

Os Algoritmos terapêuticos de disritmias supraventriculares em doentes com pacing permanente são afinal úteis ?

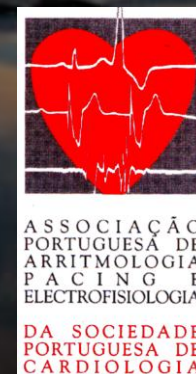
Novas Fronteiras em Cardiologia

Mesa Redonda: O que há de novo nos dispositivos implantáveis ?



Ericeira
8 de Fevereiro de 2014

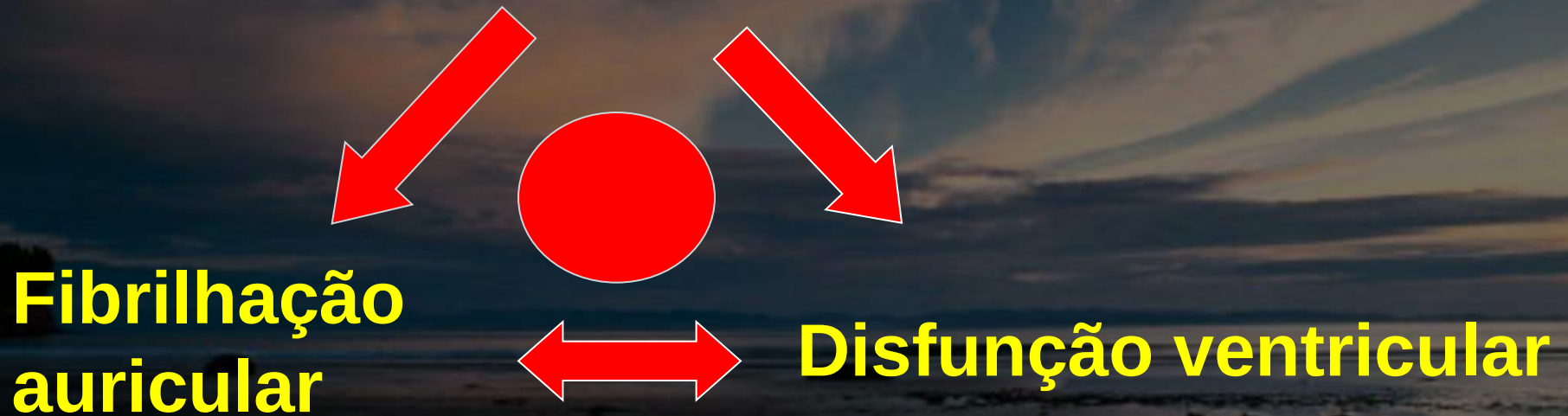
Vitor Paulo Martins



Pacing e Fibrilhação auricular

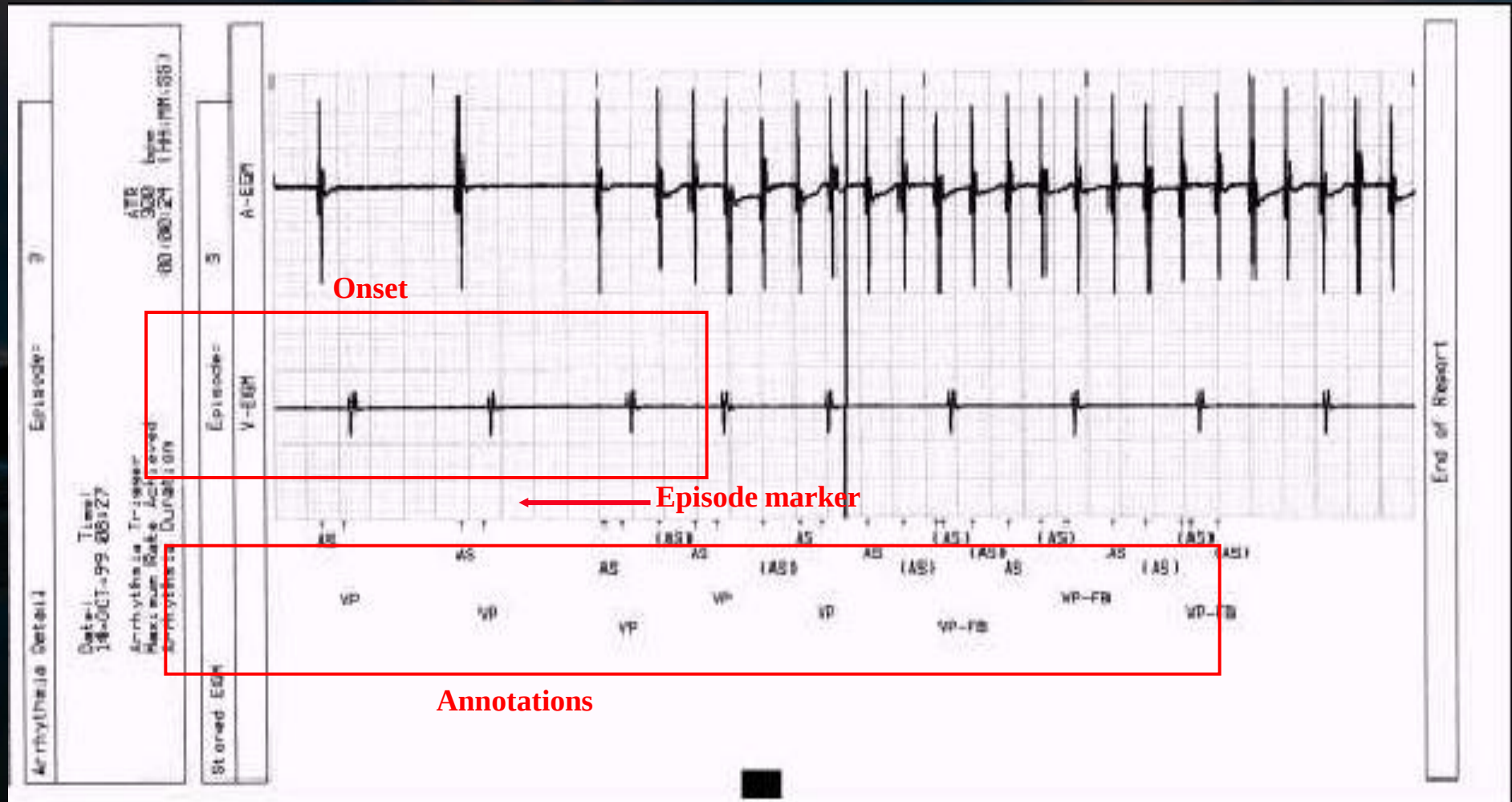
Problema em cascata

Maior % de pacing ventricular direito



Pacing e Fibrilhação auricular

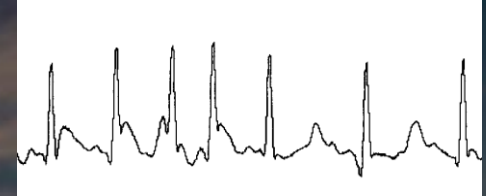
Importância do Holter intracavitário no portador de pacemaker



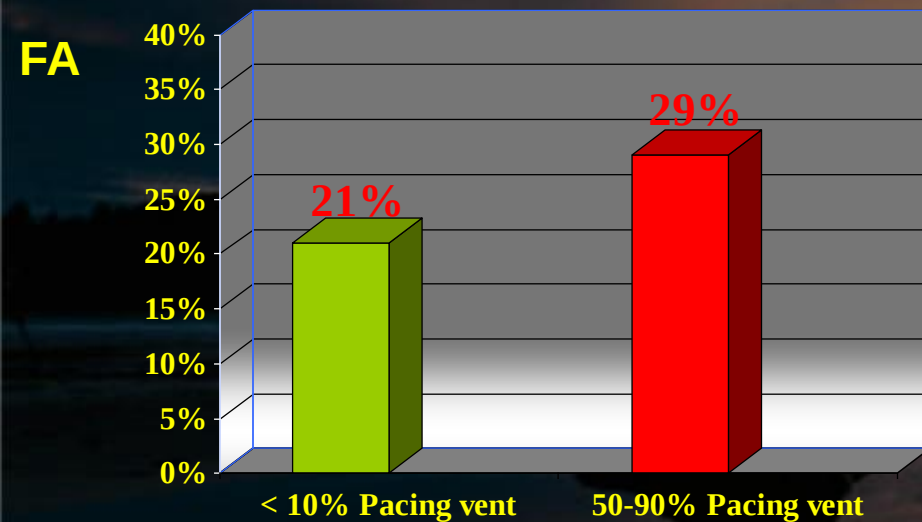
Pacing e Fibrilhação auricular

Incidência de FA no portador de pacemaker

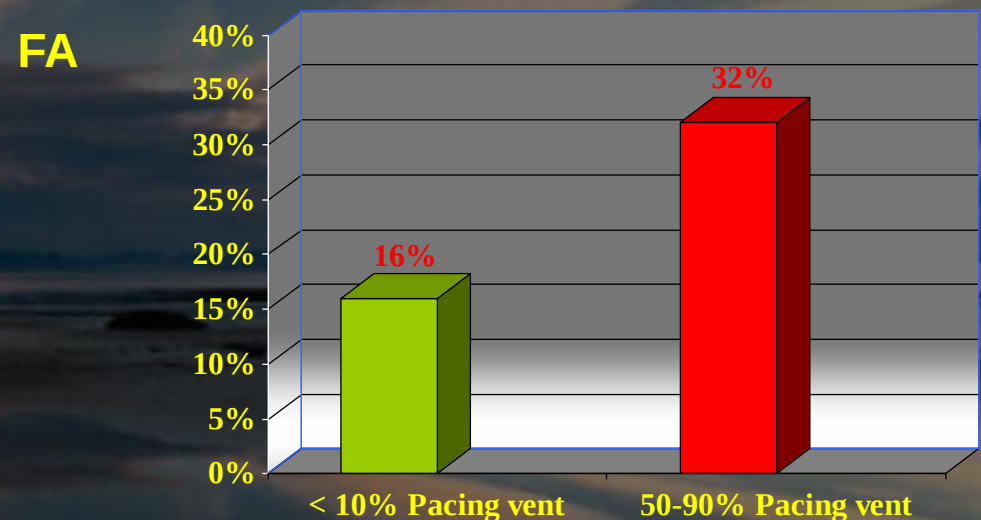
Incidência anual de FA



Sistema VVI



Sistema DDD



Interessa não só o modo de pacing mas também a % de pacing VD

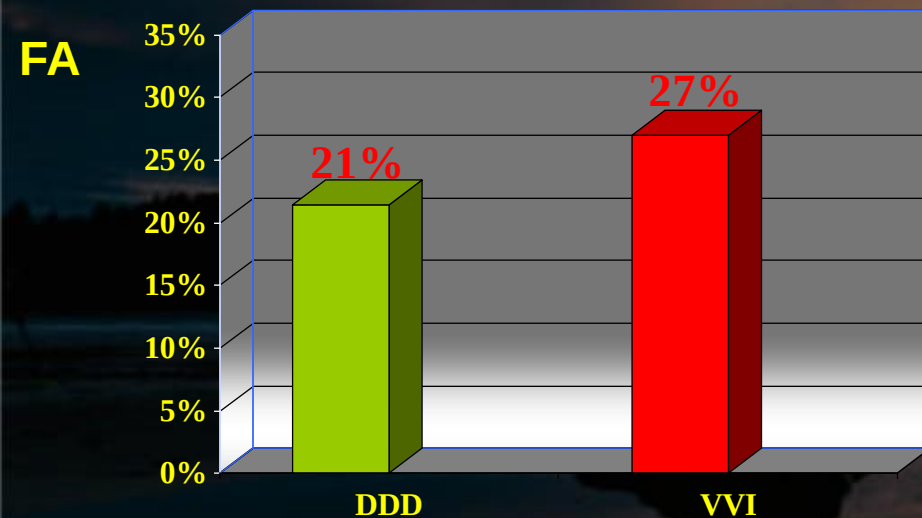
*Sweeney and al
Circulation 2003; 107:2932-37*

Pacing e Fibrilhação auricular

Incidência de FA no portador de pacemaker

Incidência de FA ao fim de 33 meses

FA paroxística

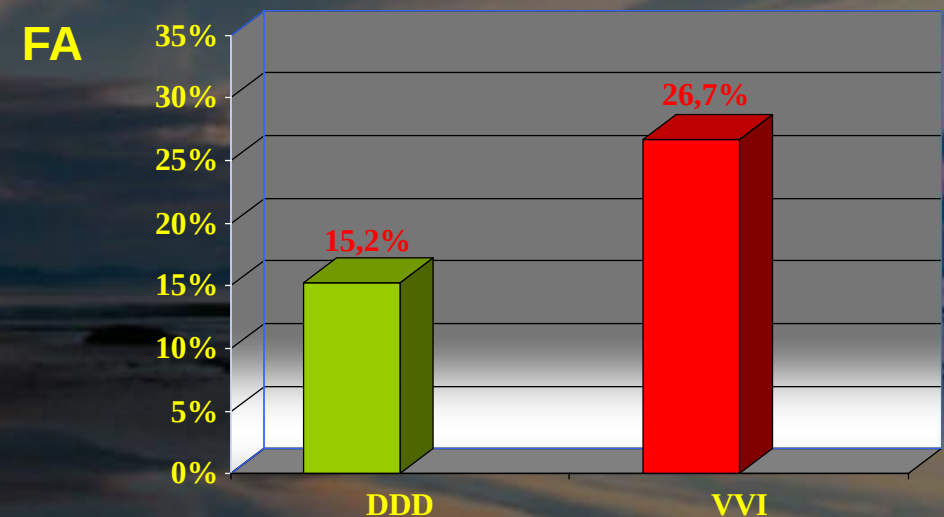


$p < 0,01$

$n = 2.010$

Dç. Nódulo Sinusal

FA permanente



$p < 0,001$

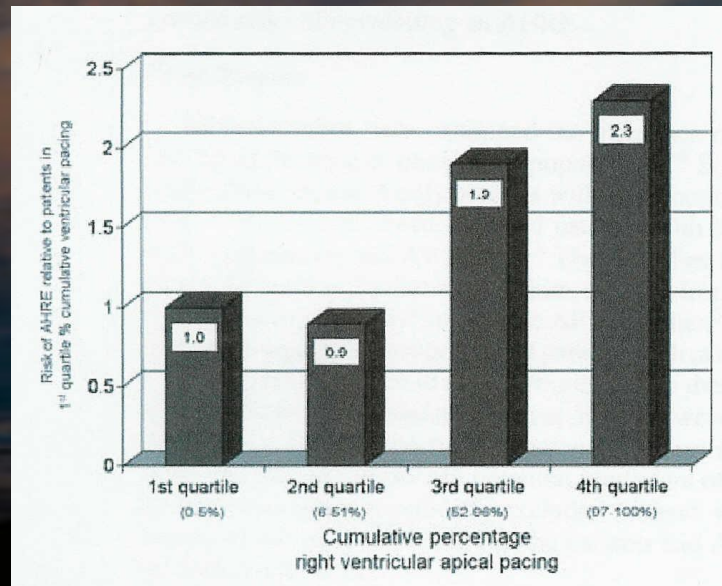
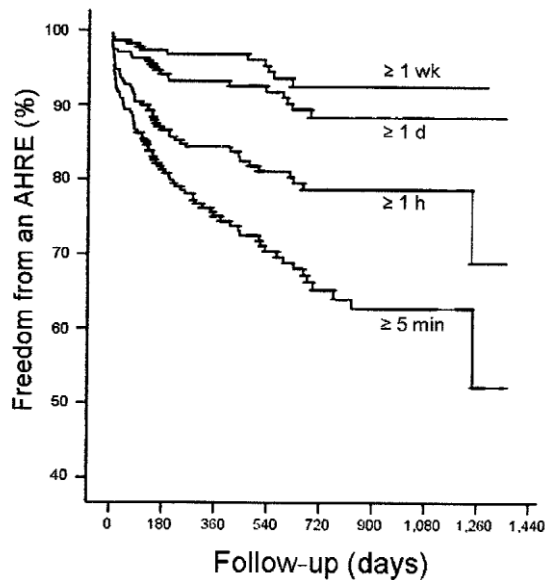
The Mode Selection Trial in Sinus Node Dysfunction
N Engl J Med 2002; 346:1854-1862

Pacing e Fibrilhação Auricular

Diagnóstico - Prevenção

Atrial high-rate episodes (AHREs)

n = 262
PM-vários
Sem AF prévia



FA : AHREs > 5 minutos

Episódios de FA
em 29% aos 2 anos

DNS: > 50% pacing VD ► 2 x risco de AHREs > 5 mn

Consequências clínicas ?

Cheung et al
J Cardiovascular Electrophysiol 2006;17:1323-1328

Pacing e Fibrilhação auricular

Diagnóstico



n = 377

**45% dos dts com DDD
tem episódios de FA
(21 meses de seguimento)**

**Em 10%, os episódios
duram mais de 20 dias**

Consequências ?

**Piager and al
PACE 2005; 28:S137-S145**

Relationship Between Clinical/Pacing Variables and FMS Incidence

	FMS = 0 (n = 208)	FMS > 0 (n = 169)	P
Men/women, n (%)	26/17 (%)	34/21 (%)	ns
Age, [years (mean ± SD)]	75.8 ± 10.2	74.5 ± 13.7	ns
<i>Pacing indications (%)</i>			
AVB	28.7	19.8	ns
SND	8.2	7.8	
BTS	1.9	3.4	
AVB + SND	12.7	6.3	
AVB + BTS	3.7	2.2	
BTS + SND	3.7	1.5	
<i>Underlying heart disease (%)</i>			
Ischemic	29.7	27.0	ns
Dilated cardiomyopathy	8.1	2.7	
Valvular	4.0	2.7	
Other	10.8	14.9	
<i>NYHA functional class (%)</i>			
Class I	16.8	8.4	P = 0.09
Class II	23.2	32.6	
Class III	7.4	11.6	
<i>Underlying diseases (%)</i>			
Hypertension	7.6	10.8	P = 0.16
Diabetes	0.8	2.0	
Prior stroke	0	1.6	
<i>Drug therapy (%)</i>			

Pacing e Fibrilhação auricular

Diagnóstico

Análise quantitativa dos electrogramas de sistemas de Pacing

- A maioria dos episódios de AT/AF são assintomáticos
- SPAF (Stroke Prevention in Atrial Fibrillation) mostra que o risco de AVC isquémico é semelhante na FA intermitente ou permanente
- Risco de AVC é elevado na presença de episódios com duração > 5 mn

Ziegler et al
Heart Rhythm 2006; 3:1445-1452

Importância das arritmias supraventriculares

Estudo Assert

Table 2. Clinical Outcomes Occurring after the 3-Month Visit, According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

Clinical Outcome	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months				Hazard Ratio with Subclinical Atrial Tachyarrhythmias (95% CI)	P Value
	Present (N=261)		Absent (N=2319)			
	no. of events	%/yr	no. of events	%/yr		
Ischemic stroke or systemic embolism*	11	1.69	40	0.69	2.49 (1.28–4.85)	0.007
Ischemic stroke	10	1.54	36	0.62	2.52 (1.25–5.08)	0.01
Systemic embolism	1	0.15	4	0.07	2.24 (0.25–20.10)	0.47
Myocardial infarction	7	1.07	39	0.67	1.52 (0.68–3.42)	0.31
Death from vascular causes	19	2.92	153	2.62	1.11 (0.69–1.79)	0.67
Stroke, myocardial infarction, or death from vascular causes	29	4.45	206	3.53	1.25 (0.85–1.84)	0.27
Hospitalization for heart failure	20	3.07	131	2.24	1.36 (0.85–2.19)	0.20
Clinical atrial fibrillation or flutter on surface electrocardiogram	41	6.29	71	1.22	5.56 (3.78–8.17)	<0.001



n = 2580 pts; PMD; Ep. Taq. Aur. > 6 mn

Healey and al. N Engl J Med 2012;366:120–9.

Importância das arritmias supraventriculares

Estudo Assert

Table 3. Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline CHADS₂ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

CHADS ₂ Score	No. of Patients	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months						Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*
		Present			Absent			
		<i>no. of patients</i>	<i>no. of events</i>	<i>%/yr</i>	<i>no. of patients</i>	<i>no. of events</i>	<i>%/yr</i>	
1	600	68	1	0.56	532	4	0.28	2.11 (0.23–18.9)
2	1129	119	4	1.29	1010	18	0.70	1.83 (0.62–5.40)
>2	848	72	6	3.78	776	18	0.97	3.93 (1.55–9.95)

Estratégias de redução da carga arrítmica

- Algoritmos de prevenção
- Algoritmos de tratamento (ATP)
- Estimulação auricular única em local alternativo, pacing auricular duplo (dual site) ou multisítio (multi site)
- Novos locais de estimulação do ventrículo direito (pacing septal, CSVS)
- Algoritmos de minimização da estimulação apical do VD (MVP; AAISafe R, VIP, IRS, etc)

Algoritmos de Prevenção em Pacing

Mecanismos envolvidos

Mechanisms Involved in Atrial Fibrillation Prevention by Pacing Algorithms

1. Suppression or conditioning of premature atrial beats
2. Prevention of short-long atrial cycle phenomenon
3. Block of spontaneous firing rate of all natural subsidiary atrial foci

Algoritmos de Prevenção em Pacing

Classificação

Classification of Prevention Algorithms

1. Dynamic sinus rhythm overdrive
2. Premature atrial beats response
3. Posttachycardia overdrive to prevent early recurrence of atrial fibrillation
 - i. Short-long cycle prevention
 - ii. Ectopy overdrive
4. Prevention of inappropriate rate fall after exercise

Importância das arritmias supraventriculares

Estudo Assert

Table 4. Effect of Continuous Atrial Overdrive Pacing on Clinical Outcomes.

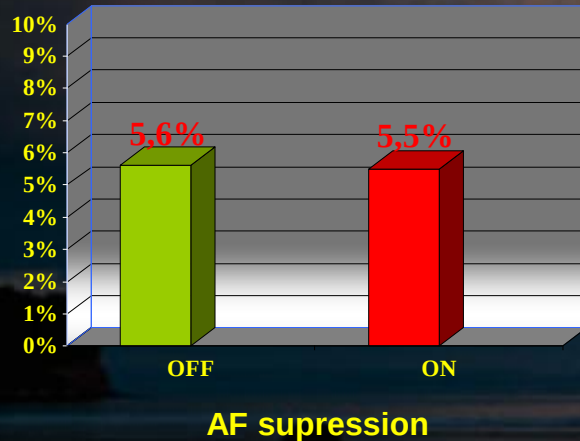
Outcome	Continuous Atrial Overdrive Pacing Turned On (N=1164)		Continuous Atrial Overdrive Pacing Turned Off (N=1179)		Hazard Ratio with Continuous Atrial Overdrive Pacing Turned On (95% CI)	P Value
	No. of Patients	Annual Rate*	No. of Patients	Annual Rate*		
Atrial tachyarrhythmia†	60	1.96	45	1.44	1.38 (0.94–2.03)	0.10
Symptomatic	29	0.95	22	0.71	1.35 (0.78–2.35)	0.29
Asymptomatic	36	1.17	28	0.90	1.31 (0.80–2.16)	0.29
Device-detected atrial tachyarrhythmia with duration >24 hr	134	4.37	125	4.01	1.11 (0.87–1.41)	0.42
Stroke, systemic embolism, myocardial infarction, death from vascular causes, or hospitalization for heart failure	160	5.22	146	4.69	1.13 (0.90–1.41)	0.29
Stroke	21	0.68	25	0.80	0.85 (0.48–1.52)	0.59
Systemic embolism	3	0.10	2	0.06	1.52 (0.25–9.12)	0.64
Myocardial infarction	22	0.72	20	0.64	1.13 (0.62–2.08)	0.69
Death from vascular causes	82	2.67	80	2.57	1.05 (0.77–1.42)	0.78
Hospitalization for heart failure	77	2.51	59	1.89	1.34 (0.95–1.88)	0.09

Pacing na Prevenção da Fibrilhação auricular

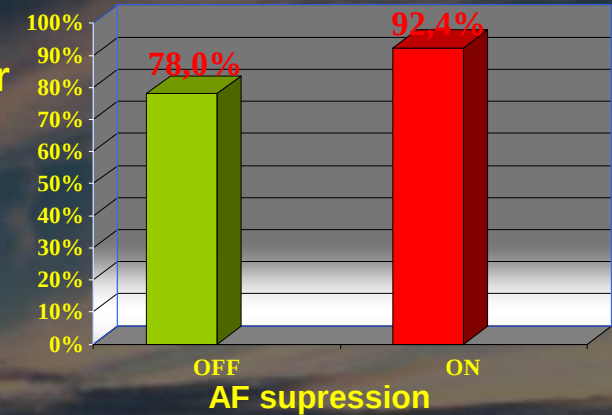
Algoritmos de Prevenção – Overdrive pacing

Estudo Stadim

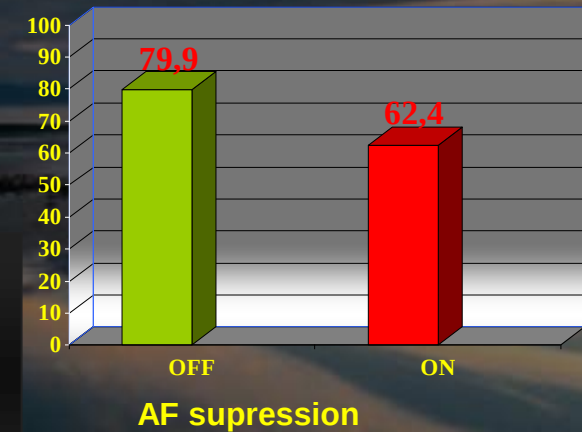
AMS
(%)



Pacing
auricular
(%)



Freq. Card
Média
(bpm)



Embora não haja redução da carga arritmica, há maior % de pacing auricular e menor frequência cardíaca ventricular o que poderá levar a menor incidência de eventos cardiovasculares adversos.

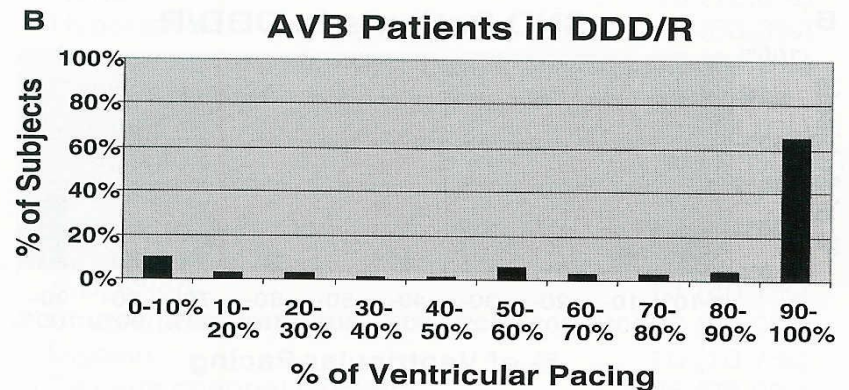
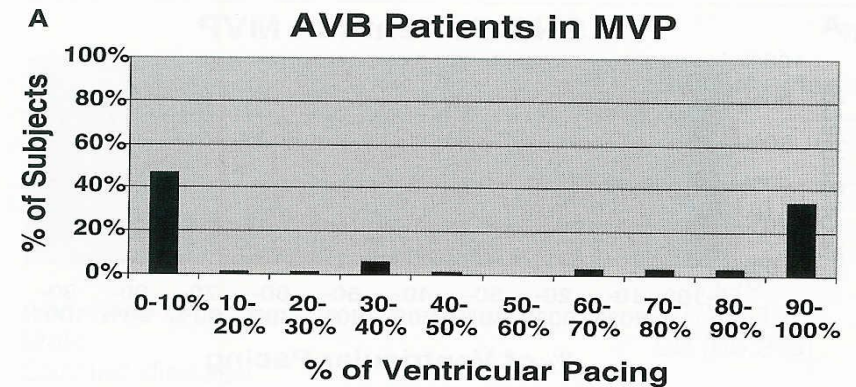
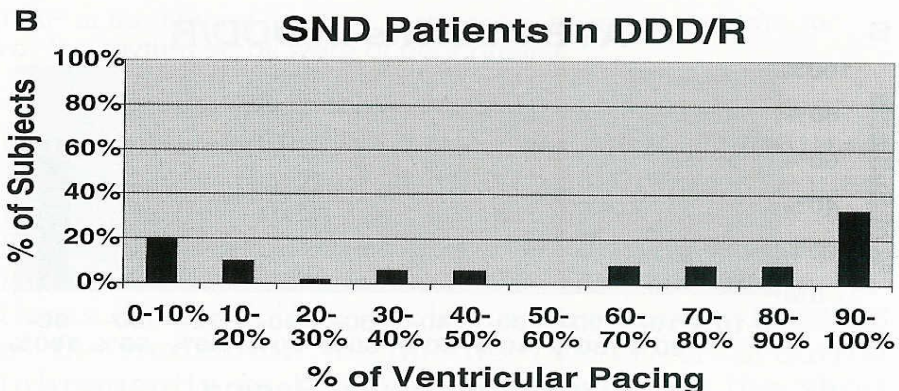
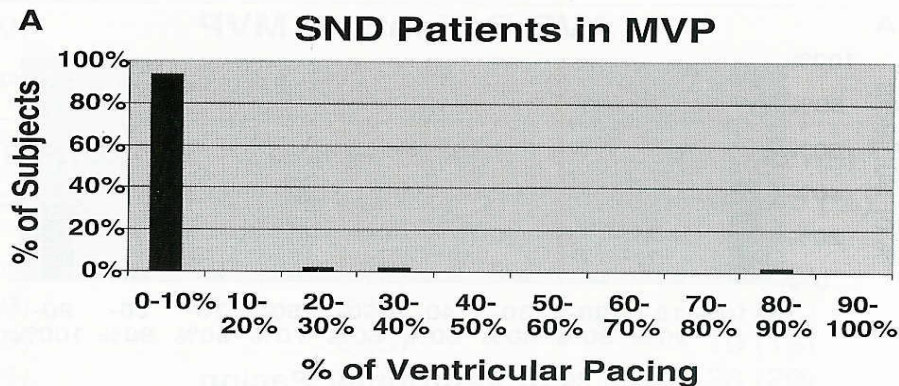
Simone et al
PACE 2007; 30: S71-S74

Pacing na Prevenção da Fibrilhação auricular

Algoritmos de minimização de Pacing

n = 129
(DNS-51;BAV-68)

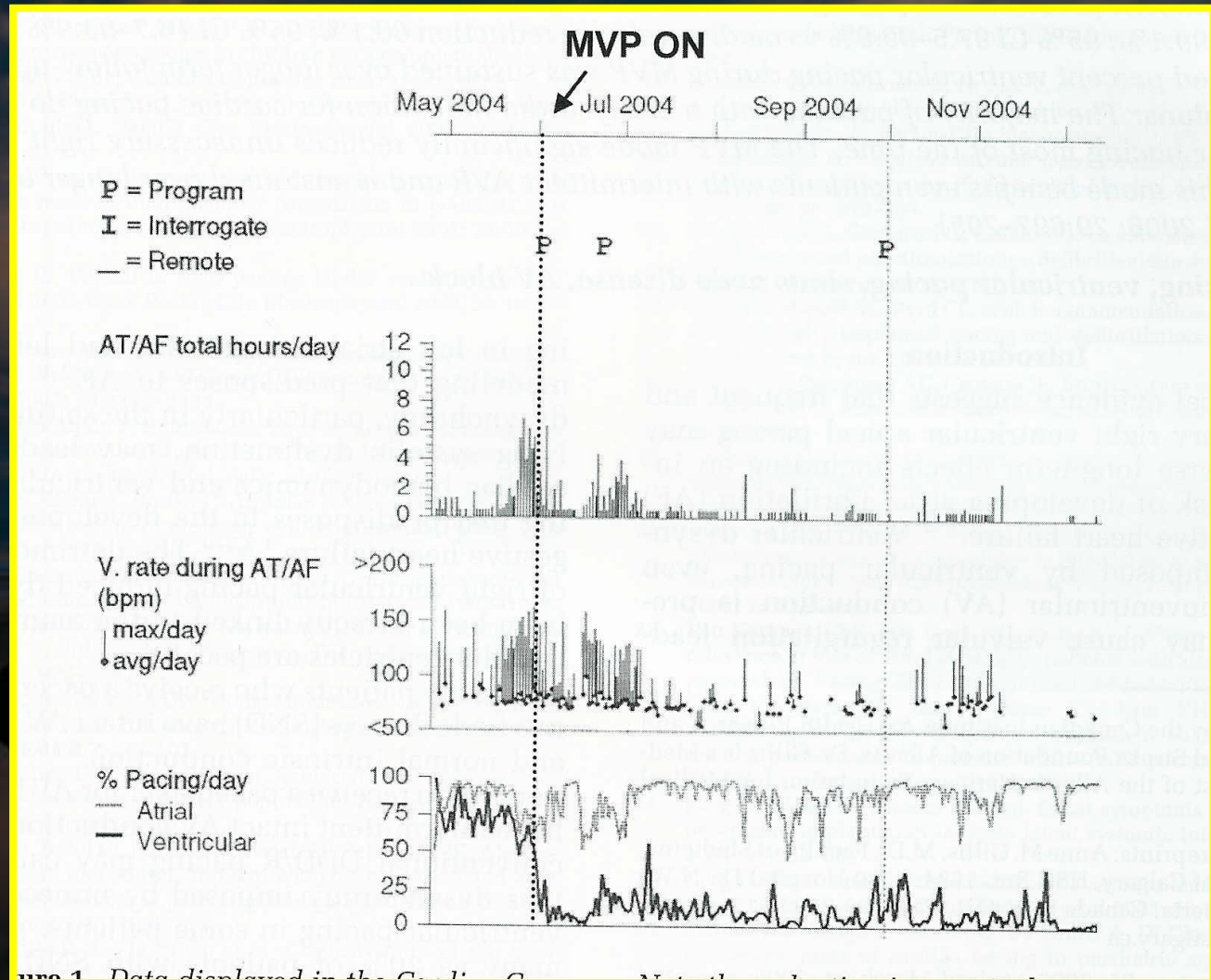
MVP MODE



Pacing na Prevenção da Fibrilhação auricular

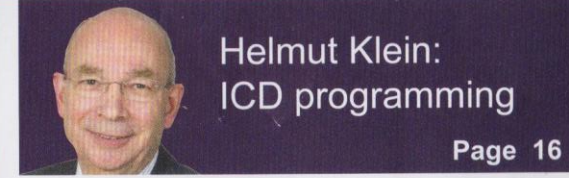
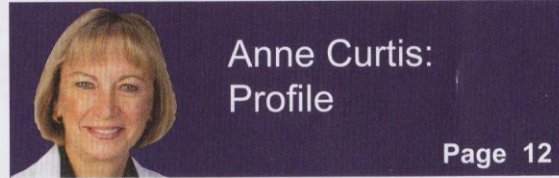
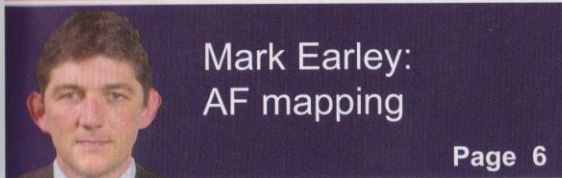
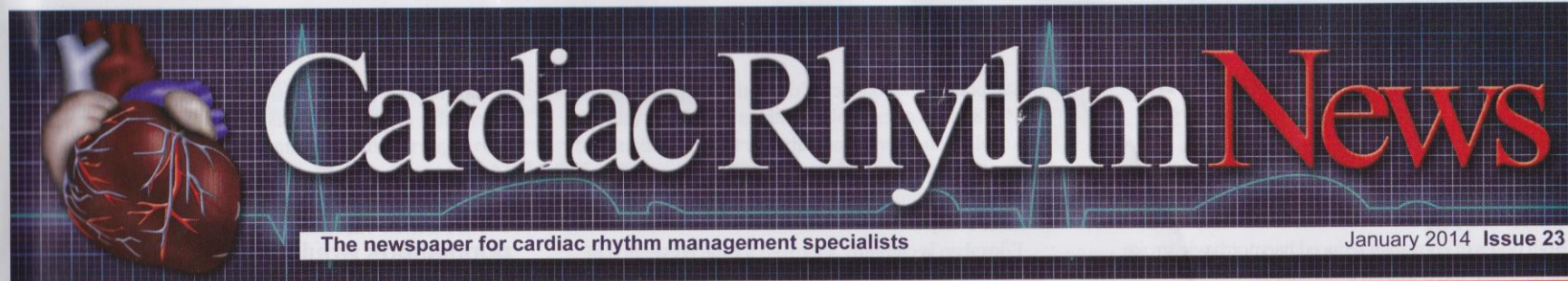
Modos alternativos de Pacing

MVP MODE



Algoritmos Terapêuticos em Pacing

Minerva Study



Largest anticoagulant trial in atrial fibrillation shows edoxaban is as effective as warfarin

Preliminary results from the ENGAGE AF-TIMI 48 clinical trial, the longest and largest novel oral anticoagulant trial in atrial fibrillation, have demonstrated that the investigational, oral, once daily direct factor Xa-inhibitor edoxaban (Lixiana, Daiichi-Sankyo) is as effective as warfarin in preventing stroke or systemic embolic events in patients with atrial fibrillation. Edoxaban was also associated with a lower rate of bleeding than warfarin

New generation pacemakers reduce atrial fibrillation progression by 61% at two years

Results of the MINERVA study have shown that pacemakers with enhanced capabilities to decrease unnecessary right ventricular pacing are associated with reduction of atrial fibrillation, fewer deaths, fewer hospitalisations and better quality of life

Algoritmos Terapêuticos em Pacing

Minerva Study

Atrial Antitachycardia Pacing and Managed Ventricular Pacing Reduce the Endpoint Composed by Death, Cardiovascular Hospitalizations and Permanent Atrial Fibrillation Compared to Conventional Dual Chamber Pacing in Bradycardia Patients:
Results of the MINERVA Randomized Study

Presenter: Giuseppe Boriani, Univ of Bologna, Policlinico S.Orsola-Malpighi, Bologna, Italy
Authors: Giuseppe Boriani, M.D., Ph.D., Raymond Tukkie, M.D., Lluís Mont, M.D., Helmut Pürerfellner, M.D., Antonis S. Manolis, M.D., Massimo Santini, M.D., Giuseppe Inama, M.D., Paolo Serra, M.D., Silvia Parlanti, M.S., Lorenza Mangoni, M.S., Andrea Grammatico, Ph.D., Luigi Padeletti, M.D., on behalf of the MINERVA Investigators.

Sponsor: Medtronic Inc.

Clinical Registration: clinicaltrials.gov ID NCT00262119

Algoritmos Terapêuticos em Pacing

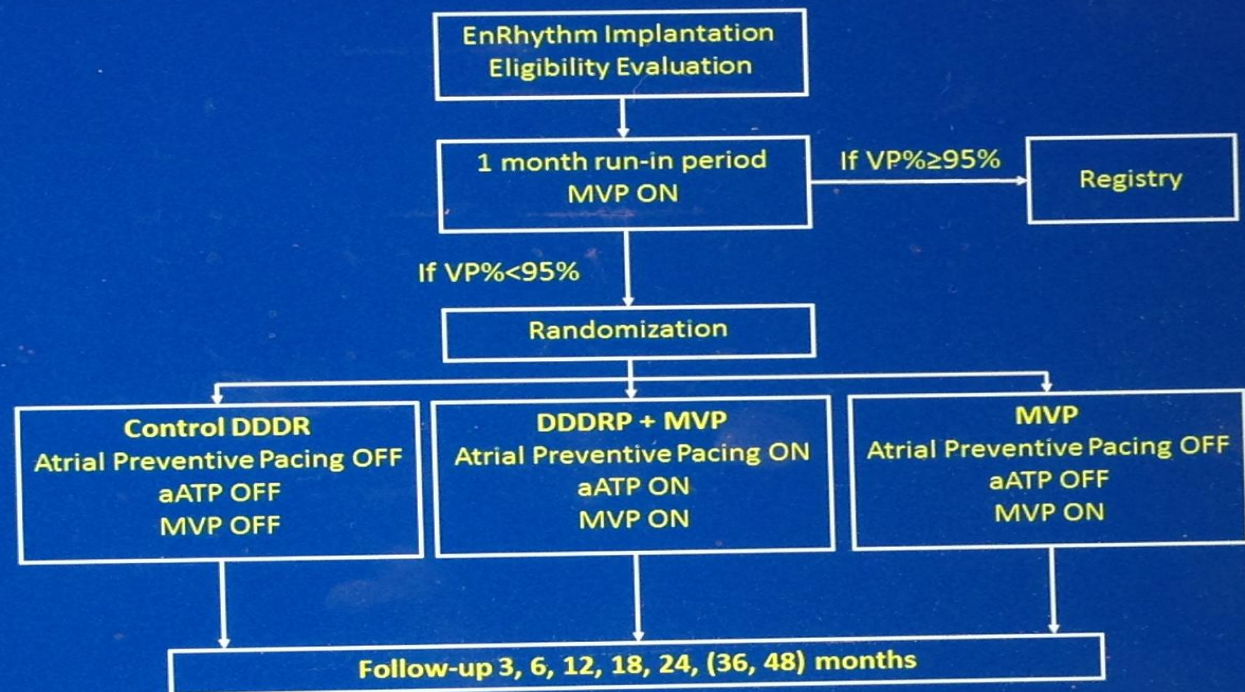
Minerva Study

Study Aim and Design

Aim: to evaluate whether DDDRP+MVP or MVP reduces mortality, morbidity, or progression to permanent AF compared with standard dual-chamber pacing.

Multicenter (63 centers), international, randomized, single blind study with 3 arms enrolling patients with:

- Class I or class II indications for dual-chamber pacing
- Previous atrial tachyarrhythmias
- No history of permanent AF or third-degree AV block



Algoritmos Terapêuticos em Pacing

Minerva Study

Primary and Secondary Objectives

PRIMARY OBJECTIVE: To assess if DDDRP+MVP is superior to Control DDDR in terms of 2-year incidence of a composite clinical outcome composed by all-cause death^{*}, cardiovascular hospitalizations^{*} or permanent AF [investigator decision not to cardiovert the patient and long duration AF (at least two consecutive follow-up visits with documented AF)]^{*}

^{*} All events were reported by study investigators according to pre-defined conditions and was then adjudicated by an independent Event Adjudication Committee.

SECONDARY OBJECTIVES:

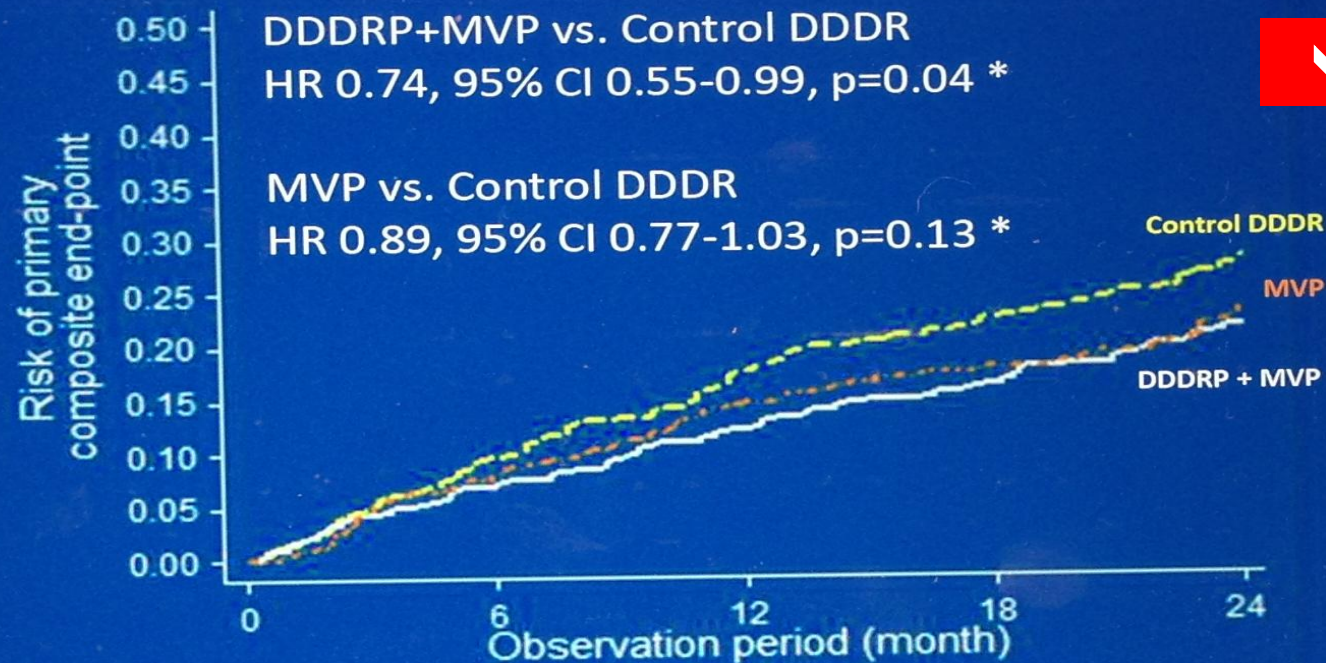
1. Compare primary endpoint in MVP arm vs. Control DDDR arm
2. Compare DDDRP+MVP vs. Control DDDR and MVP vs. Control DDDR in terms of other variables such as incidence of components of the composite endpoint and incidence of persistent AF

Algoritmos Terapêuticos em Pacing

Minerva Study

Primary Outcome
(All-Cause Death, CV hospitalizations, or Permanent AF)

Intention-to-treat survival analysis using time to first event



Number at risk					
Control DDDR	385	335	299	275	224
DDDRP+MVP	383	338	311	288	221
MVP	398	350	318	295	228

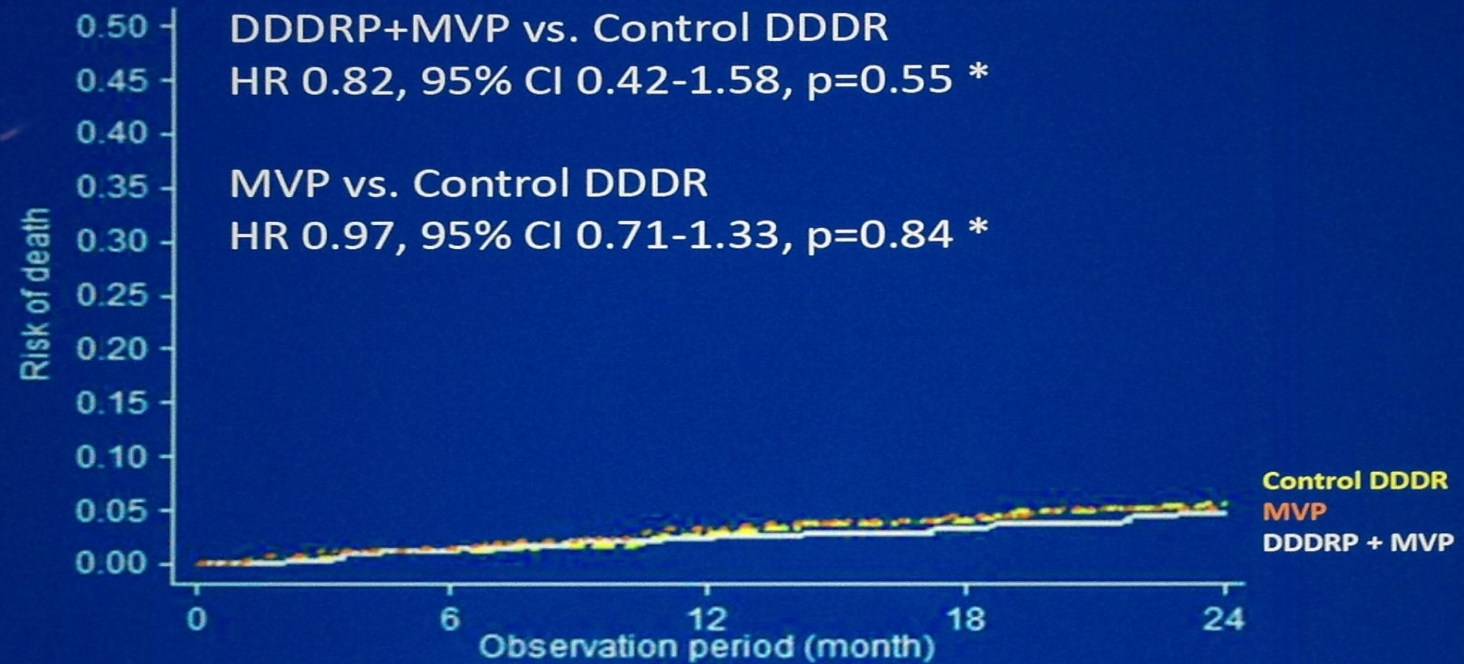
*After adjustment for gender HR 0.73, $p=0.04$, and HR 0.89, $p=0.12$, respectively

Algoritmos Terapêuticos em Pacing

Minerva Study

All-Cause Death

Intention-to-treat survival analysis using time to first event



Number at risk					
Control DDDR	385	366	352	340	288
DDDRP+MVP	383	360	346	334	269
MVP	398	375	360	342	282

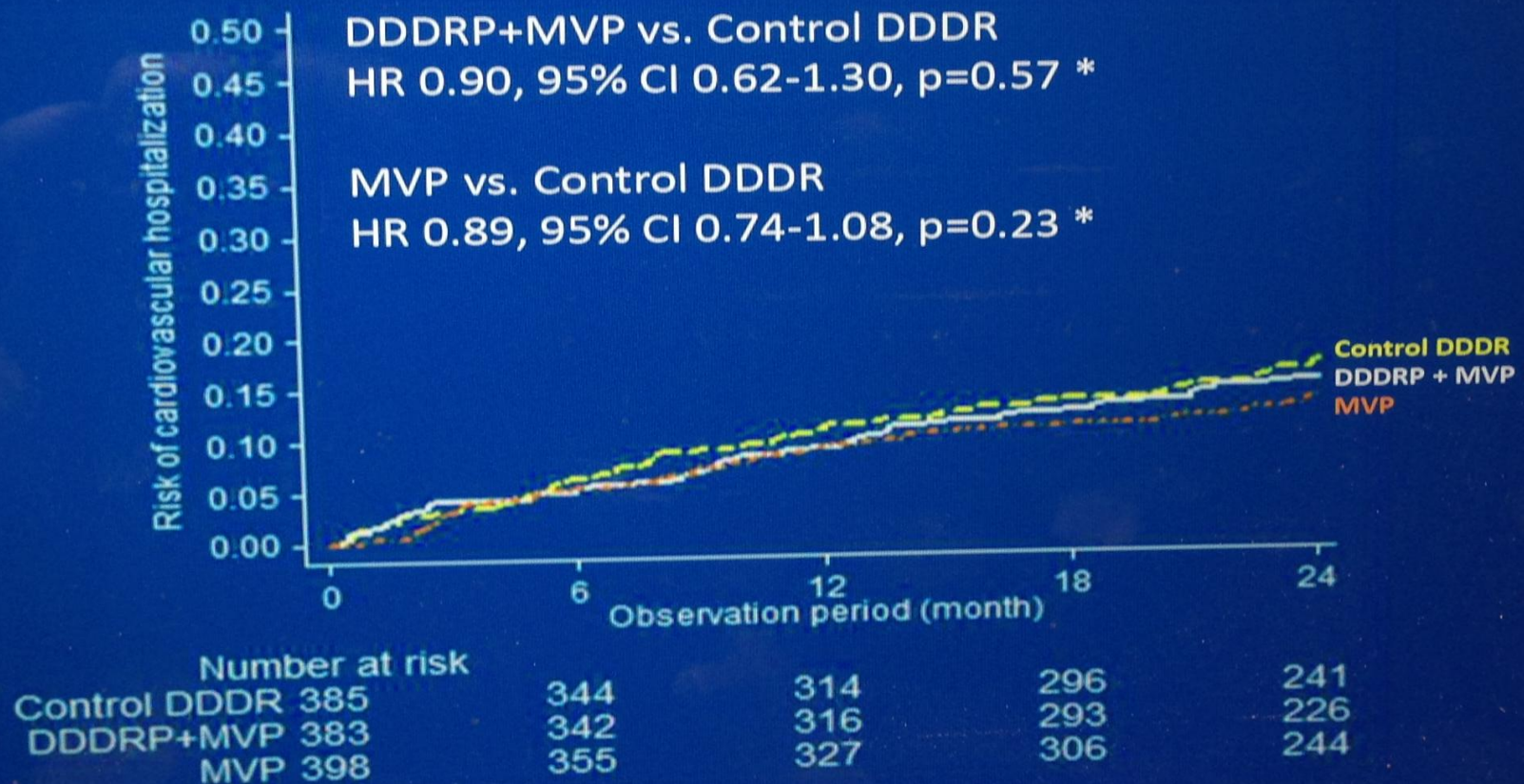
*No change after adjustment for gender

Algoritmos Terapêuticos em Pacing

Minerva Study

CV Hospitalizations

Intention-to-treat survival analysis using time to first event

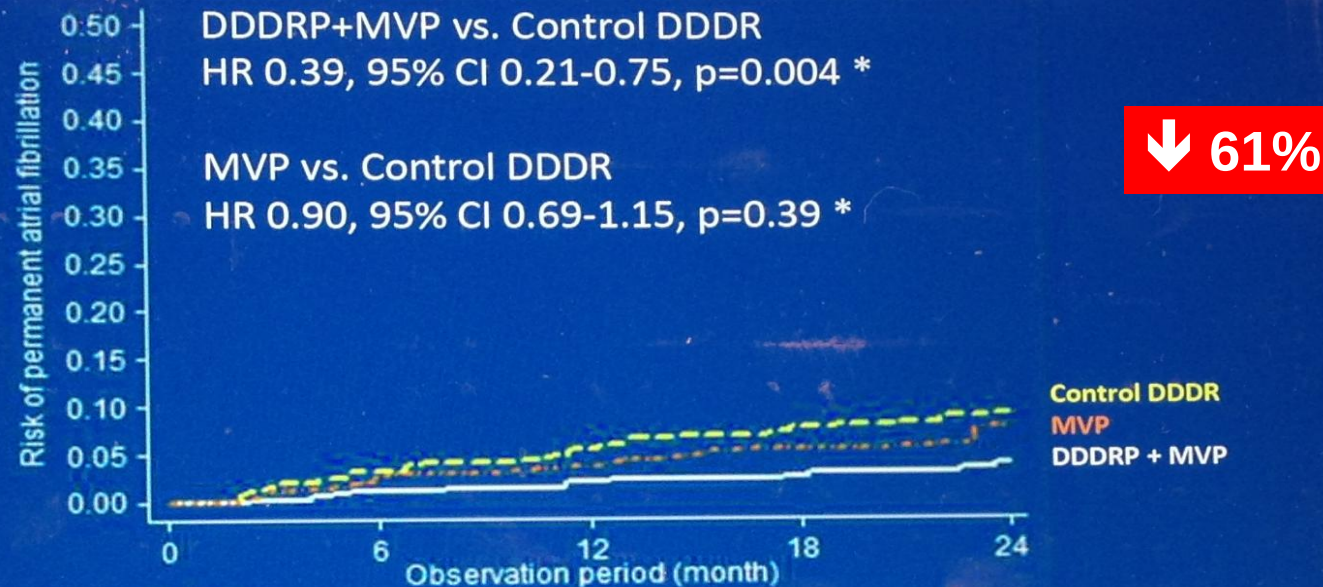


*No change after adjustment for gender

Algoritmos Terapêuticos em Pacing Minerva Study

Permanent AF

Intention-to-treat survival analysis using time to first event



Number at risk					
Control DDDR	385	355	336	316	265
DDDRP+MVP	383	356	339	325	260
MVP	398	366	347	325	260

*No change after adjustment for gender

- Atrial cardioversion occurred less frequently in the DDDR+MVP vs. Control DDDR (49% relative reduction, $p=0.001$)
- AF-related hospitalizations and ER visits occurred less frequently in the DDDR+MVP vs. Control DDDR (52% relative reduction, $p<0.0001$)

Algoritmos Terapêuticos em Pacing

Minerva Study

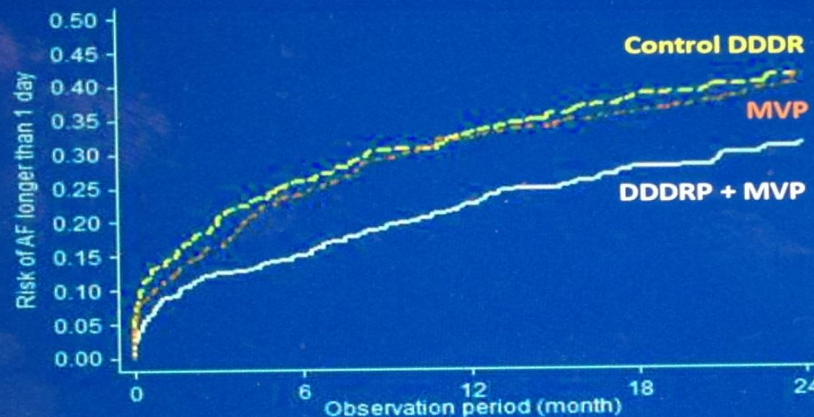
Incidence of AF

Intention-to-treat survival analysis using time to first event

>1 Day

DDDRP+MVP vs. Control DDDR
HR 0.66, 95% CI 0.52-0.85, $p=0.001^*$

MVP vs. Control DDDR
HR 0.98, 95% CI 0.87-1.10, $p=0.71^*$

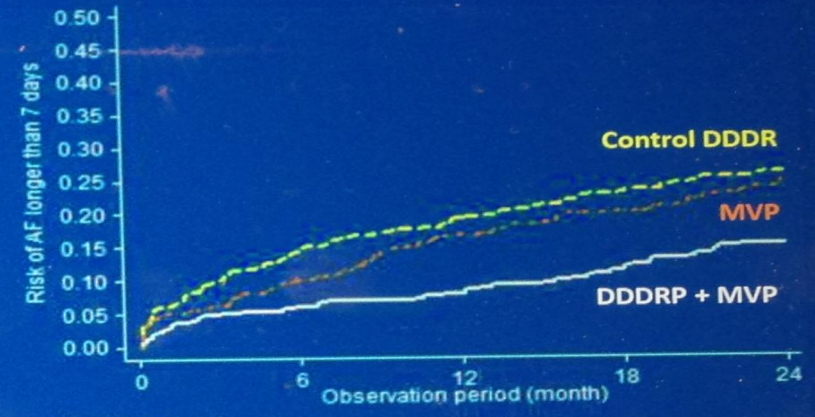


Number at risk					
Control DDDR	383	261	224	194	152
DDDRP+MVP	373	285	241	206	146
MVP	389	266	226	190	134

>7 Days

DDDRP+MVP vs. Control DDDR
HR 0.52, 95% CI 0.36-0.73, $p<0.001^*$

MVP vs. Control DDDR
HR 0.95, 95% CI 0.82-1.10, $p=0.49^*$



Number at risk					
Control DDDR	383	298	266	239	190
DDDRP+MVP	373	313	283	253	173
MVP	389	314	272	238	170

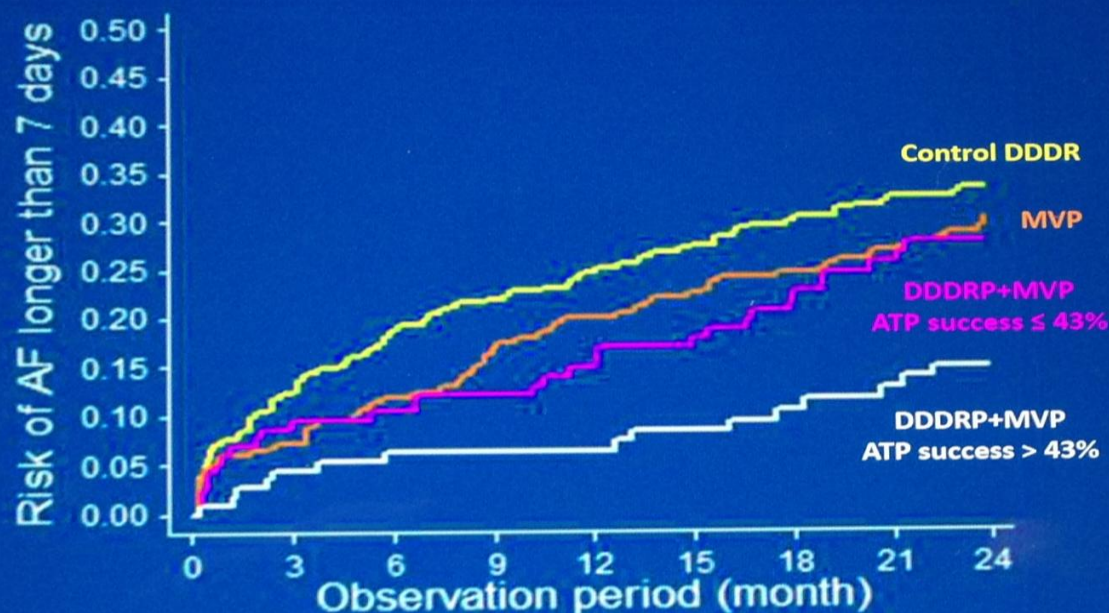
*No change after adjustment for gender

Algoritmos Terapêuticos em Pacing

Minerva Study

Risk of AF > 7 days and aATP efficacy

Median (25th-75th percentile) aATP efficacy: 43% (17%-62%)



Log Rank p value comparing
Control DDDR vs.
MVP $p=0.274$
DDDR+MVP
(ATP success $\leq 43\%$)
 $p=0.193$
DDDR+MVP
(ATP success $> 43\%$)
 $p<0.001$

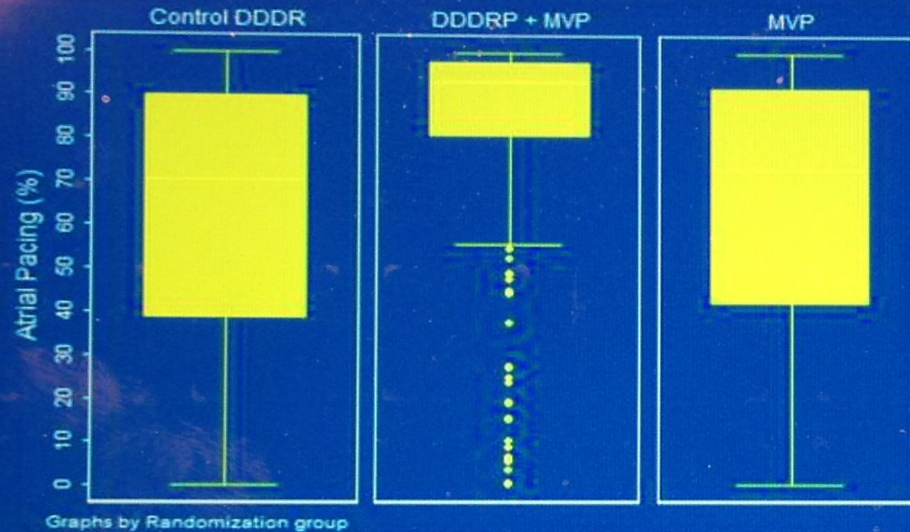
	Number at risk								
	0	3	6	9	12	15	18	21	24
Control DDDR	279	239	215	205	188	176	164	155	133
MVP	266	242	223	205	191	182	168	155	121
DDDR+MVP, low ATP Efficacy	116	104	101	96	90	86	81	70	49
DDDR+MVP, high ATP Efficacy	113	105	100	100	93	89	82	77	58

Note: since ATP treated only episodes longer than 2 minutes, to compare the different groups in a correct and balanced way, this analysis considered only patients with at least 2 minutes of AF

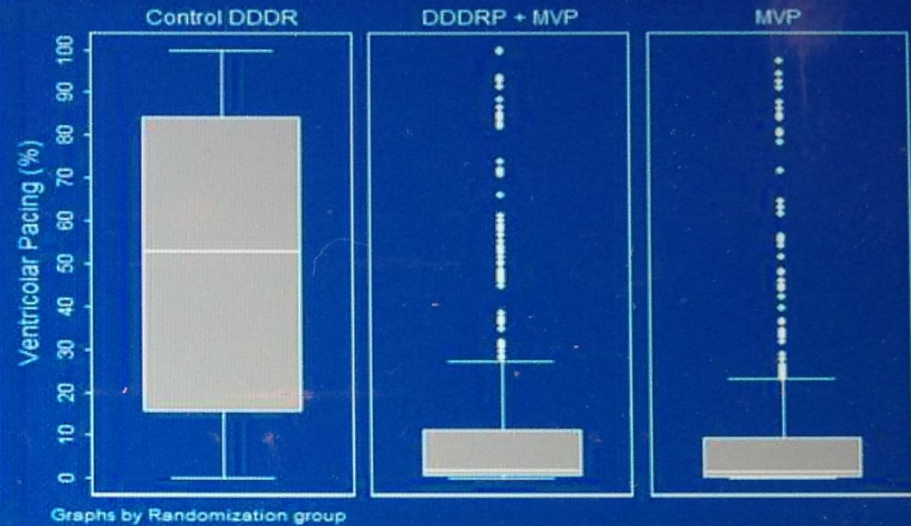
Algoritmos Terapêuticos em Pacing

Minerva Study

% of Atrial Pacing



% of Ventricular Pacing



AP%	Control DDDR n=374	DDDRP + MVP n=370	p-value Control DDDR vs DDDRP + MVP	MVP n=392	p-value Control DDDR vs MVP
Median (Q1-Q3)	70% (39%-90%)	93% (81%-97%)	<0.001	73% (42%-92%)	0.66

VP%	Control DDDR n=374	DDDRP + MVP n=370	p-value Control DDDR vs DDDRP + MVP	MVP n=392	p-value Control DDDR vs MVP
Median (Q1-Q3)	53% (15%-84%)	2% (0%-11%)	<0.001	1% (0%-9%)	<0.001

Algoritmos Terapêuticos em Pacing

Minerva Study

Conclusions

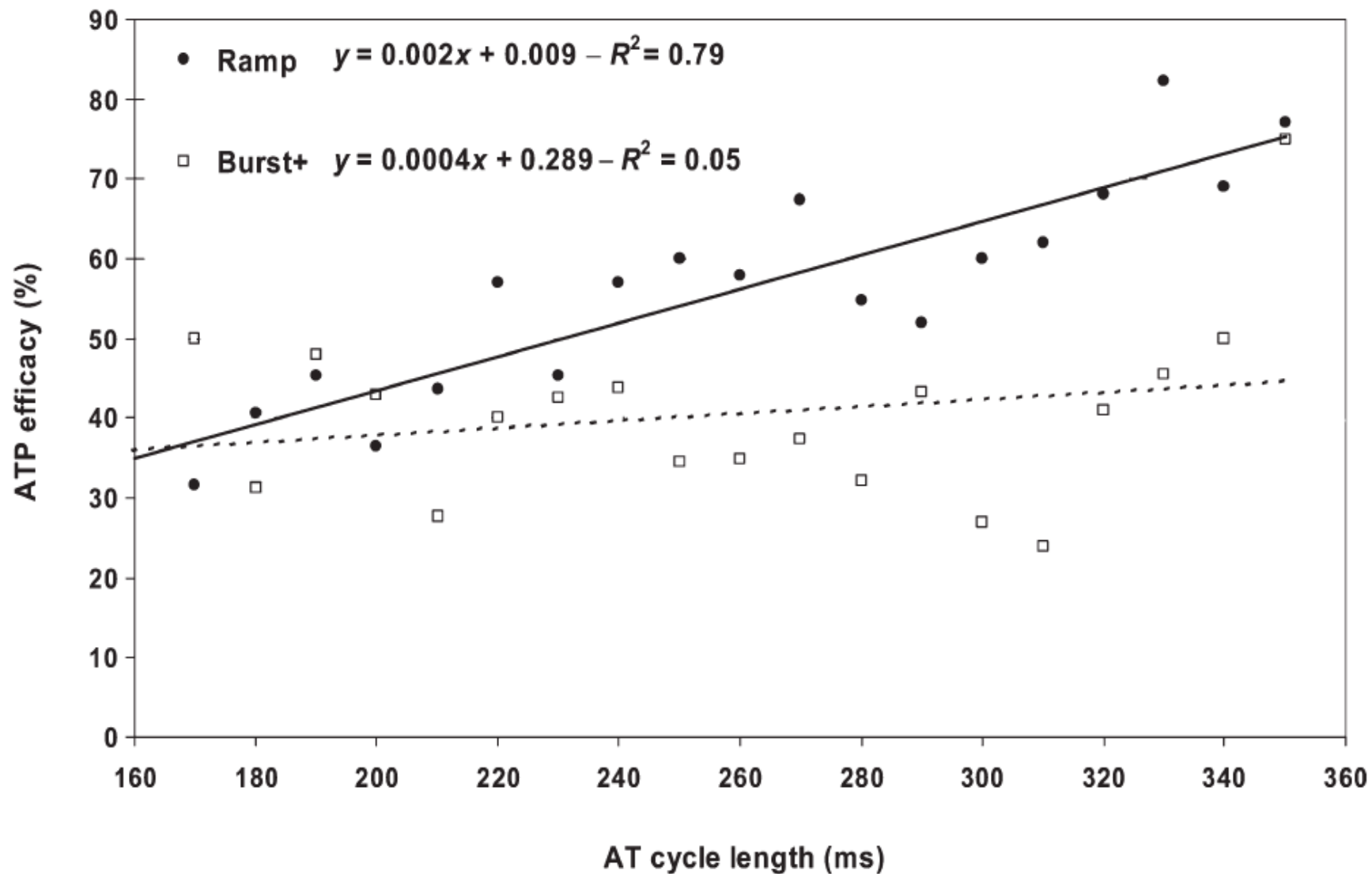
- In patients with bradycardia, previous atrial tachyarrhythmias and no history of permanent AF or third-degree atrioventricular block, DDDRP+MVP proved superior to standard dual-chamber pacing, in that it led to a significant **26% relative risk reduction** in the combined endpoint of mortality, cardiovascular hospitalizations, and permanent AF.
- DDDRP+MVP positive effect was mainly driven by a significant reduction in the progression of atrial tachyarrhythmias to permanent AF (**61% relative risk reduction**) over 2 years of follow- up.
- For DDDRP+MVP the number needed to treat (NNT) to prevent evolution to permanent AF over 2 years is 20 patients.

Terminação precoce das taquiarritmias auriculares pode limitar o “*remodeling*” auricular

ECG recording showing EGM-V, Intervalo A-A, Marker Channel, and Intervalo V-V. The EGM-V trace shows a series of sharp, narrow QRS complexes. The Intervalo A-A trace shows a series of numbers representing the interval between A waves. The Marker Channel trace shows a series of letters (S, T, P, V) indicating the type of wave. The Intervalo V-V trace shows a series of numbers representing the interval between V waves. The recording is on a grid background.

ECG recording on a grid showing EGM-V, Intervalo A-A, Marker Channel, and Intervalo V-V. The EGM-V trace shows several sharp spikes. The Intervalo A-A trace shows numerical values for each beat. The Marker Channel trace shows letters (T, S, A, P, V) indicating the type of beat. The Intervalo V-V trace shows numerical values for each beat.

Terapias: Ramp VS Burst+



Eficácia das terapias de pacing auricular anti taquicardia no tratamento da fibrilhação auricular paroxística em doentes portadores de pacemaker

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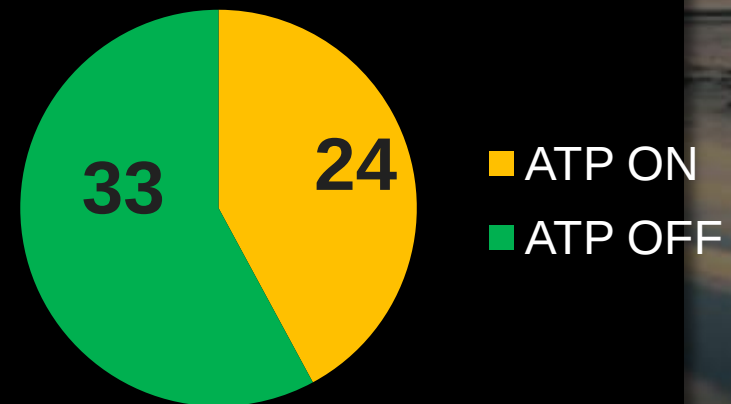
³Universidade Metodista de Angola, Departamento de Cardiopneumologia

- Doentes que implantaram PMD Medtronic Enrhythm P1501 DR entre 2005 e 2010 no Lab. Pacing de Santarém
- Follow-up de 15 meses



3º mês(M1); 9º mês (M2); 15º mês (M3)

Amostra



n = 57 doentes

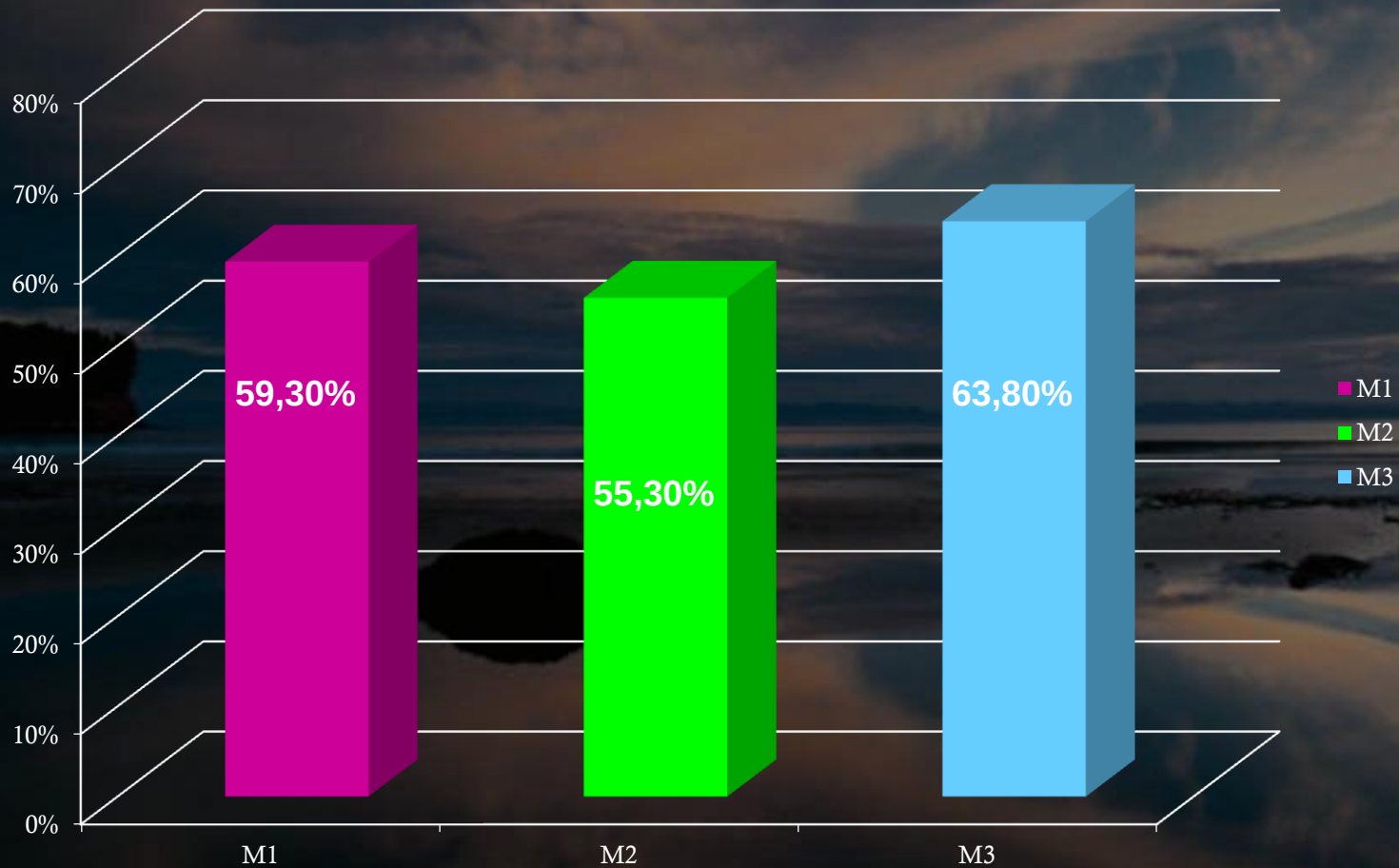
	ATP ON	ATP OFF	Valor de p
% ♂	58,3% n = 14	42,4% n = 14	p = 0,289
DNS	87,5% n = 21	75,8% n = 25	p = 0,288
BAV 2º grau	0% n = 0	9,1% n = 3	p = 0,288
BAVC	12,5% n=3	15,2% n=5	p = 0,288
HTA	87,5% n = 21	90,9% n = 30	p = 0,501
DPOC	20,8% n = 5	9,1% n = 3	p = 0,191
Dislipidemia	58,3% n = 14	48,5% n =16	p = 0,593
Disf.tiroideia	12,5% n = 3	15,2% n = 5	p = 0,546
FA/Flutter auricular	79,2% n = 19	78,8% n = 26	p = 1,000
DM II	25% n = 6	18,2% n = 6	p = 0,743
ICC	16,7% n = 4	27,3% n = 9	p = 0,524
IRC	12,5% n = 3	15,2% n = 5	p = 0,546
CAD	12,5% n = 3	15,2% n = 5	p = 0,564
AVC	8,3% n = 2	6,1% n = 2	p = 0,565
Anti-arrítmicos	60,9% n = 14	45,5% n = 15	p = 0,289
IECA	66,7% n = 16	54,5% n = 18	p = 0,420

Dados demográficos, indicação para implante, medicação prévia e factores de risco cardiovascular.

Resultados

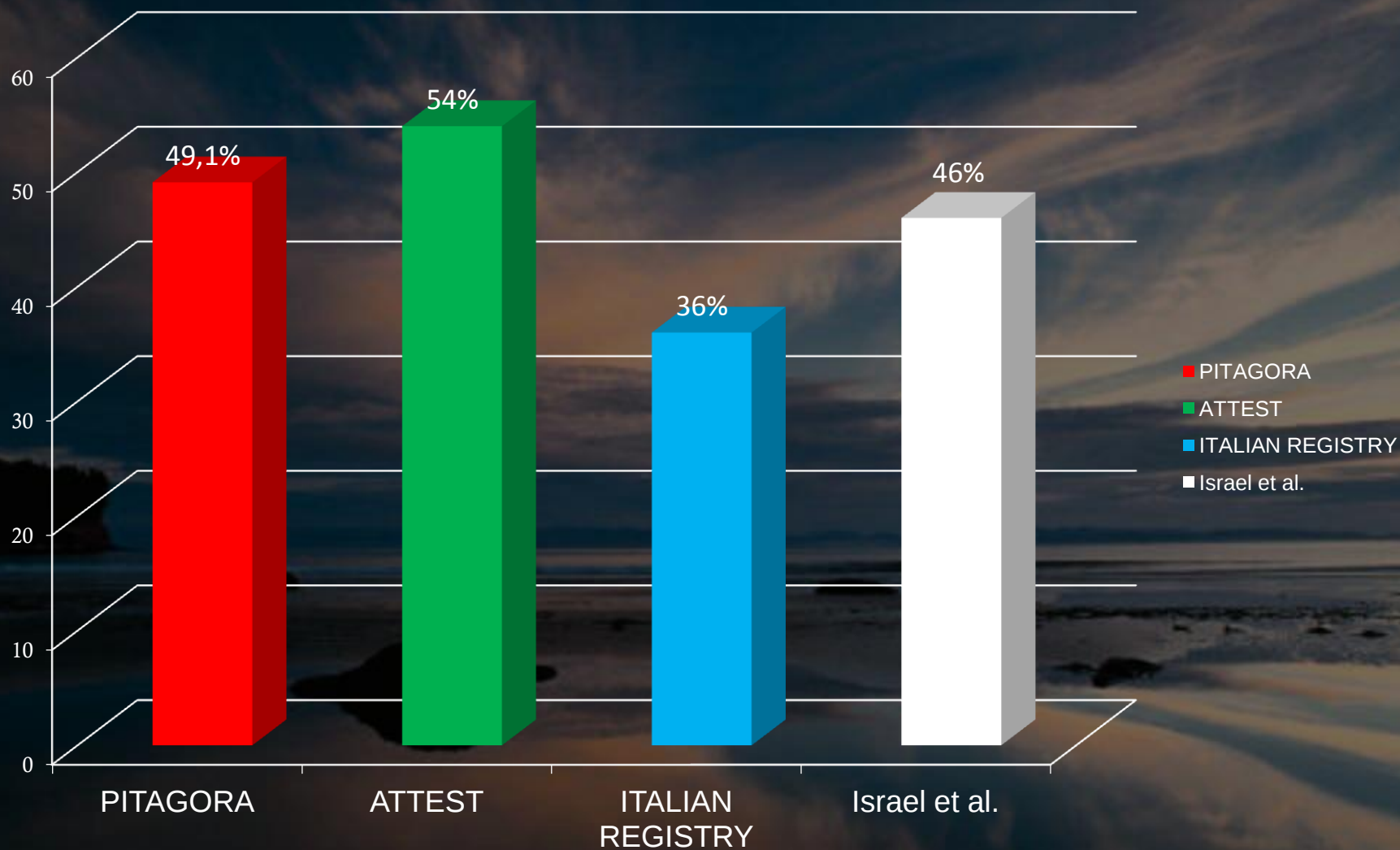
Total – 12428 episódios

EFICÁCIA ATP

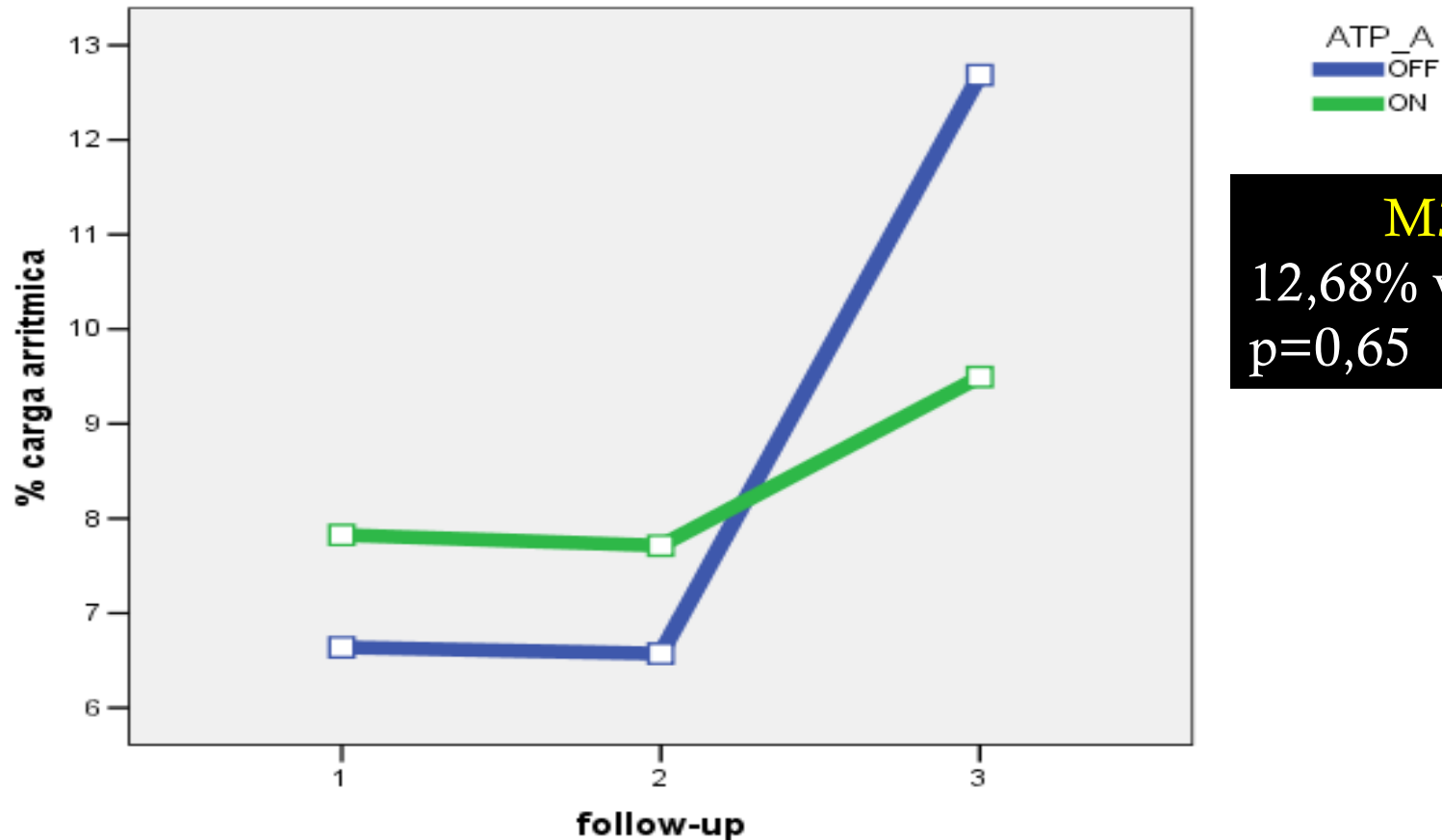


R Silva, V Martins, 2014

Eficácia ATP

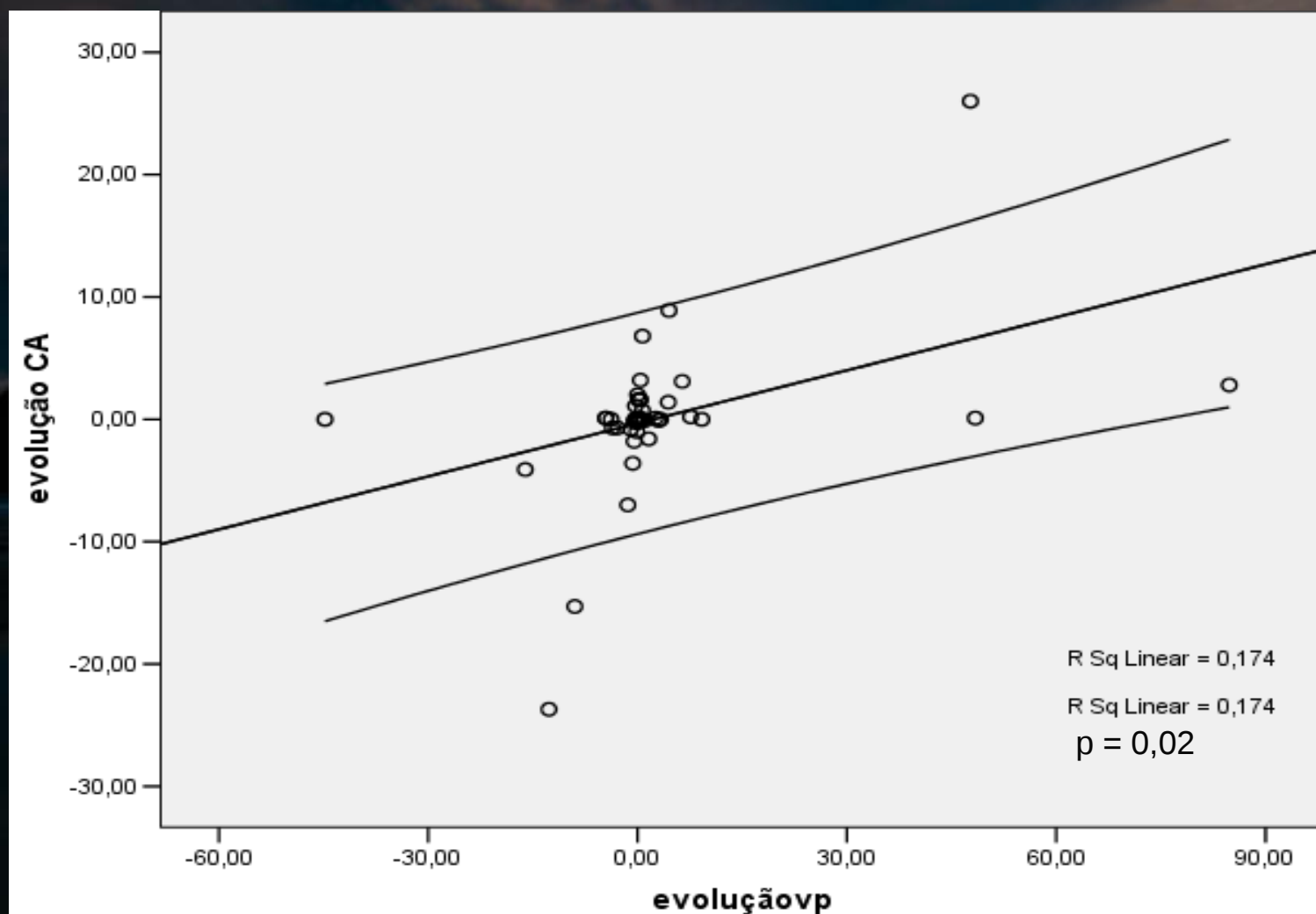


Carga Arritmica / ATP

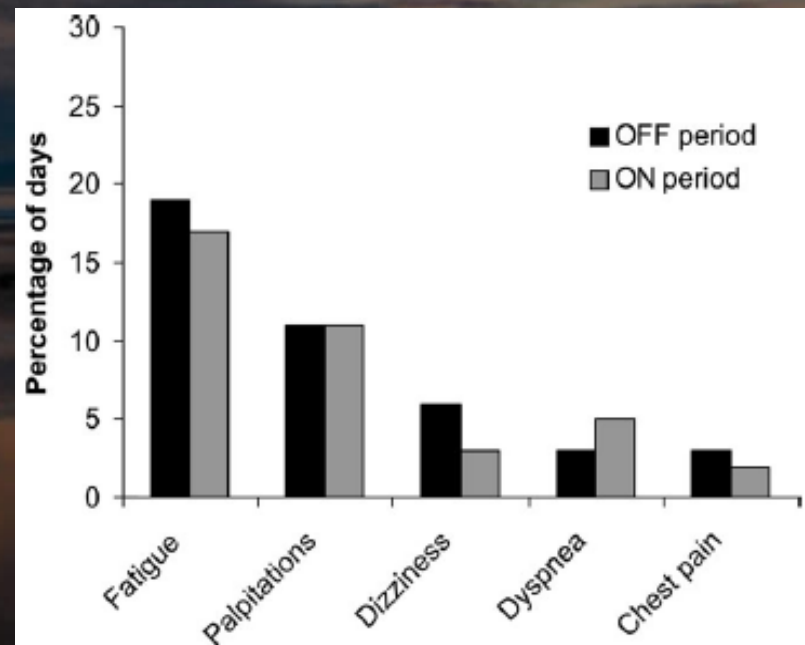
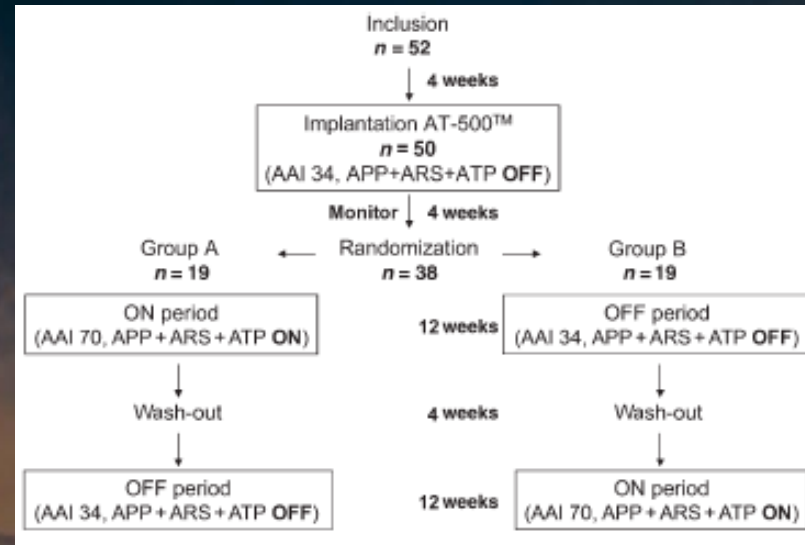
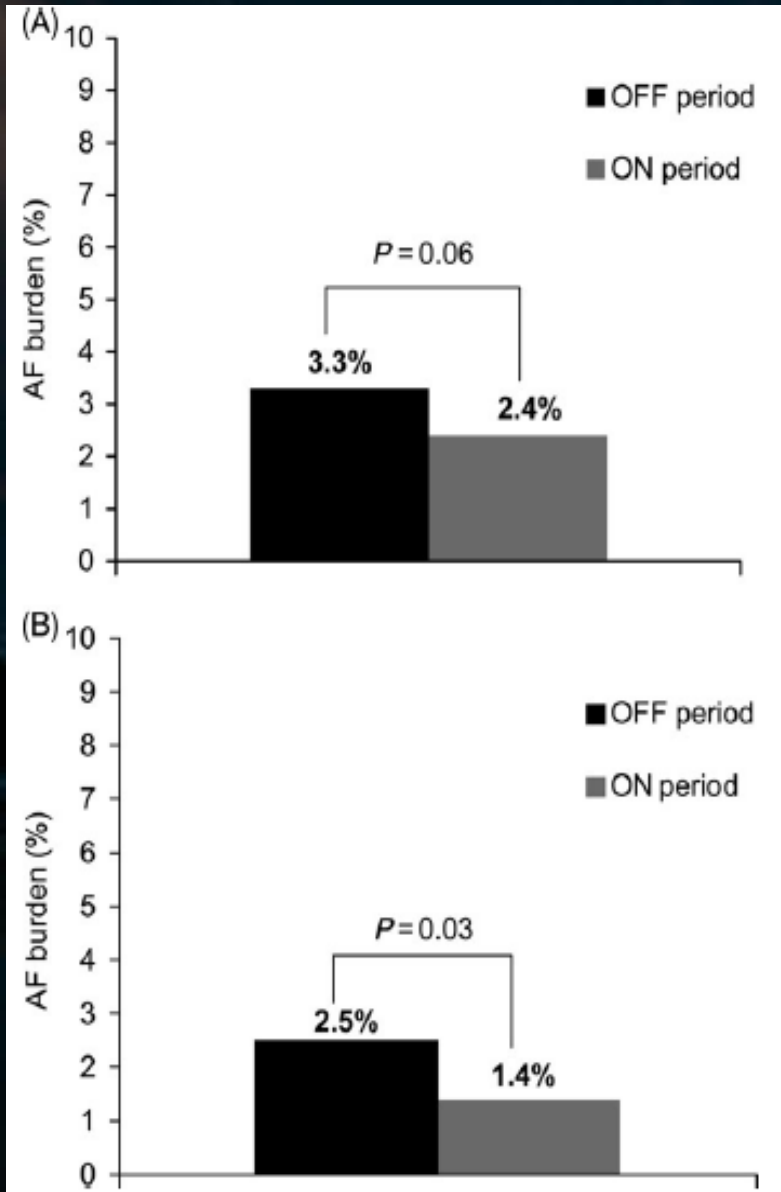


M3
12,68% vs 9,5%
 $p=0,65$

Correlação da evolução da % VP com evolução da % CA



Algoritmos Terapêuticos em Pacing



Algoritmos Terapêuticos em Pacing

Conclusões

- Os algoritmos terapêuticos para as arritmias supraventriculares parecem diminuir a progressão para a fibrilhação auricular permanente
- Percentagem média de sucesso do ATP ronda os 40 a 50%.
- Correlação significativamente positiva entre a evolução da percentagem de pacing ventricular e a evolução da carga arrítmica.
- Estes algoritmos devem estar presentes nos pacemakers e devem ser sempre activados dado o benefício que não sendo imediato é importante a longo prazo

A wide-angle photograph of a beach at dusk or dawn. The sky is filled with wispy, light-colored clouds against a dark blue background. The sun is low on the horizon, creating a warm glow. The beach is wet, reflecting the sky and clouds. Several large, dark rocks are scattered across the sand. In the distance, a dark silhouette of a forested hill or cliff is visible on the left side. The word "OBRIGADO" is written in large, white, serif capital letters across the center of the image, with a subtle drop shadow.

OBRIGADO