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Cardiac Resynchronization Therapy-Anesthetic Considerations

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Abstract

Chronic heart failure is the leading cause of hospital admissions among the elderly population. In spite of the optimal treatment, the risk of morbidity and mortality remains high in these patients. Cardiac resynchronization in the past few decades has revolutionized the management of heart failure and has shown to reduce the symptoms in a subgroup of patients with severe systolic dysfunction associated with ventricular dyssynchrony. In this article, we described the procedure, the associated risks and highlighting the anesthetic implications in these critically ill patients.

Keywords: Chronic heart failure; Cardiac resynchronization; Pacemaker; Coronary sinus; Leads; Biventricular pacing; Ventricular dyssynchrony

Abbreviations

NYHA: New York Heart Association; LV: Left Ventricle; LBBB: Left Bundle Branch Block; RBBB: Right Bundle Branch Block; RV: Right Ventricle; RA: Right Atrium; ICD: Implantable Cardioverter Defibrillator; CRT-P: Cardiac Resynchronization Therapy with Pacemaker; CRT-D: Cardiac Resynchronization Therapy with ICD; dp/dt: Measure of LV contractility; LVEDV: Left Ventricular End Diastolic Volume; LVESV: Left ventricular End Systolic Volume

Introduction

Congestive heart failure is a complex clinical syndrome that results from any structural or functional myocardial dysfunction that impairs the heart's ability to circulate blood at a rate sufficient to maintain the metabolic needs of peripheral tissues and various organs. The syndrome usually manifests as dyspnea, poor exercise tolerance, fatigue, and peripheral edema. This can be either acute or chronic. Chronic heart failure is a major public health problem in the UK affecting between 2 and 3% of general population. The incidence of heart failure in the UK is 140 per 100,000 men and 120 per 100,000 women. Approximately 900,000 people in England and Wales have heart failure, of which at least half have left ventricular systolic dysfunction [1]. The incidence and prevalence of heart failure increase with age and the average age at first diagnosis is 76 years. Despite many recent advances in the evaluation and management of heart failure, the development of symptomatic heart failure carries a poor prognosis. Although it's difficult to predict the prognosis in an individual, NHYA classification of functional status is an important predictor of patient outcome.

Cardiac failure can be classified in several ways: acute and chronic cardiac failure, left and right heart failure, high output and low output and systolic and diastolic heart failure. Although there is no unified system of classification, cardiac failure symptoms are graded using the New York Heart Association system (NYHA). Systolic dysfunction is characterized by reduced ejection of the blood, enlarged left ventricle with hypertrophy and remodeling of the chamber, increase in left ventricular end-diastolic and end-systolic volume and represented by poor ejection fraction on the echocardiogram. Diastolic dysfunction is characterized by abnormal left ventricular relaxation, filling or diastolic dispensability or stiffness. These patients often have preserved ejection fraction and left ventricular hypertrophy on echocardiogram.

The causes of heart failure can be multifactorial and include diabetes mellitus, congenital problems, infections, cardiomyopathies, infiltrative diseases, toxins and valvular lesions. However the predominant risk factors are ischemic heart disease, hypertension, male gender, and advancing age [2]. The pathophysiological changes that cause chronic failure involve a complex series of maladaptive neurohumoral responses, principally involving the sympathetic and renin-angiotensin axes. The resultant increased peripheral vascular resistance and sodium and water retention serve to increase workload and worsen left ventricular failure. The longstanding changes that occur secondary to the death or dysfunction of cardiac myocytes can lead to diminished cardiac reserve and increase in end- diastolic pressure and volume. This, in turn, can lead to cardiac re-modeling [3]. The left ventricular re-modeling is triggered by prolonged pressure or volume overload, loss of contracting myocytes from myocardial infarction, genetic abnormalities of contractile proteins or exposure to cardiotoxic agents [4]. Cardiac re-modeling involves myocardial hypertrophy, chamber enlargement, and increase in myocardial oxygen demand and ventricular wall stress. Left ventricular re-modeling is the final pathway for severe systolic dysfunction.

Approximately 10% of the patients with systolic Heart failure have left ventricular dyssynchrony. The dyssynchrony can be either interventricular or intraventricular dyssynchrony. The electromechanical dyssynchrony of the left ventricle is electrically represented as prolonged QRS on the electrocardiogram. In patients with heart failure, the dyssynchrony may further impair the ability of the left ventricle to pump effectively, resulting in decreased cardiac output and stroke volume, an increase in mitral valve regurgitation and thereby resulting in increased backflow and pulmonary congestion.

Heart failure should be viewed as a continuum and treatment can be variable depending on the stage of the heart failure as per the NYHA functional status. Current drug therapies in chronic failure are directed at preventing sodium and water retention and antagonizing the

humoral responses that cause peripheral vasoconstriction. Emphasis should be given to treat the underlying cause along with the treatment of the symptoms.

The Various Treatment Modalities for Heart Failure Include

Non-Pharmacological: change of life style, exercise training, sodium restriction, fluid restriction, continuous positive airway pressure and cardiac rehabilitation in selective patients.

Identifying and treatment of reversible causes: Coronary artery bypass grafting, correction of anemia, thyroid, diabetes, hypertension, etc.

Pharmacological treatment: Includes diuretics, beta blockers, ACE inhibitors, Angiotensin II receptor blockers, aldosterone receptor blockers, antiarrhythmic drugs etc.

Device therapy: ICD, Cardiac resynchronization therapy with or without ICD.

Mechanical circulatory support: Intra-aortic balloon pump, ventricular assist devices. These are used as a bridge to definitive therapy or as a bridge to recovery following an intervention in acutely hemodynamically unstable patients.

Cardiac transplantation: This is the only definitive treatment of end-stage heart failure.

Device therapy, mechanical support devices, and cardiac transplantation are offered for patients with refractory heart failure.

Cardiac Resynchronization Therapy

Cardiac resynchronization therapy is one of the breakthrough treatment modalities with marked proven benefit to the subgroup of patients with heart failure secondary to severe systolic dysfunction associated with cardiac dyssynchrony. CRT was introduced into clinical practice by Dr. Mowler [5] in 1990 for the treatment of myocardial dysfunction associated with left bundle branch block. Cardiac resynchronization therapy (CRT), at times also known as biventricular pacing, involves simultaneous pacing of the right ventricle (RV) and the left ventricle (LV). The heart can essentially be retimed to contract in a synchronized manner with improved efficiency and hemodynamic parameters. The CARE-HF trial (Cardiac Resynchronization in Heart Failure) has shown a relative reduction in mortality by 36% in patients who are treated with CRT compared to patients who are established on optimal medical therapy alone. The patients who were enrolled had NYHA class III/IV symptoms, QRS interval of more than 150 milliseconds, QRS interval of 120 milliseconds with echocardiographic dyssynchrony and left ventricular ejection fraction of 35% or less [6].

The prevalence of atrial fibrillation increases with age from 5% at the age of 60 years to about 22% by the age of 90 years. Evidence suggests that patients with atrial fibrillation and heart failure carry high mortality regardless of the left ventricular function. There are several observational studies and a randomized study which showed similar benefits to patients with sinus rhythm in terms of functional capacity and reverse remodeling in patients with permanent atrial fibrillation [7]. However, CRT is shown to be more effective in patients in sinus rhythm. Left bundle branch block causes asynchronous contraction of the left ventricle with the ventricular septum contracting early and the lateral left ventricular wall contracting late. This leads to a reduction in cardiac output and myocardial contraction efficiency and systolic mitral regurgitation. The longer the ORS duration the more likely benefit is. CRT is shown to reduce the adverse events in heart failure more in patients with baseline QRS interval of more than 150 milliseconds compared to the patients with less than 150 milliseconds.

CRT is of little benefit in patients with RBBB. There is limited evidence to support the benefit of CRT in patients who are acutely decompensated or catecholamine dependent. Although CRT is a valuable additional treatment in patients with moderate to severe dyssynchronous heart failure, 30-40% patients may not respond to the treatment.

CRT is of two types: CRT-Pacemaker (CRT-P) and CRT-Defibrillator (CRT-D)

The cost of CRT-P is less than the CRT-D device. The Typical cost of CRT-P is £4000 compared to £15000 for the CRT-D device approximately.

Indications of CRT: As per the most recent recommendations of European Society of Cardiology guidelines (2010) (Table 1) [8]:

Level of Evidence	Aim
Class IA	
NYHA III/IV, QRS ≥ 120 ms, SR, LVEF ≤ 35%	Reduce morbidity and mortality
NYHA II, QRS ≥ 150 ms, SR, LVEF ≤ 35%	Reduce morbidity or prevent disease progression
Class IB	
NYHA III/IV, QRS ≥ 120 ms, LVEF ≤ 35%, class I PM indication	Reduce morbidity
Class IIA	
NYHA III/IV, LVEF ≤ 35%, QRS ≥ 130ms, AF+AVN ablation	Reduce morbidity
NYHA III/IV, LVEF ≤ 35%, QRS ≥ 130 ms, AF with slow ventricular rate	Reduce morbidity

NYHA III/IV, LVEF ≤ 35%, QRS <120 ms, class I PM indication	Reduce morbidity
Class IIB	
NYHA II, LVEF ≤ 35%, QRS <120 ms, class I PM indication	Reduce morbidity
CRT: Cardiac Resynchronisation Therapy; NYHA: New York Heart Association; SR: Sinus Rhythm; LVEF: Left Ventricular Ejection Fraction; PM: Cardiac Pacemaker; AF: Atrial Fibrillation; AVN: Atrioventricular Node	

Table 1: Focused update of European Society of Cardiology guidelines on device therapy in heart failure with respect to CRT, by indication.

CRT with Implantable cardioverter defibrillators is recommended as a possible treatment for patients who have had a serious ventricular arrhythmia, an inherited heart condition linked to a high risk of sudden death, or post-surgical repair of congenital heart disease. Sudden cardiac death syndrome can occur either due to primary causes likes Brugada Syndrome, familial cardiac death syndrome or secondary to malignant arrhythmias following cardiac disease of any nature. ICD is not considered in patients with limited life expectancy. The COMPANION trial (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) has shown a greater reduction in mortality of patients treated by CRT-D compared with CRT-P alone or medical therapy in>or = Stage III cardiac failure [9].

Procedure

CRT is performed usually under local anesthetic and conscious sedation provided the patient is hemodynamically stable and the procedure is tolerated well. But patients with severe orthopnea or who are hemodynamically unstable either need deep sedation or a general anesthetic.

The CRT device consists of three parts

1. A metal titanium case containing battery powered generator. The size of the metal case is a pocket watch and weighs about 50 grams. CRT-D device is slightly heavier than the CRT-P device.

2. The programmer software which operates the device.

3. Insulated wires called leads. They carry information signals from the heart to the programmer software and to carry electrical impulses to the heart. CRT-P have leads with consistent texture and thickness on radiographs but CRT with an ICDs have shocking coils toward the distal tip of the lead which are brighter on radiograph and are thicker (Figure 1).

The implantation of a CRT pacing leads is similar to insertion of a conventional pacemaker or ICD except for the placement of a third lead along the lateral wall of the left ventricle through one of the tributaries of the coronary sinus. The major differences between the conventional pacemaker and the CRT are highlighted in the table below (Table 2). Pacing leads are placed in the right atrium, right ventricle endocardially and along the lateral wall of left ventricle epicardially (Figure 2). The Coronary sinus is located at the junction of the inferior vena cava to the tricuspid valve. It is guarded by the thebesian valves (Figure 3). The lateral or the posterior lateral vein is the ideal vein [10]. Successful resynchronization can be achieved with placement of the LV lead in almost any coronary sinus branch, provided that the lead can stimulate proximal third to the middle third of the LV. Placement of leads through left subclavian is preferable because of ease of insertion of left ventricular lead through the coronary sinus as it is less angulated and the defibrillation threshold being less. Anterior interventricular vein cannulation can lead to diaphragmatic stimulation as it lies in close proximity to the phrenic nerve. Optimal lead placement in the vein is by adequate pacing capture, lack of diaphragmatic stimulation and lead stability. Placing the LV lead can be tricky and time-consuming because of the complexity of the process. Significant tricuspid regurgitation can make it difficult to place the LV lead [11].

Left ventricular lead placement is followed by the right atrial and right ventricular leads. The placement of leads is done under radiological guidance, hence the possibility of contrast induced nephropathy with difficult insertions.

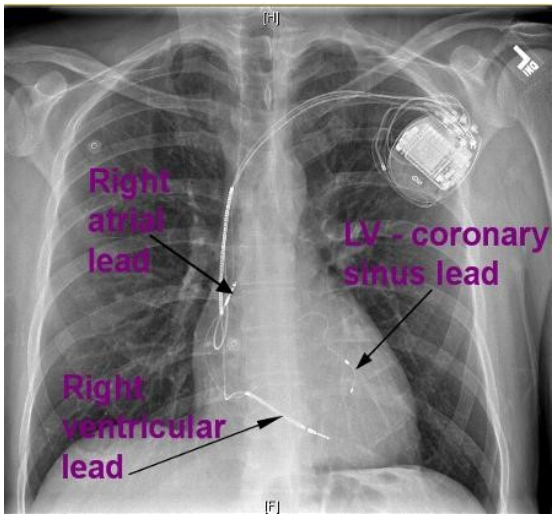

Figure 1: CRT-D device with three pacing leads.

	Conventional pacemaker	CRT
Indications	Sick sinus syndrome, AV blocks, post cardiac arrest	Severe systolic dysfunction with ventricular dyssynchrony
Mode of action	Pacing	Biventricular synchronization
Duration of procedure	1-2 hours	2-3 hours
Mode of pacing	Demand/ fixed	Fixed
Route	Transcutaneous, Trans venous, Epicardial, & Transoesophageal	Transvenous

Position of leads	RA / RV/Both	LV, RV, and RA
Chest X-Ray findings	One or two leads	Three leads

Table 2: Differences between conventional pacemakers to CRT.

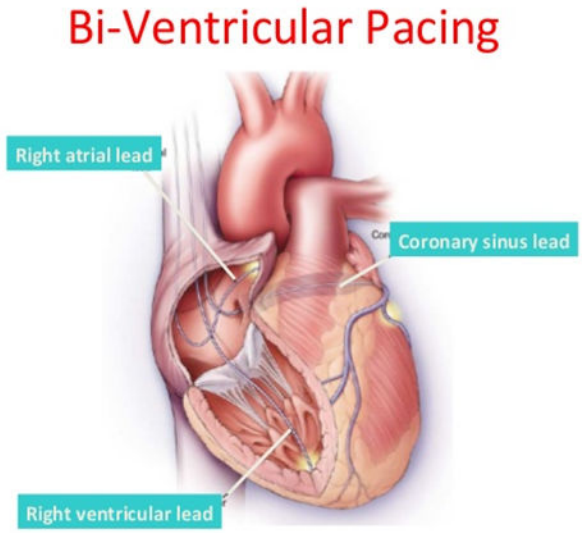

Figure 2: CRT leads *in situ*.

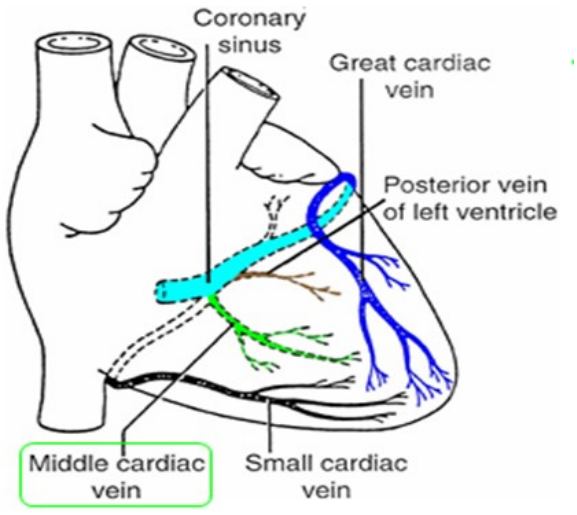

Figure 3: Anatomy of the coronary sinus.

Mechanism of Action

Bi-ventricular pacing allows the optimization of atrio-ventricular timing and resynchronization of septal and postero-lateral left ventricular contraction (Figure 4) [12].

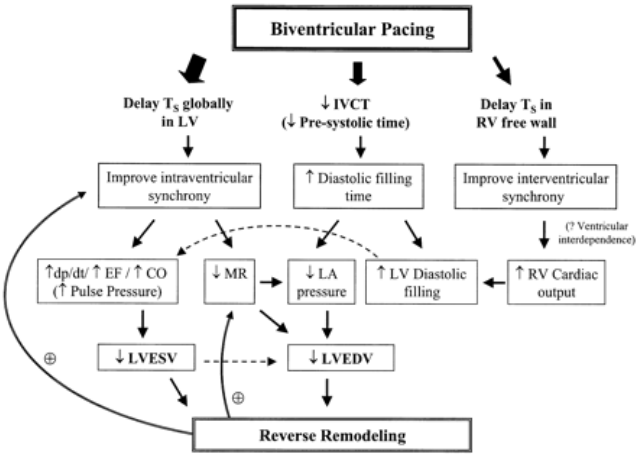

Figure 4: Mechanism of action.

Benefits of CRT

The benefits of CRT can be seen immediately after the procedure. The X-Ray changes seen before and 3 days post procedure are shown below (Figure 5). CRT can lead to marked improvement in cardiac function, improvement in 6-minute walking distance increased left ventricular filling time, decreased septal dyskinesia, reduction in mitral regurgitation, improvement in ejection fraction, and improved blood pressure, peak intraventricular pressures, and stroke volume. CRT has shown to reverse ventricular re-modelling in heart failure and overall improvement in survival and reduce hospitalisations [13].

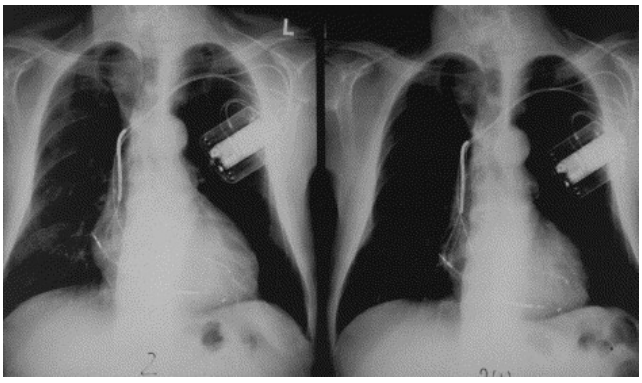

Figure 5: X-Ray changes before (Left) and after CRT (Right).

Complications: Early

Venous access: Pneumothorax, hemothorax, air embolism, inadvertent injury to subclavian artery, perforation of coronary vein, coronary vein dissection [14].

Lead placement: Diaphragmatic stimulation, Brady or tachyarrhythmia, acute LVF, perforation of heart, damage to heart valve, hemopericardium, cardiac arrest.

Generator: Pocket hematoma, improper or inadequate connection to the leads.

Systemic: Local anesthetic toxicity.

Complications: Delayed

Lead related: Thrombosis/embolization, superior vena cava obstruction, lead dislodgement, infection, lead failure, perforation, and pericarditis

Generator: Pain, erosion, infection, migration, electric shock.

Systemic: Radiation injuries, contrast induced nephropathy.

Anesthetic Considerations

The various cardiac interventions for which an anesthetist can be involved are the insertion of a pacemaker, intra-aortic balloon pump, percutaneous coronary intervention, implantable cardioverter defibrillator, Cardio version and Cardiac Resynchronization Therapy.

Pre-operative

All patients should be medically optimized before the procedure. Unless indicated, medications should be continued throughout the perioperative period. Patients with heart failure often require preinduction optimization of intravascular volume status, pharmacological manipulations of inotropy and afterload, adjustments to pacemaker settings (where present), and on occasion elective placement of an Intra-aortic balloon pump. If anxiolytic is required it is prudent to provide supplemental oxygen and monitor closely since this population of patients tolerate poorly to the sudden decreases in sympathetic tone, hypoxemia, or the potentially increased pulmonary vascular resistance that may accompany a respiratory acidosis. Patients with advanced heart failure are at risk of developing cardiac complications including cardiogenic shock and multi-organ failure. High risk consent should be taken explaining all the risks and possibility of organ support post procedure. These patients should be dealt by an experienced anesthetist with adequate external support when needed. Premedication has not shown to be of any benefit in these patients.

Intra-operative

Intraoperative monitoring should include essential monitoring including five lead ECG. Invasive arterial pressure monitoring should be established before the start of the procedure where ever possible. Invasive blood pressure has not shown to be of proven benefit over the non-invasive blood pressure but subtle changes in blood pressure can be picked up early [15]. Central venous access is needed only if inotropic support is anticipated. Central venous access is not recommended for monitoring purposes as it is a poor estimate of left ventricular filling when left ventricular compliance is reduced. Intra-aortic balloon pump is considered in high risk patients as a bridge to CRT. Defibrillator pads should be attached to the patient. Access to the patient is limited and hence all the monitoring, endotracheal tube, intravenous access should be secured properly before the start of the procedure. These patients are dependent on preload for adequate perfusion and hence maintaining preload as normal to as possible is ideal. A Slight reduction in afterload is beneficial.

There is little evidence that any particular anesthetic technique is superior over other [3]. A cardiovascular stable anesthetic with minimal myocardial depression, maintaining a sinus rhythm, with as minimal changes as possible to the preload and afterload would be the reasonable goals to achieve in these patients. The failing heart is chronically compensated by a heightened adrenergic state, and removal of the sympathetic tone may lead to rapid decompensation with cardiovascular collapse. Emphasis should be given to maintain cardiovascular stability with minimal changes during Induction and emergence. A close attention to detail is necessary to prevent acute exacerbation of left ventricular failure and other cardiac complications. Vasoactive drugs should be made readily available and judiciously used at the first sign of refractory hemodynamic instability. The rate of sudden death is high in patients undergoing this procedure. Human cohort studies have shown that CRT can have a differential effect on the arrhythmogenic substrate, antiarrhythmic in some and proarrhythmic in others [16]. Blood loss can be significant in prolonged procedures and hence should be monitored and corrected. Good effective communication among the team members is crucial. There's significant amount of radiation exposure and hence, adequate protective measures have to be taken by the medical personnel. The procedure can last up to few hours and hence the use of warming devices to maintain normothermia is recommended.

Postoperative

Anesthetic technique should be tailored for early extubation and fast track anesthesias technique should be adopted with adequate postoperative pain management. Analgesic requirements are usually minimal and avoidance of strong opioids which cause respiratory depression would be appropriate. Meticulous management of hemodynamic stability, electrolytes, coagulation and renal function is necessary. Contrast induced nephropathy can occur in prolonged procedures and hence post procedure renal support should be considered in high risk patients. These patients are closely monitored for cardiac complications and adequately dealt with as they arise.

Conclusion

Cardiac resynchronization therapy is biventricular continuous pacing and is the treatment modality of choice in certain subgroup of patients with severe systolic dysfunction with ventricular dyssynchrony. Prolong QRS is a negative prognostic marker. Greater the QRS, greater is the benefit from CRT. CRT has shown be of proven benefit in these subgroup of patients with an overall improvement in quality of life. However careful selection of patients with good medical optimization is essential because of the associated risks of the procedure. Attention to detail and expertise is required when anaesthetizing these critically ill patients.

Conflict of Interests

The authors declare that there is no conflict of interest.

References

1. Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (TA314), NICE technology appraisal guidance, June 2014.
2. Magner JJ, Royston D (2004) Heart Failure. Br J Anaesth 93: 74-85.
3. Kotze A, Howell SJ (2008) Heart failure: pathophysiology, risk assessment, community management and anaesthesia. Contin Educ Anaesth Crit Care Pain 8: 161-166.
4. Thomas A, Mower M (1995) Multiple chambered pacing for treatment of congestive heart failure. Pacing and Clinical Electrophysiology 18: 749-750.

5. Sutton MS, Keane MG (2007) Reverse remodeling in heart failure with cardiac resynchronization therapy. Heart 93: 167-171.
6. Cleland J, Daubert J, Erdman E, Freemantle N, Gras D, et al. (2005) The effect of cardiac resynchronisation on morbidity and mortality in heart failure, N Engl J Med 352: 1539-1549.
7. Delnoy PP, Ottervanger JP, Luttikhuis HO, Elvan A, Misier AR, et al. (2007) Comparison of usefulness of cardiac resynchronization therapy in patients with atrial fibrillation and heart failure versus patients with sinus rhythm and heart failure. Am J Cardiol 99: 1252-1257.
8. Dickstein K, Vardas PE, Auricchio A, Daubert JC, Linde C, et al. (2010) 2010 Focused Update of ESC Guidelines on device therapy in heart failure: an update of the 2008 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy. Developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. Eur Heart J 31: 2677-2687.
9. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, et al. (2004) Cardiac resynchronisation therapy with or without an implantable defibrillator in advanced chronic heart failure, N Engl J Med 350: 2140-2150.
10. Butter C, Auricchio A, Stellbrink C, Fleck E, Ding J, et al. (2001) On behalf of the PATH-CHFII Study Group. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. Circulation 104: 3026-3029.
11. Mayank S, Manoj KR, Parag B(2015) Cardiac Resynchronisation Therapy – An Approach to Difficult Left Ventricular Lead Placement. European Journal of Arrhythmia & Electrophysiology 1: 25-26.
12. Yu CM, Chau E, Sanderson JE, Fan K, Tang MO, et al. (2002) Tissue Doppler echocardiographic evidence of reverse remodeling and improved synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. Circulation 105: 438-445.
13. Cleland JGF, Calvert MJ, Verboven Y, Freemantle N (2009) Effects of cardiac resynchronization therapy on long-term quality of life: an analysis from the CArdiac Resynchronisation-Heart Failure (CARE-HF) study. Am Heart J 157: 457-466.
14. Colquitt JL, Mendes D, Clegg AJ, Harris P, Cooper K, et al. (2014) Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure: systematic review and economic evaluation. Health Technol Assess 18.
15. Groban L, Butterworth J (2006) Perioperative management of chronic heart failure. Anesth Analg 103: 557-575.
16. Leyva F, Foley PWX (2008) Is cardiac resynchronisation therapy proarrhythmic? Indian pacing and electrophysiology journal 8: 268-280.