

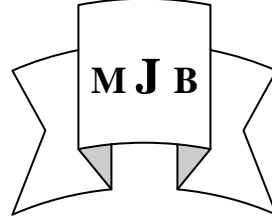
Clinical Comparison between Single and Dual Chamber Pacemakers in Patients with Advanced Atrioventricular Block

Hayder Abdul-Amir Alhindi

Saad Mirza Alaaraji

Mohammed Hashim Almyahi

College of Medicine, University of Babylon, Hilla, Iraq.



Abstract

Background: Several trials have compared (single chamber) ventricular pacing with dual chamber pacing. Dual chamber pacing is believed to have an advantage over ventricular pacing.

Objective: The aim of the study was to determine whether patients with implanted pacemaker (PM) for complete atrioventricular block (AVB) gain significant benefit from dual chamber compared with single chamber ventricular demand.

Design: The study was cross sectional parallel, all results were expressed as means (SD); a P value less than 0.05 were regarded as significant. Pair T - test was used to study all the variations. All data were processed with SPSS 18.

Setting: Al-nasyria heart center, Dhyqar.

Patients; sixty patients with high grade AVB who already underwent permanent pacemakers implant (single or dual chamber) were attending heart center for following up their devices.

Methods: the patients completed a (within-patient) comparison of symptoms, clinical finding, programming data, and echocardiographic finding during long term dual (VDD, DDD) pacing and long term ventricular demand (VVI) pacing.

Results: the study involved sixty patients, 23(38.3%) were males and 37(61.7%) were females. Thirty three (55%) patients had dual and twenty seven (45%) patients had single chamber PM. 36(60%) patients were hypertensive while 23.3(14%) patients were diabetic and the number of the smokers was only 7(11.7%). Majority of the patients from both groups lied within the age group (40-80y). The most common indication was complete heart block. The incidence of symptoms, systolic (but not diastolic) BP, and echocardiographic characteristics in both groups were parallel.

Conclusion: In patients with advanced AVB, there was no superiority of dual over single chamber PM concerning symptoms, systolic (but not diastolic) BP, programming data, and echocardiographic characteristics.

مقارنة سريرية بين نابض القلب احادي الحجيرة والثنائي الحجيرة في مرضى انحصار القلب

المتقدم

الخلاصة:

قامت عدة دراسات بمقارنة بين نابض القلب الاحادي والثنائي الحجيرة ، يعتقد بان النابض الثنائي ذا فائدة تفوق النابض الاحادي. كان الهدف من هذه الدراسة لتحديد ما اذا كان المرضى الذين زرع لهم نابض ثنائي الحجيرة لمعالجة انحصار القلب الكامل قد استفادوا اكثر من زرع النابض الاحادي. كان تصميم الدراسة عرضي ومتوازي وكل النتائج عبر عنها بالمعدل (الانحراف المعياري) وقيمة P اقل من ٠,٠٥. اعتبرت ذات مغزى . استخدم فحص T المزدوج لدراسة كل المتغيرات، وكل المتغيرات تم معالجتها بنظام SPSS 18. تمت الدراسة في مركز الناصرية للقلب في محافظة ذي قار. تم اختيار ستون مريضاً من المصابين بانحصار القلب الكامل ممن زرعت لهم

اجهزة النابض (الاحادي او اثنائي) الذين كانوا يراجعون المركز لغرض متابعة اجهزتهم. اجريت مقارنة بينية للمرضى من حيث الاعراض ، والمكتشفات السريرية، ومميزات البرمجة ومميزات فحص الصدى خلال النبض طويل الامد للناض التثائي (VDD, DDD) والاحادي الحجيرة (VVI) . شملت الدراسة ستون مريضاً، كان الذكور منهم ٢٣ (٣٨,٣%) والانات كان عددهم ٣٧ (٦١,٧%) . 33(55%) مريض كان لديهم نابض ثنائي بينما ٢٧ (٤٥%) مريض كان لديهم نابض احادي الحجيرة . ٣٦(٦٠%) مريض كان مصابا بارتفاع ضغط الدم و ٢٣(١٤%) كان مصابا بداء السكري. وقع اكثر المرضى في المجموعة العمرية بين عمر (٤٠-٨٠ سنة) . كان انحصار القلب الكهربي هو الموجب الاكثر شيوعا للزرع . كان حدوث الاعراض وضغط الدم الانتقاضي (ليس الانبساطي) ومميزات فحص الصدى للمرضى في كلا المجموعتين متشابه. الاستنتاج النهائي هو انه في مرضى انحصار القلب الكامل لم يكن النابض التثائي بافضل من النابض الاحادي فيما يخص الاعراض وضغط الدم الانتقاضي (ليس الانبساطي) ومعلومات البرمجة وكذلك مميزات فحص الصدى.

Introduction

Dual chamber has several theoretical advantages over ventricular demand pacing.

These include the ability of dual pacing to maintain the normal activation sequence of AV synchrony, provide a degree of rate responsiveness, better haemodynamic function, a greater effort tolerance, and fewer symptoms than long term ventricular demand pacing. Maintaining the normal sequence of atrial and ventricular activation will tend to optimize ventricular filling and cardiac output. This, in turn, should improve symptoms and cardiac function [1-5]. There is also evidence that patients who require pacing for SAN disease suffer fewer symptoms during dual pacing than during ventricular pacing [2, 4].

However, the ability of ventricular PM with rate-adaptive ability to raise rate in response to exertion appears to minimize the benefit of dual over single chamber pacing [3- 5].

In contrast, dual pacing usually causes some degree of RV unnecessary pacing, which changes the electrical activation and contraction pattern of the ventricles. This may result in ventricular remodeling, with decreased LVEF and left atrial dilatation [4].

It is therefore appropriate to evaluate seriously the evidence supporting the

proposed benefits of dual chamber pacing.

Patients and Methods

Patients selection; we studied 60 patients aged 30 – 84 years (mean 60y) who already underwent permanent PM implant (single or dual chamber) for high grade AVB which were attending heart centers for following up their devices regardless their ages. Patients were eligible if PM implantation for advanced AVB not other else, had neither heart diseases (congenital or structural) nor LV dysfunction prior to PM implantation, and PM implanted for a period of at least one year. Those with hemoglobin (<10 gm/dl) or with pacing percent (< 50%) of the time were excluded. The patients are classified into 2 groups: single (n=27) and dual PM (n=33).

Study Design; we had to take all the patients that visit the cardiac consultation clinic, then, take history, performing examination, sending them for hematological, biochemical and radiological investigation. Then performing programming session (interrogation) and echocardiographic examination for all also; thereafter, eligible patients were chosen.

Pacemaker programming; throughout interrogation, the baseline characteristics of the PM was recorded including: pacing mode, lower basal rate, pacing %, battery life, AV delay

(in case of dual PM), atrial and ventricular thresholds (pacing and sensing), and finally lead impedances of atrial and ventricular leads. These parameters programmed according to the clinical data and interrogation result [21].

Echocardiographic evaluation; performed by Philips® Envisor CHD (Netherlands origin) both supine and left lateral position examination using both M-mode and Doppler echocardiographic assessment for measurement of LVESD, LVEDD and LVEF %. The later is a valuable index of ventricular function [7], measured by using the formula [22]:

$$\text{Ejection fraction (EF)} = \frac{\text{LVEDD}^2 - \text{LVESD}^2}{\text{LVEDD}^2}$$

Where the LVEDD is the LV internal diameter at end diastole while the LVESD is the narrowest diameter in systole. Normal LV function has EF

>55% while LV dysfunction has EF <50% [6].

Statistical analysis: our study was cross sectional parallel study, all results are expressed as means (SD); a P value less than 0.05 were regarded as significant. Pair T - test was used to study all the variations of the two groups. All data were processed with SPSS software version 18.

Results

Table (1) shows that the total number of patients is sixty. The number of the males were 23 and 37 were females. Their mean age was 60 ± 18.5 years, minimum age was 3y and the maximum age was 84y, 36 (60%) of the patients had hypertension, 14 (23.3%) were suffering from DM, 12(20%) had IHD, 2(3.3%) were affected with heart failure and 7 (11.7%) were smokers (4) of them had stopped smoking.

Table 1 Baseline characteristics of patients with advanced AVB

Characters	Patients No. & (%)		
	Mean±SD	Min.	Max.
Age (year)	±18.5 60	3	84
Hypertension	36 (60%)		
Diabetes Mellitus	14 (23.3%)		
Ischemic Heart Disease	12 (20%)		
Heart Failure	2 (3.3%)		
Smoking	7 (11.7%)	Stop Smoking	4 (6.6%)

Table 2 shows the distribution of the patients according to the sex, where the numbers were relatively equal in single chamber while the females were double

the males in those with dual chamber PM (22:11). Females number were 37(61.7%) and 23 (38.3%) were males.

Table 2 Distribution of Patients with advanced AVB to the sex for those with single and dual chamber pacemakers

Type of PM	Male (No.&%)	Female (No.&%)	P value
Single chamber	12 (44.5)	15 (55.5)	0.9
Dual chamber	11 (33.3)	22 (66.6)	0.045
Total patients' No.	23 (38.3)	37 (61.7)	0.5

Table (3) shows that there was no statistically significant variation between the two groups in all baseline

characters except for the incidence of DM being more in dual 11(33.3%) than in single chamber 3(11.1%).

Table 3 comparison of baseline characteristics in patients with advanced AVB between single and dual chamber pacemakers

Characters (No. & %)	Single Chamber	Dual Chamber	P value
Total patients	27 (45%)	33 (55%)	
Age of patients (years)	Mean ± SD 60.5 ± 20.8	Mean ± SD 59.6 ± 16.8	0.85
	Min 3	Min 17	
	Max 84	Max 80	
Hypertension	15 (55.5%)	21 (63.6%)	0.53
Diabetes Mellitus	3 (11.1%)	11 (33.3%)	0.03
Ischemic Heart Diseases	3 (11.1%)	9 (27.2%)	0.12
Heart Failure	2 (7.4%)	0	0.11
Smoking	3 (11.1%)	4 (12.1%)	0.9

Table (4) demonstrates the age groups of patients, according to the types of PM. Majority of the patients of both

groups lied in age group (40-80y) being more at (60-80y) age group.

Table 4 age groups of patients with advanced AVB

Pacemaker Type	< 20 y	20-40y	40-60 y	60-80 y	> 80y	Total
Single Chamber (No. & %)	2 (7.4)	1 (3.7)	6 (22.2)	12 (44.4)	6 (22.2)	27
Dual chamber (No. & %)	1 (3)	4 (12.1)	8 (24.2)	17 (51.5)	3 (9.1)	33

Table (5) illustrates the duration of PMs' implantation for patients; it shows that most of the patients of both groups

lied within the duration of 1-2y, then the number decreasing gradually with the subsequent durations.

Table 5 Duration of pacemakers' implantation for patients with advanced AVB.

Pacemaker Type	1-2 y	2-3 y	3-4 y	4-5 y	> 5 y	Total
Single chamber & %No(10 (37)	7 (26)	8 (29.5)	0 (0)	2 (7.5)	27
Dual chamber & %No(21 (63.6)	4 (12.1)	5 (15.1)	1 (3)	2 (6)	33

Table (6) explains the indication of PM implantation in patients, the most common indication was CHB in more

than two third of the patients and the least one being the trifascicular block.

Table 6 indication of pacemaker implantation in patients with advanced AVB at follow up visit

Indication (No& %)	Single chamber	Dual chamber
Complete Heart Block	19 (70.3%)	25 (75.8%)
Second Degree Block	5 (18.5%)	6 (18.2%)
Trifascicular Block	3 (11.2%)	2 (6%)

Table (7) points up the programming characteristics of dual and single chamber PM in patients, there were no

significant differences between both groups.

Table 7 programming characteristics of dual and single chamber pacemaker in patients with advanced AVB at follow up visit

Programmed Mode (No & %)	VDD		DDD		VVI		
		7 (11.6%)		26 (43.4%)		27 (45)	
Rate (pace/minute)	Mean ± SD 58.4 ± 7.7		Min 40	Max 70	Mean±SD 58.9 ±6.2	Min 45	Max 70
Battery Life (No. & %)	ERI		Good		ERL		Good
	1	(3)	32	(97)	1	3.7	26 96.3
Pacing %	Mean ± SD		Min	Max	Mean±SD	Min	Max
	84 ± 20.8		5%	100%	76.3±32.2	100	50
AV Delay (ms) (Mean ± SD)	191 ± 51				Not applicable		
Pacing Threshold (Mean ± SD)	Atrial	Pacing(V)	Sensing(mV)		Not applicable		
		3.7 ± 4.9	1 ± 1				
	Ventricular	Pacing(V)	Sensing(mV)		Pacing(V)	Sensing(Mv)	
		2.3± 1.2	3.4 ± 3		.48±1.1	3.9 ± 3.5	
Lead Impedance(Ω) (Mean ± SD)	Atrial	613 ± 363		Atrial	Not applicable		
	Ventricular	512 ± 136		Ventricular			

ERI: Elective Replacement Indicator, **AV:** atrioventricular

Table (8) shows the clinical characteristics at programming session of patients. Again, no statistically significant differences between the single and dual chamber PM patients. The only exceptions were both diastolic BP and mean pulse rate. The

mean diastolic BP was (81±13.4 and 91.2±15.2) mmHg with (*p* 0.009) whilst the mean pulse rate was 67±14.9 p/m and 75.7±16.4 p/m with *P* value 0.04 for single and dual chamber PM respectively.

Table 8 clinical characteristics at programming session of patients with advanced AVB in single and dual chamber pacemakers

Characters (No.&%)	Single Chamber		Dual Chamber		P value
Dizziness	13 (48.1%)		16 (48.5%)		0.98
Postural Dizziness	7 (25.9%)		8 (24.2%)		0.88
Fainting	4 (14.8%)		4 (12.1%)		0.67
Syncope	1 (3.7%)		3 (9.4%)		0.39
Orthopnea	7 (25.6%)		9 (27.3%)		0.9
Shortness of Breath	8 (29.6%)		9 (27.3%)		0.84
Leg Swelling	10 (37%)		8 (24.2%)		0.29
Blood Pressure mmHg (Mean ± SD)	Systole	Diastole	Systole	Diastole	0.62
	143.5	81	147.5	91.2	
	32.9	13.4	29.3	15.2	0.009
Pulse rate (p/min) Mean ± SD	67 ± 14.9		75.7 ± 16.4		0.04
Postural Drop	0		1 (3%)		0.37

Table (9) illustrates the echocardiographic findings at programming session of patients. Both groups having a good LVEDD (47 ±

9.6, 50.4±9.6), LVESD (34.2± 11.3, 35.1±11) and EF% (59.9±15.8,59.11.5) respectively and no significant statistical variations were found.

Table 9 Echocardiographic findings at programming session of patients with advanced AVB for single and dual pacemakers

Echocardiographic Finding	Single Chamber	Dual Chamber	P Value
LVEDD (mean ± SD)	47 ± 9.6	50.4 ± 9.6	0.23
LVESD (mean ± SD)	34.2 ±11.3	35.1 ± 11	0.7
Ejection Fraction (Mean ± SD)	57.9 ±15.8	59 ± 11.5	0.7
LVH (No. & %)	2 (7.4)	0	0.11
Functional MR (No. & %)	2 (7.4)	2 (6.5)	0.8
Functional TR (No. & %)	3 (11.1)	1 (3.2)	0.44
Functional AR (No. & %)	1 (3.7)	1 (3.2)	0.75

LVEDD: left ventricular end diastolic dimension, **LVESD:** left ventricular end systolic dimension, **LVH:** left ventricular hypertrophy, **MR:** mitral regurgitation, **TR:** tricuspid regurgitation **AR:** aortic regurgitation.

Discussion

The study run over 8 months, we exclude the anemic patients as anemia may affect the physiology of heart and initiating signs and symptoms that interfere with that of the PM. Those with congenital or structural heart disorders had been excluded as both may affect the heart

pathophysiology also. Those with PM implantation for a time interval less than one year also excluded because the PM may require a time after implantation to create physiological changes

in the heart so we took a time interval of one year as a cut off value. Same

thing could be applied for the reason behind the exclusion of PM patients whom ventricular pacing percent less 50%. Therefore in our study to confirm that these clinical as well as echocardiographical findings were attributed to the pure effect of the PM we put them in an (exclusion criteria).

Furthermore, if the battery status was on end of life indicator has been excluded also as this PM

has no enough energy to induce its full ability to pace the myocardium. But, this is not the case for the (ERI) battery indicator. As still the PM working very well; but, only had a few months of appropriate work before elective replacement.

Those PMs that were working practically as VVI in the interrogation for 2 separate sequential sessions are considered as VVI in our recordings even though their shipping parameters are VDD or DDD.

In table (1) which showed, the mean age of all patients in this study was 60 ± 18.5 years while in comparison, Tehran study [14] showed that the mean age of patients was 65 years. Hypertensive patients were 60%, this is actually may signify some association between hypertension and PM implantation and could be attributed to the fact that hypertension can be associated with aortic valve calcification. Moreover, hypertension is a well known risk factor for atherosclerosis and IHD, and this may play a role in the pathogenesis of AVN diseases [7]; however, it needs further working and a larger sample of patients to prove this association.

Table (2) shows the female preponderance of the total patients that could be attributed to a known difference in the frequency of underlying structural heart disease. Women have smaller cardiac size and smaller coronary artery diameter than men. Additionally, there is a cyclical variation in the occurrence of episodes

of arrhythmia with regards to the menstrual cycle [8].

The finding of female preponderance is concordant to what is published by a study [9] who reported a sex differences in the selection of a PM which can't be explained by the underlying cardiac disorder depending on a retrospective study that have including 634 hospital in Germany. On the other side, a retrospective analysis in USA from a single-center database of PM implants during the years 2001-2003 aimed to assess gender-related differences in PM mode selection in 274 patients found no difference in PM mode selection between male and female patients [10].

Table (3) illustrates no any statistical significant differences in the incidence of baseline characteristics between the 2 groups (the exception was the incidence of DM). In fact, this eliminated the confounders in the comparison between the two groups. Nevertheless, the percent of smokers was 11.1% of the patients with the single and 12.1% of the dual chamber patients which is very low and might be a coincidental finding (because of relatively small sample size).

There was a significant incidence of DM, where 33.3% of the dual and 11.1% of the single chamber patients was diabetic. This is may be due to the incidence of DM in Iraq. Moreover, the incidence of DM was more in patients with dual than in single chamber PM. This is because DM usually associated with some structural heart disease that increasing the risk factors making the operator decision biased for dual than single PM in diabetics [20].

Table (4) showed that age of (50%) all patients in both groups concentrated in (60- 80 years) age group which can be explained by the fact that with the age the degenerative changes of the heart conductive system expected to be increased [11]. But, those whom > 80 years the number not

increased so much may be correlated with the life expectancy in Iraq which is around 66 years [12].

Table (5) shows that most of the patients lied within the duration of 1-2 years. This is in part due to most patients were poor compliant, at most they visit the PM clinic if they have been recently implanted and their interest in programming of their PM decreasing with time as far as they are symptoms free. Then there was a relative increment at duration of ≥ 5 y (2%). The later rising might be attributed to their battery lives being start to be depleted or near ERI.

Table (6) shows that the commonest indication for PM in this study was a CHB for both groups. This is similar to the finding that been available in ACC/AHA Guidelines 2010 [13]. As well as this concurs to a previously published by Tehran study [14], which lasted for one year, 1635 patients were studied and received permanent PM implanted at 27 centers all over the country and the CHB was consistently the most common indication at all centers.

Table (7) shows basically similar programming parameters of the patients. In our programming, despite the (AV delay) in a dual chamber PM is programmed according to a special known formula to produce the best AV synchrony.

Table (8) showed that there were no significant statistical differences in presence of symptoms that included dizziness, postural dizziness, syncope, orthopnea, leg swelling, systolic BP and postural BP dropping between the groups. We assume however, that this to some extent correlated to the general Iraqi patient's personality whom satisfied with suboptimal programming results unlike people in other modern countries (whom insisting on an optimal standardization). Another justification is that most of VVI patients in this study were programmed

to VVIR which enable increase the pacing rate with the exercise mimicking dual chamber response. Other likely explanation is that the contribution of atrial contraction (AV synchrony) to cardiac output is more essential in those with structural heart diseases than with a structurally normal heart. i.e. those with structural heart disease showed more symptomatic benefit from dual chamber PM. However, patients with structural heart diseases had been excluded.

This is concordant to what had been documented by the (UK-PACE trial) that had been conducted in 46 centers in the UK where patients were recruited from 1995 to 1999 [15].

However, in a study involved fifteen patients with dual PM that was implanted for AVB and lasted for 10 weeks. It reported significantly less shortness of breath, dizziness, and fatigue during DDD pacing [3].

Moreover, the table showed also that dual chamber patients had a higher pulse rate than those with single chamber. A same finding was presented by two studies [16, 17]. This could be explained by the fact that normally the SAN action raises with activity and so the SAN could effectively increase rate in a dual PM and dual PM on the whole depends on SAN activity and this make it more dynamic or more physiological [15, 18].

What's more, table (8) shows that there is statistically significant ($p < 0.01$) higher diastolic BP (91.2 ± 15.2) among dual than those with single chamber (81 ± 13.4).

Anyhow, other study [3] reported that a systolic BP tended to be lower and was significantly more variable during VVI pacing than during DDD pacing. They had been explained this difference by an AV dissociation rather than rate responsiveness.

Meanwhile, another study had showed that a dual chamber had a higher BP

(systolic and diastolic) than does a single chamber pacing. That's to say, the cardiac pacing mode may influence sympathetic outflow simply through arterial baroreflex mechanisms [19].

The higher diastolic BP in the study can't be explained absolutely, nevertheless, might be due to the unintentional increase of DM among dual PM may play a role in a higher diastolic BP.

Conclusion

This study confirms that in patients with advanced heart block the dual chamber pacemaker has no significant benefit over the single chamber at the level of symptoms, clinical finding, programming data, and echocardiographic finding.

References

- 1) Nielsen J., Thomsen P., Højberg S., Møller M., Vesterlund T., Dalsgaard D.; the DANPACE Investigators (2011): A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. *European Heart Journal* 32, 686–696.
- 2) Hargreaves M., Channon K., Cripps T., Gardner M. and Ormerod O. (1995): Comparison of dual chamber and ventricular rate responsive pacing in patients over 75 with complete heart block. *Br Heart J*; 74:397-402.
- 3) Boon N., Frew A., Johnston J., Cobbe S. (1987): A comparison of symptoms and intra-arterial ambulatory BP during long term dual chamber atrioventricular synchronous (DDD) and ventricular demand (VVI) pacing. *Br Heart J*; 58:34-9.
- 4) Brunnera M., Olschewskib M., Geibela A, Bodea C., Manfred Z. (2004): Long-term survival after pacemaker implantation Prognostic importance of gender and baseline patient Characteristics. *European Heart J* 25, 88-95.

- 5) Ovsyshcher E., Hayes D. and Furman S. (1998): Dual-Chamber Pacing Is Superior to Ventricular Pacing : Fact or Controversy? *Circulation*, 97: 2368-2370.
- 6) Kim E. Barre, *et al.* (2010): *Ganong's Review of Medical Physiology*, 23 Ed.
- 7) Libby P. (2011): *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 8th ed. Saunders, an Imprint of Elsevier.
- 8) Gowda RM, Wilbur SL, Schweitzer P. (2006): Gender differences in cardiac electrophysiology and arrhythmias. Part1. *Cardiol*; 15(6):296–302.
- 9) Schüppel R., Büchele G., Batz L., Koenig W. (1998): Sex differences in selection of PM: retrospective observational study. *BMJ*; (4): 316:1492–5.
- 10) Veerareddy S, Arora N, Caldito G, Reddy PC. (2007): Gender differences in selection of pacemakers: a single-center study. *Gend Med.* ; 4(4):367-73.
- 11) Topol, Eric J. (2007): *Textbook of Cardiovascular Medicine*, 3rd Edition.
- 12) WHO Iraq health profile 2010.
- 13) American College of Cardiology/American Heart Association (ACC/AHA), (2010) *Guidelines Implantation of Cardiac PM Antiarrhythmia Devices*, (A Report of the ACC/AHA, Task Force on Practice Guidelines). Developed in Collaboration with the North American Society of Pacing and Electrophysiology (NASPE).
- 14) Oraii S., Eftekhazadeh M., Mirmasoumi M., Ghorbani A., Taraghi M. & Hasanzadeh M. (2006): The National Survey of Cardiac PM and ICD. *The Journal of Tehran Heart Center*, (1): N 2 95-99.
- 15) Toff, W.; Camm, A.; Skehan, J. (2005): UK-PACE trial; Single Chamber versus Dual Chamber Pacing for High Grade AVB, *Nejm*; 353: 145-155.

- 16) Iwase M, Miyaguchi K, Aoki T, Kato K, Hatano K, Hayashi H, (1991): Evaluation of maintenance of cardiac output during DDD and VVI pacing by exercise Doppler Echocardiography. J Card. 1991; 21(3): 727-33.
- 17) Vootiprux W.; Sermsawan A.; Kasemsuwan P. (2009). Effect of Heart Rate on Tissue Doppler Measures of E/E', Thai Hear J; 22:12-125.
- 18) Michael J., Michael R. (2006): The control of heart rate: the physiology of the SAN and the role of the *I_f* current. Dialogues in Cardiovascular Medicine (11); 11:5-17.
- 19) Andrew, T.; Morillo, A.; Eckberg, D.; Ellenbogen, K. (1996): Higher sympathetic nerve activity during ventricular (VVI) than during dual-chamber (DDD) pacing JACC; 28:1753– 8.
- 20) Andrea N. (2007): Handbook of Cardiac Electrophysiology. The Cleveland Clinic Foundation, Cleveland, Ohio, USA.
- 21) Kenny, T. (2005): The Nuts and Bolts of Cardiac Pacing, Clinical Education & Training. St Jude Medical, Austin, Texas. Blackwell Futura.
- 22) Bonow. R.; Mann, D.; Zipes, D.; Libby, p. (2011): Braunwald's Heart Disease. A Textbook of cardiovascular medicine. 9th ED, Elsevier.