dipole.

As will be demonstrated by the experiments reported here, despite the fact that the mass of the left ventricle does not change in response to the immunophylline, tacrolimus, the height of the R wave in lead aVF decreases and the height of the P wave increases dramatically. It will be shown by echocardiography, that the left ventricular and atrial lumena become small, the left ventricular free-wall and atrial walls thick (pseudohypertrophy), and that the alterations in amplitudes can be explained by application of the Brody effect. This may limit the ability to identify hypertrophy of the left ventricular free-wall, and may falsely suggest enlargement of the atria.

The P waves increased in amplitude and the R waves decreased in amplitude, acutely, in response to tacrolimus. Obviously in the 15 minutes between baseline and the administration of tacrolimus neither change could reflect a change in muscle mass, the depolarization of which produces the ECG deflections; thus an alternative explanation must be offered. It is reasonable to assume that the topographical relationship between the electrodes on the torso surface and the heart did not change enough to account for altered voltages. Similarly it is reasonable to assume that the unit dipole ( $\Phi$  in Figure 3) – sheets of which constitute the waves of depolarization – did not change substantially. Since the amplitude of the P wave increased while the amplitude of the R wave decreased, and both dipole sources are nearly equidistant from the electrodes on the torso surface, the differences between baseline and tacrolimus cannot be explained by altered resistivity ( $k_1$  in Figure 3) of the body as a volume conductor. Thus, there are only 2 possibilities to explain the divergent effects of tacrolimus on the amplitudes. First an increased amplitude of the P wave and a decreased amplitude of the R wave could be explained by changes in the magnitude of the solid angle formed by the radii from the boundary between depolarized and resting myocardium ( $\Omega$  in Figure 3); i.e., the sheet representing atrial depolarization became larger and that representing ventricular depolarization – actually depolarization of the left ventricular free-wall which generates the R wave in lead aVF – became smaller. However, observation of the atria and ventricles on the echocardiograms show that both became smaller after tacrolimus. Furthermore, although we could not observe the entire left ventricular geometry on the echocardiogram, it is clear that both atria and ventricles became smaller. Thus, it would be inconsistent to explain an increase in P wave amplitude and a decrease in R wave amplitude on the decrease in magnitude of the sheets of dipoles producing the respective deflections. Thus, the only explanation to account for the increase in amplitude of the P wave and decrease in amplitude of R wave is the Brody effect.

Both atria and ventricles became smaller; i.e., their epicardial perimeters decreased. Since the muscle mass could not have changed, it follows that both must have become thicker,

which was observed unequivocally on the echocardiograms. Thus the image dipole in the left ventricular volume would be reduced in magnitude, since the primary dipole in the free-all of the left ventricle would be more distant from the ventricular cavity. This occurs because the spread of depolarization through the left ventricular free-wall is radial through the wall. Thus, the sum of the primary and image dipoles would be reduced (the primary being normal but the image reduced), and the height of the R wave would be reduced. But because the spread of activity through the atrial wall is tangential to the volumes of blood within the atria, the thickening of the atrial walls would increase the image dipole, thus making the sum of the primary and image dipoles greater after tacrolimus than during baseline. Further studies may evaluate the effect of phi change differently for atria versus ventricles and resistivity of myocardium change differently for atria and ventricles.

The severe tachycardia caused by tacrolimus may be related with binding to the 12-kDa FK506-binding protein (FKBP12.6) modulating calcium conductance through ryanodine channels in pace-maker cells and a decrease in conductance of potassium over the inward rectifying  $K^+$  (IK1) and transient outward  $K^+$  (IKTO) channels.<sup>3,7</sup> Furthermore, the profound myocardial thickening and reduced luminal cavity by the influence of tacrolimus were noted concurrent with the ECG changes resulting in tachycardia and increased contractility.

In conclusion, the hypothesis that ECG voltages would decrease as luminal volume decreases and the wall thickens was accepted. This study demonstrates that factors other than wall mass must be considered in electrocardiology.

**CONFLICTS OF INTEREST:** None.

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## Case Report

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E-mail: [srinivasan.sattiraju@carle.com](mailto:srinivasan.sattiraju@carle.com)**Volume 2 : Issue 3****Article Ref. #: 1000HROJ2117****Article History:****Received:** July 10<sup>th</sup>, 2015**Accepted:** July 22<sup>nd</sup>, 2015**Published:** July 23<sup>rd</sup>, 2015**Citation:**Cho JH, Sattiraju S, Mehta S, Cook LS, Ayenew W. Surgical removal of left atrial appendage thrombus in a patient with acute ischemic stroke. *Heart Res Open J.* 2015; 2(3): 100-102.

# Surgical Removal of Left Atrial Appendage Thrombus in a Patient with Acute Ischemic Stroke

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Atrial fibrillation is a major risk factor for ischemic stroke. Left atrial appendage thrombus is responsible for the majority of cardioembolic stroke caused by atrial fibrillation. Left atrial appendage thrombus in a patient with acute ischemic stroke is usually managed medically with anti-coagulation. We present a case of left atrial appendage thrombus causing acute ischemic stroke in a patient with atrial fibrillation, who underwent surgical removal of left atrial appendage thrombus. The surgical approach was chosen due to several embolic infarcts and a left atrial appendage with a high clot burden.

**KEYWORDS:** Thrombosis; Atrium; Atrial Fibrillation; Stroke.**INTRODUCTION**

Atrial fibrillation is recognized as a major risk factor for stroke accounting for approximately 15 % of all strokes.<sup>1</sup> Atrial fibrillation is the most common cause of cardioembolic stroke accounting for approximately 60% of all cases.<sup>2</sup> Left Atrial Appendage (LAA) thrombus in a patient with acute ischemic stroke is usually managed medically with anti-coagulation. We present a case of LAA thrombus causing acute ischemic stroke in a patient with atrial fibrillation, who underwent surgical removal of LAA thrombus due to several embolic infarcts and high clot burden in left atrial appendage.

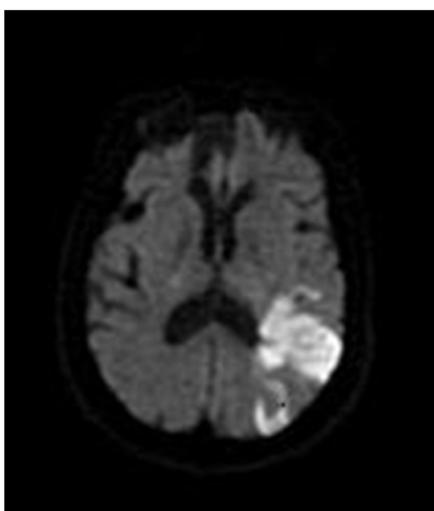
**CASE REPORT**

A 65-year-old male was brought to the emergency department with expressive aphasia and right-sided weakness. His past medical history was significant for hypertension and seizure disorder. Initial vital signs were notable for an irregular pulse at 83 beats per minute and BP of 222/127 mm Hg. He was alert but could not speak. He had right-sided hemiparesis. CT brain without contrast was unremarkable without hemorrhage. He was not a candidate for thrombolytics due to delayed presentation. His malignant hypertension was managed with Labetalol drip. Electrocardiogram showed atrial fibrillation. MRI of the brain revealed multiple acute infarctions in left parietal and occipital lobes (Figure 1) along with small focus of petechial hemorrhagic conversion of left parietal infarcts. Transesophageal echocardiogram, performed two days after admission, revealed a large echogenic density in the LAA suggestive of thrombus with mobile elements (Figure 2, Video 1). With multiple brain infarcts, large LAA clot burden with mobile elements, with high potential of recurrent stroke, it was decided on neurology consultation that it would be reasonable to surgically remove the LAA clot and then

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plan for long term anticoagulation. During hospitalization, telemetry revealed paroxysmal atrial arrhythmias including atrial fibrillation and atrial flutter. Patient underwent surgical removal of LAA clot and resection of LAA (Figure 3) three days after his presentation. His post-operative course was remarkable for new small cerebellar infarctions with small areas of microhemorrhage on repeat MRI of the brain. Serial imaging of the brain was performed to assess the stability of the hemorrhages. With stability of the neurological findings and imaging, he was started on Heparin and Coumadin to decrease the risk of future cardioembolic stroke with chronic atrial fibrillation. After the INR was therapeutic on Coumadin, he was transferred to rehabilitation facility to address his neurological deficits. Patient has residual aphasia and right hemiparesis.



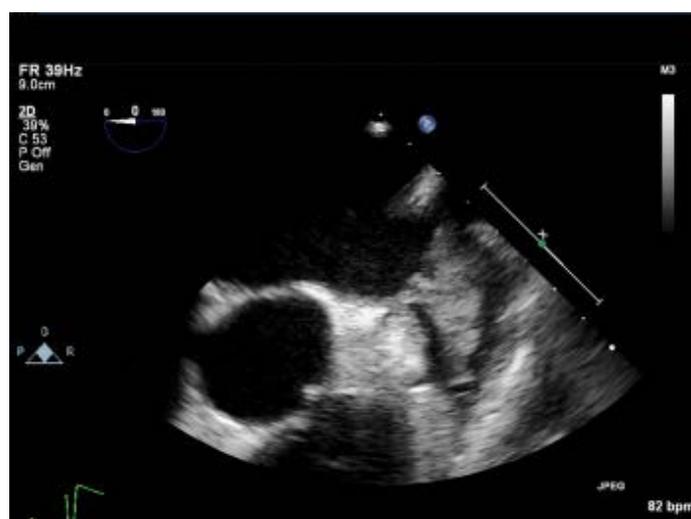
**Figure 1:** MRI of brain revealed multiple acute infarctions in left parietal and occipital lobes along with evidence of small focus of hemorrhagic conversion of left parietal infarction.



**Figure 2:** Transesophageal echocardiogram reveals a large echogenic density (asterisk) in LAA suggestive of thrombus with mobile elements.

## DISCUSSION

A study on a large series of patients with LAA thrombus on transesophageal echocardiogram showed increased risk of embolic events approximately 10.4% per year and mortality of 15.8% per year.<sup>3</sup> LAA thrombosis is occasionally detected in patients with atrial fibrillation and managed medically with anticoagulation to prevent the development of stroke.<sup>4</sup> Although anti-coagulant therapy is considered relatively safe, embolic events after the initiation of therapy because of the partial fragmentation of the thrombus have been reported.<sup>5-7</sup> Our patient presented with cardioembolic stroke due to large LAA thrombus with mobile elements and had evidence of several embolic strokes. The surgical approach was chosen due to concern for recurrent systemic embolization from the extensive LAA thrombus with mobile elements. To our knowledge, this case represents the first



**Video 1:** Transesophageal echocardiogram reveals a large echogenic density (asterisk) in LAA suggestive of thrombus with mobile elements.

**Note:** To best view

1. Kindly open the pdf file in Adobe Reader XI version.
2. Please save the pdf file in your local computer.
3. To watch the video kindly install the latest adobe flash player. Click here to download: <http://get.adobe.com/flashplayer/otherversions/>



LAA: Left Atrial Appendage; LA: Left Atrium

**Figure 3:** A. Intraoperative view shows the exposed thrombus (asterisk) in LAA. B. LAA thrombus is fragmented and removed. C. LAA was surgically removed along with a retained thrombus (asterisk).

report where surgical thrombectomy and LAA resection is undertaken, with acute stroke, in place of anticoagulation to decrease the chance of recurrent systemic embolization. The best timing for surgical removal of thrombus from LAA is unknown and this approach may be based on clinical context, residual clot in LAA, potential for further embolization and the risk with surgical approach.

#### CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

#### CONSENT

No consent is required to our article publication/The patient has provided written permission for publication of the case detail.

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## Mini Review

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E-mail: [z.sun@curtin.edu.au](mailto:z.sun@curtin.edu.au)**Volume 2 : Issue 3****Article Ref. #: 100HROJ2118****Article History:****Received:** September 27<sup>th</sup>, 2015**Accepted:** October 8<sup>th</sup>, 2015**Published:** October 9<sup>th</sup>, 2015**Citation:**

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# 3D Printed Models of Complex Anatomy in Cardiovascular Disease

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Three-dimensional (3D) printing technology has undergone rapid developments over the last decades. The application of 3D printing has reached beyond the engineering field to medicine, with research showing many applications in cardiovascular disease. Due to the complexity of the cardiovascular system, application of 3D printing technology has shown potential value to benefit patients with cardiovascular disease. This mini-review provides an overview of applications of 3D printing in cardiovascular disease, with evidence of some of examples using patient-specific 3D printed models in the two common cardiovascular diseases, aortic dissection and abdominal aortic aneurysm.

**KEYWORDS:** 3D printing; Cardiovascular disease; Abdominal aortic aneurysm; Aortic dissection; Model.

**ABBREVIATIONS:** 3D: Three-dimensional; RP: Rapid Prototyping; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; MSCT: Multislice CT; CAD: Computer Aided Design; STL: Standard Tessellation Language; AAA: Abdominal Aortic Aneurysm.

**INTRODUCTION**

The recent growth and development of three-dimensional (3D) printing has enabled the generation of 3D models of complex anatomy with high resolution and accuracy of depicting cardiovascular disease.<sup>1-3</sup> The concept of 3D printing was first introduced in the late 19<sup>th</sup> century, and then further advanced in 1980's.<sup>4</sup> 3D printing is a common term for Rapid Prototyping (RP), which is commonly used in the engineering and industry field to generate prototype models. 3D printing provides several significant advantages over traditional manufacturing, which include increased rapidity and removing the use of molds or production line. In recent years, this technology has been increasingly used in the medical field, with benefits of RP technology demonstrated in assisting clinical diagnosis, pre-surgical planning and surgical guidance.<sup>5-9</sup>

The expanded applications of this technology to cardiovascular disease allow for rapid generation of 3D complex anatomical structures from medical imaging datasets such as echocardiography, Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) data of patients. This editorial provides an overview of current applications of 3D printing in cardiovascular disease.

**IMAGING POST-PROCESSING OF 2D IMAGES OF CARDIOVASCULAR SYSTEM TO 3D MODELS**

Although, 3D reconstructed visualizations from CT and MRI data are widely available, images are still presented on a computer screen, which impedes comprehensive understanding and interpretation of pathologies due to the differences between actual anatomical structures and reconstructed 3D images.<sup>10</sup> This limitation can be overcome with the development of RP technology through replication of the cardiovascular system. The procedure of creating 3D printed models consists of steps from image acquisition, image post-processing and 3D printing.

Acquisition of high resolution images is a very important step in generation of 3D objects as the quality of the object for 3D printing is determined by the quality of the original data. Superior resolution images (350-400 microns) can be achieved with modern CT or MRI scanners.<sup>11,12</sup> In most cases, slice thickness of submillimeter is required for generation of isotropic voxels to minimize the partial volume artifacts during image post-processing.<sup>13</sup> Currently, Multislice CT (MSCT) imaging is more commonly used for rapid prototyping than MRI due to the wide availability of MSCT scanners, excellent spatial resolution and less complexity of image post-processing for cardiac MSCT data.<sup>14</sup> Regardless of imaging modality used for image acquisi-

tion, the acquire data is saved in the Digital Imaging and Communications in Medicine (DICOM) for post-processing.

3D post-processing of DICOM images is performed on high performance workstations equipped with post-processing tools and software packages, which allow for image segmentation, semi-automatically or automatically. A variety of visualization tools are used during this process, such as multiplanar reformation, surface or volume rendering and maximum-intensity projection. Figure 1A is an example of 3D surface rendered visualization of a patient with aortic dissection with both contrast-enhanced arteries and bony structures displayed, while Figure 1B shows image post-processing of removing the bony structures. Figure 1C indicates the visualization of only vascular details for 3D models. Image post-processing can be enhanced with use of Computer Aided Design (CAD) software which enables automatic optimization of the geometry. Finally, the data is saved as Standard Tesselation Language (STL) file format which is commonly used for 3D printing.

The principle of RP in 3D printing is to use 3D computer models for the reconstruction of a 3D physical model through the additive manufacturing of material layers.<sup>15</sup> These layers correspond to the virtual cross-sectional slices from the 3D CAD model and are joined together to create the final shape



**Figure 1:** The process of using CT angiographic data for image post-processing, segmentation and generation of 3D aorta model. A: 3D surface rendering showing visualization of contrast-enhanced thoracic and abdominal aorta, as well as bony structures. B: Only anatomical vascular structures are displayed with most of the bony details removed through image post-processing. Arrow refers to the aortic dissection in the descending thoracic aorta. C: After image segmentation, only contrast-enhanced aorta and its branches are visualized for 3D models.

or geometric feature of the 3D printed models.

**3D PRINTING MATERIALS**

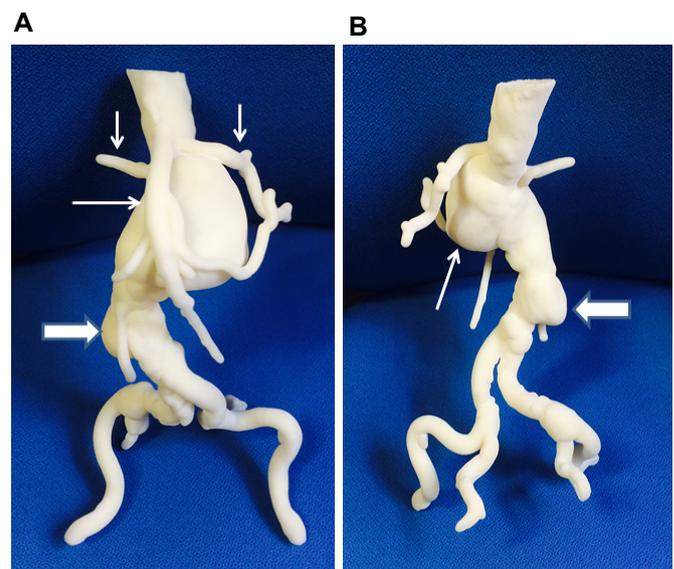
3D physical models may be printed in a variety of materials using different 3D printing technologies, depending on the application purposes, such as education or training, surgical planning, device sizing or diagnostic testing, etc. Each of these technologies has its own advantages and limitations.<sup>14,16,17</sup> Table 1 summarizes the currently available 3D printing technologies using different materials with corresponding clinical applications. The materials available from these technologies have different properties, minimum wall thicknesses and maximum part sizes, which also influences the material or technology selected for a particular purpose.

**CLINICAL APPLICATIONS OF 3D PRINTING IN CARDIOVASCULAR DISEASE**

3D printed models have been reported to benefit patients with cardiovascular disease in many different applications. Individualized or patient-specific 3D printed models have been shown to improve understanding of cardiovascular structure abnormalities, assist in predicting intraoperative complications, choose the best surgical procedures, improve the skills of young or junior surgeons with the use of 3D printed models for simulation training, and reduce operating times through efficient utilization of operating rooms.<sup>1,10,18-20</sup> Furthermore, 3D printing technology enables the manufacture of personalized cardiac stents to reduce the rate of in-stent restenosis,<sup>1</sup> optimize designs of biological scaffolds for tissue engineering of cardiac valves for valve replacement,<sup>21,22</sup> and fabrication of human microvasculature for organ transplantation.<sup>23,24</sup> We will present our preliminary experience of using 3D printed models in the two common cardiovascular diseases: abdominal aortic aneurysm and aortic dissection.

Abdominal Aortic Aneurysm (AAA) is a common vascular disease which most frequently involves abdominal aorta below the renal arteries. Once an aneurysm is detected by imaging studies (most commonly by ultrasound or CT), the risk of rupture is weighed against the risk of surgical repair for each

individual patient.<sup>25</sup> The major determinant for risk of rupture is aneurysm diameter. The traditional approach of open surgery is less commonly performed due to its invasiveness and procedure-related complications, while endovascular stent graft repair is increasingly used as a minimally invasive technique with many advantages compared to open surgery.<sup>25</sup> The success of endovascular stent graft repair of AAA depends on imaging assessment, and currently computed tomography angiography has been confirmed as the best single imaging technique for both preoperative patient assessment and aortic stent-graft surveillance.<sup>25-27</sup> 2D and 3D reconstructions are routinely used to assist planning of endovascular repair by providing information about aneurysm extent and relationship between the aneurysm and the arterial branches. 3D printed models further enhance the role of CT angiography by demonstrating the patient-specific anatomical details of aortic aneurysm in relation to the surrounding structures (Figure 2).



**Figure 2:** 3D printed aorta model of aortic aneurysm. A: anterior view of a full-sized 3D printed model in a patient with an infrarenal Abdominal Aortic Aneurysm (AAA). Arterial branches including superior mesenteric artery (long arrow), renal arteries (short arrows) are clearly visualized. Another small aneurysm (open arrow) is seen just above the common iliac arteries. B: posterior view of the 3D printed model. The long arrow refers to AAA.

Aortic dissection is a common vascular disease and it is the most frequent cause of aortic emergency. Aortic dissection can be a life-threatening event which is characterized by splitting of the aortic wall by high blood pressure entering the

Techniques	Materials	Advantages	Limitations
Stereolithography (SLA) Selective Laser Sintering (SLS) Fused Deposition Modeling (FDM) Laminated Object Manufacturing (LOM)	Photopolymers Polymers, metals Thermoplastic materials or eutectic metals Layers of paper or plastic films	High detail and precision, smooth surfaces High accuracy, good strength Low cost, good strength Low cost, material stock easy to obtain	Moderate strength, high cost High cost, powdery surface Low speed High material waste, slower printing
Inkjet printing techniques (such as ZPrinter 450, PolyJet and PolyJet Matrix)	Fine powers such as plaster or starch	Low cost, high speed, multiple materials	Moderate strength, fail to mimic true tissue properties

**Table 1:** Overview of 3D printing techniques and medical applications.<sup>14,16</sup>

media through an intimomedial entrance tear.<sup>28</sup> Multislice CT angiography is the preferred method for diagnosis of aortic dissection with a sensitivity and specificity of nearly 100%.<sup>29-31</sup> CT angiography has been shown to be more sensitive than invasive angiography for diagnosis of aortic dissection. The 3D aortic arch is difficult to assess on an axial CT plane. Although, 3D reconstructions serve as valuable tools for more accurate assessment of aortic dissection,<sup>30,31</sup> the complex anatomical structures of thoracic aorta, in particular when dissection involving aortic arch present a challenge to decision-making process (Figure 3). The 3D printed models overcome these limitations by providing the exact individual anatomy of the cardiovascular pathology in each patient. Figure 4 is an example of 3D printed model of thoracic aorta based on CT angiographic images (Figure 1) of a patient with Stanford type B aortic dissection. The model was evaluated with measurement of certain anatomical structures of the model comparable to the data from CT angiography (Table 2). The differences in dimensions are due to the process of preparing the digital model to make it suitable for 3D printing, e.g. wall thickening to meet the material's minimum thickness. However, these will be more fully investigated with the intention to match dimensions much more closely and reliably.

Anatomic structure	CT measurements (mm)	3D printed model (mm)
Ascending aorta	40	38
Aortic arch	36	38
Brachiocephalic artery	17	16
Left common carotid artery	13	14
Left subclavian artery	15	15.5
Descending aorta	36	35

Table 2: Correlation of CT angiography and 3D printed model.

### SUMMARY AND CONCLUDING REMARKS

3D printing is an emerging and promising technique with many applications in cardiovascular disease with a focus on surgical training and device design. High resolution images, especially from cardiac CT make the use of 3D printing technology become a reality to assist patients with cardiovascular disease. Development of materials used for rapid prototyping is a key area to guarantee successful implementation of 3D printing technology. Another limitation lies within the time and cost spent in generation of 3D printed models. Further studies with inclusion of more patients and more data are needed to confirm



Figure 3: 3D printed model of aortic aneurysm in aortic arch. A: Stereolithographic model of the aortic arch (outside view) and the aneurysm. B: Stereolithographic model of the aortic arch (inside view) and preoperative testing of the interventional procedure with the custom-made occlude device.<sup>19</sup>

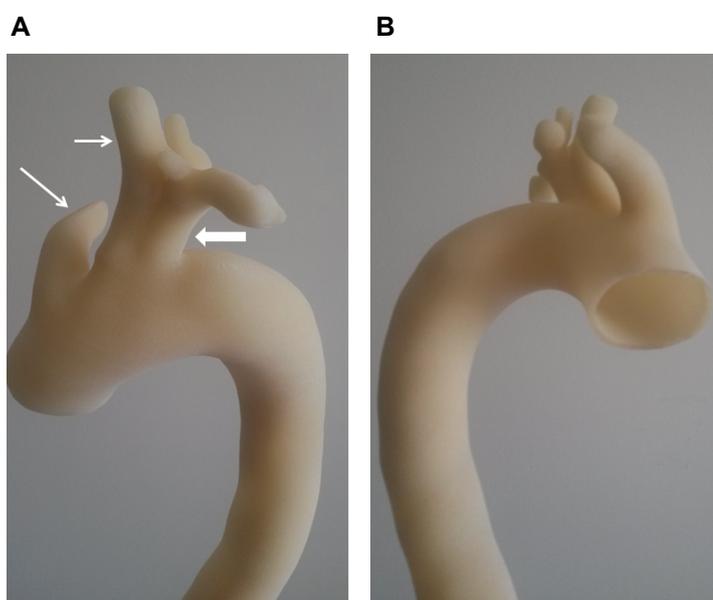


Figure 4: 3D printed model of aortic dissection. A: anterior view of a patient-specific 3D printed model based on CT angiographic images of aortic dissection (Figure 1). Aortic branches consisting of brachiocephalic artery, left common carotid and left subclavian arteries (long, short and open arrows, respectively) are seen arising from the aortic arch. B: posterior view of 3D printed model. Note that the intimal flap that separates the aortic dissection was not printed in the 3D model due to removal of the thin fibrous membrane of the flap during image post-processing.

its clinical value of using preoperative 3D printed models for reduction of perioperative/postoperative mortality.

#### CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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## Research

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# Clinical Characteristics of Children with Pulmonary Vein Abnormalities in a Tertiary Centre in an Urban Community in Nigeria

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**ABSTRACT**

**Background:** Pulmonary vein abnormalities are rare. Prompt intervention is needed to salvage the children affected. There are very few reports on occurrence of pulmonary vein abnormalities among Nigerian and African children. The aim of this study is to report the clinical characteristics of Nigerian children with Pulmonary vein abnormalities.

**Method:** A prospective study involving consecutive subjects diagnosed with pulmonary venous abnormalities using echocardiography at the Lagos State University Teaching Hospital (LASUTH), Nigeria between January 2007 and December 2014. Data were analysed using Microsoft Excel program supplemented by Megastat statistical package. Statistical significance was set at p-value<0.05.w

**Results:** There were 21 cases of pulmonary venous abnormalities, which accounted for 2.07% of cases of congenital heart disease and 6 per 100,000 of the total children that presented in LASUTH during the study period, with male to female ratio of 0.8:1. Sixteen (76.2%) of the studied subjects presented in infancy and five (23.8%) cases presented above one year of age. The commonest indication for echocardiography was cyanosis, other mode of presentation were breathlessness, recurrent respiratory tract infection, congestive cardiac failure and murmur. Total anomalous pulmonary venous return accounted for 66.7%, Cortriatriatum was seen in 6 subjects (28.6%) and a case of Partial Anomalous Pulmonary Venous Connection (PAPVC) was seen (4.8%). Most of the subjects had other associated cardiac defects.

**Conclusion:** The prevalence of pulmonary vein abnormalities among Nigerian children is comparable to that in other parts of the world. High degree of suspicion is needed to enable prompt diagnosis and intervention.

**KEYWORDS:** Pulmonary; Venous; Abnormalities; Children; Nigeria.

**ABBREVIATIONS:** LASUTH: Lagos State University Teaching Hospital; PAPVC: Partial Anomalous Pulmonary Venous Connection; TAPVC: Total Anomalous Pulmonary Venous Connection; CHD: Congenital Heart Disease; LUTH: Lagos University Teaching Hospital; APVC: Abnormal Pulmonary Venous Connection; GE: General Electric; MDCT: Multi Detector Computed Tomography.

**INTRODUCTION**

Pulmonary veins abnormalities include total and partial anomalous pulmonary venous connection, cortriatriatum and pulmonary vein stenosis or hypoplasia/atresia.

Total Anomalous Pulmonary Venous Connection (TAPVC) is a cyanotic congenital

heart defect in which all the pulmonary veins are connected to the right atrium or the tributaries of the systemic veins. It accounts for 1 to 3 percent of congenital heart disease.<sup>1</sup> It is the fifth commonest cyanotic congenital heart disease.<sup>2</sup> The incidence of TAPVC is 1:15,000 live births.<sup>2</sup> It is classified into supracardiac, cardiac, infracardiac and mixed pattern based on the site of anomalous venous union. There is a 3:1 male preponderance in infants with infradiaphragmatic lesion.<sup>3</sup> There is a natural history of death in 80% of symptomatic infants with TAPVC that present before the age of one year.<sup>4</sup>

Cortriatriatum is a rare congenital cardiac anomaly in which a fibromuscular membrane divides the atrium into two. This results in abnormal incorporation of the pulmonary venous structures into the right or left atrium. It accounts for 0.1% of Congenital Heart Disease (CHD).<sup>5</sup>

Partial anomalous pulmonary venous return (PAPVC) is a rare CHD with one or pulmonary veins connects to the venous circulation. The estimated prevalence rate is 0.5% of the general population. It is commonly associated with atrial septal defect.<sup>6</sup>

Congenital pulmonary vein stenosis and hypoplasia/atresia is a rare cause of neonatal pulmonary oedema and can present later in life with pulmonary artery hypertension or hemotypsis.<sup>7</sup> In a seven years population based study in Atlanta by Reller, et al.<sup>2</sup> TAPVC was seen in 0.95% of infants with congenital heart disease with a prevalence of 0.8 per 10,000 live births.

In a retrospective analysis of patients with anomalous pulmonary venous return in India by Vimal Raj, et al.<sup>8</sup> anomalous pulmonary connection occurred in 10.3% of subjects with CHD. TAPVC and PAPVC occurred in 6 and 4.3% percent of the studied subjects respectively. Out of the subjects with TAPVC, supracardiac type was the commonest.

In a retrospective study by Chinawa, et al.<sup>9</sup> in Enugu, Nigeria, data of 71 children with CHD aged 6 months to 12 years that presented between January 2007 to April 2015 were analysed. Only one case of TAPVC was seen which accounted for in 1.4% of the studied subjects.

Okoromah, et al.<sup>10</sup> in Lagos University Teaching Hospital (LUTH), Nigeria did a two years prospective study on children with CHD aged 3 to 192 months, a case of TAPVC (2.4%) was seen among the 41 cases of cyanotic CHD. A case of Cortriatriatum was also documented. No other form of Abnormal Pulmonary Venous Connection (APVC) was seen. There have been other reports on Congenital Heart Disease in Nigeria, but no case of APVC was mentioned.<sup>11,12</sup>

In Nigeria, there are very few Paediatric centres with echography machine with doppler facility and expertise which may explain why only very few cases of abnormal pulmonary venous connections have been reported. To the best of the au-

thors knowledge, there has been no report in Nigeria on the clinical characteristics of children with anomalous or abnormal pulmonary venous connections hence the need for this study which aim to describe the clinical characteristics of subjects with abnormal pulmonary venous connections to be able emphasize the need to look out for these subjects to enable improved outcome by early diagnosis and prompt intervention in these subjects.

## SUBJECTS AND METHODS

The study was a prospective study of consecutive subjects diagnosed with abnormal pulmonary venous connections using echocardiography at the Lagos state university teaching hospital (LASUTH), Nigeria between January 2007 and December 2014 as part of a large study. LASUTH serves as a major referral centre form both private and public hospitals within Lagos and other neighbouring states.

Transthoracic echocardiography was done by a Paediatric Cardiologist using a General Electric (GE) Vivid I machine ref number 14502 WP SN 2084 with an appropriate size probe. All subjects referred for echocardiography had clinical evaluation, physical examination, chest radiograph, electrocardiogram before echocardiography.

Subjects bio-data and indications for echocardiography and echocardiographic findings were analysed using Microsoft Excel program supplemented by Megastat statistical package. Mean, standard deviation and other parameters were generated as necessary for continuous data. Means of continuous variables were compared using the student t test and proportions using chi-square test. The coefficients of correlation and associated p-values were derived. Statistical significance was set at p-value <0.05.

## RESULTS

A total of 315,150 children less than 13 years presented at the Paediatric department of LASUTH as both in and out patients within the study period, out of which 1495 had echocardiography done for various indications. Among the total children that had echocardiography done, 354(23.7%) of them had structurally normal heart and 1141(76.3%) had structural heart defect. Among the children with structural heart defect, 1011(88.6%) of them had congenital heart defect and 130(11.4%) of them had acquire heart defect. There were 21 cases of pulmonary venous abnormalities within the studied period, which accounted for 2.07% of cases of congenital heart disease and 6 per 100,000 of the total children that presented in LASUTH within the study period.

Of the 21 cases seen, 16(76.2%) of the studied subjects presented in infancy and 5(23.8%) cases were diagnosed above one year of age. The mean age at diagnosis of all subjects was 8.01±25 months. The mean age at diagnosis for boys was 8.7±3.1 months and 7.5±3.2 months for girls. There was

no statistical significance for the age at diagnosis between both sex ( $p=0.804$ ). This is highlighted in Table 1. Among the studied subjects, 57.1% were female and 42.9% were male with male to female ratio of 0.8:1.

Age group of subjects	Frequency	Percentage
<1 month	5	23.8
1 month-12 months	11	52.4
>12 months	5	23.8
Total	21	100.0

Table 1: Age of subjects at presentation.

The commonest indication for echocardiography was a suspicion of cyanotic congenital heart disease based on cyanosis at presentation. This accounted for 38.1% of echocardiography evaluation. Seven subjects (28.6%) presented with breathlessness. Five subjects (23.8%) presented with recurrent respiratory tract infection and had echocardiography done on suspicion acyanotic CHD. One of the subjects was evaluated on account of congestive cardiac failure which accounted for 4.8% of the indication for echocardiography while another had echocardiography done after presenting with murmur. Indication for echocardiography is shown in Figure 1.

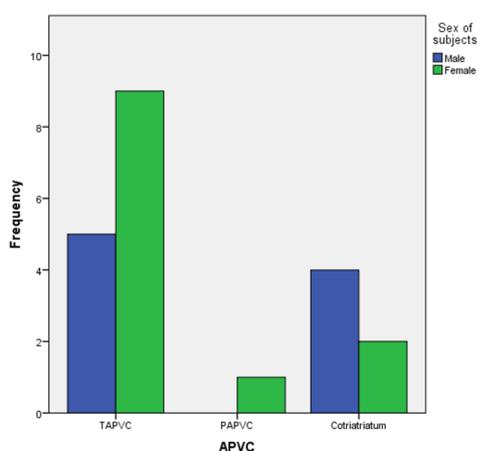


Figure 1: Sex distribution of the types of pulmonary vein abnormalities in subjects.

Total anomalous pulmonary venous return accounted for 66.7% of the subjects with APVC. Cortriatrium was seen in 6 subjects (28.6%) and a case of PAPVC was seen (4.8%). The mean age at diagnosis of TAPVC was  $8.4\pm 4.2$  months. The child with PAPVC was diagnosed at 8.5 months of age. Mean age at diagnosis of cortriatrium was  $7.0\pm 5.1$  months. There was not statistical significance at the age of diagnosis of the APVC with a  $p$  value of 0.917. These are highlighted in Tables 2 and 3.

Out of the 14 cases with TAPVC, supracardiac type was seen 12 subjects (85.7%) and 2 patients (14.3%) had mixed TAPVC.

No other associated cardiac anomaly was seen in 6 (42.8%) out of the 14 subjects with TAPVC. ASD was seen in

3 subjects diagnosed with TAPVC. Cortriatrium alone occurred in 4 (66.7%) out of 6 subjects with the cardiac lesion. The only subject with PAPVC had associated large secundum ASD. Associated cardiac anomalies are highlighted in Figure 1.

Indications for Echocardiography	Frequency	Percentage
Recurrent RTI	5	23.8
Cyanosis	8	38.1
Murmur	1	4.8
Breathlessness	7	28.6
CCF	1	4.8
Total	21	100.0

RTI: Respiratory Tract Infection.

Table 2: Indication for echocardiography.

Types of APVC	Frequency	Percentage
TAPVC	14	66.7
PAPVC	1	4.8
Cortriatrium	6	28.6
Total	21	100.0

Table 3: Types of pulmonary venous abnormalities in the subjects.

## DISCUSSION

Anomalous pulmonary venous connection is a rare congenital heart disease with a lethal natural course because of progressive pulmonary artery hypertension and heart failure.<sup>13</sup> In this study, 6 per 100,000 of the total children that presented in LASUTH within the study period had abnormal pulmonary vein connections. A prevalence of 1 in 15,000 live births was reported for TAPVC by Reller, et al.<sup>2</sup> among children in Atlanta. Abnormal pulmonary vein connections was found in 2.07% of cases with CHD in the current study. This is low compare to finding in a study by Vimal Raj, et al.<sup>8</sup> in an eight years retrospective study where APVC accounted for 10.3% of cases with CHD. The larger number of cases of congenital heart diseases, geographical differences, differences in methodology including mode of diagnosis with Doppler echocardiography compared with Multi Detector Computed Tomography (MDCT) and Cardiac Magnetic Resonance which are more sensitive used by Vimal Raj, et al.<sup>8</sup> Cardiac Multi detector computed tomography (MDCT) and Cardiac Magnetic Resonance evaluation is still at fetal stage in Nigeria.

A major finding in this study is that about one quarter of the subjects (23.8%) with diagnosis of APVC within one month of life. This may account for why earlier reports from the country reported fewer cases since these reports were on subjects

older than three months generally.<sup>9,10</sup> Another probable reason for the lower prevalence reported in the earlier studies may be lack of doppler facility in the echocardiography machine used.<sup>7</sup> Although the proportion reported in this study proportion is lower than the earlier report by Correa-Villasenor<sup>1</sup> where 98% of subjects with TAPVC presented during the neonatal period. This emphasises the need for more surveillance for these subjects to enable early diagnosis. In the current study about a quarter of the subjects were diagnosed after infancy. This is quite late considering the fact that the disease is a progressive one which requires early intervention.<sup>7</sup> The presentation of this group of subjects is also late when compared to the study by El-Said, et al.<sup>14</sup> where 20 (57%) out of 35 subjects had diagnosis of TAPVC by 6 weeks of life. In the study by El-Said, et al.<sup>14</sup> surgical intervention before six months resulted in high mortality but early and intensive medical treatment resulted in a favourable outcome. Most patients with TAPVC were found to be asymptomatic at birth and majority died within first year of life if surgical repair was not implemented.<sup>14</sup>

In this study, 57.1% of the subjects were female but there was no statistical significant difference in the sex of studied subject. Male preponderance has been documented in some cases of TAPVC.<sup>15-17</sup> whereas there appears to be no sex prevalence in some other reports.<sup>17</sup>

Two third of the subjects (66.7%) had TAPVC, while PAPVC occurred in one patient (4.8%). This is similar to the report by Ussiri, et al.<sup>15</sup> where TAPVC was seen in 60% of the studied subjects and PAPVC in 40% of the cases. TAPVC is said to be the commonest form of APVC occurring ten times more than PAPVC<sup>18</sup> as documented also in this report. Among subjects with TAPVC, supracardiac lesion was seen in 86% of cases while mixed lesion occurred in 14% of the cases. This is not surprising because supracardiac lesion is the commonest form of TAPVC but mixed type has the worst prognosis. Vimal Raj, et al.<sup>8</sup> and Ussiri, et al.<sup>15</sup> also documented higher proportion of the supracardiac type among the Indian children. Although, it occurred in 46% and 43.6% respectively.

The diagnosis of TAPVC was made much earlier than PAPVC in cases seen in this study. The earliest diagnosis of APVC seen was in subjects with cortriatrium although there was no statistical significant difference in the age at diagnosis. The earlier presentation of subjects with TAPVC may be due to the fact the timing and severity of symptoms in Pediatric patients with pulmonary vein abnormalities depend largely on the number of pulmonary veins involved and the severity of obstruction to individual pulmonary veins. Since all the four pulmonary veins are involved in TAPVC, they are more likely to have more severe symptoms which will necessitate earlier presentation. This finding is similar to the study by Ussiri, et al.<sup>15</sup> where the mean age at presentation was 21.6 months for TAPVC and 135.2 months for PAPVC. (Table 4) The mean age at diagnosis of cortriatrium in this study was 7.0±5.1 months. This is similar to a mean age of 6 months documented by Alphonso, et al.<sup>19</sup>

Form of APVC	N	Age at presentation in weeks (Mean± SD)	p-value
TAPVC	15	35.57±11.86	0.971
PAPVC	1	36.00±00	
Contriatrium	6	30.17±20.57	

Table 4: Types of pulmonary venous abnormalities and mean age of presentation in months.

The commonest indication for diagnosis in this study was cyanosis (38.1%). The reason for low prevalence of cyanosis in these subjects is not immediately clear but may be due to the fact that about that proportion presented in the neonatal period when cyanosis may not be so visible to the naked eye at that age due to patency of the duct at that age and coexisting lesions such as ASD which can help improve mixing of blood at the atrial level in them.<sup>17</sup> In a study by Tubianosa, et al.<sup>20</sup> all patients that had TAPVC correction presented with cyanosis and 83% of them had congestive cardiac failure. Breathlessness was the second commonest indication for diagnosis in this study but this was found as the commonest indication in a study by Am-mash, et al.<sup>21</sup> on subjects with PAPVC.

TAPVC is usually an isolated cardiac anomaly and associated complex cardiac lesion is seen in 30% of the cases.<sup>22</sup> Mortality with complex anomalies exceeds 50% than in patients with isolated TAPVC. In this study, isolated TAPVC was seen in 42.9% of the cases. In 57.1% of the cases, other associated cardiac lesions were seen. The commonest associated cardiac lesion was ASD. Other cardiac lesions seen were VSD, TGA, PDA and DORV.

ASD is a common associated cardiac lesion with PAPVC.<sup>23</sup> ASD was seen in the only subject that was diagnosed with PAPVC in this study. Cortriatrium is often associated with other congenital cardiac anomalies with ASD being the commonest.<sup>24</sup> In this study, isolated cortriatrium was seen in 4 out of 6 subjects. Two subjects each had a VSD and ASD as an associated anomaly. (Table 5)

Other associated cardiac anomalies	Frequency	Percentage
TAPVC only	6	28.6
Contriatrium only	4	19.0
TAPVC and ASD	3	14.3
TAPVC and VSD	1	4.8
Cortriatrium with VSD	1	4.8
Cortriatrium with ASD	1	4.8
PAPVC and ASD	1	4.8
TAPVC and TGA	1	4.8
TAPVC, ASD and PDA	1	4.8
TAPVC, VSD, ASD, PDA and TGA	1	4.8
TAPVC, ASD, Single Ventricle and DORV	1	4.8
Total	21	100.0

Table 5: Other associated cardiac anomalies in subjects with pulmonary vein abnormalities.

**CONCLUSION**

The prevalence of pulmonary vein abnormalities among Nigerian children is comparable to that in other parts of the world. High degree of suspicion is needed to enable prompt diagnosis and intervention.

**CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

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**FINANCIAL DISCLOSURE**

The study was sponsored by both authors.

**CONSENT**

Informed consent was obtained from the parent and caregivers before being included in the study.

**AUTHOR'S CONTRIBUTION**

BA Animasahun was the project leader, Study concept and design was done by BA Animasahun.

Acquisition of data was done by Animasahun. Animasahun, Akinbami and Awe participated in the analysis and interpretation of data and drafted the manuscript. Critical revision of the manuscript for important intellectual content, administrative, technical, and material and financial support were done by all the authors.

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