DDD is Superior to VVI?

Jeong-Gwan Cho, MD, FACC

Division of Cardiology
Chonnam University Hospital

What is your answer?

My answer is "no", based on the several randomized clinical trials.

The era of evidence-based medicine has come since 1992.

Our medical practice should be based on the evidence confirmed by randomized clinical trial.

Pacemaker Implantation: CNUH

Indication	n	VVI(R)	D(V)DD(R)	AAI(R)
SSS	347	204(58.8)	115(33.1)	28(8.1)
AVB-2nd D	81	37(45.7)	44(54.3)	0
AVB-3rd D	530	274(51.7)	256(48.3)	0
Total	958	515(53.8)	415(43.3)	28(2.9)

What is DDD Pacing?

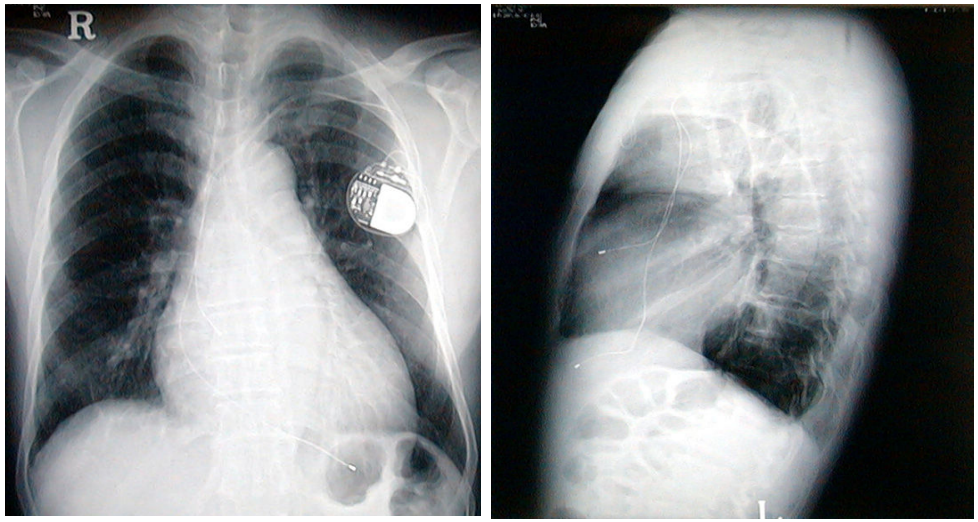
Dual chamber pacing

AV sequential pacemaker

'so-called' physiologic (?) pacemaker

'so-called' universal pacemaker

Most expensive and complex pacemaker



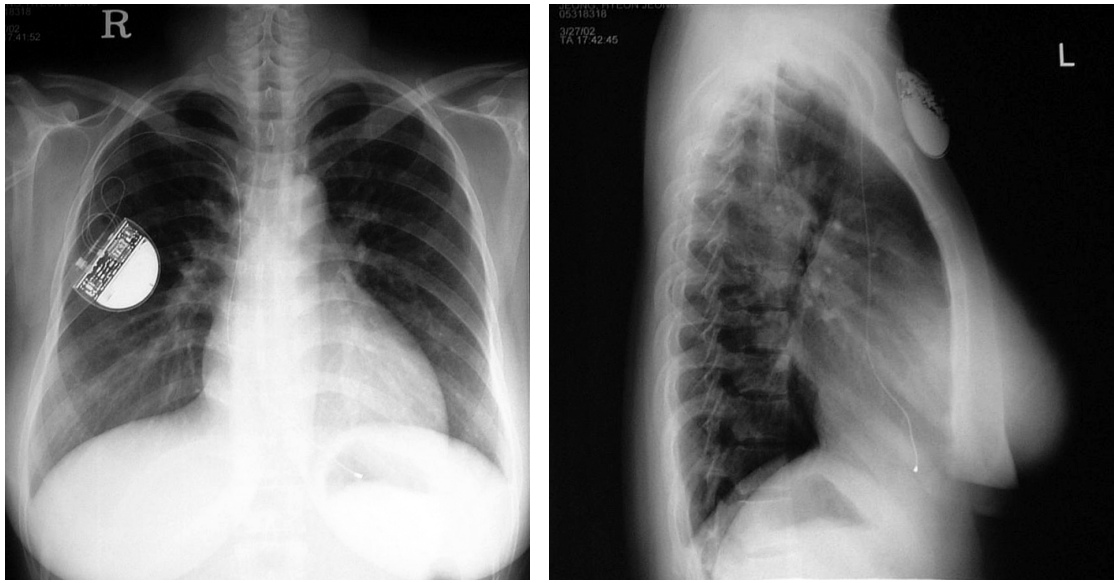
What is VVI Pacing?

Single chamber pacing

Atrial-asynchronous ventricular pacing

'so-called' non-physiologic pacemaker

Most cheap and simple pacemaker



What is the Difference between DDD and VVI?

DDD: RV pacing + AV synchrony
VVI: RV pacing – AV synchrony

DDD pacing preserves AV synchrony, but disturbs ventricular synchrony resulting from RV pacing like VVI. However, AAI pacing preserves AV synchrony and ventricular synchrony.

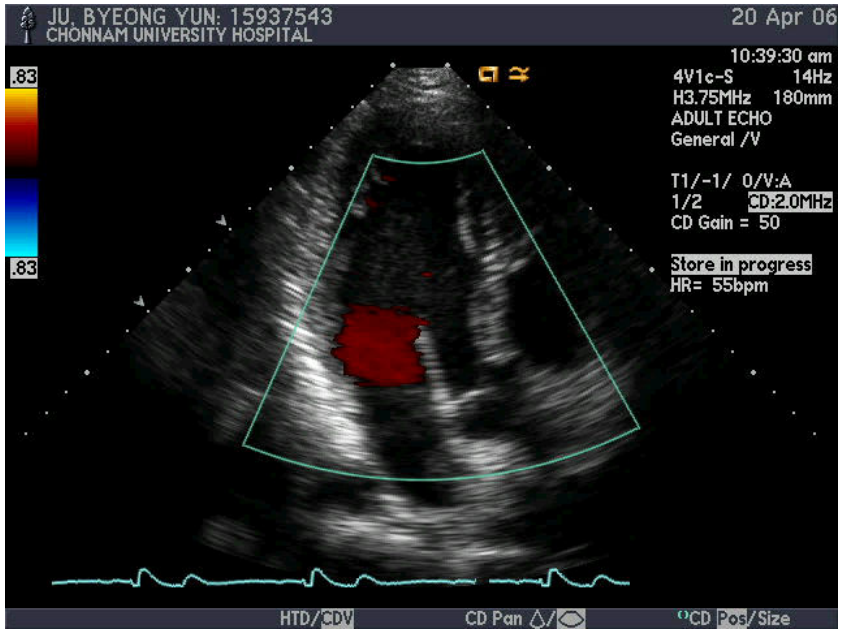
Determinants of Cardiac Function

Heart rate: chronotropy

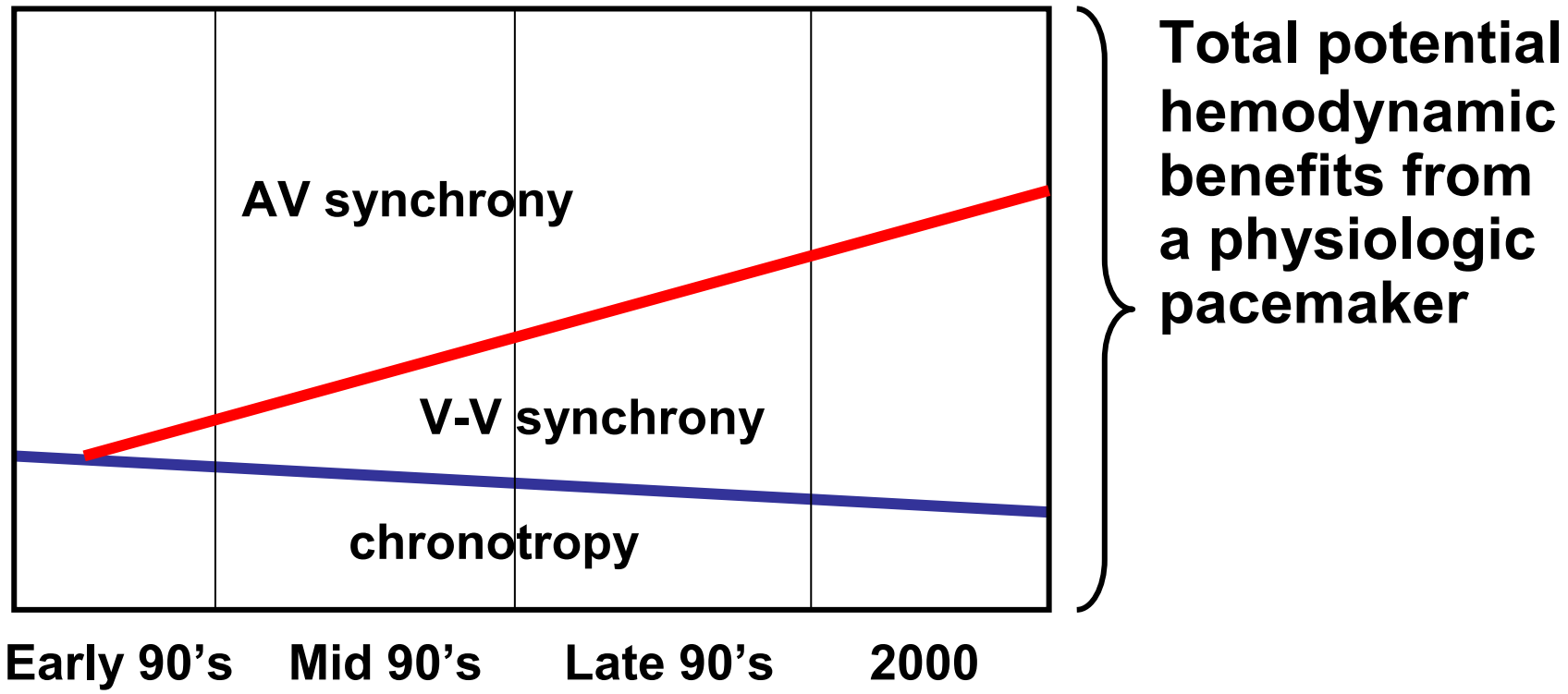
Afterload

Preload: AV synchrony

Contractility: ventricular synchrony



Role of each PM Function in Hemodynamic Benefits



Clinical Trials Comparing DDD with VVI Pacing

Clinical Trial	Pacing Indication	No. of Patients	Modes	Selected Endpoints	Summary of Results
Andersen 1997	SND	225	AAI vs VVI	Mortality: AAI relative risk, 0.66 (0.44–0.99); $P=0.045$ Thromboembolism: AAI relative risk, 0.47 (0.24–0.92); $P=0.023$ Atrial fibrillation: AAI relative risk, 0.54 (0.33–0.89); $P=0.012$	Long-term follow up favored atrial pacing in all clinical endpoints
PASE 1998	SND+AVB	407	DDDR vs VVIR	Mortality: DDDR 16%; VVIR 17%; $P=0.95$ Stroke or death: DDDR 17%; VVIR19%; $P=0.75$ Atrial fibrillation: DDDR 17%; VVIR 19%; $P=0.80$	Quality of life was the primary endpoint and was similar between pacing modes in the overall group; subgroup analysis of SND patients suggested benefit for DDDR pacing in quality of life and atrial fibrillation
Mattioli 1998	SND+AVB	210	VVI(R) vs AAI, DDD(R) or VDD	Stroke: VVI(R) 19 patients; atrial-based 10 patients; $P<0.05$.	Physiological pacing associated with less stroke and atrial fibrillation
PAC-A-TACH 1998	SND	200	DDDR vs VVIR	Death: DDDR 3.2%; VVIR 6.8%; $P=0.007$ Atrial tachycardia: DDDR 48%; VVIR 43%; $P=0.09$	Mortality benefit for atrial-based pacing; no difference in recurrence of AF
CTOPP 2000	SND+AVB	2568	DDD(R) or AAI(R) vs VVI(R)	Stroke and cardiovascular mortality: reduction in relative risk, 9.4% (−10.5 to 25.7%) Atrial fibrillation: reduction in relative risk, 18% (3 to 32.6%)	No difference in stroke or death between pacing modalities; AF less frequent in atrial-based pacing

Clinical Trials Comparing DDD with VVI Pacing

MOST 2002	SND	2010	DDDR vs VVIR	Mortality and stroke: DDDR hazard ratio, 0.91 (0.75–1.10); P=0.32 Atrial fibrillation: DDDR hazard ratio, 0.77 (0.64–0.92); P=0.004 Heart failure hospitalization: DDDR hazard ratio, 0.73 (0.56–0.95); P=0.021	No difference in death or stroke between pacing modalities; atrial fibrillation and heart failure less in DDDR-paced patients
UKPACE 2002	AVB	2000	DDD vs VVI or VVIR	Mortality primary endpoint	No difference between groups (ACC 2003 late-breaking trials presentation only)
STOP-AF	SND	350	VVI vs AAI or DDD	Atrial fibrillation primary endpoint	Results not reported
RAMP 1999	SND+AVB	400	DDD vs DDDR	Quality of life primary endpoint	No difference between groups (NASPE abstract presentation only)
ADEPT 2003	SND+AVB+chronotropic incompetence	870	Factorial trial: DDD vs DDDR mode switch-on vs off	Quality of life primary endpoint	No difference between groups (NASPE 2003 late-breaking trials presentation only)
DANPACE	SND	2000	AAI vs DDD with ventricular capture	Mortality primary endpoint	Currently enrolling; results in 2004
SAVE-PACE	SND	1800	DDD+search AV vs DDD	Endpoints: reduction in %ventricular pace; atrial fibrillation; LV remodeling	Currently enrolling; results on % ventricular pace in 5/04; clinical results in 2005

1st Randomised Trial of AAI vs. VVI Pacing for SSS

Andersen HR, et al. Lancet. 1997;350:1210.

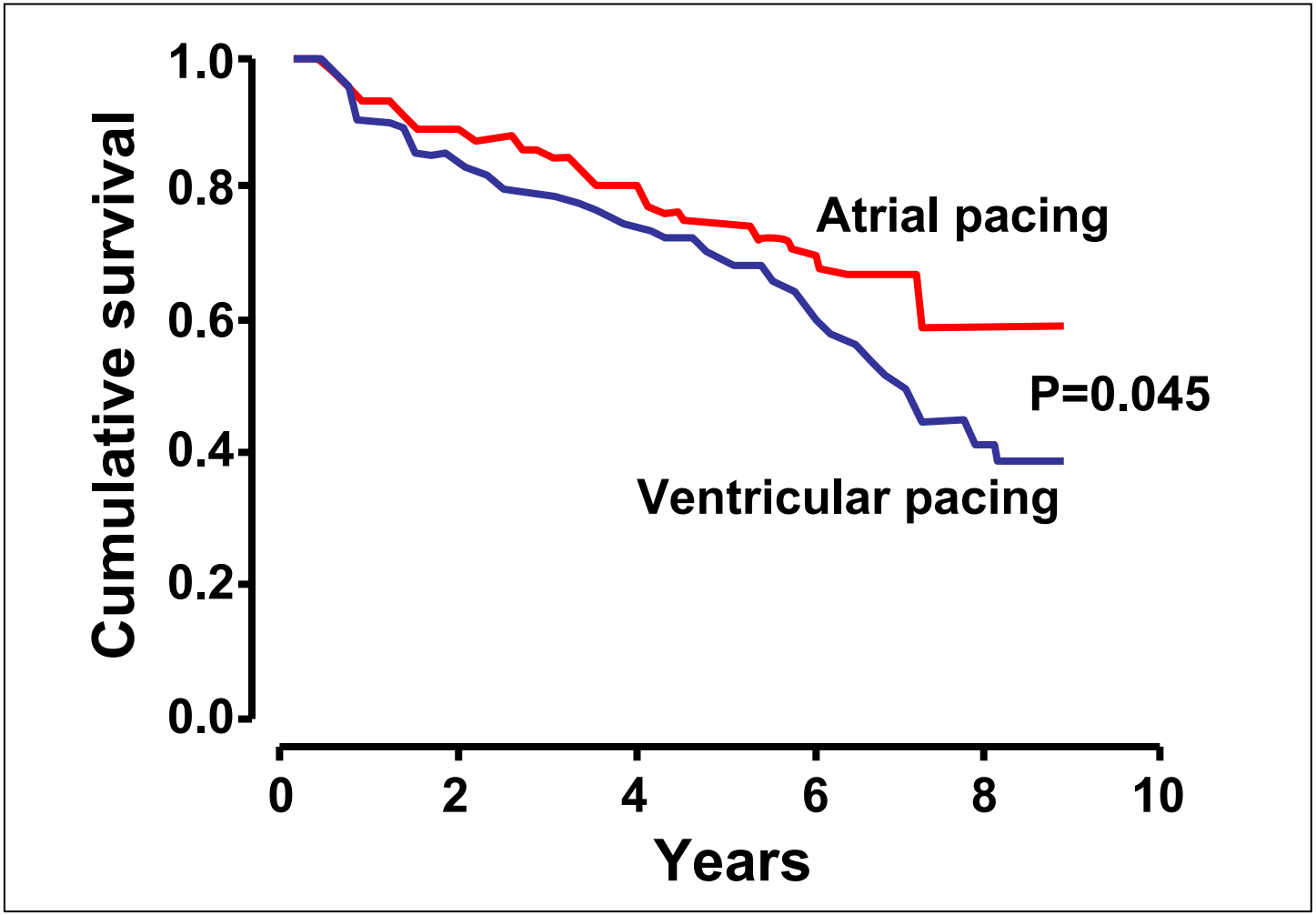
225 patients with SSS randomised to either single-chamber atrial pacing (n=110) or single-chamber ventricular pacing (n=115)
Follow-up: up to 8 years
Endpoints were mortality, CV death, AF, TE events, heart failure, and AV block.

1st Randomised Trial of AAI vs. VVI Pacing for SSS

Andersen HR, et al. Lancet. 1997;350:1210.

	Total death	CV death	AF	TE
AAI	39	19	26	13
VVI	57	39	40	26
RR	0.66	0.47	0.54	0.47
P	0.045	0.0065	0.012	0.023

Clinical Outcome: Total Death



1st Randomised Trial of AAI vs. VVI Pacing for SSS

Andersen HR, et al. Lancet. 1997;350:1210.

	Total death	CV death	AF	TE
AAI	39	19	26	13
VVI	57	39	40	26
RR	0.66	0.47	0.54	0.47
P	0.045	0.0065	0.012	0.023
Multivariate analysis				
RR	0.71	0.52	0.45	0.47
P	0.11	0.022	0.063	0.028

1st Randomised Trial of AAI vs. VVI Pacing for SSS

Andersen HR, et al. Lancet. 1997;350:1210.

Conclusions:

Compared to VVI pacing, atrial pacing is only associated with a significantly lower CV death and fewer TE events.

AAI appears superior to VVI.

This can not be extrapolated to comparison of DDD vs VVI.

Pacemaker Selection in the Elderly (PASE)

Lamas GA, et al. NEJM. 1998;338:1097.

PASE: 30-month, single-blind, randomized, controlled comparison of DDD and VVI pacing in 407 pts ≥65 years of age in 29 centers

Background: Ventricular pacemakers are less expensive, but dual-chamber pacemakers are believed to be more physiologic. However, it is not known whether either type of pacemaker results in superior clinical outcomes.

Pacemaker Selection in the Elderly (PASE)

Lamas GA, et al. NEJM. 1998;338:1097.

Primary End-Point

QOL by the 36-item Medical Outcomes Study Short-Form General Health Survey (SF-36)

Subjects

- **The average age was 76 years (65 to 96), and 60 percent were men.**
- **SVT including AF, 29%; HF (NYHA FC ≥III), 27%; CV disease 13%; low EF, 44%**
- **AVB, 49% (CHB: 59%); SSS, 43%; VAC, 29%**

PASE Study: Quality of Life

Subscale	base	3	9	18 mos
Physical function	0.55	0.23	0.22	0.99
Social function	0.45	0.37	0.54	0.54
Physical role	0.54	0.051	0.36	0.78
Emotional role	0.41	0.052	0.27	0.31
Mental health				
Energy				
Pain	.67	0.91	0.64	0.42
Health perception	0.97	0.99	0.95	0.33

no significance!

PASE Study: Clinical Outcomes

End-points	Total	SND	AVB
All-cause death	0.95	0.09	0.41
Stroke or all-cause death	0.75	0.11	0.68
Stroke or HF admission or all-cause death	0.18	0.07	0.49
Atrial fibrillation	0.80	0.06	0.26

Pacemaker Selection in the Elderly (PASE)

Lamas GA, et al. NEJM. 1998;338:1097.

Results:

- **QOL improved significantly ($p<0.001$).**
- **There were no differences between VVI and DDD in either the QOL or clinical outcomes including cardiovascular events or death.**

Canadian Trial of Physiologic Pacing (C-TOPP)

Connolly SJ, et al. NEJM. 2000;342:1385.

Large, randomized, controlled, 32 center-trial to evaluate the effects of physiologic (DDD or AAI) pacing versus ventricular pacing on the risk of stroke and CV death

Subjects: Patients without chronic AF who were scheduled for a first implantation of a PM to treat symptomatic bradycardia.

Canadian Trial of Physiologic Pacing (C-TOPP)

Connolly SJ, et al. NEJM. 2000;342:1385.

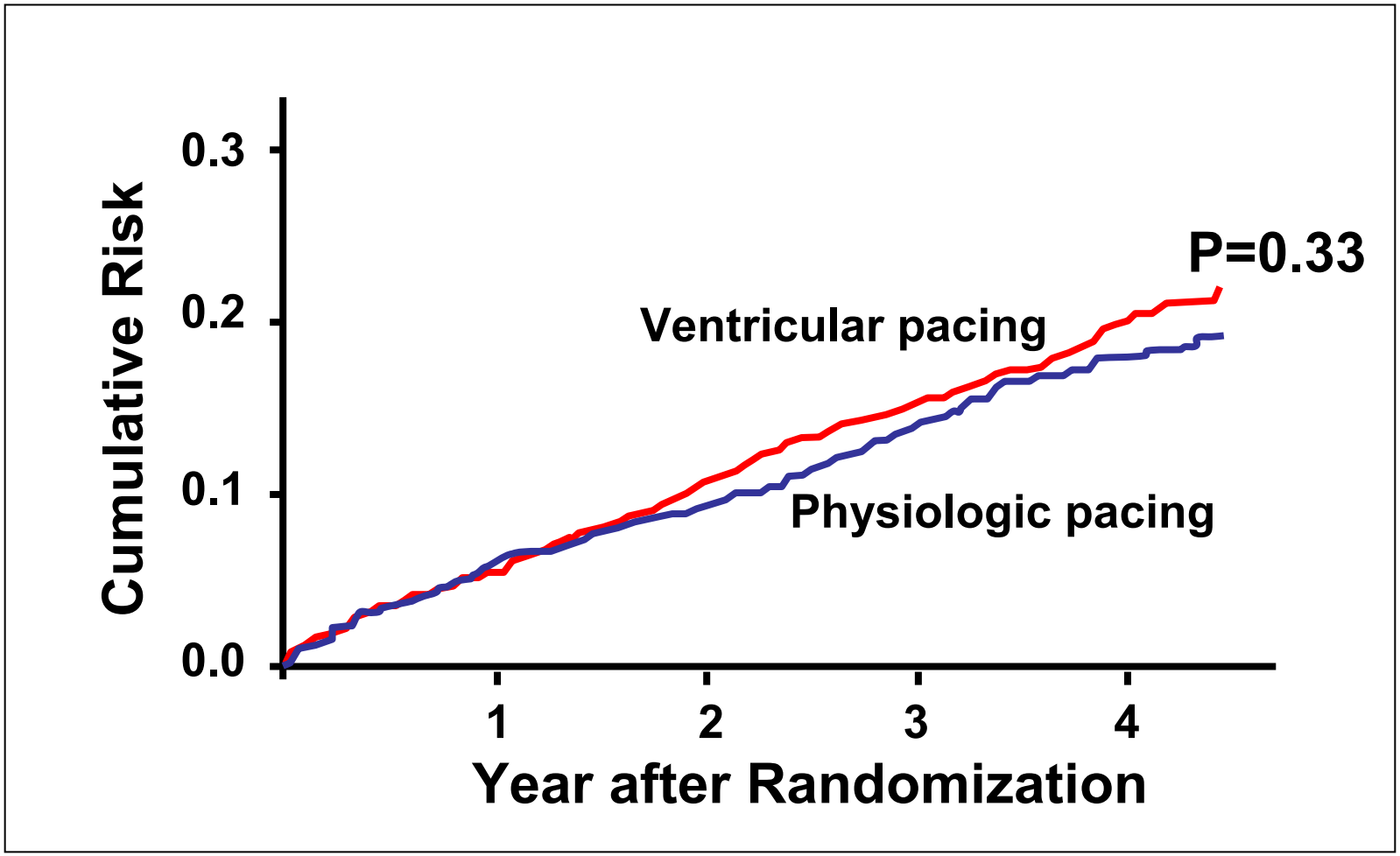
Follow-up for an average of 3 years

Results: 1474 pts were randomly assigned To VVI and 1094 to DDD or AAI pacemaker.

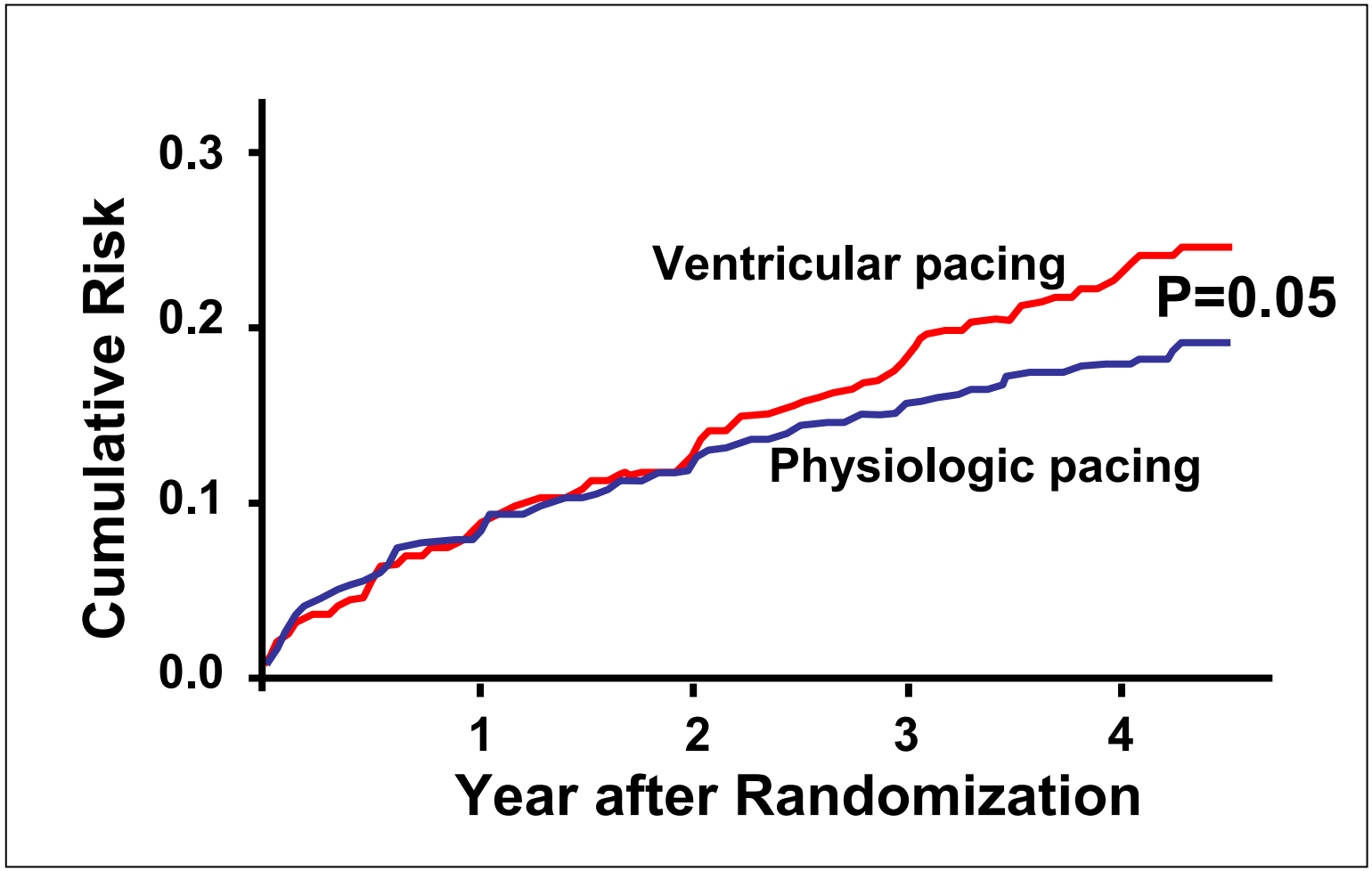
Annual CV events (VVI vs DDD or AAI):

- **All-cause mortality: 6.6% vs 6.3% (p=ns)**
- **Stroke, CV death: 5.5% vs 4.9% (p=ns)**
- **Hospitalized HF: 3.5% vs 3.1% (p=ns)**
- **AF: 6.6 vs 5.3 (p<0.05)**
- **Peri-Op Cx: 3.8% vs 9.0% (p<0.001)**

CTOPP: Stroke & CV Death



C-TOPP: Atrial Fibrillation



CTOPP: Peri-Op Complications

Complication	Ventricular Pacing (%)	Physiologic Pacing (%)	P value
Any	3.8	9.0	<0.001
Pneumothorax	1.4	1.8	0.42
Hemorrhage	0.4	0.2	0.32
Inadequate pacing	0.3	1.3	0.002
Inadequate sensing	0.5	2.2	<0.001
Device malfunction	0.1	0.2	0.40
Lead dislodgement	1.4	4.2	<0.001

Mode Selection Trial in Sinus Node Dysfunction (MOST)

Lamas GA, et al. NEJM. 2002;346:1854.

Background: DDD and VVI pacing are alternative treatment approaches for SND. However, it is unknown which type of pacing results in the better outcome.

Subjects: 2010 pts with SND received DDD in 1014 pts and VVI in 996 pts, followed for a median of 33.1 months.

Mode Selection Trial in Sinus Node Dysfunction (MOST)

Lamas GA, et al. NEJM. 2002;346:1854.

The primary end point was death from any cause or nonfatal stroke.

Secondary end points were the composite of death, stroke, or hospitalization for HF; AF; heart-failure score; the PM syndrome; and the quality of life.

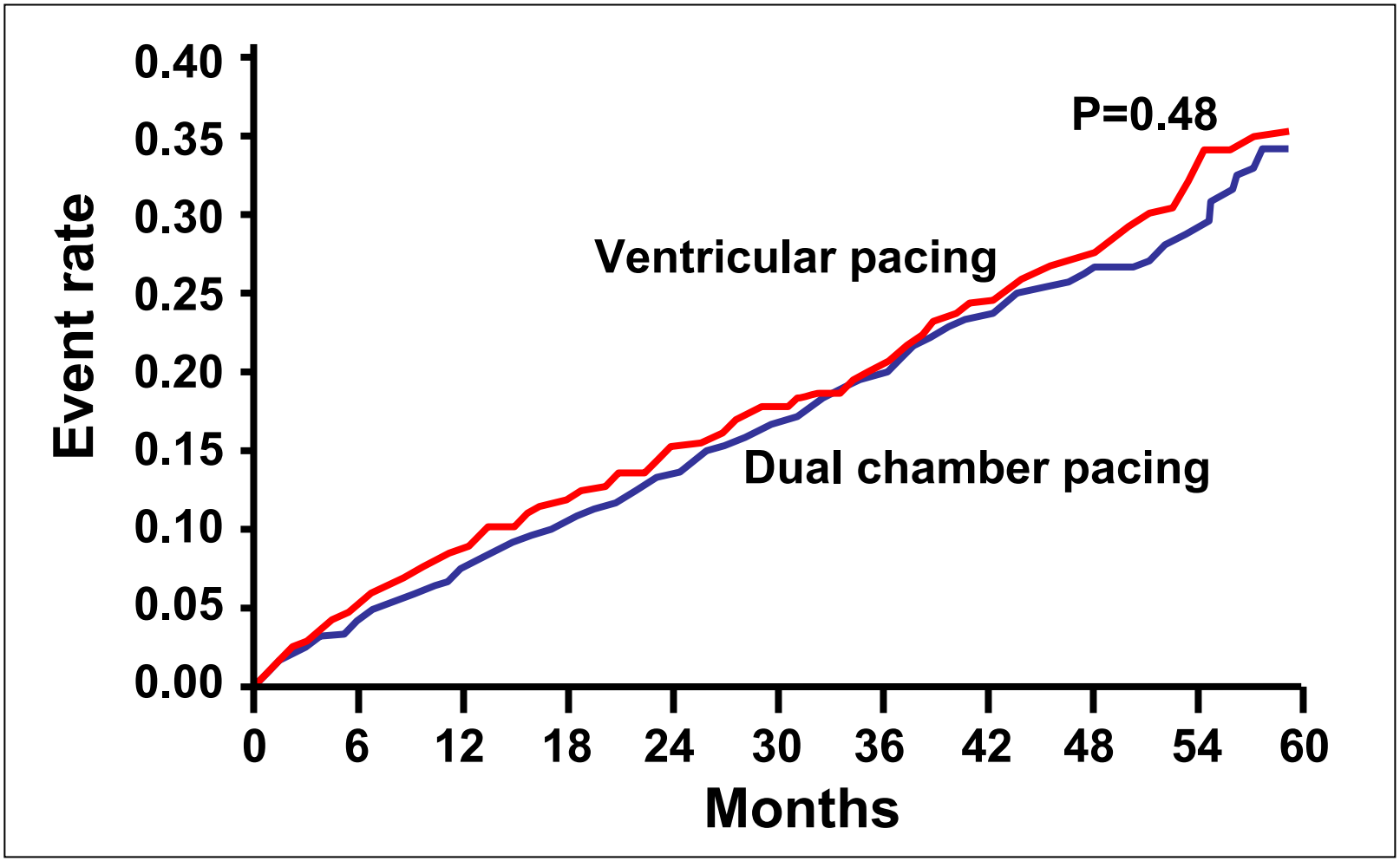
Mode Selection Trial in Sinus Node Dysfunction (MOST)

Lamas GA, et al. NEJM. 2002;346:1854.

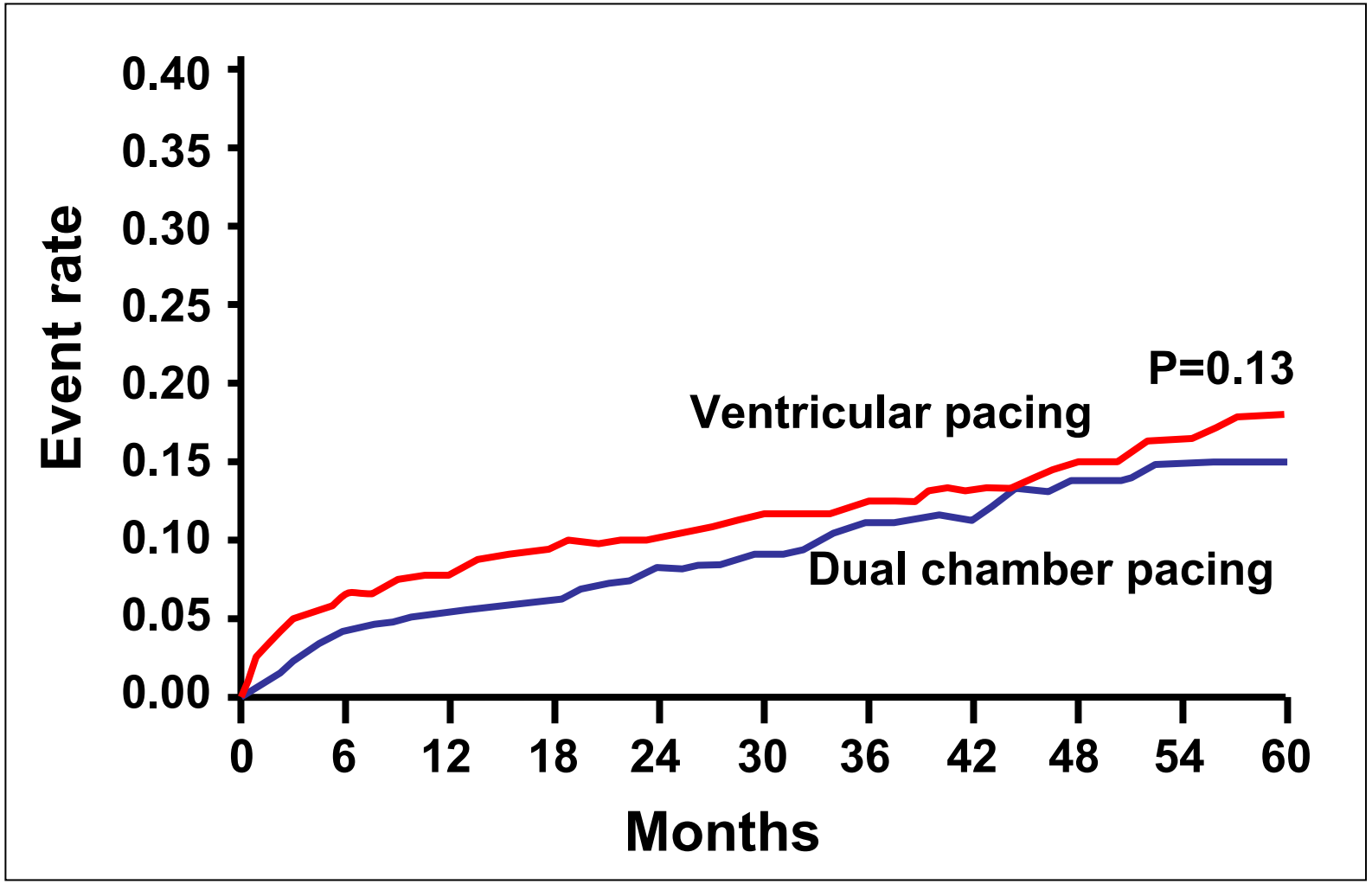
Results (VVI vs DDD)

- PEP: 23.0% vs 21.5% (p=0.48)
  Death: 20.5% vs 19.7% (p=0.78)
  Stroke: 4.9% vs 4.0% (p=0.36)
- CV Death: 9.2% vs 8.5% (p=0.61)
- AF: 27.1% vs 21.4% (p=0.008)
- HF scores: 1.75 vs 1.49 (p<0.001)
- HF admission: 12.3% vs 10.3% (p=0.13)

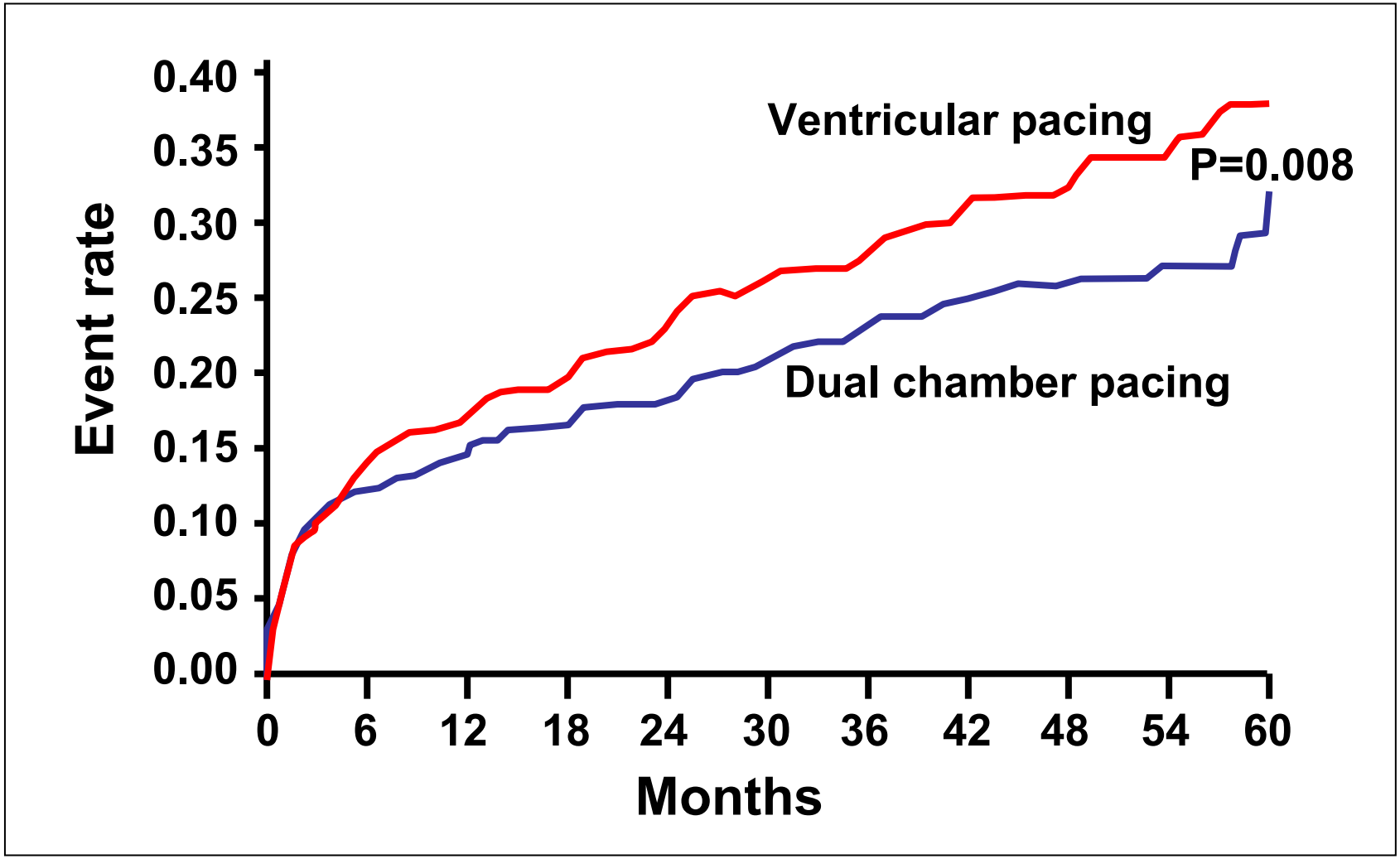
MOST: Primary End-Point



MOST: Admission for HF



MOST: AF


0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Event rate
Ventricular pacing
P=0.008
Dual chamber pacing
0
6
12
18
24
30
36
42
48
54
60
Months

UK Pacing & Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

Dual-chamber cardiac pacing is thought to confer a clinical benefit as compared with ventricular pacing, but the supporting evidence is mainly from retrospective study.

UKPACE is a prospective multicenter, randomized, parallel-group trial comparing the clinical benefits of ventricular pacing and dual-chamber pacing in elderly patients with AV block.

UK Pacing and Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

2021 patients ≥70 years of age who were undergoing their first pacemaker implant for high-grade AV block were randomly assigned to receive a ventricular PM (1009 pts; 504: VVI; 505: VVIR) or a dual-chamber PM (1012 pts) and followed for 4.6 yrs for mortality and 3 yrs for other CV events. AV block was second degree in 26.1% and complete in 73.3%.

UK Pacing and Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

Mean annual total and CV mortality rate were 7.2% and 3.9% in the ventricular pacing group and 7.4% and 4.5% in the dual-chamber group (P=0.56, 0.07, respectively).

UK Pacing and Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

There were no significant differences between the group with ventricular pacing and that with dual-chamber pacing in the rates of AF (3.0% vs 2.8%; P=0.74), HF (3.2% vs 3.3%; P=0.80), or a composite of stroke, TIA, or other TE (2.1% vs 1.7%; P=0.20).

UK Pacing and Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

Procedural Cx's were more common in the dual-chamber group than in the ventricular group (7.8% vs 3.5%, P<0.001). Therapeutic intervention was more frequent in the dual-chamber group (8.8% vs 5.6%, P=0.005), as were Cx's requiring repeated Op before discharge (4.2% vs 2.5%, P=0.04), usually due to problems with the placement or stability of atrial leads.

UK Pacing and Cardiovascular Events (UKPACE) Trial

Toff WD, et al. NEJM 2005;353:145.

Conclusions:

In elderly patients with high-grade AV block, the pacing mode does not influence the rate of death from all causes during the first 5 years or the incidence of CV events during the first 3 years after implantation of a PM.

So,
DDD is not superior to VVI.

The several randomized clinical trials such as Andersen's first randomized clinical trials, PASE, CTOPP, MOST, and UKPACE demonstrated that DDD pacing is not superior to VVI pacing in the prevention of death and stroke.

What's the Problem with DDD?

DDD pacing forces the pacemaker to stimulate the ventricle to tract atrial activity and to maintain AV synchrony.
This causes excessive RV pacing, resulting in inter-ventricular (V-V) and intra-ventricular asynchronous contraction (ventricular dyssynchrony).

Problems of RV Pacing

원 저

Korean Circulation J 1998;28(4):506-515

영구형 심박조율기 이식 환자에서 심근 관류와 국소벽운동의 변화

전남대학교병원 순환기내과,[1] 동아대학교병원 순환기내과,[2] 전남대학교병원 핵의학과[3]

차광수[2] · 민정준[3] · 김주한[1] · 김준우[1] · 김성희[1] · 배 열[1] · 안영근[1] · 박종철[1]
서정평[1] · 박주형[1] · 정명호[1] · 범희승[3] · 조정관[1] · 박종춘[1] · 강정채[1]

Alterations in Myocardial Perfusion and Regional Wall Motion in Patients with Permanent Pacemaker

Kwang Soo Cha, MD[2], Jung Jun Min, MD[3], Ju Han Kim, MD[1], Jun Woo Kim, MD[1], Sung Hee Kim, MD[1], Youl Bae, MD[1], Young Keun Ahn, MD[1], Jong Cheol Park, MD[1], Jeong Pyeong Seo, MD[1], Joo Hyung Park, MD[1], Myung Ho Jeong, MD[1], Hee Seung Bom, MD[3], Jeong Gwan Cho, MD[1], Jong Chun Park, MD[1] and Jung Chaee Kang, MD[1]

[1]Department of Cardiology, Chonnam University Hospital, [2]Dong-A University Hospital, Pusan, [3]Department of Nuclear Medicine, Chonnam University Hospital, Kwangju, Korea

Problems of RV Pacing

ABSTRACT

Background : The effect of right ventricular pacing on myocardial perfusion and regional wall motion is not well known, although some studies have suggested that it may be adverse. We investigated the effects of right ventricular pacing on myocardial perfusion and regional wall motion in patients with permanent pacemakers. **Method** : Thirty patients receiving permanent pacemakers for complete heart block or sick sinus syndrome were included in this study. All the patients showed normal coronary angiograms. Myocardial scintigraphy and two-dimensional echocardiography were performed to assess myocardial perfusion and to evaluate regional wall motion and global function of the left ventricle (LV). **Results** : 1) Mean age was 66.2±8.2 (41 – 84) years, and the male
ntation
were co
pacing
modes w
l by 2-
dimensic
patients
includin
l (50%)
out of 2
r in 17
(57%), apical in 16 (53%), lateral in 3 (10%), and anterior in 2 (7%). Extent of maximal perfusion defects was 17.
0±9.5 (0 – 44)%. 3) Regional wall motion abnormalities were noted mainly over the apical region of the LV in 26 (93%) of 28 patients with ventricular pacing. However, LV ejection fraction did not differ significantly before and early after implantation of the pacemaker (62.7±5.8% vs. 61.0±5.8%, p=0.313). **Conclusions** : Right ventricular apical pacing frequently caused myocardial perfusion defects and regional wall motion abnormalities.

RV apical pacing frequently caused myocardial perfusion defects and regional wall motion abnormalities.

Problems of RV Pacing

대한내과학회지 : 제 63 권 제 2 호 2002

장기적인 우심실 첨부 조율 시 좌심실 기능부전의 발생에 관여하는 인자

전남대학교병원 심장센터 순환기내과, 전남대학교 의과학연구소*

류제영 · 고점석 · 이상현 · 양보라 · 임상엽 · 홍영준 · 이승현 · 박옥영
김 원 · 김주한 · 염주협 · 박형욱 · 안영근 · 정명호* · 조정관* · 박종춘* · 강정채*

=Abstract=

Factors for development of left ventricular dysfunction during long-term right ventricular apical pacing

Jay Young Rhew, M.D., Jeom Seok Koh, M.D., Sang Hyun Lee, M.D., Bo Ra Yang, M.D., Sang Yup Lim, M.D., Young Joon Hong, M.D., Seung Hyun Lee, M.D., Ok Young Park, M.D., Weon Kim, M.D., Ju Han Kim, M.D., Ju Hyup Yum, M.D., Hyung Wook Park, M.D., Young Keun Ahn, M.D., Myung Ho Jeong, M.D.*, Jeong Gwan Cho, M.D.*, Jong Chun Park, M.D.* and Jung Chaee Kang, M.D.*

Division of Cardiology, The Heart Center, Chonnam National University Hospital, Chonnam National University Research Institute of Medical Sciences, Gwangju, Korea*

Problems of RV Pacing

dysfunction with the paced QRSd (cut-off value: 180 ms), sensitivity, specificity, positive and negative predictive values were 60.0%, 88.7%, 50.0% and 99.2%, respectively. The paced QRSd at the last follow-up was significantly correlated with paced QRSd immediately after implantation ($r=0.542$, $p<0.01$).

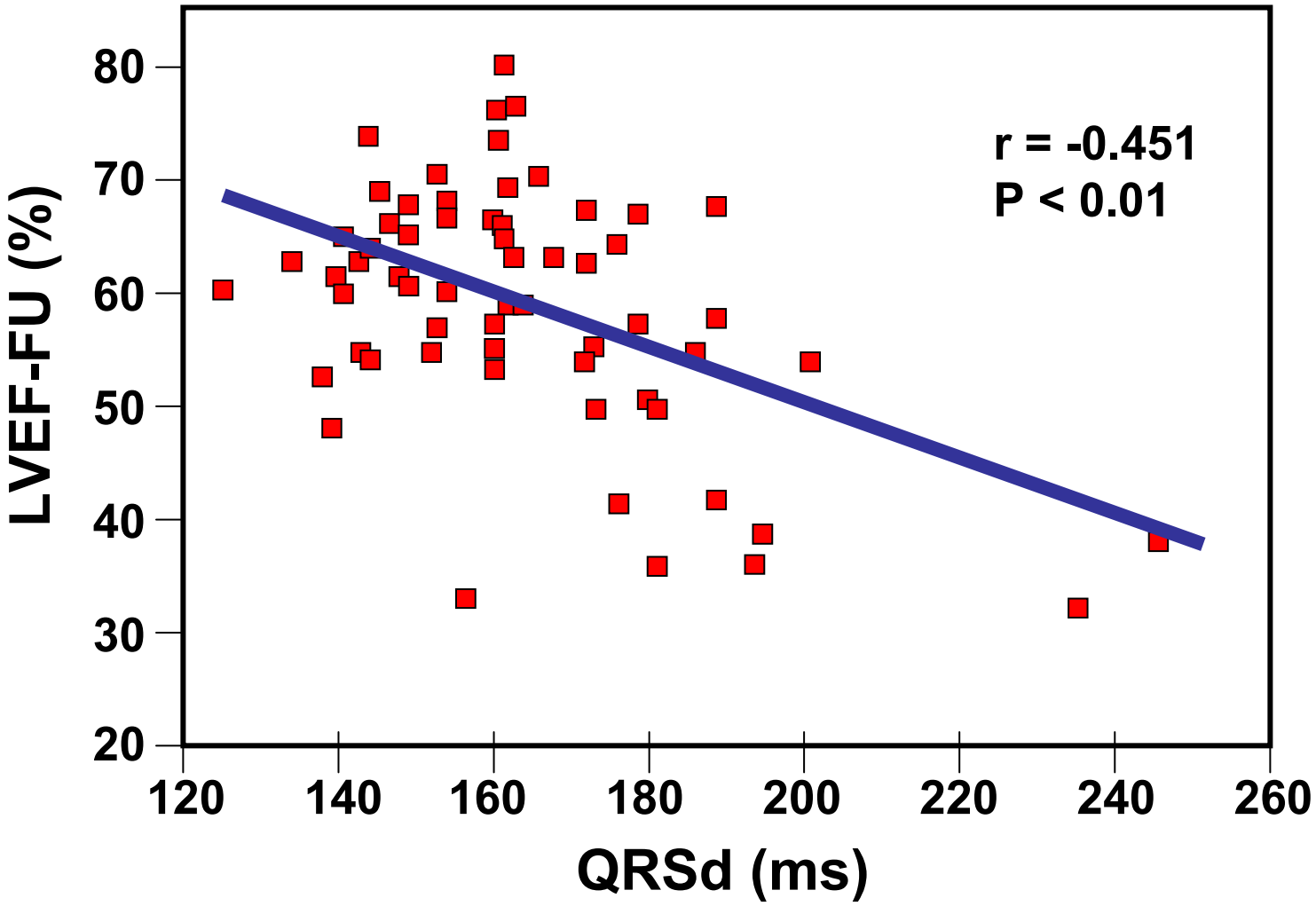
Conclusion LV systolic dysfunction after long-term right ventricular apical pacing may develop. Prolongation of paced QRSd ≥180 ms during follow-up may suggest development of LV systolic dysfunction. New technologies to minimize prolongation of paced QRSd should be investigated to prevent LV systolic dysfunction after permanent ventricular pacing.(Korean J Med 63:169-176, 2002)

Key Words : Cardiac pacing, Artificial, Ventricular function

LV systolic dysfunction may develop after long-term RV apical pacing.

Prolongation of paced QRSd ≥180 ms suggests development of systolic LVD.

Problems of RV Pacing



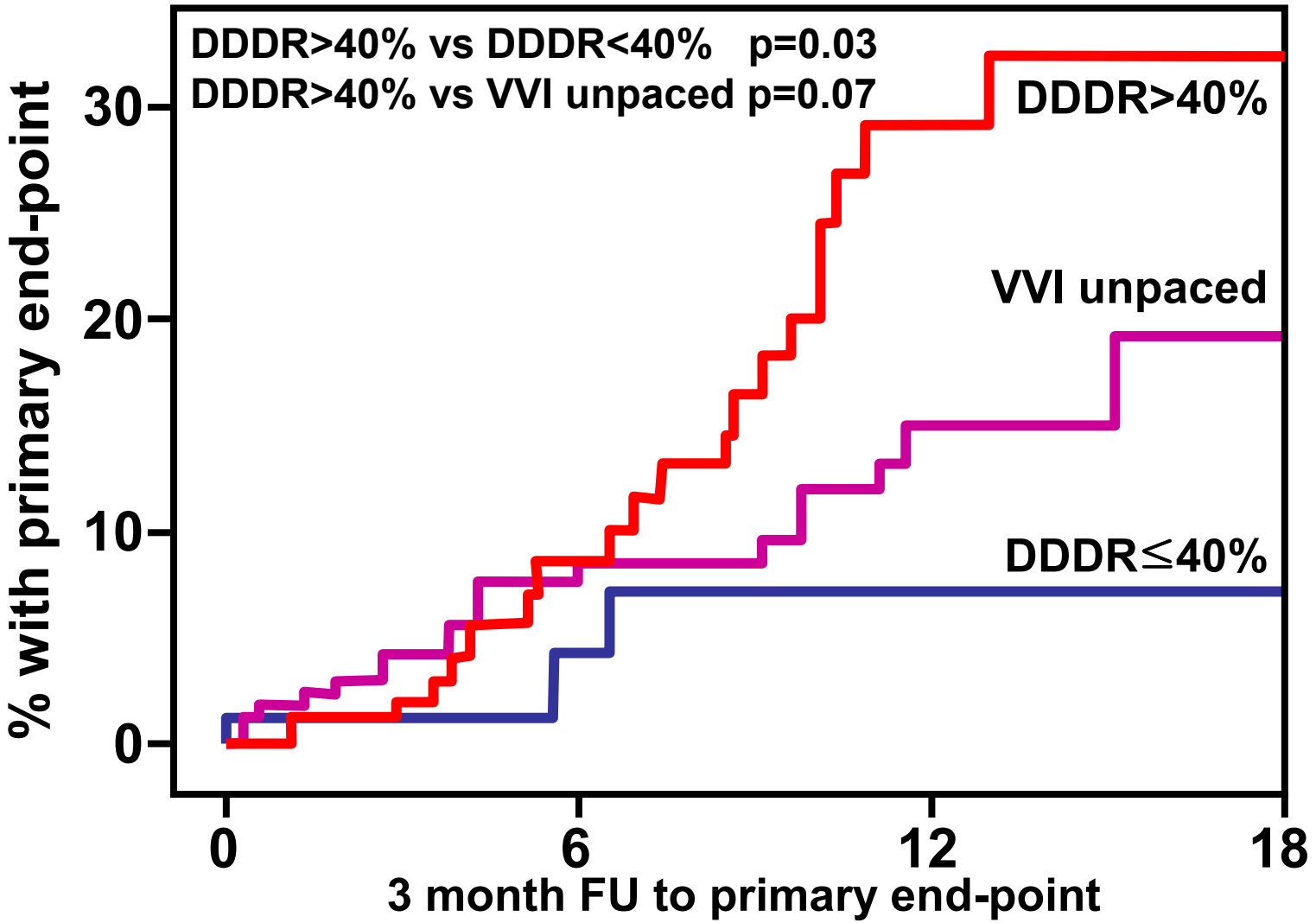
Percent RV Pacing Predicts Outcomes in the DAVID trial

Sharma AD, et al. Heart Rhythm. 2005;2:830.

The relationship of % RV pacing to the composite endpoint of death or admission for CHF was evaluated in VVI group (n=195) and DDDR group (n=185).

Results: Percent RV pacing was correlated with the primary endpoint. As a dichotomous variable, the best separation for predicting endpoints occurred with DDDR RV pacing >40% vs DDDR RV pacing ≤ 40% (P=0.025).

% RV Pacing and Outcomes



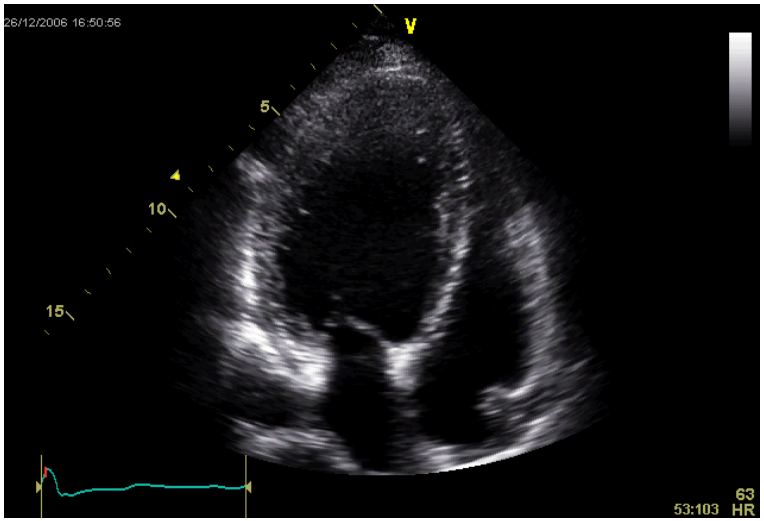
Relative Importance of AV and V-V Synchrony

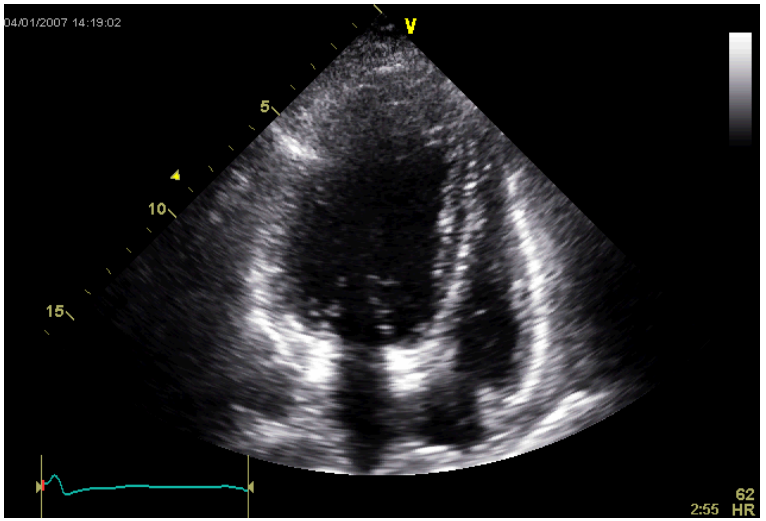
Heart rate: chronotropy

Afterload

Preload: AV synchrony

Contractility: ventricular synchrony





New Algorithm for PM Selection