Pathophysiology and clinical use of Baroreflex Sensitivity (BRS)

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Baroreflex sensitivity (BRS)

- **Definition**
  - **Amount of response in heart beat interval to a change in blood pressure, expressed in ms/mmHg**

Baroreflex sensitivity (BRS)

- Established tool for the assessment of autonomic control of the cardiovascular system

- Valuable information in the clinical management, particularly in **prognostic evaluation** and assessment of treatment effect, in a variety of cardiac diseases

Pathophysiology

- The arterial baroreceptor reflex system
  - Plays a dominant role in preventing short-term wide fluctuations of arterial blood pressure
  - Arterial baroreceptor denervation results in an increase of the variability of blood pressure

Pathophysiology

Rise in systemic arterial pressure

Activation of arterial baroreceptors

Increase of the discharge of vagal cardioinhibitory neurons and a decrease in the discharge of sympathetic neurons both to the heart and peripheral blood vessels

Bradycardia, decreased cardiac contractility and decreased peripheral vascular resistance, and venous return

Pathophysiology

- There are significant differences in the time delay of the response mediated by parasympathetic and sympathetic efferents
  - Following a rapid rise in arterial pressure, parasympathetic activation produces an immediate reaction (200~600 msec)
  - The reaction to cardiac and vasomotor sympathetic activation occurs with a 2~3 seconds delay and reaches maximal effect more slowly

The ability of the baroreflex to control heart rate on a beat-to-beat basis is exerted through vagal but not sympathetic activity

Pathophysiology

- Many central neural structures are also involved in the regulation of the cardiovascular system and contribute to the functioning of the baroreflex
- Respiration continuously interacts with baroreflex modulation of heart rate
  - Inspiration decreases while expiration increases baroreceptor stimulation of vagal motoneurons

Cardiovascular diseases

- Cardiovascular diseases are often accompanied by an impairment of baroreflex mechanisms
  - Reduction of inhibitory activity
  - Imbalance in the physiological sympathetic-vagal outflow to the heart
  - Resulting in a chronic adrenergic activation

Cardiovascular diseases

- Hypertension
- Coronary artery disease
- Myocardial infarction
- Heart failure

- Neurally mediated syncope

Measurement of BRS

- Pharmacological methods
- Valsalva maneuver
- Neck chamber
- Spontaneous oscillations in BP and HR
  - Sequence method
  - Spectral method
  - Cross-correlation (xBRS)

Clinical Implications of BRS

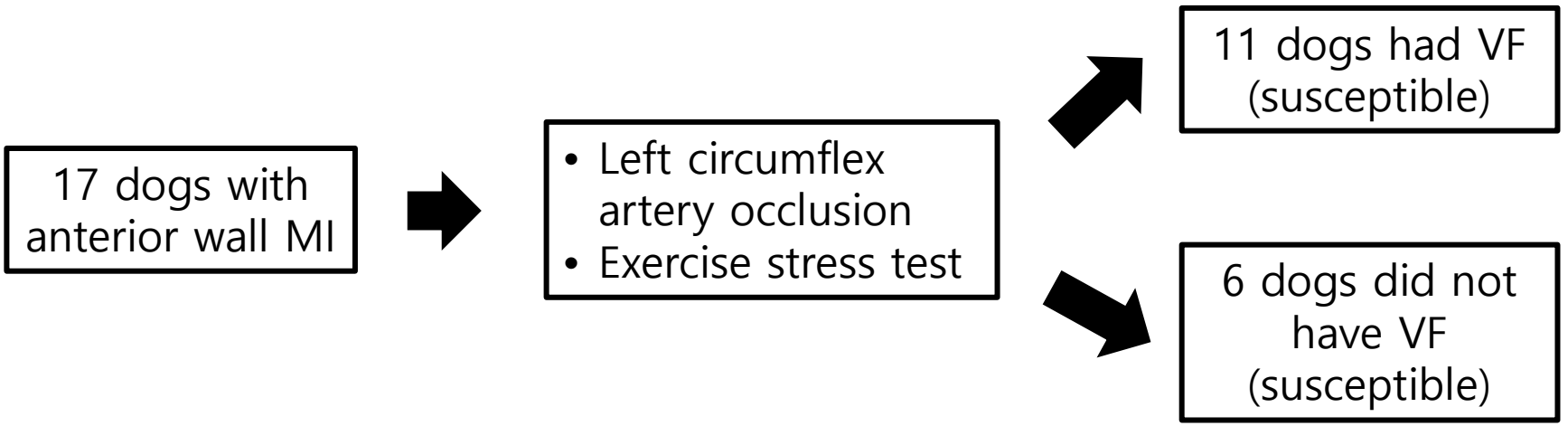
Baroreceptor Reflex Control of Heart Rate: A Predictor of Sudden Cardiac Death

GEORGE E. BILLMAN, PH.D., PETER J. SCHWARTZ, M.D., AND H. LOWELL STONE, PH.D.

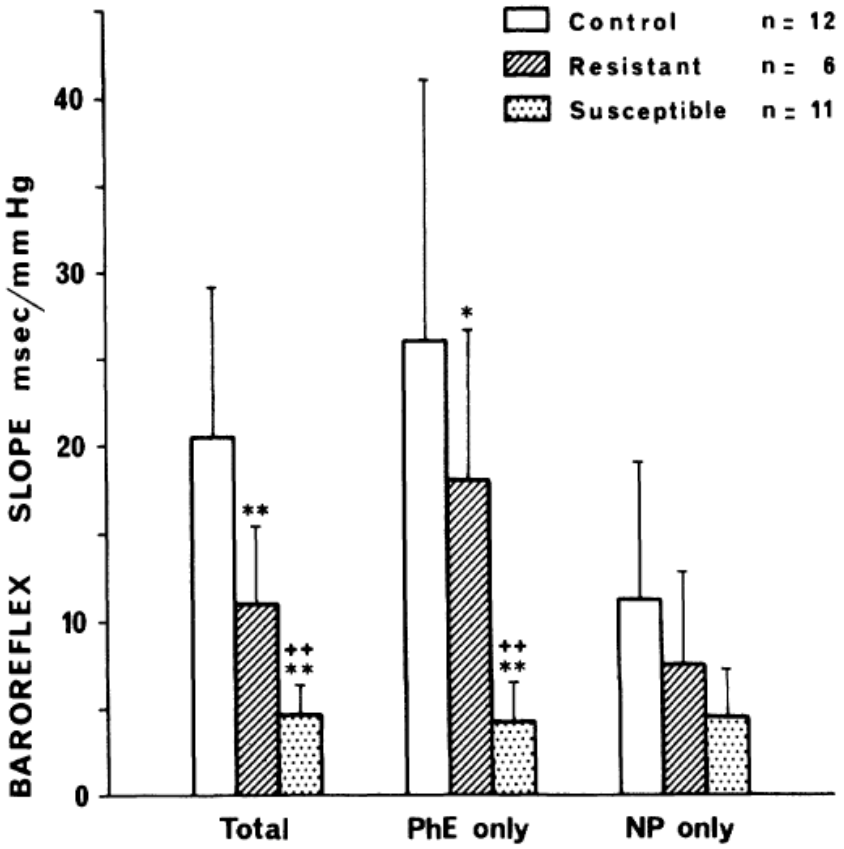
SUMMARY To explore the possibility that the analysis of autonomic reflexes could identify subgroups at high risk of ventricular fibrillation, we studied chronically instrumented mongrel dogs randomly divided into two groups. Twelve dogs served as controls and 17 were studied 3–4 weeks after anterior wall myocardial infarction (MI). After recovery, the dogs were given bolus i.v. injections of phenylephrine, 10 μg/kg, and nitroprusside, 100 μg/kg, to raise or lower systolic arterial pressure 30–50 mm Hg. The RR intervals were plotted against the systolic pressure during the preceding beats, and the slope (baroreflex slope) was determined by least-squares-fit linear regression. On a subsequent day, the left circumflex coronary artery was occluded for 2 minutes, beginning with the last minute of an exercise stress test and continuing for 1 minute after the cessation of exercise (MI group only). The dogs could be divided into two groups based on their response to this test; 11 dogs (65%) had ventricular fibrillation (susceptible), whereas six dogs (35%) did not (resistant). The baroreflex slope (control 20.49 ± 8.59; resistant 10.95 ± 4.68; susceptible 4.60 ± 1.77 msec/mm Hg) and the heart rate response to a 30-mm Hg increase in arterial pressure (control −56.5 ± 14.8; resistant −40.0 ± 12.2; susceptible −12.9 ± 5.0 beats/min) for the susceptible dogs were significantly different from those of the control and resistant dogs. This may indicate that the resistant dogs have a greater capability to activate strong vagal reflexes, which reduce vulnerability to ventricular fibrillation. We conclude that anterior wall MI significantly attenuates the baroreceptor reflex control of heart rate and that analysis of the heart rate response to arterial pressure increases allows identification of subgroups of dogs at higher risk for ventricular fibrillation. A prospective study in patients with MI is warranted.

Circulation 1982;66:874-887

- **To explore the possibility that the analysis of autonomic reflex could identify subgroups at high risk of ventricular fibrillation**
- **17 dogs with anterior wall MI (3~4 weeks ago) vs placebo (12 dogs)**
- **BRS was measured by phenylephrine methods**
- **Left circumflex artery was occluded for 2 min, beginning exercise stress test**



Circulation 1982;66:874-887



- **The baroreflex slope and the heart rate reductions associated with phenylephrine injections may useful for identifying patients vulnerable to ventricular fibrillation**

Circulation 1982;66:874-887

Laboratory Investigation

Autonomic Mechanisms and Sudden Death

New Insights From Analysis of Baroreceptor Reflexes in Conscious Dogs With and Without a Myocardial Infarction

Peter J. Schwartz, MD, Emilio Vanoli, MD, Marco Stramba-Badiale, MD, Gaetano M. De Ferrari, MD, George E. Billman, PhD, and Robert D. Foreman, PhD

We have suggested that among conscious dogs with a healed anterior wall myocardial infarction (MI) a depressed baroreflex sensitivity (BRS) carries a higher risk of developing ventricular fibrillation during a brief ischemic episode associated with an exercise stress test. The clinical and pathophysiological implications of our previous findings prompted the present study, which addressed three major questions: 1) Is, indeed, analysis of BRS after MI a specific and sensitive marker for sudden death–risk stratification? 2) Does MI modify BRS? 3) Does analysis of BRS before MI provide information about outcome during ischemic episodes occurring after MI? An anterior MI was produced in 301 dogs, and 4 weeks later, a 2-minute circumflex coronary artery occlusion beginning during the last minute of an exercise stress test could be performed in 192 animals. Ventricular fibrillation occurred in 106 (55%) dogs (susceptible to sudden death), whereas 86 (45%) dogs (resistant to sudden death) survived. BRS was assessed by the phenylephrine method and was expressed by the regression line relating RR intervals to blood-pressure changes. BRS was significantly lower among susceptible than among resistant dogs (9.1±6.0 vs. 17.7±6.5 msec/mm Hg, $p<0.0001$). The risk for sudden death increased from 20% (15 of 73 dogs) for a BRS greater than 15 msec/mm Hg to 91% (62 of 68 dogs) for a BRS less than 9 msec/mm Hg ($p<0.001$). An internal control study in 55 animals showed that BRS was reduced 4 weeks after MI compared with control conditions (13.5±6.7 vs. 17.8±6.6 msec/mm Hg, $p<0.001$) and that a reduction occurred in 73% of animals. Susceptible dogs and those that spontaneously died after MI had a lower BRS even before the MI (16.2±5.9 vs. 22.2±6.2 msec/mm Hg, $p<0.001$). The risk for sudden death after MI increased from 35% (nine of 26 dogs) for a BRS before MI greater than 20 msec/mm Hg to 85% (17 of 20 dogs) for a BRS before MI less than 14 msec/mm Hg ($p<0.001$). This study demonstrates that the presence of a reduced BRS is associated with a greater susceptibility to ventricular fibrillation during subsequent ischemic episodes. In the majority of dogs, BRS is reduced after an MI. The results in 192 conscious dogs with a healed MI indicate that analysis of BRS is a powerful tool for risk stratification not only after, but even before, the occurrence of an MI. (*Circulation* 1988; 78:969–979)

Circulation 1988;78:969-979

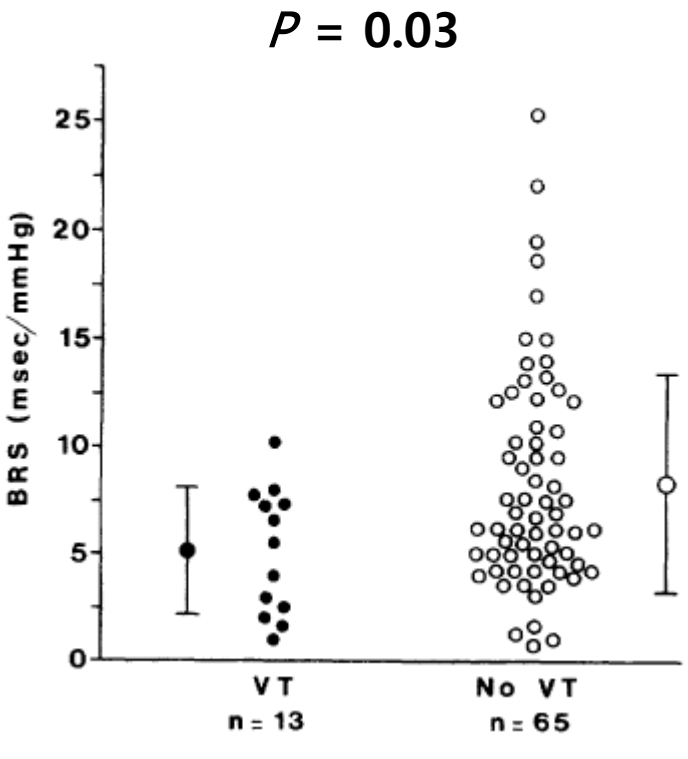
Baroreflex Sensitivity, Clinical Correlates, and Cardiovascular Mortality Among Patients With a First Myocardial Infarction

A Prospective Study

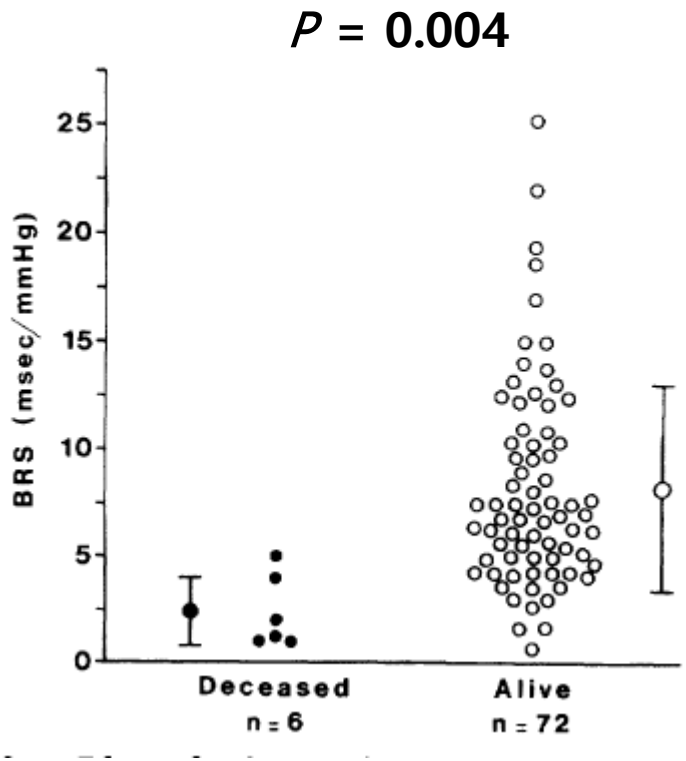
Maria Teresa La Rovere, MD, Giuseppe Specchia, MD,
Andrea Mortara, MD, and Peter J. Schwartz, MD

- **78 patients with a first MI**
- **BRS was assessed by phenylephrine methods**

Circulation 1988;78:816-824



BRS and the occurrence of VT



BRS and cardiac mortality

Circulation 1988;78:816-824

ARTICLES

Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction

Maria Teresa La Rovere, J Thomas Bigger Jr, Frank I Marcus, Andrea Mortara, Peter J Schwartz, for the ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators

- **ATRAMI**
- **Multicenter, prospective**
- **1284 patients with a recent (<28 days) myocardial infarction**
- **Heart rate variability (SDNN)**
- **Baroreflex sensitivity (phenylephrine method)**
- **Primary endpoint : cardiac mortality**

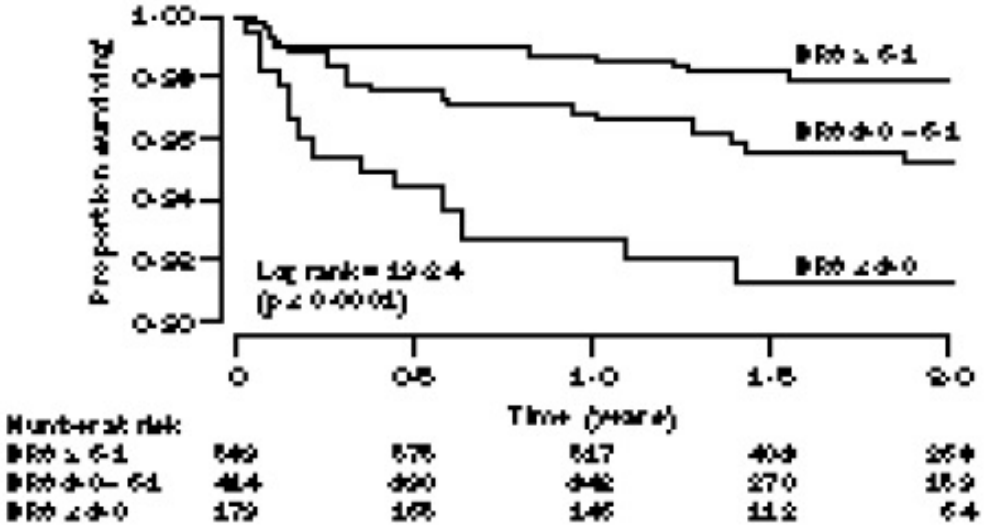
Lancet 1998;351:478-484

	BRS category			
	BRS <3·0 ms per mm Hg (n=179)	BRS 3·0–6·1 ms per mm Hg (n=414)	BRS >6·1 ms per mm Hg (n=589)	p for trend
Mean (SD) age in years	64 (7)	60 (9)*	53 (10)*†	0·001
Male (%)	70	85*	94*†	0·001
Anterior myocardial infarction (%)	56	50	46*	0·015
Mean (SD) peak creatine kinase in U/L‡	1972 (1739)	1779 (1557)	1699 (1500)	0·14
Thrombolytic therapy (%)	53	61	66*	0·003
Mean (SD) LVEF in %§	44 (14)	49 (12)*	51 (10)*	0·001
% with ⩾10 VPC per h	24	16*	15*	0·02
Mean (SD) SDNN in ms‖	86 (33)	103 (32)*	120 (33)*†	0·001
Mean (SD) BRS in ms per mm Hg¶	..	..	..	..

	SDNN category			
	SDNN <70 ms (n=172)	SDNN 70–105 ms (n=402)	SDNN >105 ms (n=573)	p for trend
Mean (SD) age in years	60 (8)	59 (9)	55 (10)*†	0·001
Male (%)	78	84*	92*†	0·001
Anterior myocardial infarction (%)	57	51	46*	0·05
Mean (SD) peak creatine kinase in U/L‡	1948 (1744)	1734 (1471)	1766 (1603)	0·48
Thrombolytic therapy (%)	56	68*	62	0·02
Mean (SD) LVEF in %§	41 (14)	49 (12)*	51 (10)*†	0·001
% with ⩾10 VPC per h	22	16*	15*	0·08
Mean (SD) SDNN in ms‖	..	..	..	..
Mean (SD) BRS in ms per mm Hg¶	4·4 (3·7)	6·8 (4·5)*	8·4 (5·0)*†	0·001

Lancet 1998;351:478-484

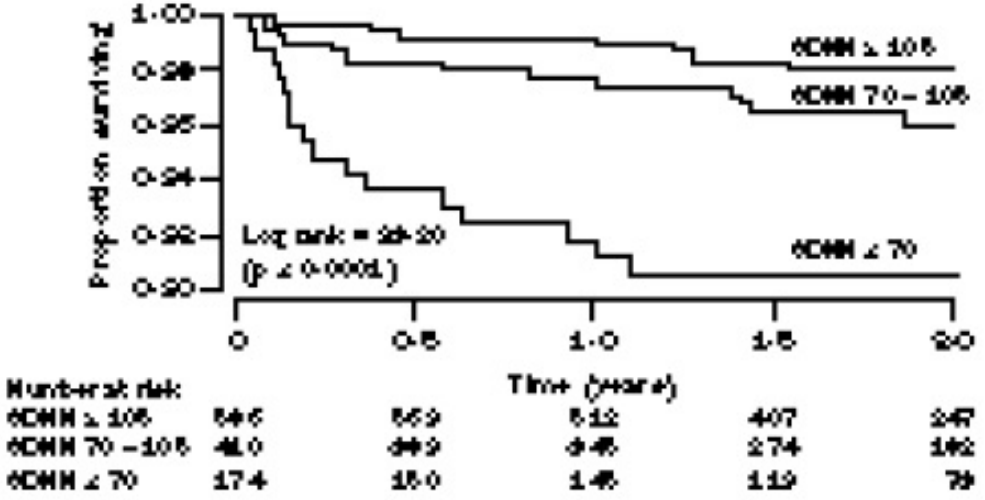
2 year cardiac mortality



BRS >6.1 ms/mmHg

BRS 3.0 – 6.1 ms/mmHg

BRS <3.0 ms/mmHg

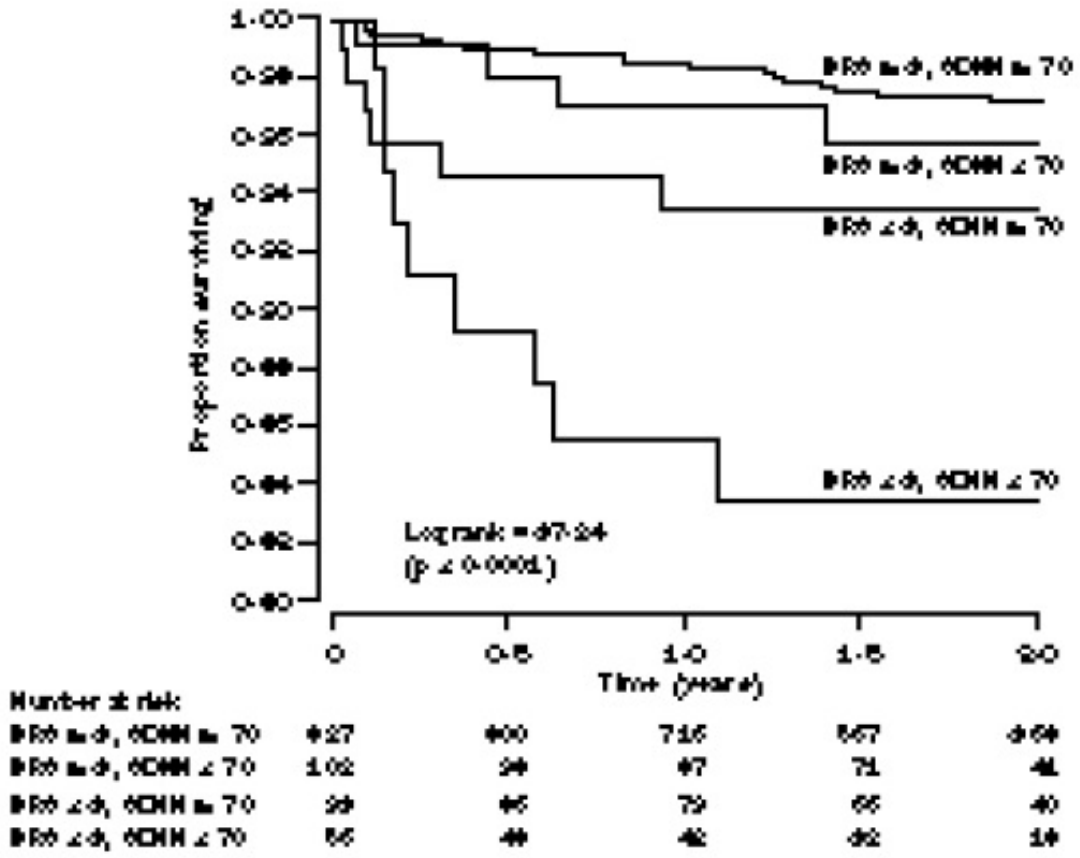


SDNN >105 ms

SDNN 70 105 ms

SDNN <70 ms

Lancet 1998;351:478-484



BRS >3.0, SDNN >70

BRS >3.0, SDNN <70

BRS <3.0, SDNN >70

BRS <3.0, SDNN <70

Lancet 1998;351:478-484

	Relative risk (95% CI)	p
Model including BRS		
LVEF		
35–50%	2·1 (0·90–4·69)	0·08
<35%	4·7 (2·04–10·9)	0·0003
BRS (ms per mm Hg)		
3·0–6·1	1·7 (0·81–3·69)	0·15
<3·0	2·8 (1·24–6·16)	0·01
⩾10 VPC/h	1·8 (0·94–3·46)	0·07
Model including SDNN		
LVEF		
35–50%	1·9 (0·87–4·49)	0·10
<35%	3·9 (1·69–9·25)	0·001
SDNN (ms)		
70–105	1·9 (0·86–4·04)	0·11
<70	3·2 (1·42–7·36)	0·005
⩾10 VPC/h	1·8 (0·97–3·50)	0·06

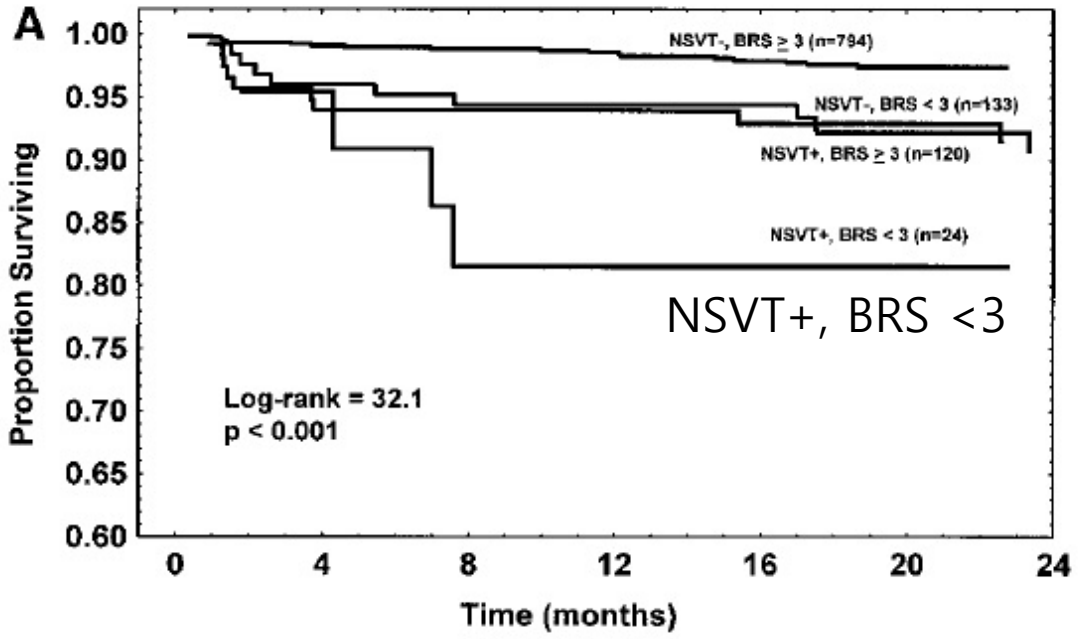
Baroreflex Sensitivity and Heart Rate Variability in the Identification of Patients at Risk for Life-Threatening Arrhythmias

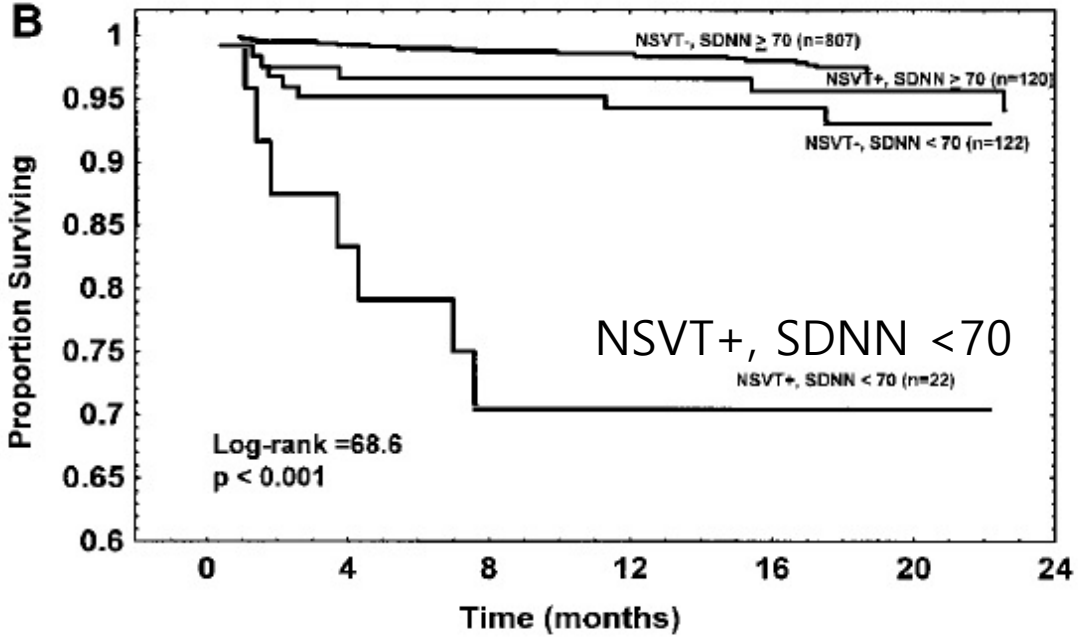
Implications for Clinical Trials

Maria Teresa La Rovere, MD; Gian Domenico Pinna, MS; Stefan H. Hohnloser, MD; Frank I. Marcus, MD; Andrea Mortara, MD; Ryuji Nohara, MD; J. Thomas Bigger, Jr, MD; A. John Camm, MD; Peter J. Schwartz, MD; on behalf of the Autonomic Tone and Reflexes After Myocardial Infarction (ATRAMI) Investigators

- To examine the role of both BRS and HRV in modifying the risk for cardiac and arrhythmic mortality associated with runs of NSVT
- Entire population of ATRAMI who had a myocardial infarction and in the subgroup with depressed LVEF

Circulation 2001;103:2072-2077


A
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
Proportion Surviving
NSVT-, BRS ≥ 3 (n=794)
NSVT-, BRS < 3 (n=133)
NSVT+, BRS ≥ 3 (n=120)
NSVT+, BRS < 3 (n=24)
NSVT+, BRS <3
Log-rank = 32.1
p < 0.001
0
4
8
12
16
20
24
Time (months)


B
1
0.95
0.9
0.85
0.8
0.75
0.7
0.65
0.6
Proportion Surviving
NSVT-, SDNN ≥ 70 (n=807)
NSVT+, SDNN ≥ 70 (n=120)
NSVT-, SDNN < 70 (n=122)
NSVT+, SDNN <70
NSVT+, SDNN < 70 (n=22)
Log-rank =68.6
p < 0.001
0
4
8
12
16
20
24
Time (months)

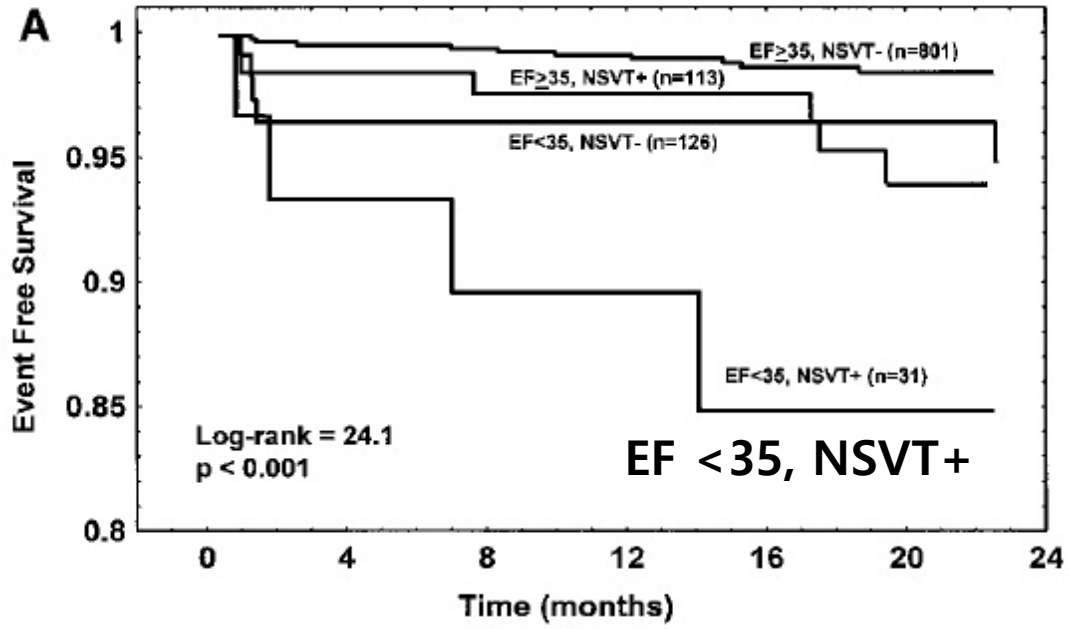
Multivariate Cox Analysis for Cardiac Mortality in total study population

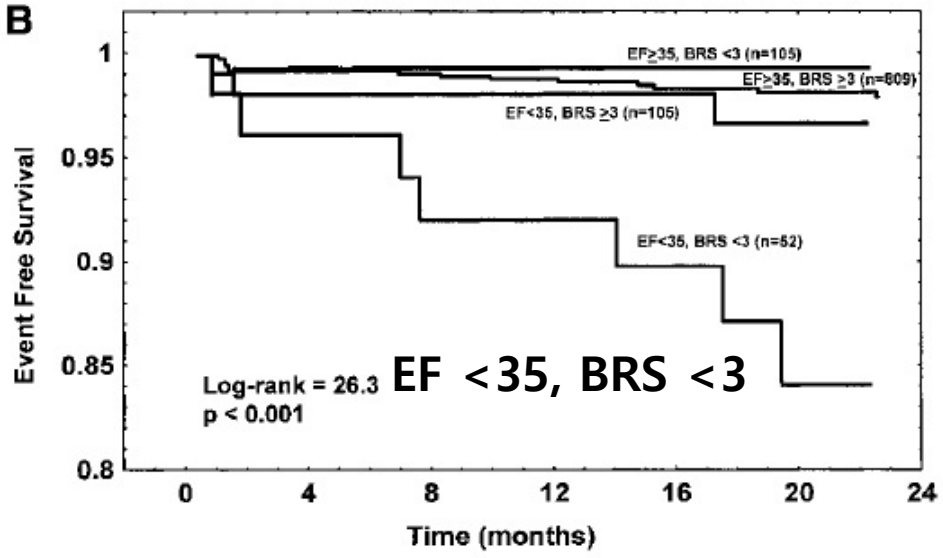
	Wald χ^2	RR (95% CI)	*P*
NSVT+	12.20	3.1 (1.6–5.9)	<0.001
SDNN<70 ms	11.65	3.2 (1.6–6.3)	<0.001
BRS<3 ms/mm Hg	4.77	2.1 (1.1–4.2)	0.03
NSVT+ and BRS<3 ms/mm Hg		9.6 (3.6–25.7)	<0.001
NSVT+ and SDNN<70 ms		17.0 (7.2–40.5)	<0.001
BRS<3 ms/mm Hg and SDNN <70 ms		7.0 (3.5–15.4)	<0.001
NSVT+, SDNN<70 ms, and BRS <3 ms/mm Hg		22.2 (7.3–66.8)	<0.001

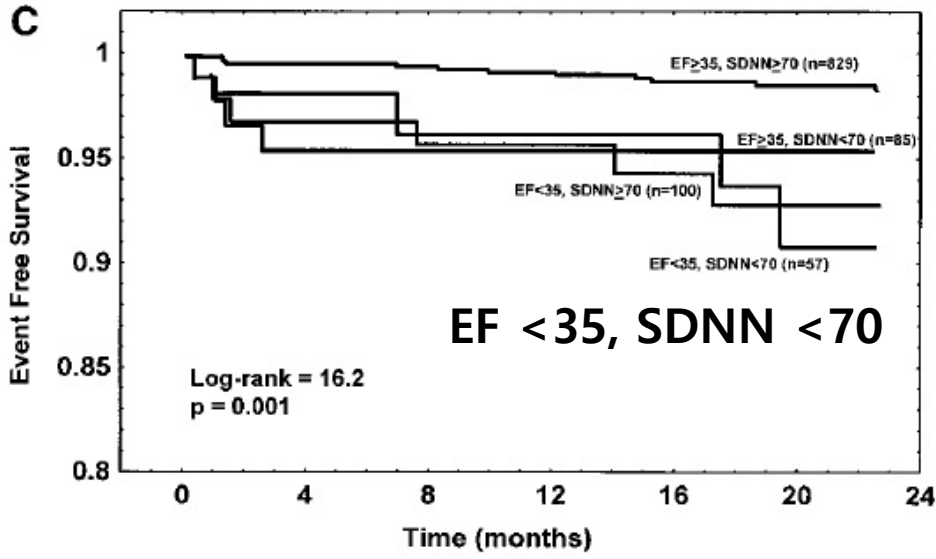
Multivariate Cox Analysis for Cardiac Mortality in patients with LVEF <35%

	Wald χ^2	RR (95% CI)	*P*
NSVT+	4.01	2.7 (1.02–7.06)	0.04
BRS<3 ms/mm Hg	3.97	2.8 (1.01–7.72)	0.04
SDNN<70 ms	0.29	1.3 (0.49–3.53)	0.58
NSVT− and BRS<3 ms/mm Hg		4.1 (1.18–13.88)	0.02
NSVT+ and BRS≥3 ms/mm Hg		4.0 (0.90–18.07)	0.067
NSVT+ and BRS<3 ms/mm Hg		7.9 (1.97–32.01)	0.003

Survival Curves for arrhythmic events







- **The integration of traditional risk stratifiers, such as LVEF and NSVT, with autonomic markers, such as BRS and HRV**

➔ **Provide a more powerful approach to the early identification of post-MI patients at a risk for cardiac and arrhythmic mortality**

Implantable Cardioverter Defibrillator (ICD)

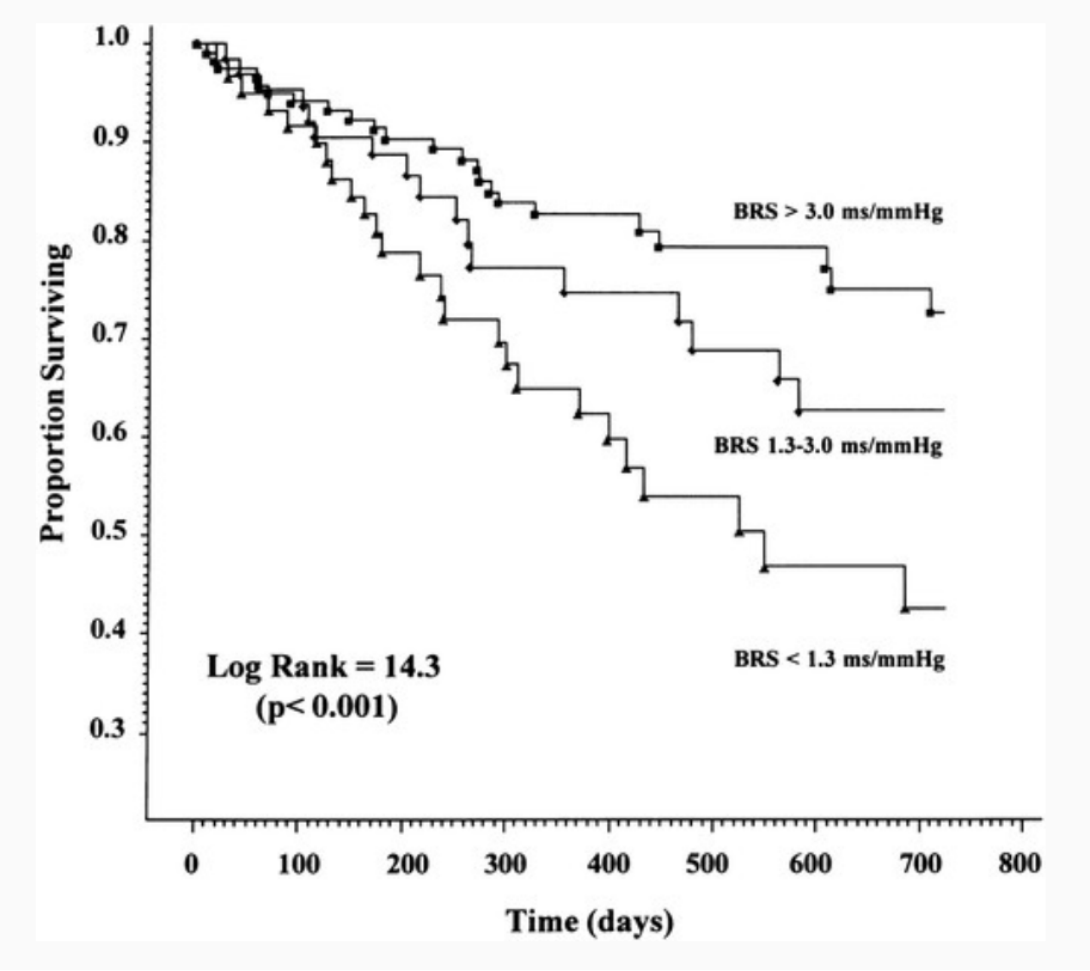
- **Mortality benefit**
  - **Ischemic and non-ischemic**

- **Primary prevention**
- **Secondary prevention**

➔ **The identification of patients at risk solely based on EF still remains a controversial issue**

- **Among post-MI patients with depressed EF and without NSVT**
  - **the presence or absence of an impaired BRS could identify two subgroups at significantly different 2-year cardiac mortality**
    - **18% vs 4.6% (P = 0.01)**

Circulation 2001;103:2072-2077

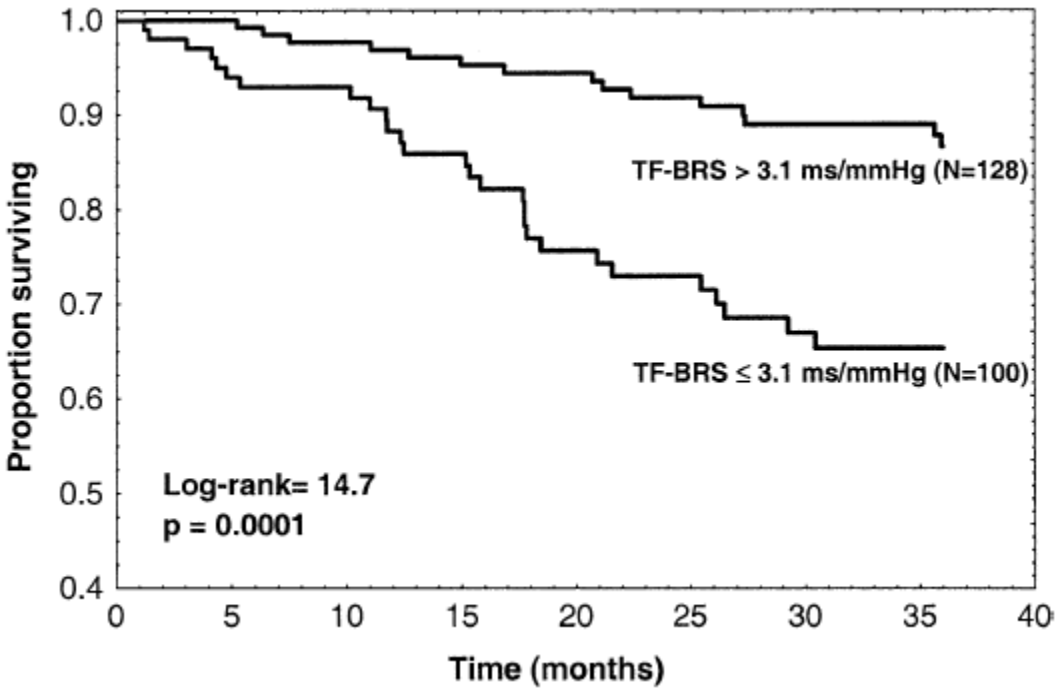


- 282 CHF patients (LVEF 23±6%)
- Primary events (cardiac death, nonfatal cardiac arrest, and status 1 priority transplantation)

Circulation 1997;96:3450-3458

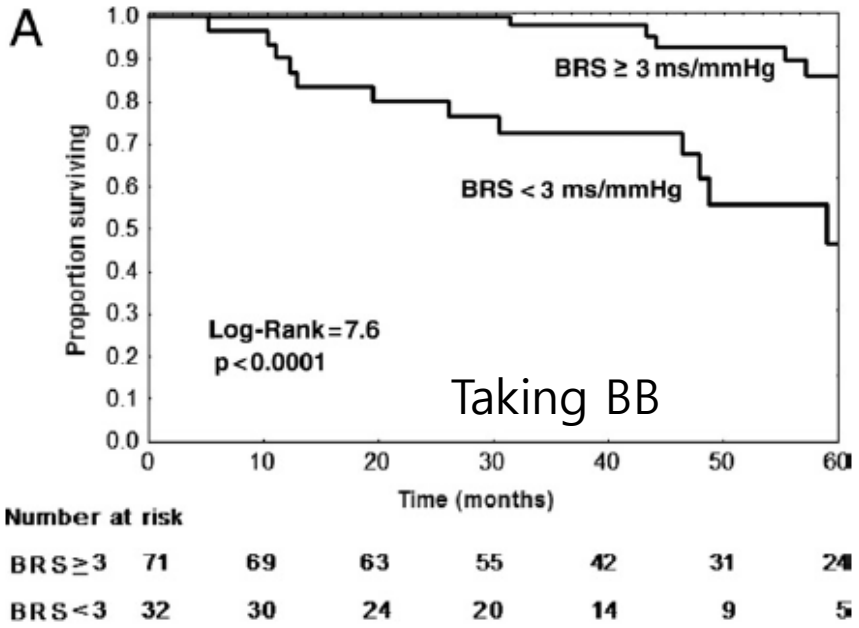
- 317 CHF patients (LVEF 27 (22-33%))
- BRS was measured by transfer function method
- Primary events (cardiac death, appropriate shock of ICD, and urgent transplantation)

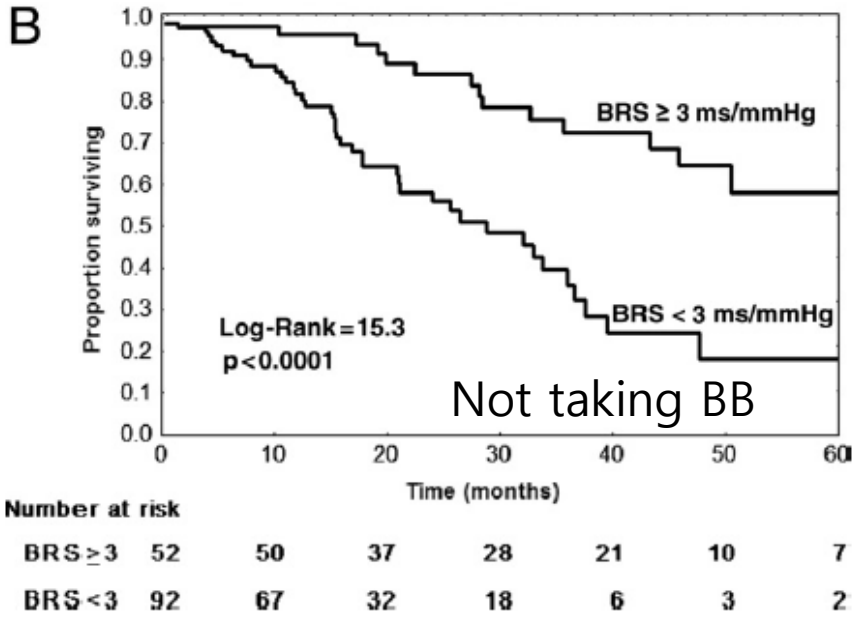
	TF-BRS (ms/mm Hg)
Etiology	
Ischemic cardiomyopathy	3.3 (1.5–5.9)
Idiopathic cardiomyopathy	4.0 (2.0–7.1)
NYHA functional class	
I–II	4.3 (2.4–8.0)
III–IV	2.2 (1.1–4.2)*
Mitral regurgitation	
0–1	4.1 (2.3–7.4)
2–3	2.2 (1.1–5.2)†
NSVT	
No	3.5 (1.8–6.6)
Yes	3.3 (1.6–6.1)



J Am Coll Cardiol 2005;40:79-84

- 103 CHF patients (LVEF 30%(22-33%))
- Treated vs. untreated of beta blocker
- BRS was measured by phenylephrine method
- Primary events (cardiac death, appropriate shock of ICD, and urgent transplantation)





J Am Coll Cardiol 2009;53:193-199

- Most of previous studies conducted before the routine use of neuroendocrine blockade and ICD

ESC European Society of Cardiology

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1306

RESEARCH ARTICLE

Assessment of baroreflex sensitivity has no prognostic value in contemporary, optimally managed patients with mild-to-moderate heart failure with reduced ejection fraction: a retrospective analysis of 5-year survival

Bartłomiej Paleczny[1,2,*], Martyna Olesińska-Mader[2], Agnieszka Siennicka[1,2], Piotr Niewiński[2,3], Krzysztof Nowak[2,3], Agnieszka Buldańczyk[1], Ewa A. Jankowska[2,3], Waldemar Banasiak[2], Stephan von Haehling[4], Beata Ponikowska[1], Stefan D. Anker[5,6], and Piotr Ponikowski[2,3]

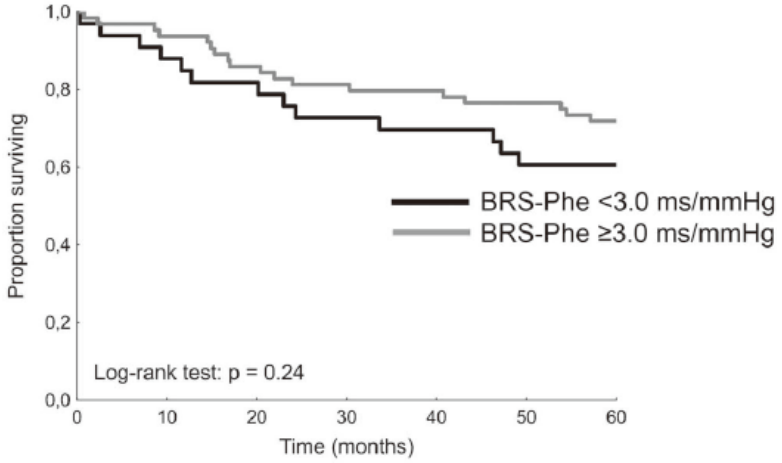
- 97 CHF patients (LVEF 32±6%)
- BRS was measured with three methods
  - Phenylephrine, sequence, and controlled breathing methods
- Mean 53±15 months f/u
- Endpoint : all-cause death and appropriate and documented ICD discharge

Eur J Heart Fail 2018 Sep 6; Epub

- **Correlations between cardiac BRS and clinical parameters in patients with HFrEF**

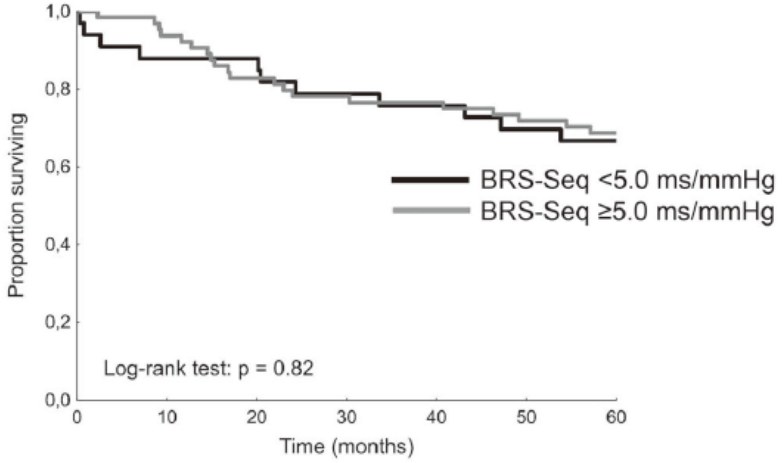
	BRS-Phe		BRS-Seq		BRS-CtrBr	
	r	*P*-value	r	*P*-value	r	*P*-value
Age, years	−0.32	0.001	−0.20	0.84	−0.26	0.01
Body mass index, kg/m^2	0.009	0.93	−0.19	< 0.05	−0.31	0.002
NYHA class I/II/III, %	−0.30	0.003	−0.16	0.12	−0.26	0.01
LVEF, %	0.27	0.006	0.06	0.57	0.06	0.66
Heart rate, b.p.m.	−0.01	0.92	−0.33	0.001	−0.14	0.20
SBP, mmHg	0.04	0.70	0.06	0.54	−0.16	0.12
Haemoglobin, g/dL	0.18	0.09	−0.22	0.04	−0.03	0.82
Creatinine, mg/dL	−0.03	0.73	−0.01	0.90	−0.04	0.71
Sodium, mmol/L	0.03	0.78	0.05	0.62	−0.09	0.39
Potassium, mmol/L	−0.02	0.88	−0.08	0.42	−0.18	0.10
Uric acid, mg/dL	−0.21	0.004	−0.27	0.008	−0.19	0.09
NT-proBNP, pg/mL	−0.13	0.19	−0.08	0.42	0.07	0.49
Peak VO_2, mL/kg/min	0.32	0.002	0.08	0.42	0.28	0.007
VE/VCO_2 slope	−0.29	0.005	−0.07	0.47	0.14	0.19
RER	0.06	0.57	0.08	0.42	0.15	0.18
KCCQ score (overall), pts	0.23	0.003	0.37	0.002	0.08	0.49
BRS-Phe, ms/mmHg	–	–	0.38	0.0001	0.29	0.004
BRS-Seq, ms/mmHg	0.38	0.0001	–	–	0.58	< 0.0001
BRS-CtrBr, ms/mmHg	0.29	0.004	0.58	< 0.0001	–	–
Mean RR, ms	0.09	0.36	0.37	0.0002	0.07	0.51
SDNN, ms	0.45	<0.0001	0.57	< 0.0001	0.23	0.03
pNN50, %	0.29	0.004	0.67	< 0.0001	0.30	0.003

A



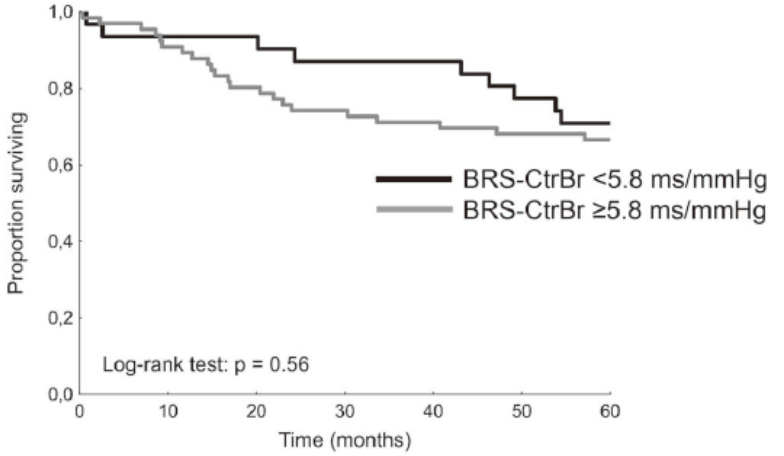
BRS-Phe <3.0 ms/mmHg	1.00	0.94	0.79	0.74	0.71	0.68	0.62
BRS-Phe ≥3.0 ms/mmHg	1.00	0.97	0.86	0.81	0.79	0.76	0.71

B



BRS-Seq <5.0 ms/mmHg	1.00	0.91	0.85	0.79	0.76	0.73	0.67
BRS-Seq ≥5.0 ms/mmHg	1.00	0.98	0.83	0.78	0.77	0.73	0.69

C



BRS-CtrBr <5.8 ms/mmHg	1.00	0.94	0.90	0.87	0.87	0.81	0.71
BRS-CtrBr ≥5.8 ms/mmHg	1.00	0.97	0.80	0.74	0.71	0.70	0.67

Neurally mediated syncope

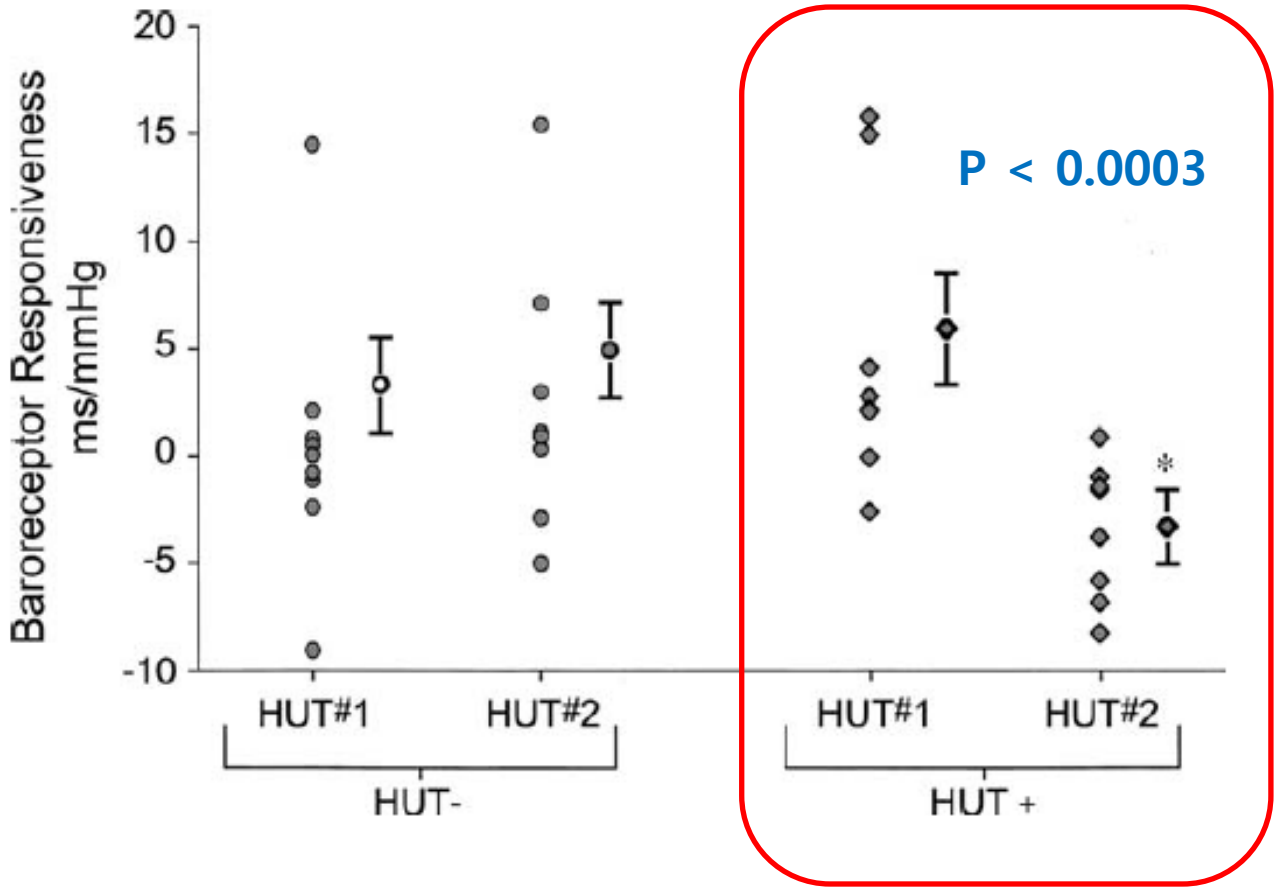
- The most common type of syncope
- Pathophysiological mechanism remain uncertain

- Autonomic nervous system
- Arterial baroreflex control of heart rate (baroreflex sensitivity, BRS) and vascular tone also play a role

Neurally mediated syncope

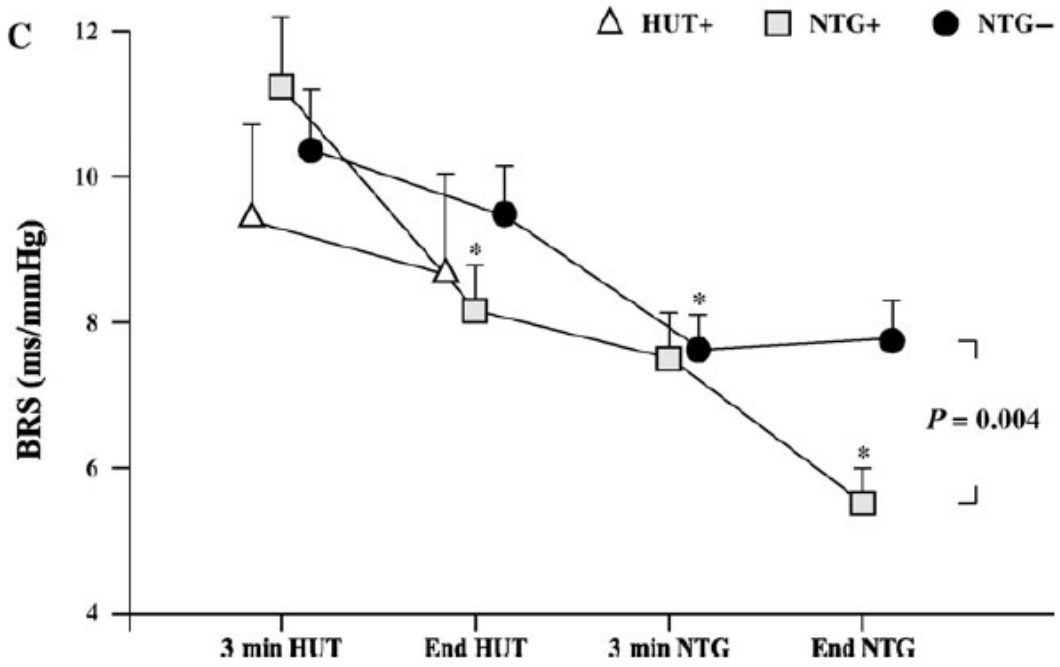
- The role of arterial baroreflex function in the pathophysiology of NMS is controversial.
- Most studies have failed to any clear evidence of alteration in arterial baroreflex control of heart rate
- A few have reported a reduction, or an increase in baroreflex activity

Circulation 1997;96:2509-13
Europace 2008;10:1170-1175
J Am Coll Cardiol 2003;41:1167-73



Europace 2004;6:48-54

	NTG−, $n = 39$	HUT+, $n = 21$	NTG+, $n = 37$	P ANOVA
Gender (M/F)	26/13	12/9	19/18	0.39
Age (years)	35 ± 13	32 ± 14	36 ± 12	0.55
Body mass index (kg/m^2)	25 ± 4	24 ± 3	23 ± 4†	0.027
Baroreflex sensitivity assessment				
SAP ramps (n/100 heart beats)	2.4 ± 2.2	2.0 ± 1.3	2.2 ± 1.7	0.75
BEI (%)	28 ± 19	44 ± 24†	48 ± 27†	<0.001
BRS (ms/mmHg)	12.8 ± 5.8	15.5 ± 7.4	16.8 ± 7.4†	0.048

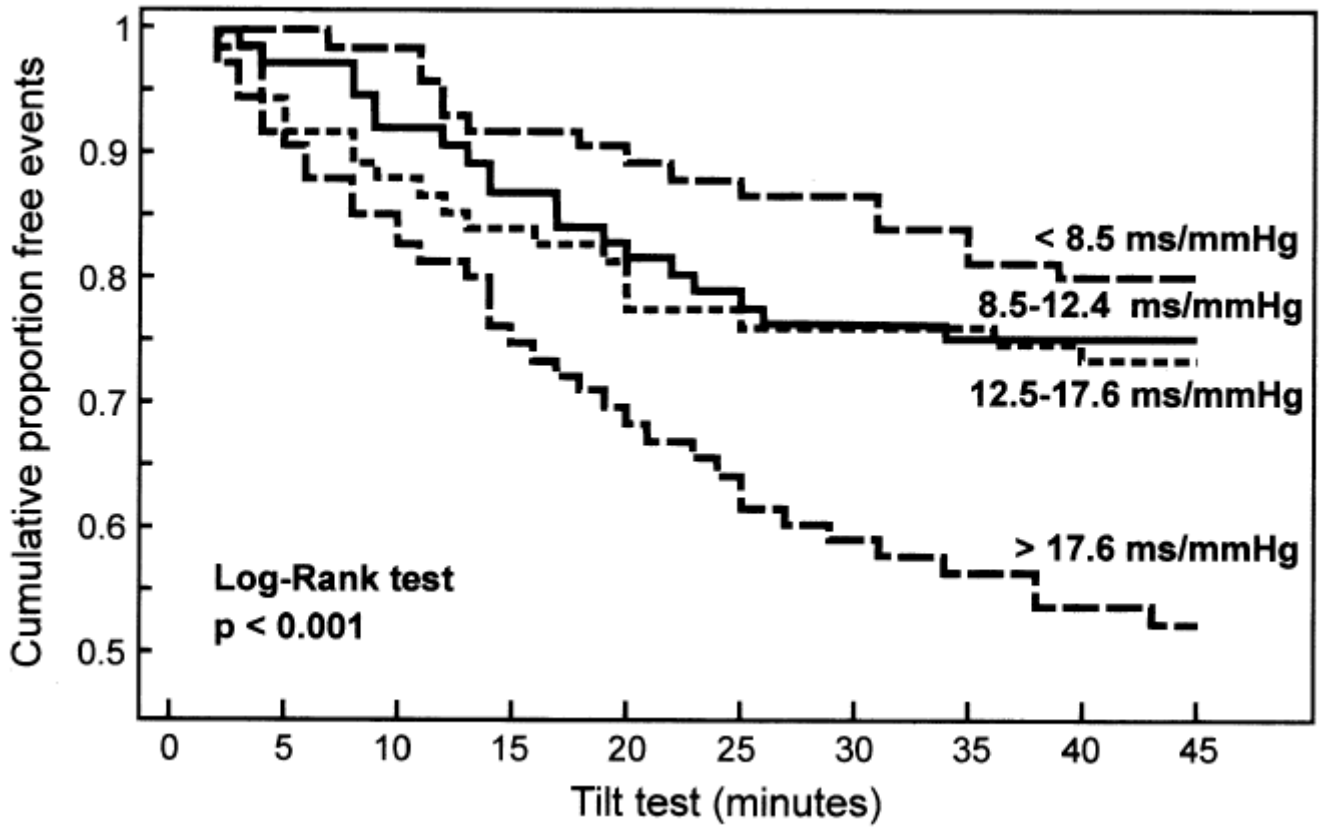


Europace 2008;10:1170-1175

	Tilt-Induced VVS (n = 94)	Negative Tilt Response (n = 216)	Control Group (n = 100)	ANOVA (p Value)	ANCOVA (Age-Adjusted p Value)
Age (yrs)	30 ± 14	38 ± 15	37 ± 14	0.00005	—
Males (%)	54	56	55	—	—
Height (m)	1.68 ± 0.12	1.67 ± 0.09	1.68 ± 0.11	NS	—
Mean R-R interval (ms)	906 ± 158	888 ± 145	883 ± 116	NS	—
Mean SAP (mm Hg)	125 ± 17	126 ± 18	123 ± 17	NS	—
Respiratory rate (breaths/min)	15 ± 3	15 ± 4	15 ± 4	NS	—
BRS-up (ms/mm Hg)	16.8 ± 10.1	13.2 ± 8.8	13.0 ± 8.8	0.003	NS
BRS-down (ms/mm Hg)	17.7 ± 9.7*	13.2 ± 7.7	12.8 ± 8.0	0.00002	0.007
BRS (ms/mm Hg)	17.4 ± 9.8*	13.2 ± 7.9	12.8 ± 8.2	0.0001	0.038
R-R intervals in baroreflex sequences (%)	30 ± 15	29 ± 15	32 ± 16	NS	—
BEI	0.59 ± 0.18	0.56 ± 0.19	0.58 ± 0.2	NS	—
Total SAP ramps (n)	102 ± 40	106 ± 41	107 ± 35	NS	—
SAP ramps in BRS-up sequences (n)	30 ± 16	29 ± 16	30 ± 16	NS	—
SAP ramps in BRS-down sequences (n)	31 ± 18	31 ± 18	33 ± 18	NS	—

- **Subjects with tilt-induced VVS showed greater resting BRS**
- **The enhanced reflex tachycardiac response to arterial baroreceptor deactivation at rest may represent a characteristic feature of subjects prone to tile-induced VVS**

J Am Coll Cardiol 2003;41:1167-1173

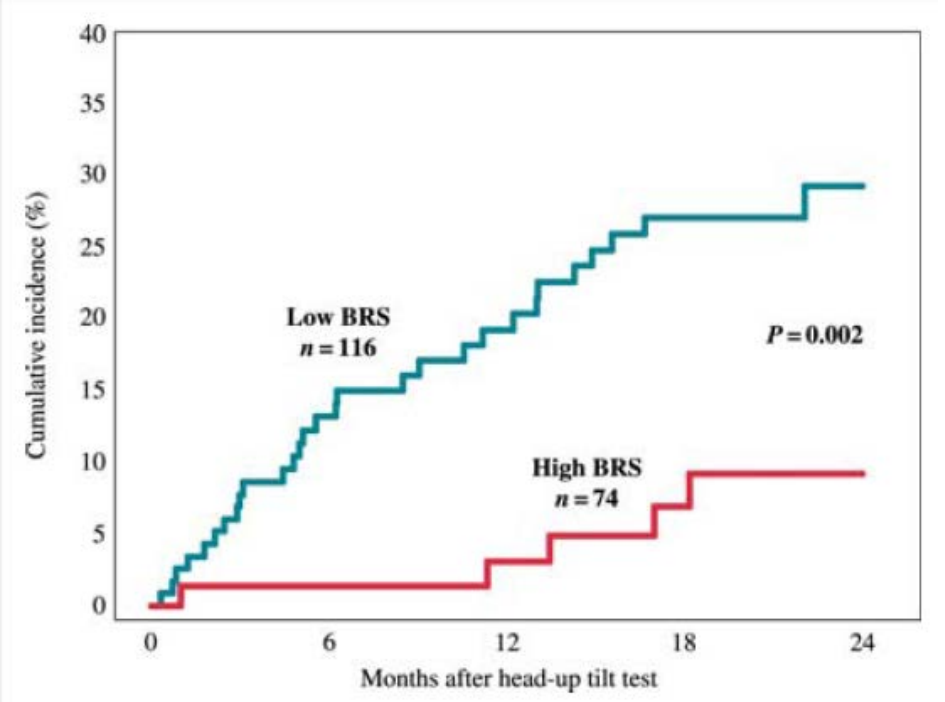


J Am Coll Cardiol 2003;41:1167-1173

Reduced BRS during HUT has independent role in predicting the recurrence of syncope

Cox's multivariate analysis of VVS recurrence during follow-up

	Hazard ratio (95% CI)	*P*-value
Model 1		
Female gender	3.19 (1.40–7.28)	0.006
≥3 syncope events before HUT	2.95 (1.26–6.87)	0.012
RR interval[a]	0.98 (0.71–1.34)	0.88
Baseline BRS	0.94 (0.88–1.00)	0.058
Model 2		
Female gender	3.01 (1.37–6.63)	0.006
≥3 syncope events before HUT	3.60 (1.46–8.83)	0.005
5 min HUT BRS	0.91 (0.84–0.99)	0.030
Model 3		
Female gender	2.86 (1.07–7.61)	0.036
≥3 syncope events before HUT3	5.49 (1.58–19.08)	0.007
5 min NTG BRS	0.73 (0.57–0.94)	0.016
5 min NTG BEI[a]	1.02 (0.74–1.40)	0.92



Europace 2010;12:1149-1155

Low BRS in supine position could be a predictor for determining the response to tilt training

Multivariate Analysis of Tilt Training Non-Response

	Hazard ratio (95% CI)	*p* value
Model 1		
BRS <8.945 in the supine position during the first session of tilt training	23.10 (1.20– 443.59)	0.037
MBP after upright posture	1.07 (0.96–1.18)	0.227
Frequency of syncope before initial diagnostic HUT	1.12 (0.87–1.43)	0.377
Total number of tilt training sessions	1.04 (0.50–2.17)	0.907
Model 2		
BRS <8.945 in the supine position during the first session of tilt training	29.62 (1.64–534.14)	0.022
MBP before syncope	1.07 (0.94–1.22)	0.312
Frequency of syncope before initial diagnostic HUT	1.08 (0.85–1.38)	0.544
Total number of tilt training sessions	0.95 (0.42–2.15)	0.895
Model 3		
BRS <8.945 in the supine position during the first session of tilt training	46.55 (1.66–1308.64)	0.024
Female gender	0.59 (0.03–12.86)	0.739
Frequency of syncope before initial diagnostic HUT	1.11 (0.88–1.40)	0.388
Total number of tilt training sessions	1.13 (0.54–2.39)	0.742

Yonsei Med J 2016;57:313-320

Summary

- **Baroreflex sensitivity**
  - **Cardiac mortality (arrhythmic event)**
  - **Neurally mediated syncope**
  - **Response of tilt training**

경청해 주셔서 감사합니다

Table 1 Number of estimates and variance for sequential (sBRS) and cross-correlation (xBRS) baroreflex sensitivity

	Number of estimates		Variance	
	sBRS	xBRS	sBRS[a]	xBRS
Lying	($n = 20$)	($n = 21$)	($n = 18$)	($n = 18$)
Mean	50	185	83	39
SD	63	84	129	53
Range	2–174	18–418	0–545	4–179
Standing	($n = 21$)	($n = 21$)	($n = 18$)	($n = 18$)
Mean	76	214	23	12
SD	78	106	34	17
Range	1–279	11–423	1–139	0–71

[a]Data from patients for whom there was no value for sBRS variance have been removed.

Table 3 Sequential (sBRS) and cross-correlation (xBRS) baroreflex sensitivity in patients with impaired baroreflex

	sBRS		xBRS	
File	Value	*n*	Value	*n*
b005s	1.2	1	0.8 ± 0.3	46
b005l	2.1 ± 0.6	2	2.3 ± 0.8	82
b010s	2.5	1	1.3 ± 0.4	11
b010l	2.2 ± 0.7	3	2.0 ± 1.8	18

Values are mean ± SD. *n*, Number of values obtained per record. Note that the number of sBRS estimates was so small that it was not always possible to establish a value for SD.

Table 2 Baroreflex sensitivity assessed by various methods

	EUROBAVAR			Local			
	Sequential	Spectral-LF	Spectral-HF	sBRS	TG-LF	TG-HF	xBRS
Lying	($n = 6^a$)	($n = 6^a$)	($n = 4^a$)	($n = 20$)	($n = 21$)	($n = 21$)	($n = 21$)
Mean	16.2	11.2	16.9	13.4	9.5	14.6	12.4
SD				9.8	10.7	12.3	12.1
Range				2.1–46	0.2–51	1.5–54	2.0–60
Standing		($n = 20^a$)		($n = 21$)	($n = 21$)	($n = 21$)	($n = 21$)
Mean		6.7		6.8	5.2	5.9	6.2
SD				3.9	3.8	4.3	3.9
Range				1.2–15.7	0.1–14.7	0.4–16.6	0.8–16.3
Ratio lying/standing	($n = 6^a$)	($n = 6^a$)	($n = 4^a$)	($n = 20$)	($n = 21$)	($n = 21$)	($n = 21$)
Mean	2.10	1.70	2.63	2.01	1.87	2.68	1.96
SD				0.97	1.02	1.43	0.92
Range				0.80–4.54	0.70–3.82	0.85–6.31	0.85–4.20

LF, HF, Low- and high-frequency; sBRS, sequential baroreflex sensitivity; TG, spectral transfer gain; xBRS, cross-correlation baroreflex sensitivity. *n*, Number of patients having at least one BRS estimate, or [a]number of procedures of that type returned by participating centres. EUROBAVAR pools the estimates obtained with the various techniques for the standing position because they differed little. Values for SD and range are between patients.