

The Cardiology Division in the Department of Internal Medicine at Texas Tech University Health Sciences Center in Lubbock, Texas, sponsors an annual symposium on congestive heart failure. The summaries below provide important updates on the management of patients with congestive heart failure

May 2019

1. Acute Heart Failure Management: Where do we stand today?

Nandini Nair MD, PhD, FACC, FACP, FAHA, FAHFSA

Abstract: *This article is a concise review on acute heart failure management with emphasis on identification of risk factors/risk stratification and using guideline directed medical therapy (GDMT) to achieve optimal results and appropriate post discharge follow up to prevent readmissions and improve quality of life. A brief treatment algorithm is presented here.*

Acute Decompensated Heart Failure (ADHF) is defined as new or worsening signs and symptoms of HF with a severity requiring unscheduled medical care/hospitalization or need for urgent/emergent therapy. About 6.2 million carry the diagnosis of HF, and approximately on half million cases per year is the current incidence of HF. The prevalence of HF is 2% in persons aged 40 to 59 years, progressively increasing to 10% for those aged 70 years and older. Sudden cardiac death is 6 to 9 times higher in the HF population.¹

Gender differences exist in presentation. Female and male patients presenting with AHF show two different clinical constellations. Women present with hypertension, valvular diseases, supraventricular arrhythmias, and preserved LV function more often than men. Male patients are younger, are more often cigarette smokers, and have coronary heart disease

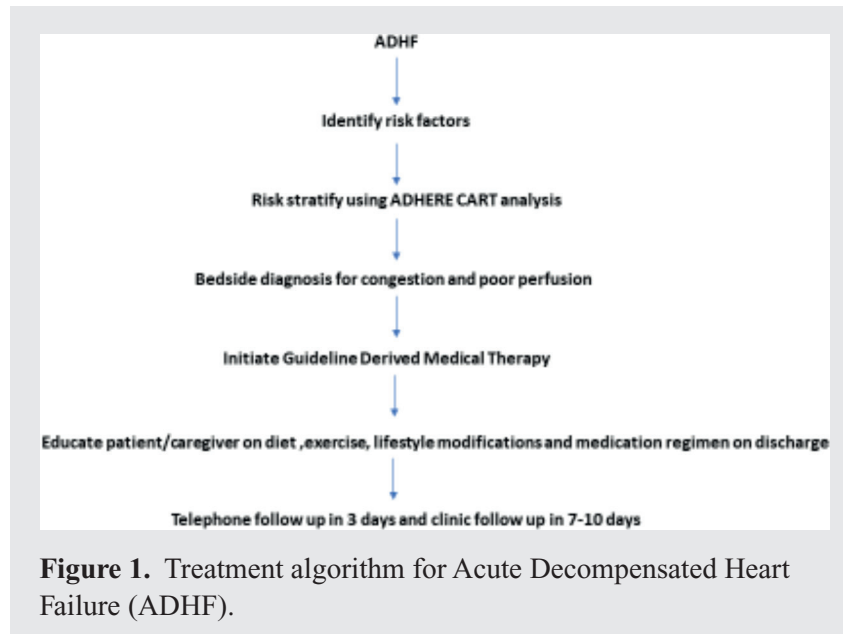
and dilated cardiomyopathy. Women more frequently have diabetes, anemia, and thyroid disease, whereas men more often have renal failure, peripheral arterial disease, and COPD. Such differences prompt a need to individualize management. This also underscores the need for more comprehensive recruitment of women into clinical trials.

Mortality secondary to ADHF varies with the type of presentation. HF patients presenting with cardiogenic shock have the highest in-hospital mortality ranging up to 40%.² Hospital readmissions present a challenge in that they increase mortality.^{3,4} Additionally, the Centers for Medicare and Medicaid Services imposes a financial penalty on the hospital if 30-day readmissions exceed 25%. Causes for hospital readmission are drug/diet noncompliance, failure to seek care, inappropriate drug regimen at discharge, and incomplete resolution of symptoms at discharge.

ADHF may be *de novo* or more commonly acute decompensation of chronic HF. Triggers for acute decompensation include hypertension, acute coronary syndrome, arrhythmias, infections, renal failure, and non-compliance. Amplifying mechanisms are usually diastolic dysfunction, endothelial dysfunction, renin angiotensin and aldosterone/sympathetic activation, oxidative stress, and inflammation. End organ dysfunction and congestion become the final consequences.

Brain natriuretic peptide (BNP) and N terminal pro BNP are the established markers of HF. High sensitivity troponins are now also used for risk stratification. Soluble ST2 and Galectin 3 are now FDA approved for use as biomarkers of fibrosis/remodeling and inflammation. However, there is no gold standard for diagnosis, but BNP is used to triage patients in the emergency rooms.

Corresponding author: Nandini Nair
Contact Information: Nandini.nair@ttuhsc.edu
DOI: 10.12746/swrccc.v7i31.613



The Acute Decompensated Heart Failure National Registry (ADHERE) makes risk stratification simple and predicts in-hospital mortality.⁶ The ADHERE registry used the classification and regression tree analysis in both the derivation and validation cohorts to assess risk. It uses three parameters, including blood urea nitrogen (BUN), systolic blood pressure (SBP), and creatinine for risk stratification. A BUN of >43 mg/dL, SBP of <115 mmHg, and a creatinine of >2.75 mg/dL will place an ADHF patient at 22% in-hospital mortality.⁶

Renal dysfunction has been historically linked to poor outcomes in ADHF, emphasizing the importance of the cardiorenal syndrome in HF. An increase in Cr by >0.3 mg/dL is associated with higher hospital and post-discharge mortality, increased length of stay, higher readmission rates, and cost. Elevated filling pressures usually precede hospitalization, and central venous pressures have been shown to have the most impact on glomerular filtration rate and worsening renal function.⁷⁻⁹

In summary, acute heart failure is a complex syndrome with multiple etiologies and targets. The main goal is symptom relief and short-term risk reduction, which are clinically important. Guideline-directed medical therapy should be initiated as soon as a diagnosis

of ADHF is made.¹⁰ A simplified treatment algorithm is shown in Figure 1. The highest priority is improving long-term outcomes and preventing readmissions, which in turn would significantly improve quality of life and mortality.

REFERENCES

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 Update: a report from the American Heart Association. *Circulation*. 2019;139:e56–e528.
2. Nieminen M S, Brutsaert D, Dickstein K, et al. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J* 2006;27:2725–2736.
3. Gheorghiu M, De Luca L, Fonarow GC, et al. Pathophysiologic targets in the early phase of acute heart failure syndromes. *Am J Cardiol* 2005;96:11G–17G.
4. Setoguchi S, Stevenson LW, Schneeweiss S. Repeated hospitalizations predict mortality in the community population with heart failure. *Am Heart J* 2007;154:260–6.
5. Yousufuddin M, Abdalrhim AD, Wang Z et al. Cardiac troponin in patients hospitalized with acute decompensated heart failure: A systematic review and meta-analysis. *J Hosp Med* 2016;11:6:446–454.
6. Fonarow GC, Adams KF Jr, Abraham WT. Risk stratification for in-hospital mortality in acutely decompensated heart

- failure: classification and regression tree analysis. *JAMA*. 2005;293:572–80.
7. Gottlieb SS, Abraham W, Butler J, et al. The prognostic importance of different definitions of worsening renal function in congestive heart failure. *J Card Fail* 2002;8:136–41.
 8. Metra M, Nodari S, Parrinello G, et al. Worsening renal function in patients hospitalized for acute heart failure: clinical implications and prognostic significance. *Eur J Heart Fail* 2008;10:188–95.
 9. Adamson PB, Magalski A, Braunschweig F, et al. Ongoing right ventricular hemodynamics in heart failure: clinical value of measurements derived from an implantable monitoring system *J Am Coll Cardiol*. 2003;41:565–71.
 10. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines *Circulation* 2013;128:e240–e32.

2. Cardiac Transplantation

Nandini Nair MD, PhD, FACC, FACP, FAHA, FAHFSA

Abstract: *This article summarizes the history of cardiac transplantation, present day surgical techniques, and the evolution of cardiac transplantation as a standard of care. Role of donor organ selection and matching and the indications and contraindications for cardiac transplant will be briefly discussed.*

Cardiac transplantation is the gold standard and the only definitive therapy at present for end stage heart failure. The average survival is now 10 years with many good candidates living >20 years. Quality of life (QOL) is optimal in that most cases return to work and enjoy an almost normal life. Donor shortage is the major limiting factor. Worldwide 3700 transplants occur in approximately 201 centers; 2500 transplants are in the USA in the 126 active heart transplant centers.

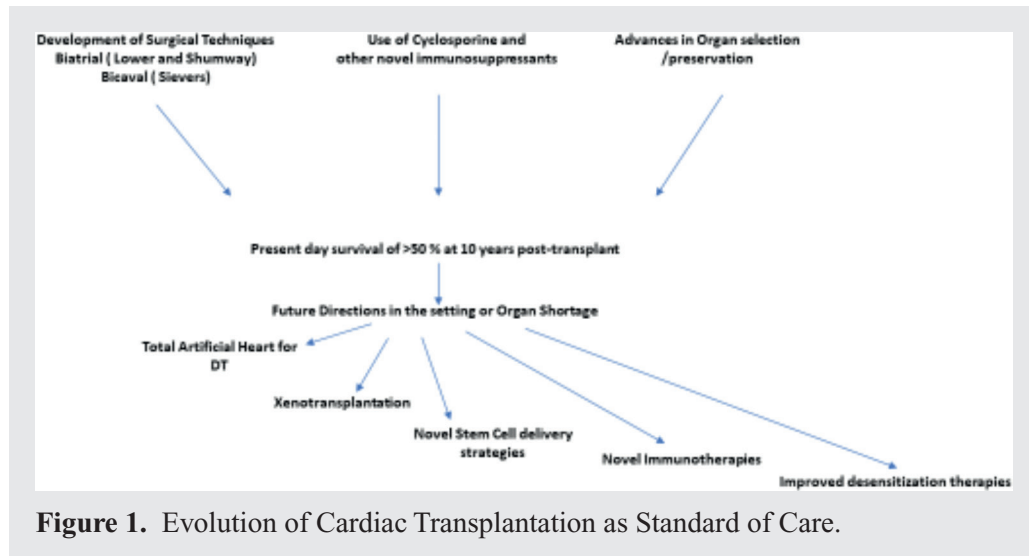
The history of cardiac transplantation starts with Alexis Carrel and Charles Guthrie who first attempted the procedure in dogs in 1905. This was followed by Frank Mann who performed canine operations in 1933 at the Mayo Clinic. Biatrial technique for orthotopic heart transplantation was also first introduced in a dog model by Richard Lower and Norman Shumway

in 1960. Christiaan Barnard performed the first ever heart transplant in December 1967 in Cape Town, South Africa. The first successful cardiac transplant in the United States was in 1968 by Norman Shumway at Stanford University Hospital.^{1–5}

Heterotopic heart transplantation was first performed by Barnard in 1974 as a left ventricular bypass and involves placing a donor heart in the right lower thorax where it is anastomosed to work in parallel to the intact recipient heart. Though rarely done today, there remain 2 possible indications for heterotopic heart transplantation: 1) patients with elevated pulmonary hypertension in whom the donor right ventricle would be unable to tolerate the increased afterload; 2) significant size mismatch (donor/recipient weight ratio <75%).

The surgical techniques for heart transplantation involve a biatrial approach versus a bicaval strategy. The classic Shumway-Lower technique was biatrial in which an excision was made at the mid atrial level and atria were re-anastomosed followed by great vessel anastomosis.⁶ The disadvantages were atrial arrhythmias, sinus node dysfunction, and increased tricuspid regurgitation (TR). In the bicaval technique by Sievers (1991) the vessels were anastomosed with atrial geometry maintained.⁷ The advantages are fewer atrial arrhythmias and less TR and less dependence on pacemakers due to lack of chronotropic incompetence. The disadvantage is a risk of superior vena cava stenosis, particularly when there is a size mismatch between the donor and recipient.

Absolute indications in appropriate patients are hemodynamic compromise due to HF, severe symptoms of ischemia that limit routine activity and are not amenable to coronary artery bypass grafting/PCI (CABG/PCI) and recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities. Contraindications include fixed pulmonary HTN (PVRI >6 Wood units). Contraindications also include trans pulmonary gradients of 16–20 mm Hg, active systemic infections, active malignancy, diabetes with end organ damage (neuropathy, nephropathy and proliferative retinopathy), severe irreversible renal, hepatic or pulmonary damage, active systemic processes with high probability of recurrence, pulmonary



infarct with high likelihood of progression to abscess with immunosuppression, and psychosocial factors, such as non-compliance, active substance abuse, and lack of adequate family support.

Organ selection is an important aspect of successful transplant outcomes. A donor heart **should not be used** in the presence of intractable ventricular arrhythmias, the need for excessive inotropic support (dopamine at a dose of 20 mcg/kg/min or similar doses of other adrenergic agents), discreet wall motion abnormalities on echocardiography, or a LV ejection fraction <40%.⁸

Donor-recipient size matching is another important factor that influences cardiac transplant outcomes. Donors whose body weight is no greater than 30% below that of the recipient is uniformly safe; a male donor of average weight (70 kg) can be safely used for any size recipient irrespective of weight, use of a female donor whose weight is more than 20% lower than that of a male recipient could pose problems with size mismatch.

Risk factors for post-transplant mortality include donor age, recipient age, recipient BMI, recipient pulmonary vascular resistance, recipient bilirubin, recipient creatinine and transplant center volume.⁹ The current survival of post cardiac transplant patients is secondary to refinement of surgical techniques,

advances in immunosuppression drugs, organ matching and selection, and the early detection and treatment of rejection and infections. However, current challenges exist in controlling primary graft dysfunction, the lack of adequate treatments for sensitized patients and remedies for long term complications, such as coronary allograft vascular disease. The major limitation is still the limited donor supply.¹⁰ The Figure summarizes the evolution of cardiac transplantation as the gold standard.

In summary, development of a total artificial heart for destination therapy (DT), improved stem cell delivery, and increasing donor pool through better organ allotment and xenotransplantation will help overcome present day challenges. The evolution of personalized medicine will possibly progress toward better organ selection.

REFERENCES

1. Hunt SA. Taking heart—cardiac transplantation past, present, and future. *N Engl J Med* 2006;355:231–5.
2. Cooper MA, Pommering TL, Koranyi K. Primary immunodeficiencies. *Am Fam Physician* 2003;68:2001–8.
3. Ventura HO, Muhammed K. Historical perspectives on cardiac transplantation: the past as prologue to challenges for the 21st century. *Curr Opin Cardiol* 2001;16:118–23.
4. McRae D. *Every Second Counts: The Race to Transplant the First Human Heart*. New York, NY: Putnam Adult, 2006.

5. Hunt SA, Haddad F. The changing face of transplantation. *JACC*. 2008;52:587–598.
6. Lower RR, Shumway NE. Studies on orthotopic homotransplantation of the canine heart. *Surg Forum* 1960;11:18–9.
7. Sievers HH, Weyand M, Kraatz EG, et al. An alternative technique for orthotopic cardiac transplantation, with preservation of the normal anatomy of the right atrium. *Thorac Cardiovasc Surg* 1991;39:70–2.
8. Costanzo, MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant* 2010;29:914–956.
9. Pettit SJ, Jhund PS, Hawkins NM, et al. How small is too small? A systematic review of center volume and outcome after cardiac transplantation. *Circ Cardiovasc Qual Outcomes*. 2012;5:783–90.
10. Kittleson MM, Kobashigawa JA. Cardiac transplantation: current outcomes and contemporary controversies. *JACC Heart Fail* 2017;5:857–868.

3. Heart Failure and Sleep Apnea- A Complex Interaction

Nandini Nair MD, PhD, FACC, FACP, FAHA, FAHFSA

Abstract: *This article is a brief summary of the complex interaction between sleep disordered breathing (SDB) and heart failure (HF). Pathophysiology of SDB involves hypoxemia, increased sympathetic activation, and decreased vagal drive leading to right ventricular dysfunction, arrhythmias, and heart failure. Current management and experimental therapies will be briefly discussed.*

Heart failure (HF) and sleep-disordered breathing (SDB) go hand-in-hand and lead to disastrous consequences if SDB is untreated. A worse prognosis

is noted in HF patients who have SDB than those without it. Sleep-disordered breathing can be divided into central sleep apnea (CSA) and obstructive sleep apnea (OSA).¹⁻⁴ Central sleep apnea is the predominant type seen in patients with more severe disease.

The global prevalence of SDB, i.e., CSA and OSA, exceeds 50% in patients with HF. Sleep-disordered breathing is common in acute and chronic HF, with reported prevalence of 44% to 97%. The prevalence of CSA increases as NYHA functional class deteriorates; CSA severity correlates with underlying cardiac dysfunction, sex, BMI, and smoking. It is also emerging as a predictor of hospital readmission and mortality. Obstructive sleep apnea has been postulated to be an independent risk factor for the development of HF with a greater incidence in males. A 2.6-fold increase in the incidence of CAD and HF after adjustment for age has been noted in this population.

Cyclic apnea and hypopnea results in sleep disturbance and fragmentation, hypoxemia, hemodynamic changes, sympathetic activation, and intrathoracic pressure swings. See the Figure.

The benefit of treatment of SDB has been noted in improved quality of life (QOL). General medical optimization using guideline derived medical treatment is recommended. Diuretics to relieve congestion and neurohormonal antagonists to reduce the sympathetic upregulation can reduce morbidity and mortality in patients with HF and SDB. Cardiac resynchronization therapy significantly improves CSA but not OSA. Advanced HF patients on LVAD support or who have had a heart transplantation show improvement in CSA. Lifestyle measures, such as weight loss, reduce the severity of SDB in obese patients with OSA. Patients

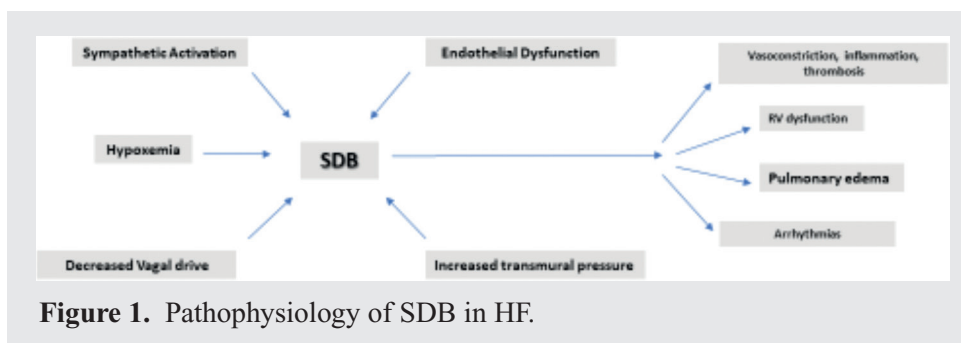


Figure 1. Pathophysiology of SDB in HF.

in whom SDB occurs when they are in a supine sleep position may benefit from “positional therapy” (using a wedge or a pillow). Avoidance of alcohol, sedatives, narcotics, and muscle relaxants will help prevent upper airway collapse.

Device therapy with oral appliances may be effective in certain OSA patients with retrognathism. Positive airway pressure (PAP) through a nasal (or nasal-oral) mask stabilizes the upper airway and benefits the cardiovascular system through increased intrathoracic pressure, reduced LV preload and afterload, and reduced transmural pressure gradients in OSA patients. Continuous PAP improves CSA by increasing functional residual capacity, decreasing blood volume in the lungs and upper airway when supine, reducing hyperventilation through direct effect on the J-receptors of the lung, and reducing preload, afterload, and cardiac transmural pressures. However, adherence to CPAP therapy is variable and can be improved with patient education, careful mask selection, and supportive management of nasal congestion or dryness. Oxygen therapy reduces CSA severity by decreasing nocturnal norepinephrine levels and hypoxemia.

Experimental therapies for SDB include phrenic nerve stimulation for CSA, hypoglossal nerve stimulation for OSA, and the use of acetazolamide which reduces AHI and improves oxygen saturation in HF and CSA.⁵ The acetazolamide effect may reflect its respiratory stimulating properties and diuretic effect; this reduces pulmonary congestion and therefore reduces CSA by reducing pulmonary J-receptor stimulation.

In summary, SDB is common in HF and a risk factor for poor outcomes. Future physiological and randomized clinical outcome trial research is needed for newer therapies. Currently, the focus is on optimally treating the HF and to treat SDB only if HF patients are symptomatic (daytime sleepiness), especially if they predominantly have CSA.

REFERENCES

1. Javaheri S, Javaheri S, Javaheri A. Sleep apnea, heart failure, and pulmonary hypertension. *Curr Heart Fail Rep* 2013; 10:315–20.

2. Krawczyk M, Flinta I, Garncarek M, et al. Sleep disordered breathing in patients with heart failure. *Cardiol J* 2013;20:345–55.
3. Javaheri S, Dempsey JA. Central sleep apnea. *Compr Physiol* 2013;3:141–63.
4. Piper AJ, BaHammam AS, Javaheri S. Obesity hypoventilation syndrome: choosing the appropriate treatment of a heterogeneous disorder. *Sleep Med Clin* 2017;12(4):587–596.
5. Costanzo MR, Ponikowski P, Coats A, et al Phrenic nerve stimulation to treat patients with central sleep apnoea and heart failure. *Eur J Heart Fail* 2018;20:1746–1754.

4. Lp (a) and Aortic Stenosis

Scott W. Shurmer, MD

Lipoprotein (a), commonly called Lp “little a”, is composed of an LDL-like particle, with an apolipoprotein B component covalently bound to apo (a). The structure of the apo (a) portion is somewhat similar to plasminogen, though number and repetition of the “kringle” portions differs.¹

The atherogenicity of Lp (a) is increasingly appreciated, and recent genetic study confirms its strong association with clinical atherosclerosis. In addition, some iso forms of Lp (a) are strongly associated with calcific aortic stenosis. Specifically, SNP rs 10455872 is strongly associated with markedly elevated Lp (a) levels (greater than 50 mg/dl) and is the only monogenetic risk factor linked to calcific aortic valve stenosis in multiple racial groups.

Autotaxin, which is involved in the lysophosphatidylcholine pathway, appears to be a promoter of inflammation, fibrosis, and cell motility.² Several clinical trials have reported an association of elevated Lp (a) levels and increased rate of progression of calcific aortic stenosis. Therapies targeting Lp (a) are in development and include highly specific antisense oligonucleotides.¹

REFERENCES

1. Tsimikas S. A test in context: lipoprotein(a): diagnosis, prognosis, controversies, and emerging therapies. *J Am Coll Cardiol* 2017 Feb 14;69(6):692–711.
2. Bouchareb R, Mahmut A, Nsaibia MJ, et al. Autotaxin derived from lipoprotein(a) and valve interstitial cells promotes inflammation and mineralization of the aortic Valve. *Circulation* 2015 Aug 25;132(8):677–90.

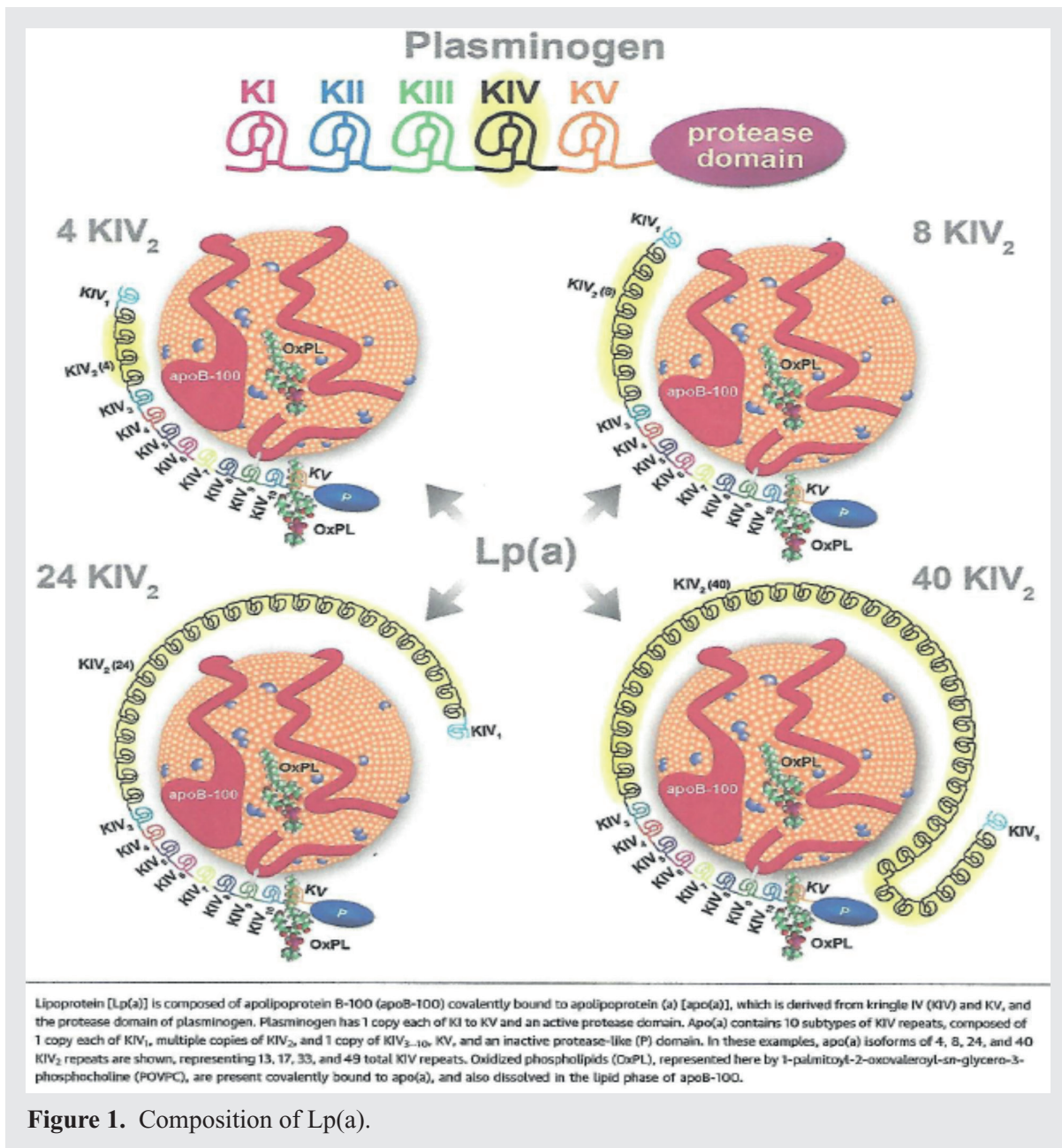


Figure 1. Composition of Lp(a).

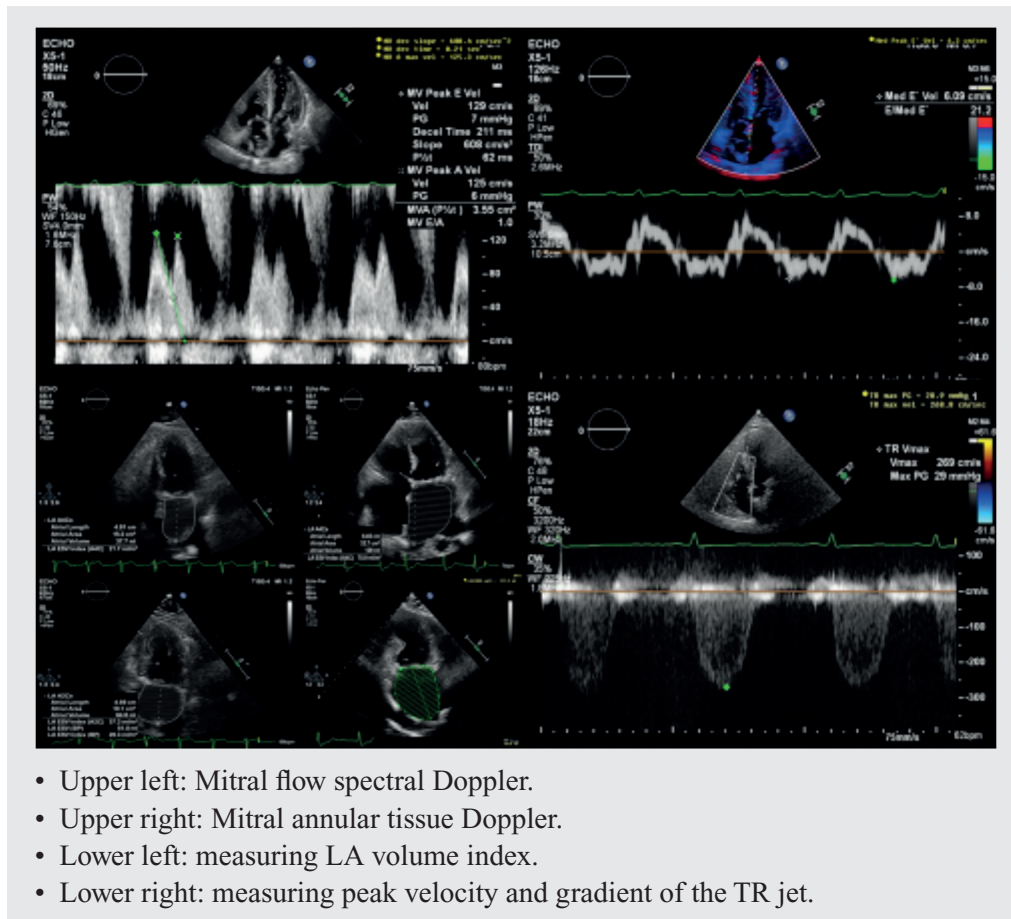
5. Role of cardiovascular imaging in management of heart failure

Aliakbar Arvandi MD

Cardiovascular imaging has an important role in different aspects of management of heart failure. It includes evaluation for etiology, pathophysiology,

treatment, and follow up after starting the treatment for heart failure. Different modalities of cardiovascular imaging include echocardiography, cardiac perfusion imaging, cardiac computed tomography (CT), and cardiac magnetic resonance imaging (MRI).

Echocardiography is the most commonly used due to its risk profile, portability, and detailed description



of cardiac structure and function. Echocardiography machines can now be as small as a hand held device that fits in a pocket and can be easily be used in emergency cases for rapid diagnosis and management. Echocardiography can be performed as a transthoracic (TTE), transesophageal (TEE), intravascular (IVUS), or intracoronary study. Transthoracic echocardiography is considered one of the safest modes of evaluation of patients with cardiovascular diseases. Adding echo contrast to the study has significantly improved volumetric and systolic function evaluations and provides results comparable to cardiac MRI.

Stress echocardiography is relatively safe and free of any radiation with very reasonable sensitivity and specificity to evaluate coronary artery disease (CAD) and tissue viability. Transesophageal echocardiography is an excellent modality to evaluate patients with

non-diagnostic TTE and is the procedure of choice for patients with endocarditis or prosthetic valve diseases and for the detection of thrombus in the left atrial appendage before cardioversion. Transesophageal echocardiography is also an important tool for interventional procedures involving patients with cardiovascular diseases, including patients with heart failure. In summary, echocardiography is the imaging procedure of choice in diagnosis and management and follow up for patients with heart failure. It is a valuable modality for the evaluation of cardiac chamber sizes, chamber volumes, cardiac function and for the evaluation of valvular structure and function, pericardial diseases, etc.

Nuclear perfusion imaging is valuable for the evaluation of patients with CAD or the possibility of CAD and for the evaluation of tissue viability and

systolic function. Cardiac computed tomography is a modality with increasing use to evaluate patients for the presence of CAD, structural heart disease, coronary anomalies, and when gated to evaluate left ventricular systolic function. Cardiac MRI is also a valuable method to evaluate patients with cardiovascular diseases and patients with heart failure. It is considered the gold standard to evaluate tissue viability. It is also a valuable method to evaluate cardiac chambers and volumetric study and function when

other modalities, especially echocardiography, are not diagnostic.

In summary, cardiac imaging has a crucial role in the diagnosis, evaluation, treatment, and follow up for patients with heart failure.

Finalized 10/15/2019
