

Effects of chronic Right Ventricular Apical Pacing (RVAP) on Left Ventricular function with a normal baseline Left Ventricular function—A descriptive study

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Abstract

Background: A common treatment option for cardiac rhythm abnormalities like sick sinus syndrome or atrioventricular block is ventricular pacing over the Right Ventricular (RV) Apex. Though several sites have come recently for ventricular pacing, RV apical pacing still holds the gold standard especially in patients with heart failure and atrial fibrillation. Limited studies exist on the long-term effects on cardiac outcome parameters following RV apical pacing. **Aim:** Assess the effects of long-term RV Apical Pacing on Left Ventricular (LV) function in patients with baseline normal LV Function. **Materials and Methods:** A descriptive study involving 51 study participants on RV apical pacing selected randomly from among those registered at the Cardiology Clinic, Chennai, India between 2009 to 2019. LV function was assessed by 2-D echocardiography at the time of pacemaker implantation and during follow-up. Only those patients with ventricular pacing of more than 90% from the time of implantation were included. Echocardiographic assessment of LV systolic and diastolic function, LV dimensions and severity of mitral regurgitation at the time of pacemaker implantation and subsequent follow-up was done for all patients. Statistical analysis was done using Statistical Package for Social Sciences ver 16.0. **Results:** Complete Heart Block was the most common (74.5%) indication for pacemaker implantation in the study population. Amongst the various pacing modes employed, VVI was the most common amounting to 52.94% followed by VVD in 31.3%. There was a significant change in Left Ventricular End systolic diameter (ESD) and End diastolic diameter (EDD) before and after pacing reflecting a change in LV dimensions following RV apical pacing (>90%) for the given indications. **Conclusions:** RV apical pacing will not cause adverse effects in all the patients. The amount of LV dyssynchrony depends on LV function at baseline and accompanying conduction disease at baseline. Though changes in LV dimensions were noted, LV dysfunction was not commonly noted in our patients undergoing RV apical pacing.

Keywords: RV apical pacing; LV dysfunction; LV dyssynchrony

Introduction

Cardiac pacing has been the cornerstone for the treatment of cardiac rhythm abnormalities.

Cardiac pacing, especially the ventricular pacing will significantly benefit the patient when symptoms of congestive heart failure or central nervous system manifestations due to the decreased cardiac output in complete heart block are present.

Improvement in central nervous system blood supply generally follows increase in the cardiac output.

Consequently, the objective signs of decreased cerebral blood flow such as the electroencephalographic findings maybe improved significantly by ventricular pacing. Error! Reference source not found.

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How to cite this article: J V Balasubramaniyan, R H Lakshmi and J S Satyanarayana Murthy. Measurement of Blood-Loss during Hip Surgery. AMHSR. 2021;11:147-153

However on the other hand, a 20% increase was demonstrated in hemodynamic indices with atrial pacing as compared to ventricular pacing by Samet et al.² However, Benchimol et al. found no increase in indices with atrial pacing compared to those with ventricular pacing in normal hearts.³ They did find, however, an advantage to the atrial pacing in diseased hearts. Sowton et al. also demonstrated increased hemodynamic indices with A-V sequential pacing as compared to those with ventricular pacing in diseased hearts.^{4,5}

Atrial pacing may be accomplished from the coronary sinus as well as from the right atrium. Befeler et al demonstrated that coronary sinus pacing produced essentially the same hemodynamics as right atrial pacing.

Error! Reference source not found. In other words, the hemodynamic consequence is identical, whether the atria are activated in forward or retrograde fashion. RV apex has become the preferred pacing site over time as it is easy to reach with the available leads and it gives stable mechanical position. In spite of these benefits, of all ventricular sites RV apical pacing appears to be hemodynamically least favourable as abnormal electrical activation changes and mechanical activation patterns have been observed, which can result in changes in cardiac metabolism, perfusion, remodelling, hemodynamics, and mechanical function.⁷⁻¹³

Chronic RV apical pacing was associated with left ventricular (LV) dyssynchrony, and deterioration of LV systolic and diastolic function in patients with congenital or acquired atrioventricular (AV) block. The adverse effects of RV apical pacing (RVAP) are more pronounced in certain patient populations, like those with Coronary artery disease, or patients with underlying conduction disturbances who find themselves at greater risk.

Various studies had also shown that as the amount of ventricular pacing increases, so do the adverse effects, especially in patients with depressed LV function. Alternatives to RV apical pacing have been explored in these populations, but without any conclusive evidence to point towards an alternative. It has also been proved that ventricular dyssynchrony is associated with increased risk of adverse cardiac events in patients with heart failure.¹⁴

Various trials showed that not all patients who receive RVAP will experience adverse events. The amount of pacing induced LV dyssynchrony was related to the presence of baseline LV dysfunction and type of underlying conduction disease at baseline.⁹

As the percentage of RVAP increases, there will be a proportional increase in adverse outcomes like development of heart failure, LV dysfunction and atrial fibrillation. Nevertheless, it remains unclear whether there is an "optimal amount" of RV pacing after which patients are more vulnerable to RV apical pacing's deleterious effects.

It is very important to note that in most of the studies, patients with structural heart disease were included which is a confounding factor that may intensify the detrimental effects of RV pacing on LV function. There has been no extensive study of the exact effects of RV apical pacing on LV function in patients without underlying structural heart disease.

Materials and Methods

A descriptive study to assess the long-term effects of RV apical pacing on LV function. 51 patients on RV apical pacing were selected randomly by computer generated random numbers from patients registered in the Cardiology Clinic, Chennai between 2009 to 2019.

Patients with a ventricular pacing more than or equal to 90% from the time of pacing, with normal baseline LV function at the time of pace maker implantation were included.

Presence of structural heart disease, atrial fibrillation and pre-existing CAD were exclusion criteria. A detailed history was elicited that included indication for pacing, duration and mode of pacing, and functional class during and after pacing.

Two dimensional echocardiographic assessment of LV function and LV dimensions and severity of mitral regurgitation at the time of pacemaker implantation and subsequent follow up was done for all patients. Statistical analysis was carried out using Statistical Package for Social Sciences ver 16.0. For continuous variables descriptive statistics was done and Student "t" test was used for dichotomous variables. 95% confidence intervals were determined and p value < 0.05 was considered significant.

Results

A total of 51 patients (29 male and 22 female) were studied, age ranging between 19 years to 80 years (Figure 1). Complete Heart Block was the most common indicator for permanent pacemaker implantation (74.5%) in the study population. Congenital complete Heart Block was present in 9.8% of the study population, explaining the younger age group for permanent pacemaker implantation.

Sick sinus Syndrome and Trifascicular Block, Second degree AV Block and Bifascicular Block (Table 1) were other indications observed. Of the various modes of pacing implemented, VVI was the most common mode of pacing (52.94%) followed by VVD in 31.3%. DDD pacing was employed in 13.7%. DDDR was observed in 2% of the study population (Figure 2). Patients were followed up for 5 to 15 years (86.3%). 13.7% patients had more than 15 years of follow-up (Table 2).

Table 1: Permanent cardiac pacing in study subjects - indications.

Indications	No. of patients	%
BFB	1	2.00%
CCHB	5	9.80%
CHB	38	74.50%
SECOND DEGREE AVB	1	2.00%
SSS	3	5.90%
TRIFASCICULAR BLOCK	3	5.90%
Total	51	100

*BFB:Bifascicularblock,CCHB: Congenital Complete Heart Block, CHB:Complete Heart Block, AVB: atrioventricular block, SSS: Sick sinus syndrome

Table 2:Follow-up (years) after pacemaker.

Follow-up (years)	No. of patients	%
10-May	51	100
15-Nov	30	58.8
>15	7	13.7

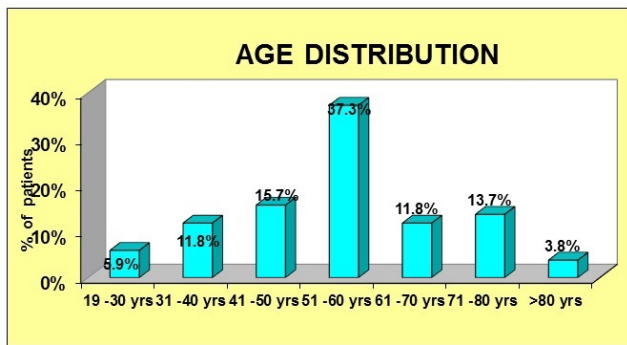


Figure 1: Age-wise distribution of the study subjects.

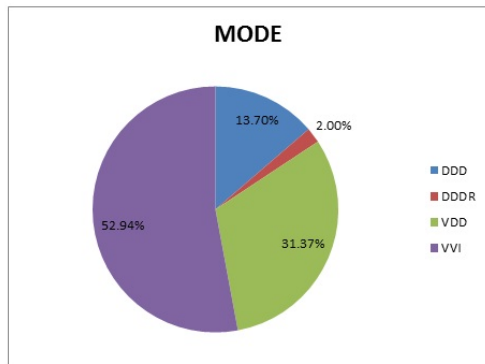


Figure 2: Distribution of pacemaker modes by clinical indication. DDD/DDDR, sequential pacing with 2 leads; VVI, single-chamber ventricular pacing.

Table 3: Echocardiographic Characteristics - pre pacemaker and post pacemaker.

	Pre pacemaker (n=51)	Post pacemaker (n=51)	p value
ESD score (mean ± SD)	29.84 ± 4.62	31.80± 3.54	p > 0.01
EDD score (mean ± SD)	46.69±5.42	49.22±4.84	p > 0.001
EF score (mean ± SD)	65.92±5.63	64.33±5.00	p < 0.05

*ESD: end-systolic dimension, EDD: end-diastolic dimension, EF: Ejection fraction

Pre-pacing and Post-pacing test scores for LV dimensions and LV function were compared.

With respect to LV dimensions, there was significant difference in ESD and EDD before and after pacing.

During pre-pacing, patients had an ESD score of 29.84 while in post-pacing, patients had a score of 31.80; the difference being statistically significant at 95% CI (p = 0.01). Patients had an EDD pre-pacing score of 46.69.

The post-pacing score was 49.22. The difference between pre-pacing and post-pacing score was 2.53, large and statistically significant (p=0.001).

However, the study did not reflect a significant change in LV function as the pre-pacing EF was 65.92 and post-pacing EF score was 64.33.

The difference of 1.59 (p=0.10) was not statistically significant (Table 3).

Results were also analysed with respect to attributes of age and sex in order to determine their association, if any, with development of LV dysfunction in RV apical pacing. ESD, EDD and EF were not affected by the age group or gender of the study population (Table 4). Gender differences did not

play a major role in determining the outcome of the study as ESD, EDD and EF were unaffected in opposite sexes (Table 5). Symptomatically most patients remained in NYHA Class II after the follow up period without much change during the follow-up period (Figure 3).

Table 4: Age-wise comparison of Echocardiographic Characteristics during pre pacemaker and post pacemaker.

	Age group (in years)	n	Mean	Std. Deviation	Oneway ANOVA F-Test
ESDdifference	19 -30	3	0.6667	11.93035	f=0.41 p=0.86 Not significant
	31 -40	6	1	2.44949	
	41 -50	8	2.125	3.87068	
	51 -60	19	1.7895	6.1335	
	61 -70	6	1.8333	2.92689	
	71 -80	7	4.4286	3.82349	
	>80	2	1.5	2.12132	
EDDdifference	19 -30	3	2	5.2915	f=0.16 p=0.98 Not significant
	31 -40	6	1.5	2.58844	
	41 -50	8	2.125	4.91172	
	51 -60	19	3.2105	4.4669	
	61 -70	6	2.8333	3.25064	
	71 -80	7	1.8571	7.3808	
	>80	2	3	0	
EFdifference	19 -30	3	0.6667	17.61628	f=0.25 p=0.95 Not significant
	31 -40	6	0.3333	3.07679	
	41 -50	8	2.5	5.23723	
	51 -60	19	2.2632	4.74742	
	61 -70	6	-0.6667	9.26643	
	71 -80	7	2.7143	8.63548	
	>80	2	-0.5	4.94975	

*ESD, end-systolic dimension; EDD, end-diastolic dimension; EF, Ejection fraction

Table 5: Gender-wise comparison of Echocardiographic Characteristics during pre pacemaker and post pacemaker.

	n	Mean	Std. Deviation	p value
End Systolic Dimension				
Male	29	3.069	±3.63447	p=0.09
Female	22	3.5	±6.36022	
End Diastolic Dimension				
Male	29	3.2414	±3.41901	p=0.19
Female	22	1.5909	±5.59472	
Ejection Fraction				
Male	29	2.5517	±5.38905	p=0.24
Female	22	2.3182	±8.06749	

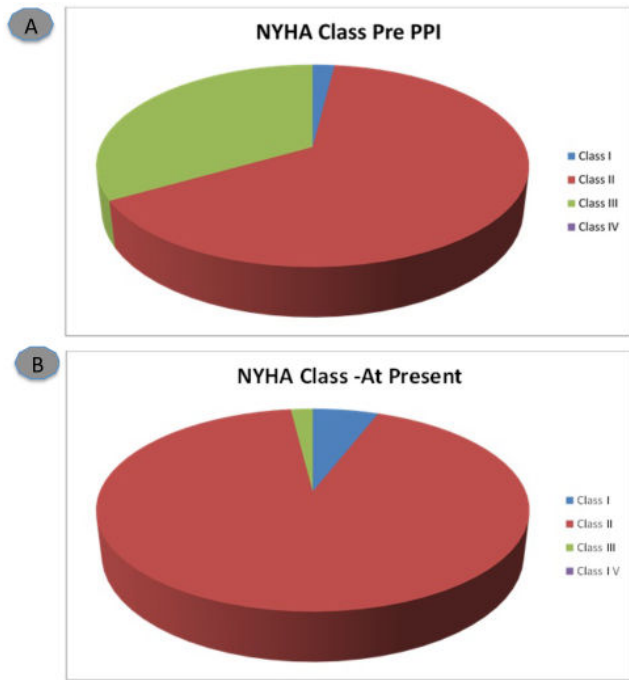


Figure 3: Functional NYHA class in patients during pre pacemaker and post pacemaker.

A. pre pacemaker; B. post pacemaker; NYHA, New York Heart Association.

Discussion

The present study was conducted to assess the effect of RVAP on study participants with a normal baseline LV function over a ten year period.

Of the 51 patients who were documented to have a high degree of ventricular pacing (>90%) over a follow up period of approximately 10 years, RV apical pacing resulted in changes in LV dimensions but did not produce significant LV dysfunction.

Recently conducted clinical trials have showed that conventional site of pacing at right ventricular apex induced more frequent episodes of HF.

The Mode selection trial (MOST) which is a randomized trial consisting of 2010 patients showed that dual chamber pacing (DDDR) reduces the risk of HF hospitalization with slight improvement in quality of life compared to Ventricular pacing (VVIR) alone.

15 DAVID trial was devised to test the hypothesis that compared to back up VVI pacing at 40beats/min, DDDR pacing at a lower rate of 70 beats / min would allow in low incidence of HF and reduce hospitalization and death.

16 Results showed that the risk of HF and HF related hospitalization is higher with DDDR pacing when compared with ventricular back up pacing.

16 This clearly demonstrated that the risk of HF and HF related hospitalization is determined by the amount of RV pacing rather than the site of pacing. MADIT II trial also showed a similar relationship between ventricular pacing and Heart failure, ventricular arrhythmias and death which was insensitive to ICD system and pacing mode.

17 There is ample evidence to show that chronic RVAP is associated with development of pathological changes in the heart. Effects of long term RVAP on cardiac perfusion and metabolism have been demonstrated in many clinical and pre-clinical studies.

18-20 Direct electrical stimulation of the RV apex results in an irregular activation sequence and erratic ventricular contraction and consequently impairment of LV output with reduced stroke volume and abnormal LV relaxation, all of which can lead to structural changes and LV remodeling.

21-23 The presence of underlying structural heart disease and impaired LV systolic or diastolic function were noted to be independent predictors of hospitalization due to HF after RVAP by Y.Hori et al.24

In patients having baseline severe LV dysfunction, abnormal LV relaxation and decrease in stroke volume will be more pronounced and permanent RVAP may result in higher risk of morbidity and mortality in long-term follow up. In experimental studies, RV apical pacing has been shown to cause myocardial fiber disarray, increased myocardial catecholamine concentration, asymmetric hypertrophy of ventricle and altered perfusion distribution.

Delgado et al noted that during RV apical pacing, 36% exhibited significant LV dyssynchrony.25 The amount of LV dyssynchrony during pacing was related to the presence of LV dysfunction at baseline.

In our study none of the participants had significant LV dyssynchrony which stresses the importance of application of pacing principle in right ventricle and its use in individuals with normal baseline LV function.

Fornwalt et al assessed the effects of RV apical pacing in paediatric patients and noted statistically significant LV dyssynchrony.

26 Liakopoulos et al observed that during RVAP, there was an exaggerated decrease in LV segmental shortening at the posterior wall.13

These findings suggest electromechanical delay as a result of LBBB pattern induced by RV apical pacing may result in systolic dyssynchrony especially in individuals with pre-existing ventricular dysfunction and may play a pivotal role in further deterioration of LV systolic function.

Interestingly, majority of patients with permanent pacemaker tolerate chronic RVAP well. In MOST study, HF was noticed only in 10% of the patients who had lower EF, MI and a worse NYHA class at baseline compared with patients who did not experience HF.¹⁵ The prevalence of mechanical dyssynchrony is again noticed at a higher frequency in patients with systolic HF and spontaneous LBBB compared to patients with normal EF and RVAP. This indicates that patients with myocardial disease, including patients with systolic HF may be more prone to mechanical dyssynchrony than compared to patients on RVAP with normal EF. The findings of these studies point to the fact that not all patients are vulnerable to the detrimental effects of long term RV apical pacing in terms of LV dysfunction.

In our study, all patients had normal baseline LVEF and majority had acquired AV block necessitating permanent RVAP (>90% pacing). After a median follow up of 7.8 years, 26% of patients developed new onset HF, majority of which required hospitalization (87%) the earliest occurring 3 years after follow-up. In patients with baseline normal EF, the adverse LV remodeling induced by RVAP took a longer time to manifest. Fang et al identified three independent determinants as predictors of heart failure, namely low normal EF during Ventricular pacing, pre-existing LVH as well as cumulative amount of RVAP > 40% in the past 6 months.²⁷ In patients receiving pacemaker therapy, particularly those with a high degree of ventricular pacing dependency, it is therefore worth assessing the vulnerability of developing systolic dyssynchrony.

Conclusions

Though studies have shown several pitfalls of RVAP including LV dysfunction, the same does not apply when the same is used as a pacing method for patients with normal LV baseline functions. The amount of LV dyssynchrony depends on LV function at baseline and accompanying conduction disease at baseline. Though changes in LV dimensions were noted, LV dysfunction was not a significant accompaniment of RV apical pacing which is still considered a gold standard among all pacing sites.

References

- Segel N, Samet P. Physiologic aspects of cardiac pacing. In: Samet P, El-Sherif N, eds. *Cardiac Pacing*. New York: Grune & Stratton, 1980:111-47.
- Samet P, Castillo C, Bernstein WH. Hemodynamic consequences of sequential atrioventricular pacing. *Am J Cardiol* 1968;21:207-12.
- Benchimol A, Ellis JG, Dimond EG. Hemodynamic consequences of atrial and ventricular pacing in patients with normal and abnormal hearts: Effect of exercise at a fixed atrial and ventricular rate. *The American journal of medicine*. 1965 Dec 1;39(6):911-22.
- Sowton E & Roy; Hemodynamics of pacing; 4th International Symposium on Cardiac Pacing, 1973.
- Sowton E; Hemodynamic studies in patients with artificial pacemakers; *Br. J Heart* 26; 737; 1964.
- Befeler, B, Hildner, FJ, Javier, RP et al. Cardiovascular dynamics during coronary sinus, right atrial and right ventricular pacing. *Am Heart J*. 1971; 81: 372-380.
- Connolly SJ, Kerr C, Gent M, Yusuf S. Dual-chamber versus ventricular pacing. Critical appraisal of current data. *Circulation*. 1996;94(3):578-583. doi: 10.1161/01.CIR.94.3.578.
- Nielsen JC, Andersen HR, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK. Heart failure and echocardiographic changes during long-term follow-up of patients with sick sinus syndrome randomized to single-chamber atrial or ventricular pacing. *Circulation*. 1998;97(10): 987-995. doi: 10.1161/01.CIR.97.10.987.
- Tantengco MVT, Thomas RL, Karpawich PP. Left ventricular dysfunction after long-term right ventricular apical pacing in the young. *J Am Coll Cardiol*. 2001;37(8):2093-2100. doi: 10.1016/S0735-1097(01)01302-X.
- Tse HF, Yu C, Wong KK, Tsang V, Leung YL, Ho WY, Lau CP. Functional abnormalities in patients with permanent right ventricular pacing: the effect of sites of electrical stimulation. *J Am Coll Cardiol*. 2002; 40:1451-1458, 8, DOI: 10.1016/S0735-1097(02)02169-1.
- Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. *J Am Coll Cardiol*. 2003; 42:614-623, 4, DOI: 10.1016/S0735-1097(03)00757-5.
- Thambo J-B, Bordachar P, Garrigue S, et al. Detrimental ventricular remodeling in patients with congenital complete heart block and chronic right ventricular apical pacing. *Circulation*. 2004;110:3766-3772. doi: 10.1161/01.CIR.0000150336.86033.8D
- Liakopoulos OJ, Tomioka H, Buckberg GD, Tan Z, Hristov N, Trummer G. Sequential deformation and physiological considerations in unipolar right or left ventricular pacing. *European journal of cardio-thoracic surgery*. 2006 Apr 1;29(Supplement 1):S188-97.
- Lieberman R, Padeletti L, Schreuder J, Jackson K, Michelucci A, Colella A, Eastman W, Valsecchi S, Hettrick DA. Ventricular pacing lead location alters systemic hemodynamics and left ventricular function in patients with and without reduced ejection fraction. *Journal of the American College of Cardiology*. 2006 Oct 17;48(8):1634-41.
- Lamas GA, Lee KL, Sweeney MO, Silverman R, Leon A, Yee R, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. *N Engl J Med*. 2002;346(24):1854-62. doi: 10.1056/NEJMoa013040.
- Wilkoff BL, Cook JR, Epstein AE, Greene L, Hallstrom AP, Hsia H, Kutalek SP, Sharma A, Blatt B, Karas B, Kirchhoffer J. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. *Journal of the American Medical Association*. 2002 Dec 25;288(24):3115-23.
- SINHA, MANISHA, SURESH CHANDRA MONDAL, and BHABOTOSH MAKHAL. "A STUDY OF HAEMATOLOGICAL PROFILE OF MEDICAL AND PARAMEDICAL STUDENTS IN NORTH BENGAL MEDICAL COLLEGE AND HOSPITAL WITH SPECIAL REFERENCE TO ANAEMIA AND HAEMOGLOBINOPATHIES." *International Journal of Medicine and Pharmaceutical Science (IJMPS)* 9.6, Dec 2019, 47-56

18. Moss AJ. MADIT-II and its implications. *Eur Heart J*2003;24:16–18.
19. Gomes JA, Damato AN, Akhtar M, Dhatt MS, Calon AH, Reddy CP, Moran HE. Ventricular septal motion and left ventricular dimensions during abnormal ventricular activation. *The American journal of cardiology*. 1977 Jan 1;39(5):641-50.
20. SHAMKHY, DR MAHMOOD SWADY, and DR MAZIN MOHAMMAD JAWAD AL-MUSSAWY. "OUTCOME ANALYSIS AND OUTCOME PROGNOSTIC FACTORS OF TRAUMATIC BRAIN INJURY IN CHILDHOOD." *International Journal of Medicine and Pharmaceutical Science (IJMPS)*9.4, Aug 2019, 35-48
21. Buchalter MB, Rademakers FE, Weiss JL, Rogers WJ, Weisfeldt ML, Shapiro EP. Rotational deformation of the canine left ventricle measured by magnetic resonance tagging: effects of catecholamines, ischaemia, and pacing. *Cardiovascular research*. 1994 May 1;28(5):629-35.
22. Sorger JM, Wyman BT, Faris OP, Hunter WC, McVeigh ER. Torsion of the left ventricle during pacing with MRI tagging. *Journal of Cardiovascular Magnetic Resonance*. 2003 Jan 1;5(4):521-30.
23. HUSSEIN, MUSTAFA RASOOL, and HASANAIN MOHAMMED ALI MAKKI. "NEUROLOGICAL ASSESSMENT OF HEMODIALYSIS PATIENTS A SINGLE CENTER STUDY." *International Journal of Medicine and Pharmaceutical Science (IJMPS)* 8.2, Apr 2018, 57-74
24. Tops LF, Schalij MJ, Holman ER, van Erven L, van der Wall EE, Bax JJ. Right ventricular pacing can induce ventricular dyssynchrony in patients with atrial fibrillation after atrioventricular node ablation. *Journal of the American College of Cardiology*. 2006 Oct 17;48(8):1642-8.
25. Wyman BT, Hunter WC, Prinzen FW, Faris OP, McVeigh ER. Effect of Single Y BiV pacing on Ventricular Contraction; *Am J PhysiolCirc*; 2002; 282-H 372 – 379.
26. Schmidt M, Brömsen J, Herholz C, Adler K, Neff F, Kopf C, Block M. Evidence of left ventricular dyssynchrony resulting from right ventricular pacing in patients with severely depressed left ventricular ejection fraction. *Europace*. 2007 Jan 1;9(1): 34-40.
27. Yasuhiko Hori et al. Presence of structural heart disease and left ventricular dysfunction predict hospitalizations for new-onset heart failure after right ventricular apical pacing. *Europace* (2011) 13, 230–236.
28. Mustafá, M. U. R. T. A. Z. A., S. Yusof, and M. U. H. A. M. M. A. D. Iftikhar. "Osteomyelitis: pathogenesis, clinical and therapeutic challenge." *Int J Med Pharma Sci* 4 (2014): 9-18.
29. Delgado V, Mollema SA, Ypenburg C, Tops LF, van der Wall EE, Schalij MJ, Bax JJ. Relation between global left ventricular longitudinal strain assessed with novel automated function imaging and biplane left ventricular ejection fraction in patients with coronary artery disease. *Journal of the American Society of Echocardiography*. 2008 Nov 1;21(11):1244-50.
30. Fornwalt BK, Cummings RM, Arita T, Delfino JG, Fyfe DA, Campbell RM, Strieper MJ, Oshinski JN, Frias PA. Acute pacing-induced dyssynchronous activation of the left ventricle creates systolic dyssynchrony with preserved diastolic synchrony. *Journal of cardiovascular electrophysiology*. 2008 May;19(5):483-8.
31. Fang F, Zhang Q, Chan JY, et al. Deleterious effect of right ventricular apical pacing on left ventricular diastolic function and the impact of pre-existing diastolic disease. *Eur Heart J* 2011;32:1891–9.