CHU Caen

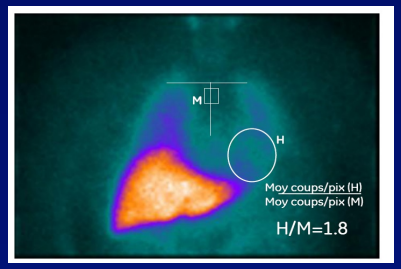
APPAC 14ème EDITION

ACTUALISATIONS ET PERSPECTIVES EN PATHOLOGIE CARDIOVASCULAIRE

UNICAEN université de Caen Basse-Normandie

Scintigraphie Cardiaque Adrénergique et Insuffisance Cardiaque

Pr Denis Agostini
Cardiologie Nucléaire
CHU Caen



Biarritz 2012

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ACTUALISATIONS ET PERSPECTIVES EN PATHOLOGIE CARDIOVASCULAIRE

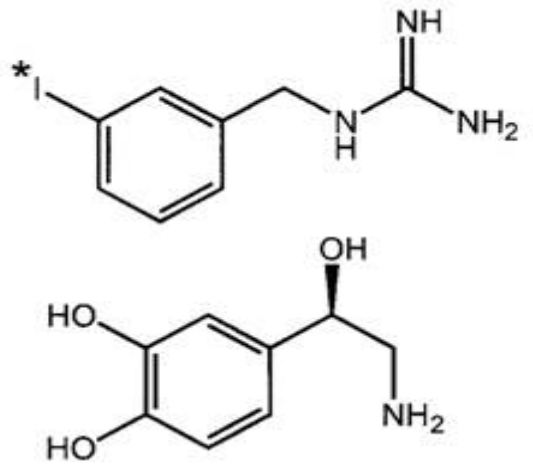
Denis Agostini

CHU Côte de Nacre
Caen

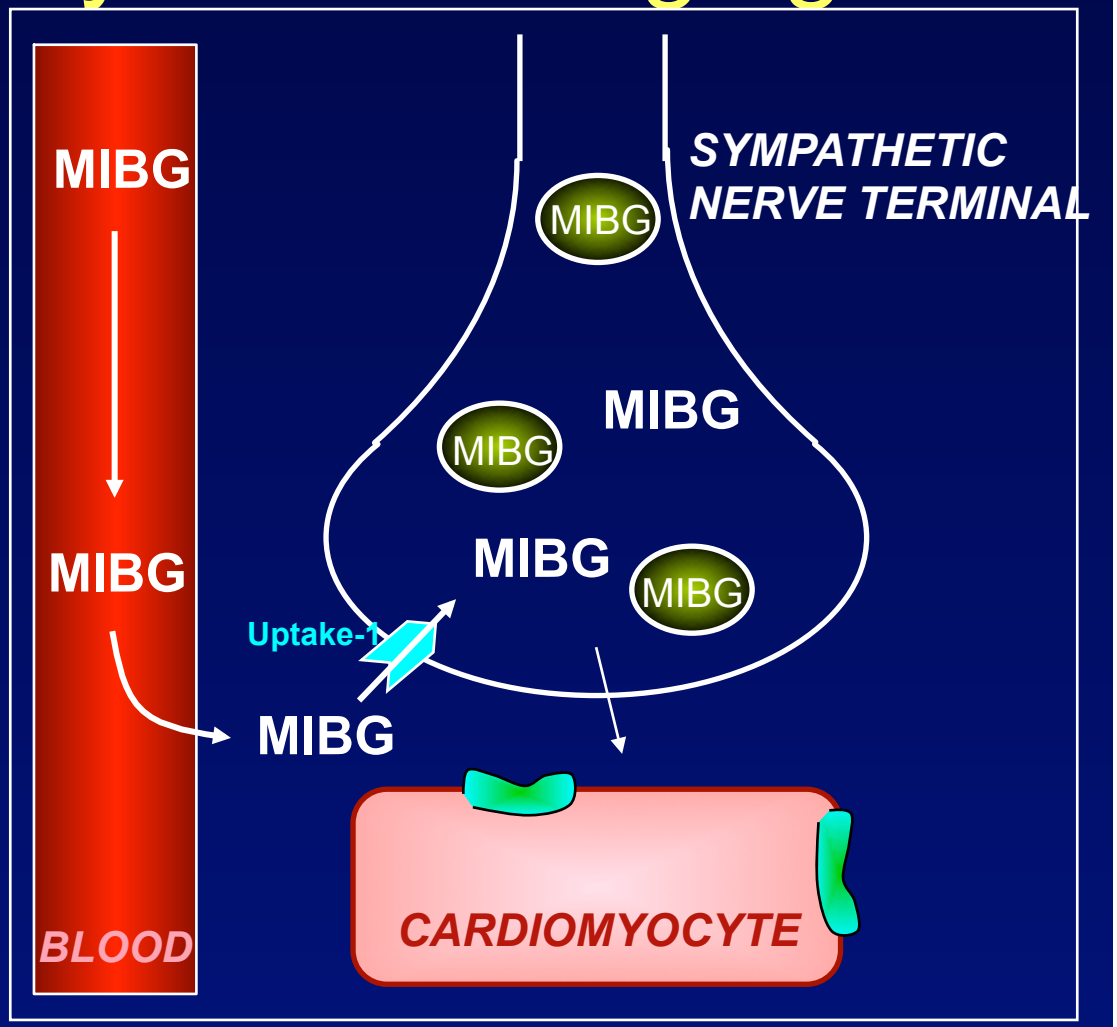
déclare avoir participé à des interventions ponctuelles (essais cliniques, travaux scientifiques, activités de conseil, conférences, colloques) pour Ge-Healthcare

Tracing Presynaptic Sympathetic Innervation by MIBG Imaging

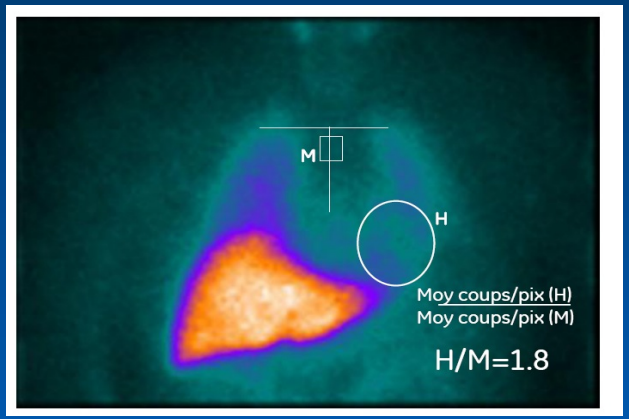
^{123}I-METAIODOBENZYL-GUANIDINE (MIBG)



NOREPINEPHRINE



Imaging the cardiac sympathetic innervation with mIBG

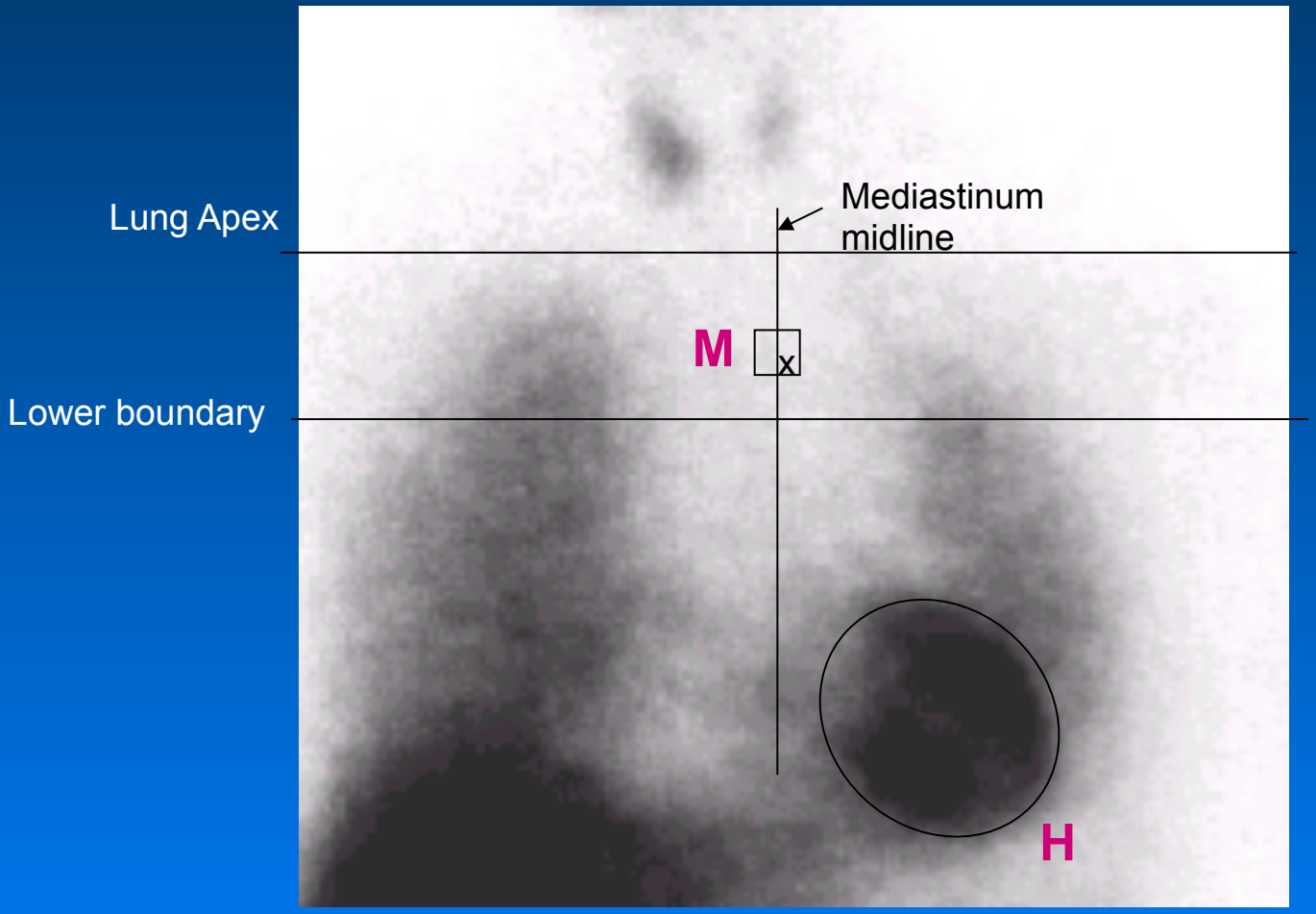


- The cardiac sympathetic innervation is measured by **Heart to Mediastinum ratio of mIBG uptake**
- **Heart / Mediastinum ratio (H/M ratio):**

  → **quantitation of cardiac uptake** of **mIBG** expressed in terms of the ratio of radioactive counts per imaging pixel between regions of interest (RoIs) **drawn around the heart (H)** and a region without noradrenaline activity such as the upper **mediastinum (M)**
- H/M ratio has been shown to have a high prognostic value in patients with heart failure
- **The lower the H/M ratio, the higher the risk of morbidity and mortality**

Agostini D *et al.* Eur J Nucl Med Mol Imaging 2008
Flotats A et al Eur J Nucl Med Mol Imaging 2010

Defining Heart and Mediastinum ROIs For H/M Ratio

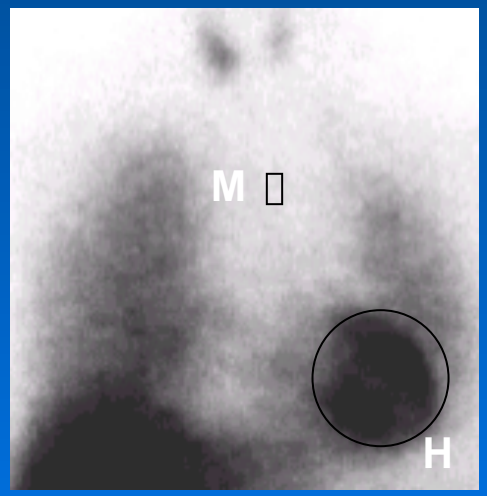


Standardized & simple procedure

Agostini et al EJNMMI 2009
Flotats et al EJNMI 2010

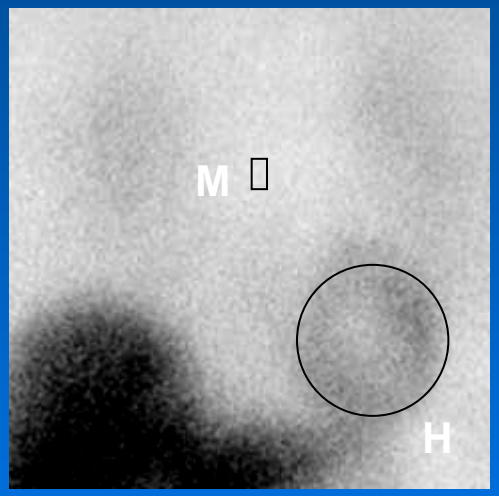
Reduction of mIBG activity and H/M Ratio reflects progressive worsening of heart failure

H/M Ratio: 2.3



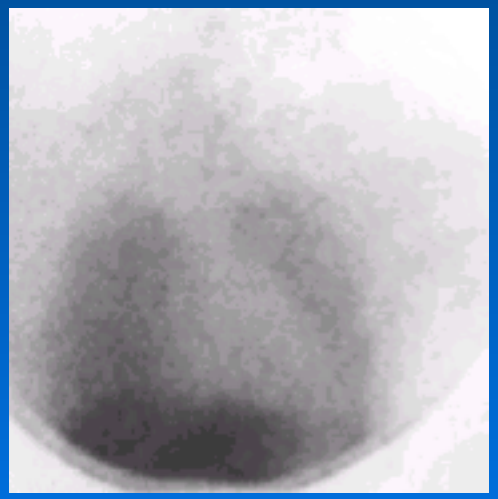
Normal innervation

1.7



NYHA Class II

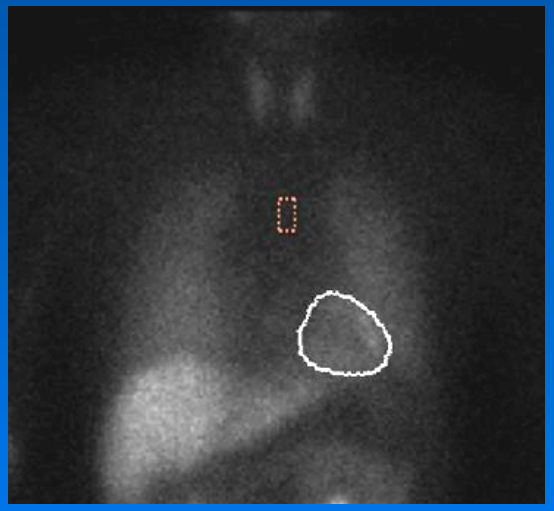
1.1



NYHA Class IV

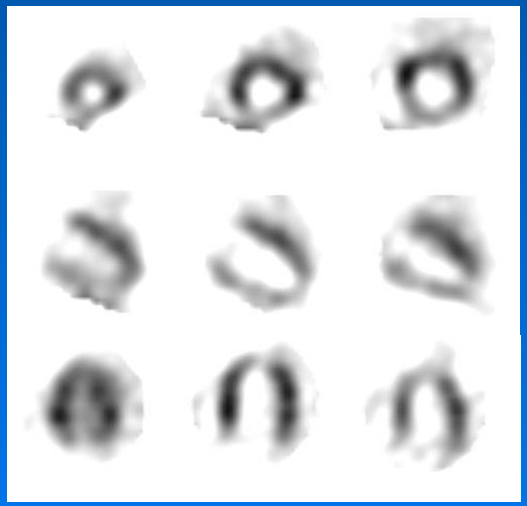
Data acquisition and analysis of MIBG imaging

Planar image



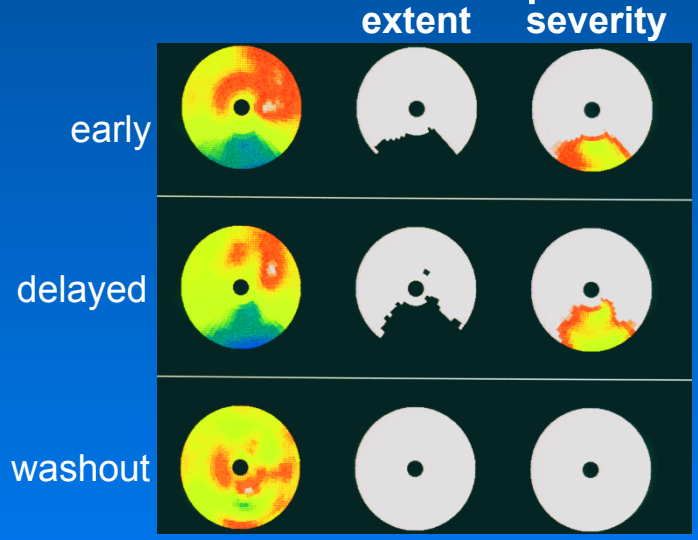
Heart/mediastinum ratio
and
washout rate

SPECT



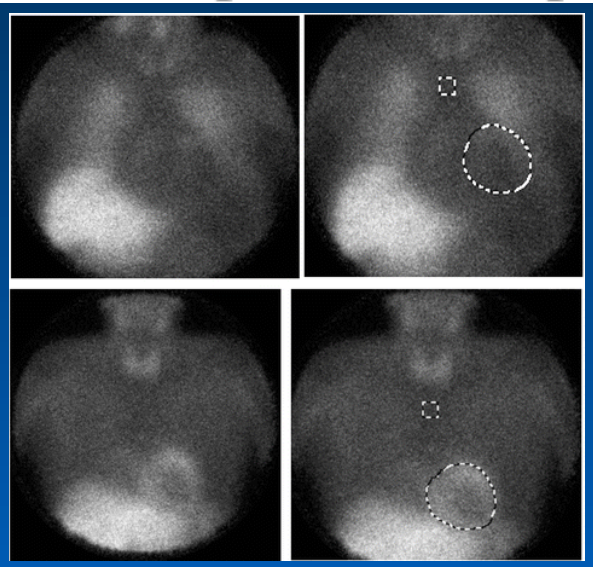
Visual assessment
defect score

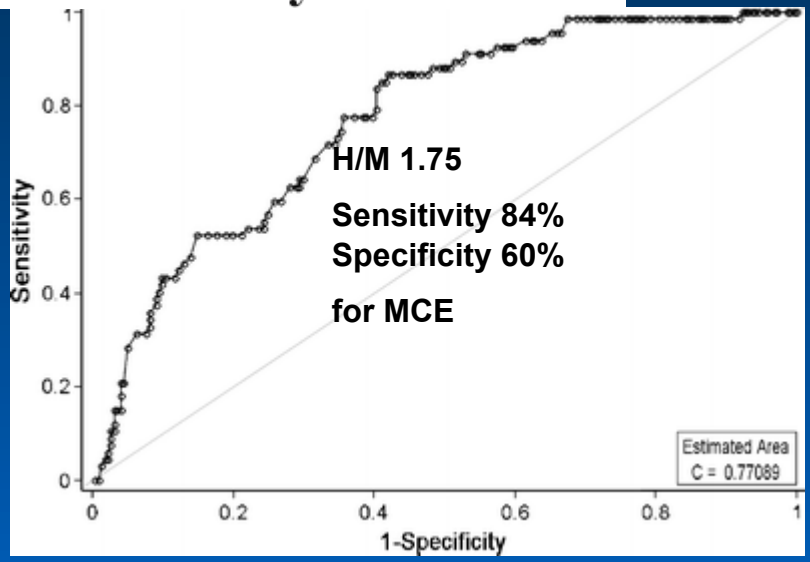
Polar map

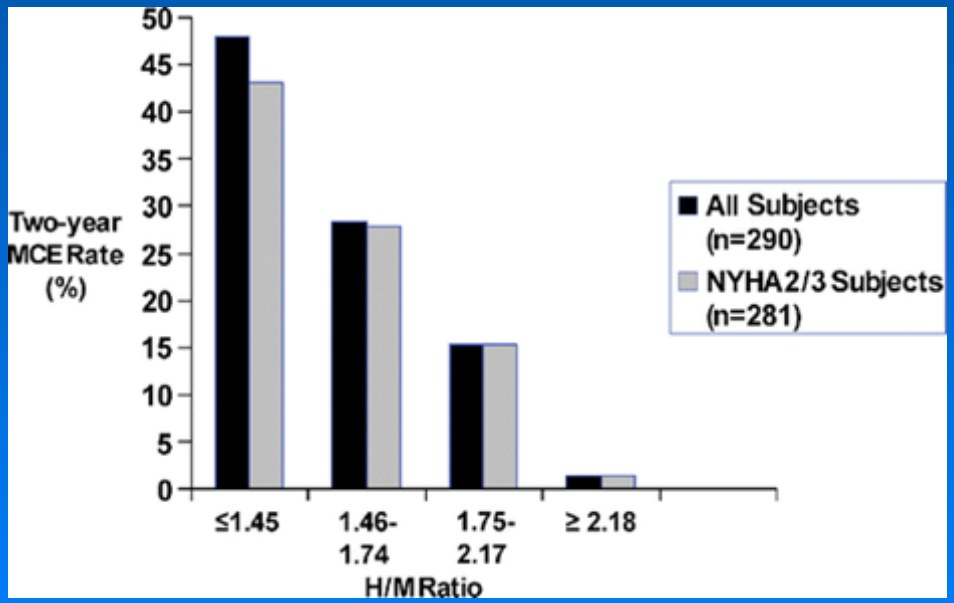


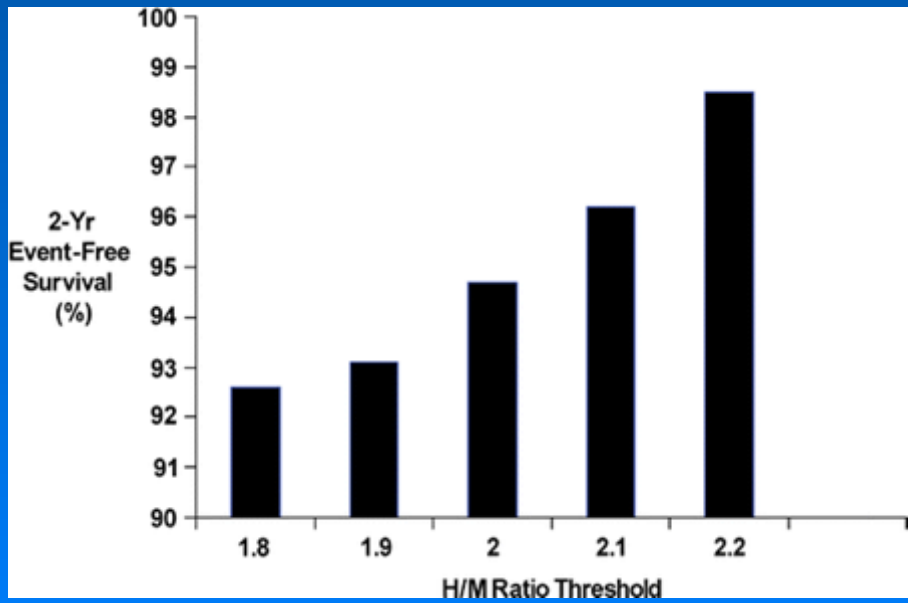
extent score
severity score
washout rate

I-123-*m*IBG myocardial imaging for assessment of risk for a major cardiac event in heart failure patients: insights from a retrospective European multicenter study



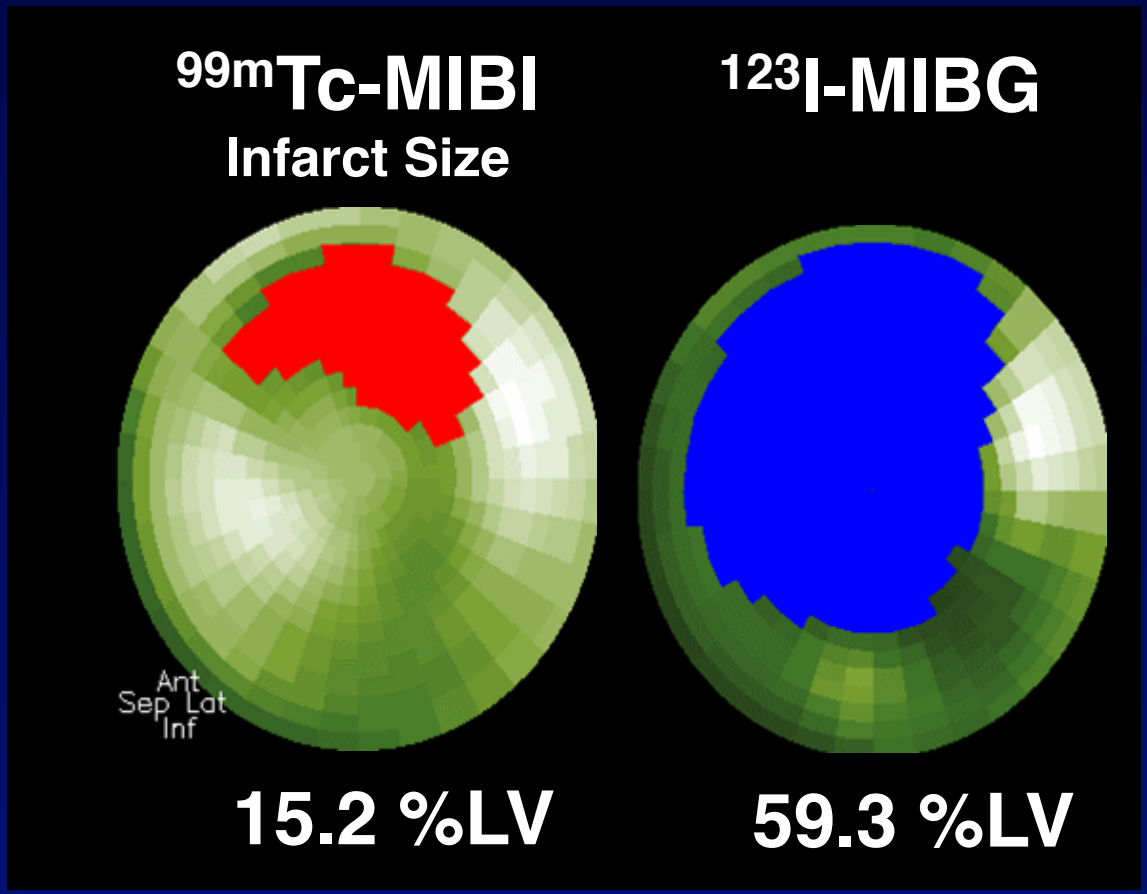






Agostini et al, EJNMMI 2008

Extent of Cardiac Sympathetic Denervation is far more EXTENSIVE than the infarct size



(perfusion – MIBG mismatch)

Matsunari et al. Circ 2000

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Myocardial Iodine-123 *Meta*-Iodobenzylguanidine Imaging and Cardiac Events in Heart Failure

Results of the Prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) Study

Arnold F. Jacobson, MD, PHD,* Roxy Senior, MD,† Manuel D. Cerqueira, MD,‡ Nathan D. Wong, PHD,§ Gregory S. Thomas, MD, MPH,§ Victor A. Lopez, BS,§ Denis Agostini, MD, PHD,‖ Fred Weiland, MD,¶ Harish Chandna, MD,# Jagat Narula, MD, PHD,§ on behalf of the ADMIRE-HF Investigators

Princeton, New Jersey; London, United Kingdom; Cleveland, Ohio; Irvine, California; Caen, France; Roseville, California; and Victoria, Texas

Jacc 2010

AdreView: New Risk Stratification Evidence from the ADMIRE-HF Study

ADMIRE-HF patients characteristics

965 pts

NYHA II/III - 83% class II, 17% class III

Ischaemic and non-ischaemic heart failure - 66% ischaemic, 34% non-isch.

LVEF ≤35%

Mean LVEF: 27% (range 5-35%)

Guidelines-based management including diuretic, statin (lipid reducer),

β-blockers, ACE inhibitors*, ARBs**, ARAs*** (Antihypertensive)

Mean age: 62.4 years

386 subjects had ICDs - 185 at baseline, 201 over course of study

*

ADMIRE-HF objective

Primary objective

- To demonstrate the prognostic value of the H/M ratio of AdreView for identifying subjects at higher risk of an adverse cardiac event

Secondary objectives

- To quantify the risks for adverse cardiac events due to heart failure and arrhythmias
- To assess myocardial sympathetic innervation H/M ratio as a continuous variable

ADMIRE-HF finding

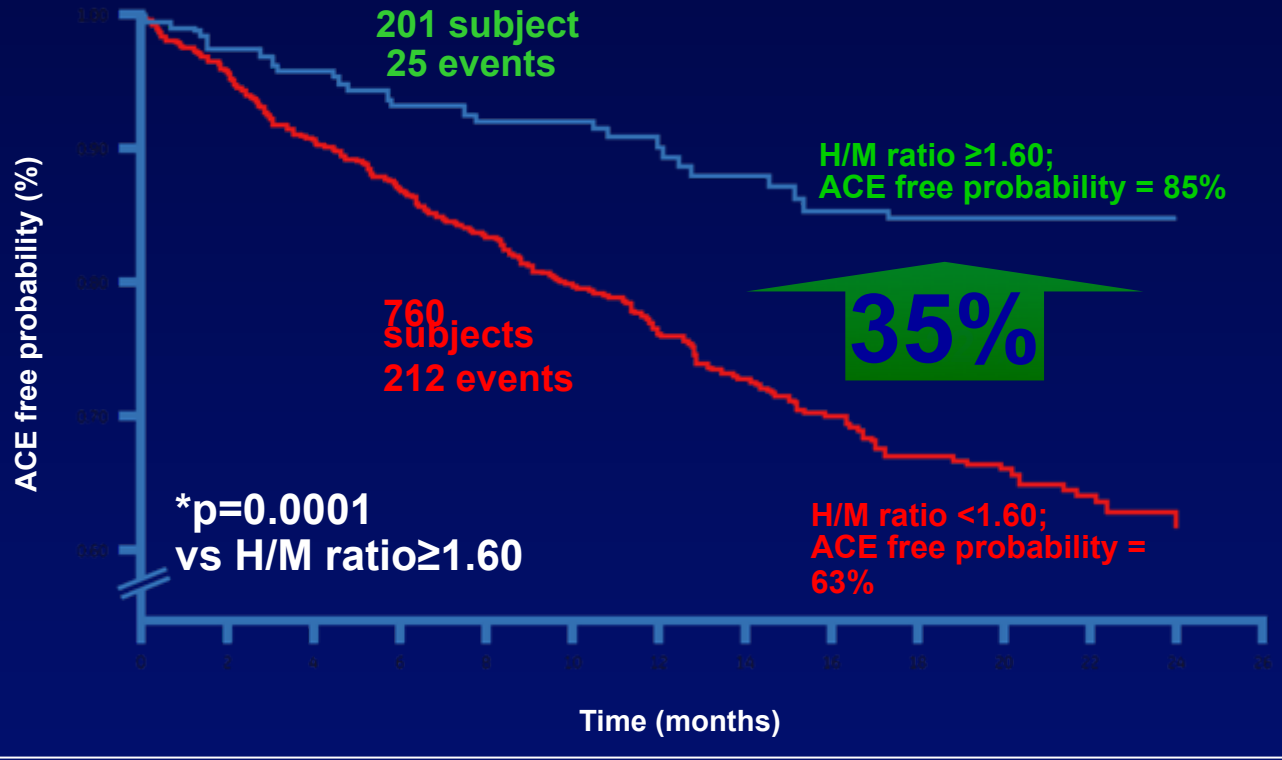
ADMIRE-HF supports a cut-off value for stratifying the risk of an adverse cardiac event

H/M ratio ≥1.6 – low risk

H/M ratio <1.6 – high risk

Kaplan-Meier estimates of ***ACE*** free probability H/M ratio

237 subjects had an adverse cardiac event on primary analysis



Separation from groups is evident within the first two months

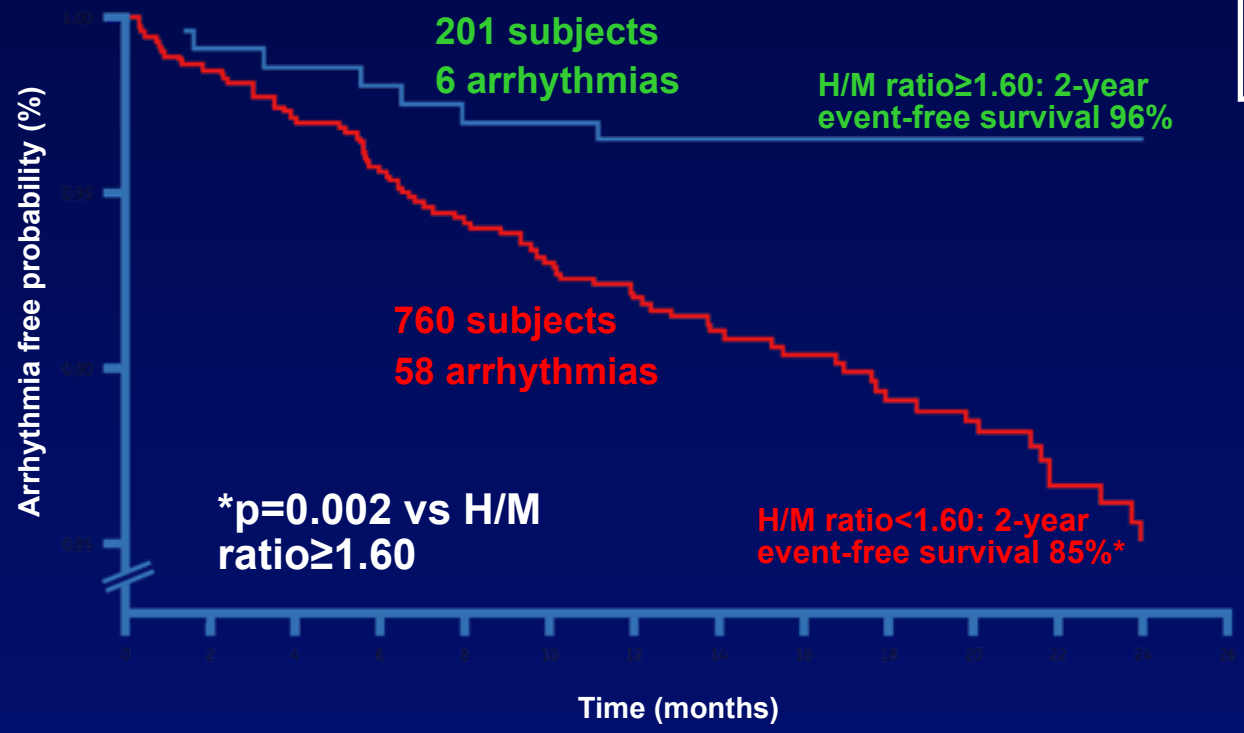
35% greater probability of not experiencing an adverse cardiac event for patients with an H/M ratio ≥1.6 vs. those with H/M ratio <1.6

AdreView: additional prognostic value for adverse cardiac event risk

Kaplan-Meier estimates of ***Arrhythmia*** free probability H/M ratio

64 patients had an arrhythmia on secondary analysis

Negative Predictive Value of arrhythmia likelihood is 96% NPV 96% for arrhythmias+++

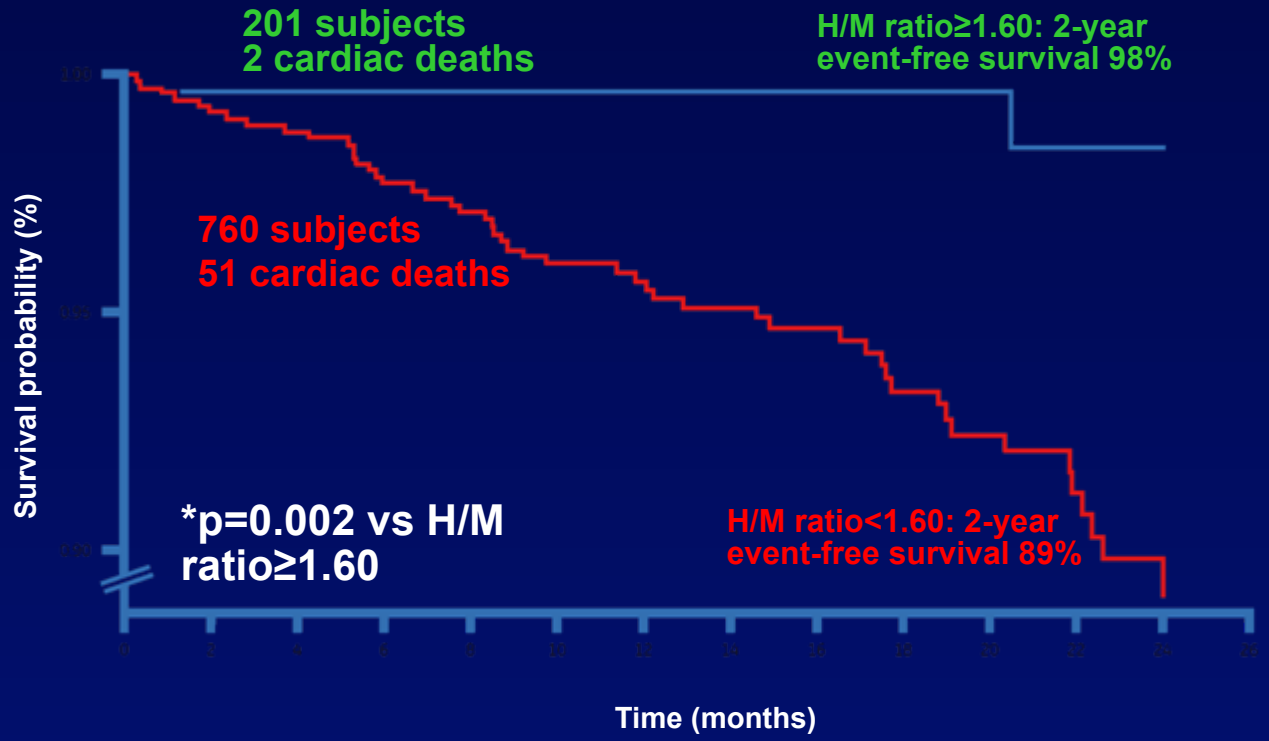


Greater arrhythmia-free survival at 2 years for patients with H/M ratio ≥1.6 vs. those with H/M ratio of <1.6

AdreView: proven prognostic value for Arrhythmias

Kaplan-Meier estimates of ***Survival*** probability H/M ratio

53 patients died of cardiac death on secondary analysis



Negative Predictive Value of cardiac death likelihood is 98%

NPV 98% for cardiac death[21]

Significantly greater probability of survival at 2 years for patients with H/M ratio ≥1.6 vs. those with H/M ratio <1.6[18]

AdreView: additional prognostic value for cardiac mortality

CONCLUSION

ADMIRE-HF demonstrated:

- A significant prognostic value of the H/M ratio (<1.60 vs ≥ 1.60) for each of the categories in the composite endpoint for identifying higher vs lower risk for adverse cardiac events in HF patients
- A 10-fold difference in cardiac mortality rate between the highest and lowest risk sub-populations (H/M ratio <1.20 and >1.60)

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Cardiac Sympathetic Denervation Assessed With 123-Iodine Metaiodobenzylguanidine Imaging Predicts Ventricular Arrhythmias in Implantable Cardioverter-Defibrillator Patients

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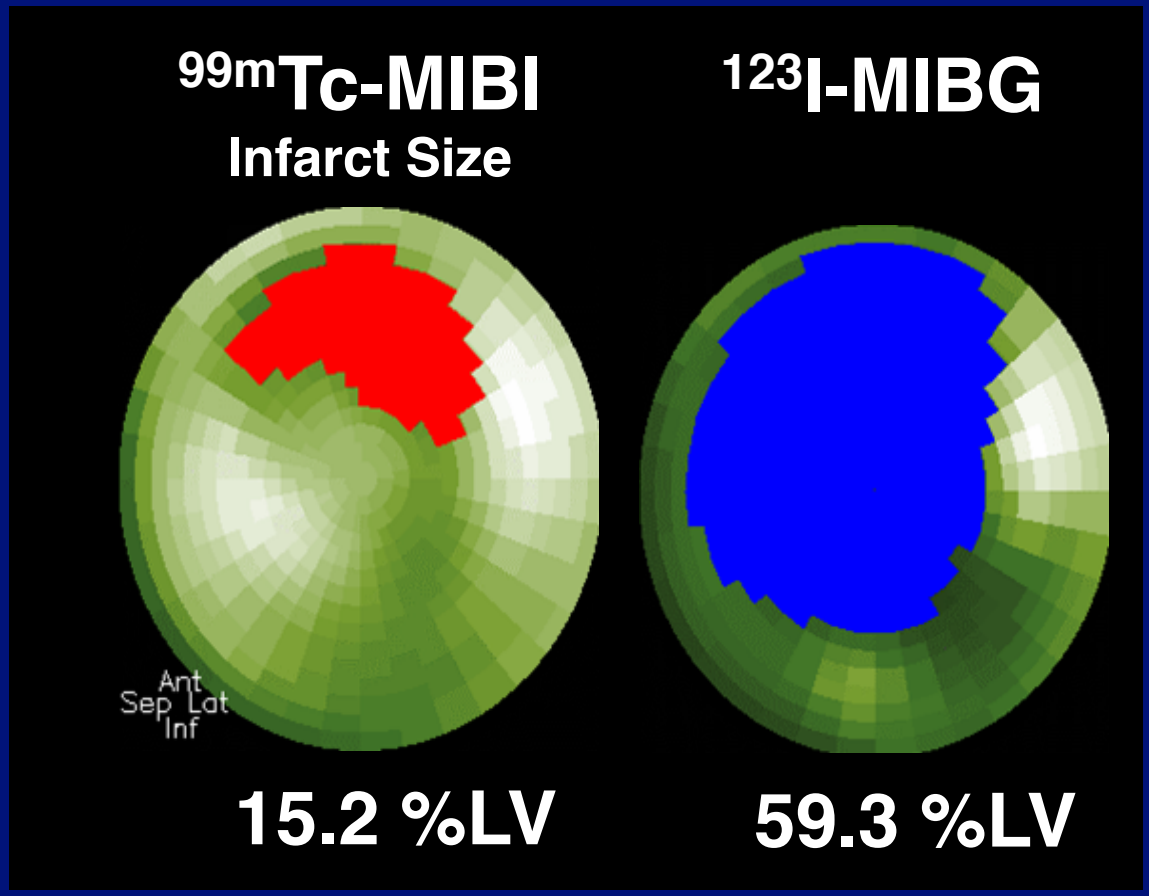
Rutger J. van Bommel, MD,* Jan van Ramshorst, MD,* Eric Boersma, PHD,§
Petra Dibbets-Schneider, MSC,† Marcel P. Stokkel, MD, PHD,† Ernst E. van der Wall, MD, PHD,*
Martin J. Schalij, MD, PHD,* Jeroen J. Bax, MD, PHD*

Leiden, Utrecht, and Rotterdam, the Netherlands

Could MIBG imaging be the gatekeeper for ICD implantation in primary prevention of sudden death?

Boogers et al. JACC 2010

Extent of Cardiac Sympathetic Denervation is far more EXTENSIVE than the infarct size



(perfusion – MIBG mismatch)

Matsunari et al. Circ 2000

Study Population (n = 116)

116 consecutive patients referred for ICD implantation based on guidelines for primary prevention

Baseline characteristics of the study population (n = 116)

Characteristics	Values
Age (yrs)	65 ± 9
Male	80 (69)
Ischemic cardiomyopathy	86 (74)
NYHA functional class	3.0 ± 0.5
LVEF (%)	27 ± 8

Study Protocol

Before ICD implantation:

123-I MIBG scintigraphy
Planar and SPECT
Early and delayed imaging

99m-Tc Tetrofosmin perfusion imaging
Stress-rest protocol (adenosine)

Endpoints

Clinical Follow-up
From ICD implantation to first documented:

Appropriate ICD therapy (prim endpoint)
ATP or ICD shock induced by ventricular tachyarrhythmia

ICD therapy + Cardiac mortality (sec endpoint)

Results at 3 yr follow-up

Primary endpoint (n = 24)

86 episodes of appropriate ICD therapy in 24 pts (21%)

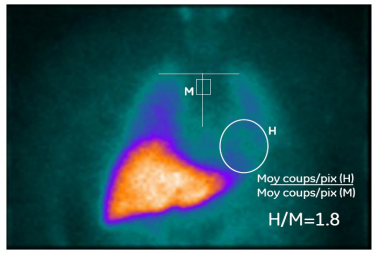
Secundary endpoint (n = 32)

Composite of appropriate ICD therapy or cardiac death in 32 pts (28%)

Predictors for ICD therapy (prim endpoint) - Imaging variables

Univariable and multivariable analyses of baseline imaging variables

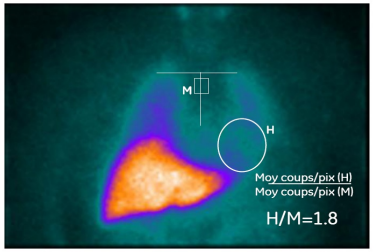
	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
123-I MIBG imaging				
Early H/M ratio	0.43 (0.05 - 4.11)	0.5		
Late H/M ratio	0.32 (0.04 - 2.81)	0.3		
Cardiac washout rate (%)	1.03 (0.96 - 1.10)	0.5		
Early summed score	1.08 (1.03 - 1.12)	<0.01*		
Late summed score	1.15 (1.09 - 1.22)	<0.01*	1.15 (1.07 - 1.23)	<0.01*
^{99m}Tc-tetrofosmin GMPS imaging				
Summed rest score	1.02 (0.98 - 1.06)	0.4		
Summed stress score	1.03 (0.99 - 1.07)	0.2		
Summed difference score	1.07 (0.98 - 1.16)	0.13*	0.98 (0.87 - 1.11)	0.7
123-I MIBG/GMPS mismatch score	1.06 (1.02 - 1.09)	<0.01*	1.01 (0.98 - 1.04)	0.5



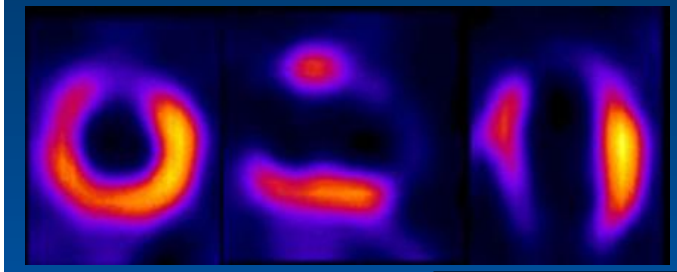
Predictors for ICD therapy or cardiac death (sec endpoint) – imaging variables

Univariable and multivariable analyses of baseline imaging variables

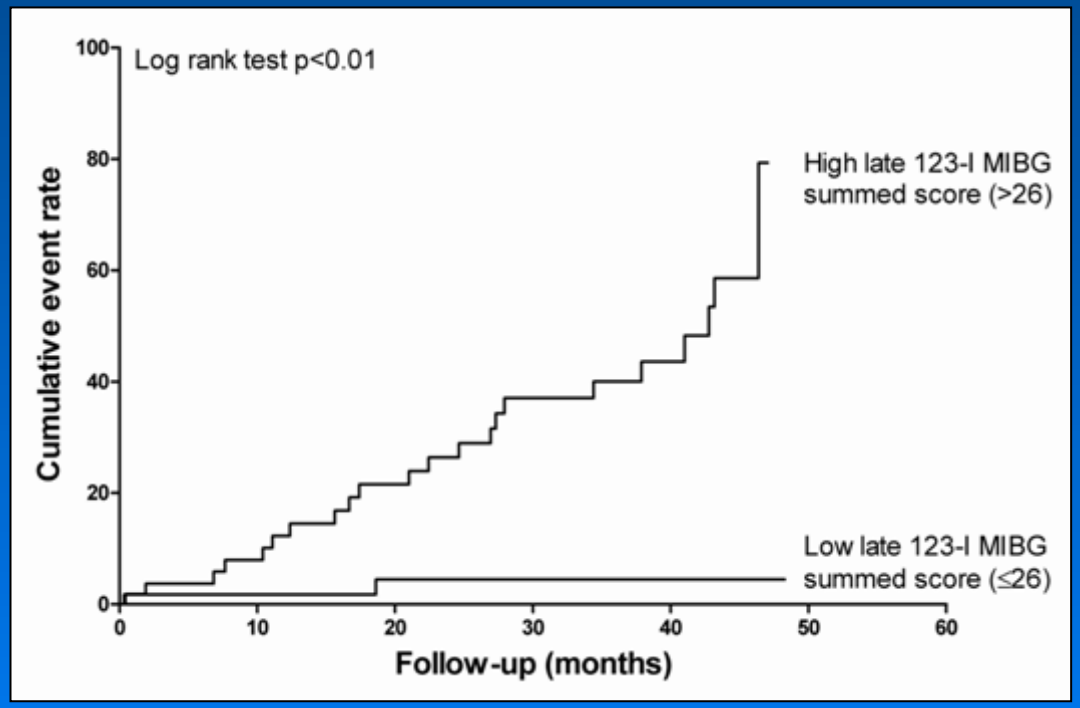
	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
123-I MIBG imaging				
Early H/M ratio	0.30 (0.04 - 2.19)	0.2		
Late H/M ratio	0.21 (0.03 - 1.36)	0.10*	0.36 (0	
Cardiac washout rate (%)	1.04 (0.98 - 1.10)	0.2		
Early summed score	1.08 (1.04 - 1.12)	<0.01*		
Late summed score	1.13 (1.09 - 1.19)	<0.01*	1.12 (1.06 - 1.18)	<0.01**
^{99m}Tc-tetrofosmin GMPS imaging				
Summed rest score	1.02 (0.99 - 1.06)	0.3		
Summed stress score	1.02 (0.99 - 1.06)	0.2		
Summed difference score	1.03 (0.95 - 1.13)	0.5		
123-I MIBG/GMPS mismatch score	1.05 (1.02 - 1.08)	<0.01*	1.01 (0.98 - 1.04)	0.5



Cumulative event rate for ICD therapy



Population divided according to median MIBG summed defect score (26)

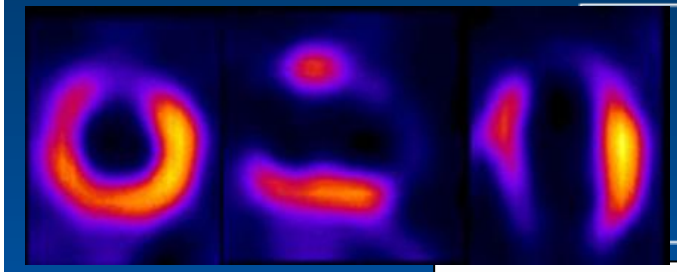


52%

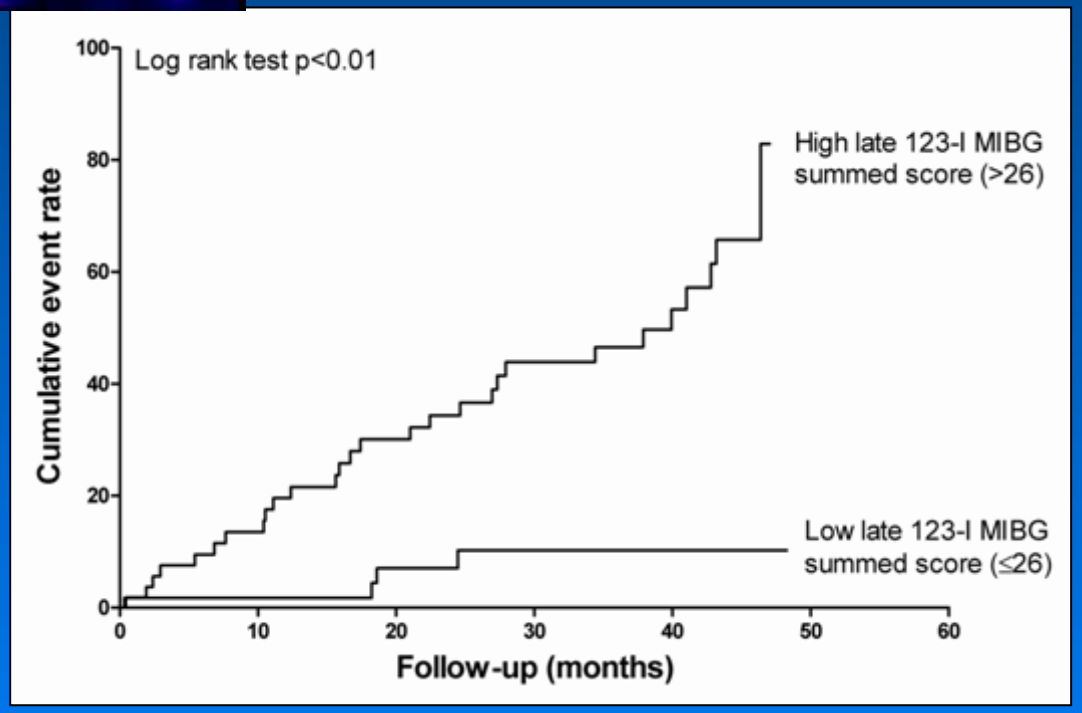
5%

Cumulative event rate 52% vs. 5%
3-year follow-up data

Cumulative event rate for ICD therapy or cardiac death



☞ Population divided according to mean MIBG summed defect score (26)



57%

10%

Cumulative event rate 57% vs. 10%
3-year follow-up data

New SPECT camera for cardiac imaging : very fast -high sensitivity- low radioactivity

Further validation REQUIRED with I-123-MIBG