DIU imagerie cardiaque et vasculaire

Rôle pronostique de l'imagerie isotopique

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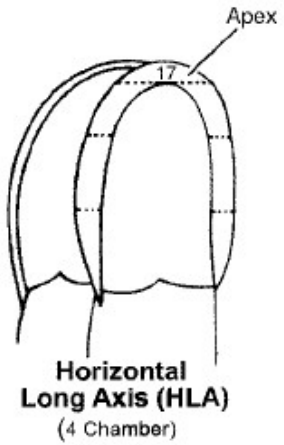
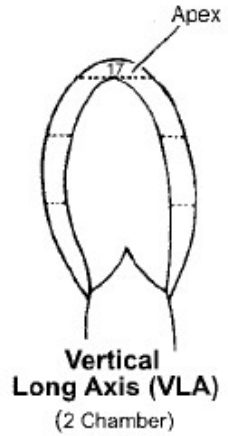
- Université Paris Diderot, Sorbonne Paris Cité, France

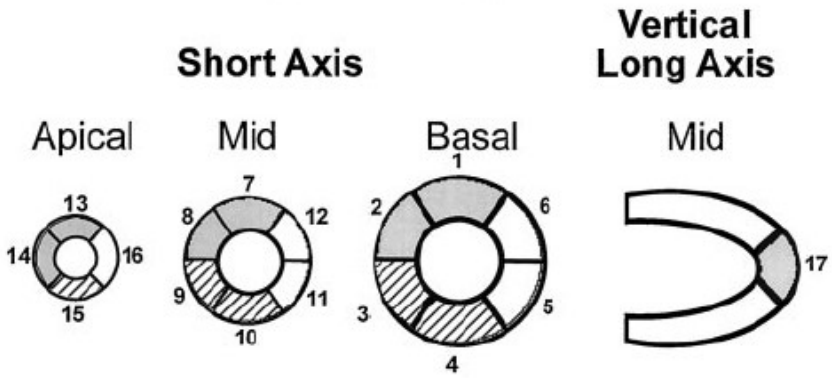
Perfusion & Fonction myocardique

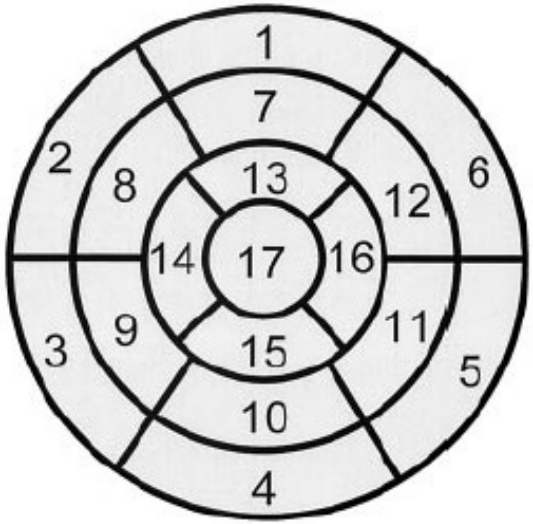
Etendue des anomalies perfusionnelles

Modèle à 17 segments

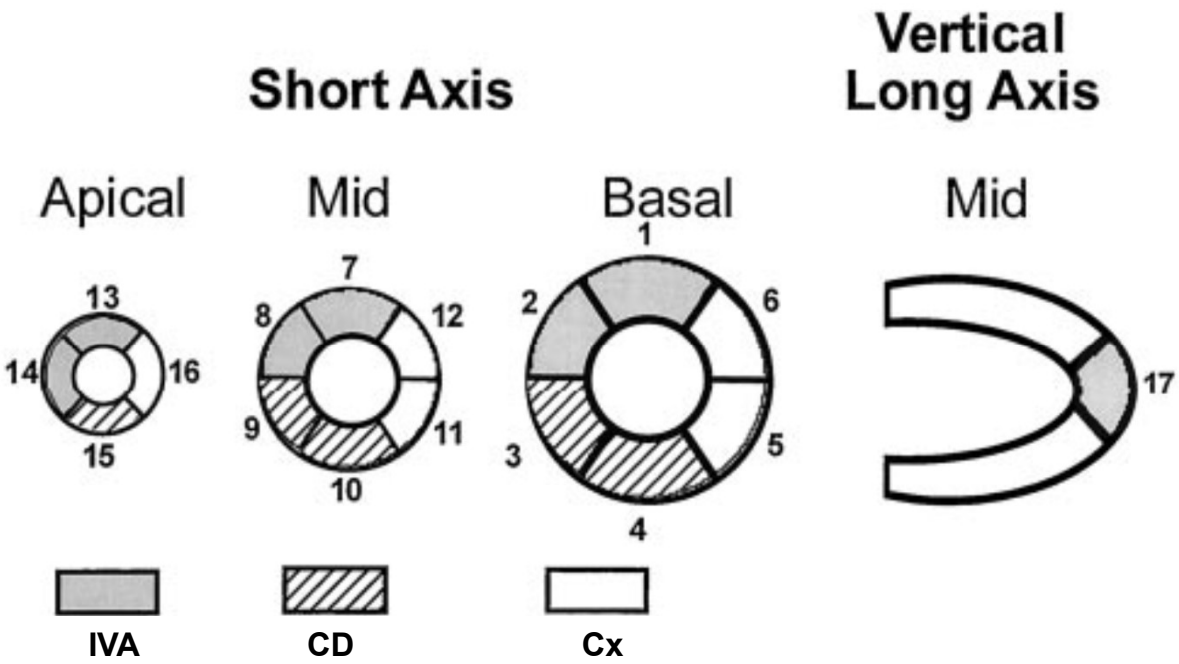








Systématisation vasculaire du myocarde



IVA : artère interventriculaire antérieure

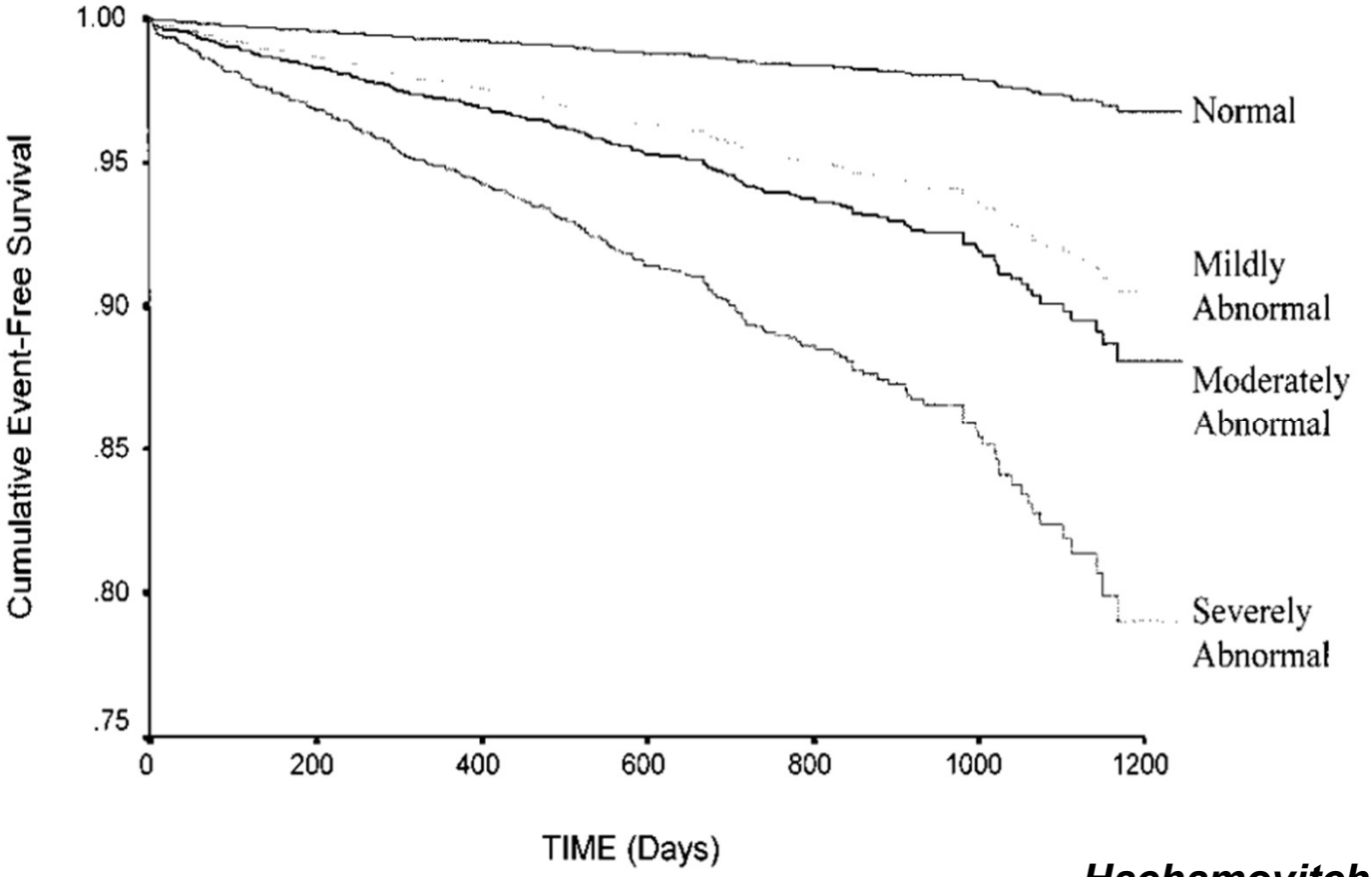
Cx : artère circonflexe

CD : coronaire droite

Valeur pronostique de la SPECT

Prognostic value (summed score)

5183 patients, follow-up 642±226 days



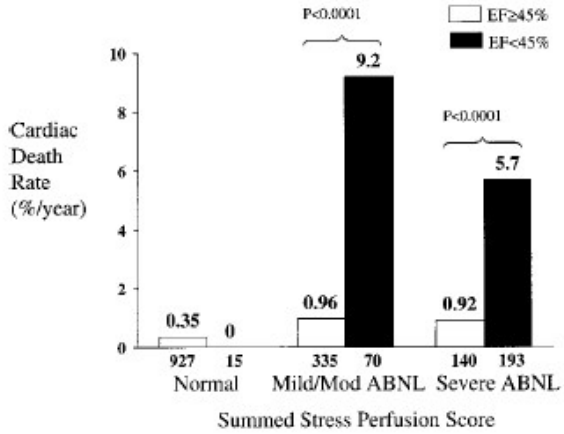
Hachamovitch et al., Circulation 1998

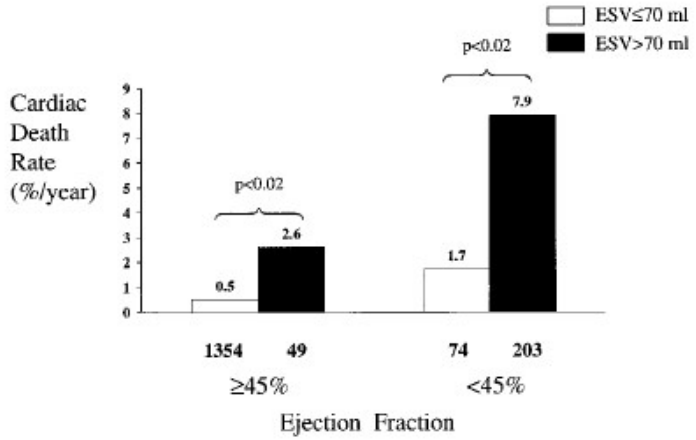
Valeur pronostique: gated-SPECT

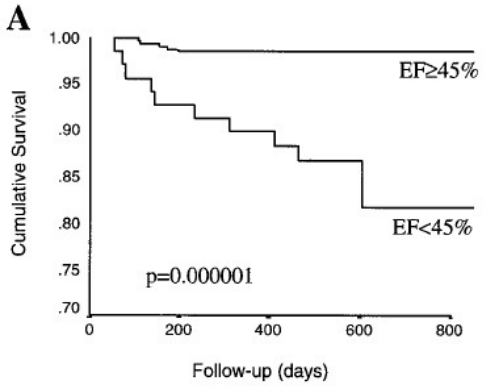
Valeur additionnelle indépendante FEVG et VTS post-stress

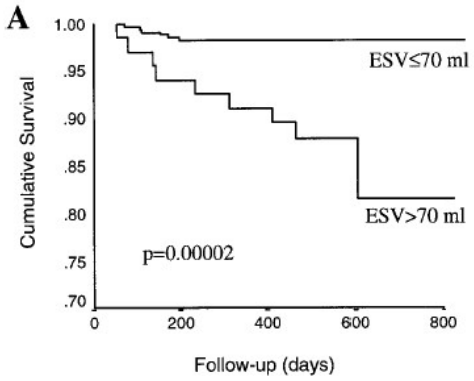
1680 patients

Suivi : 569±106 jours









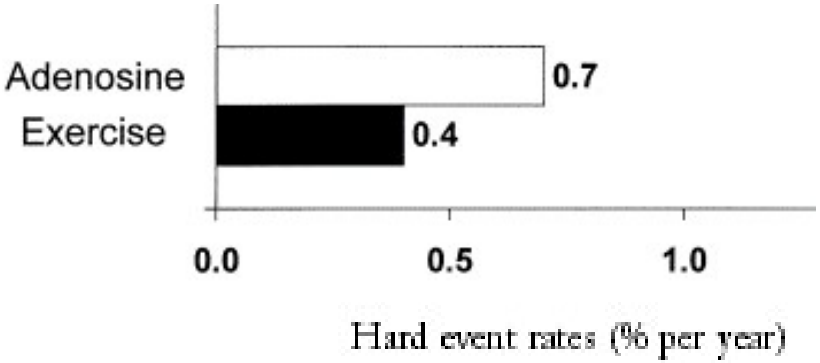
anomalies perfusionnelles légères à modérées

Sharir et al, Circulation 1999

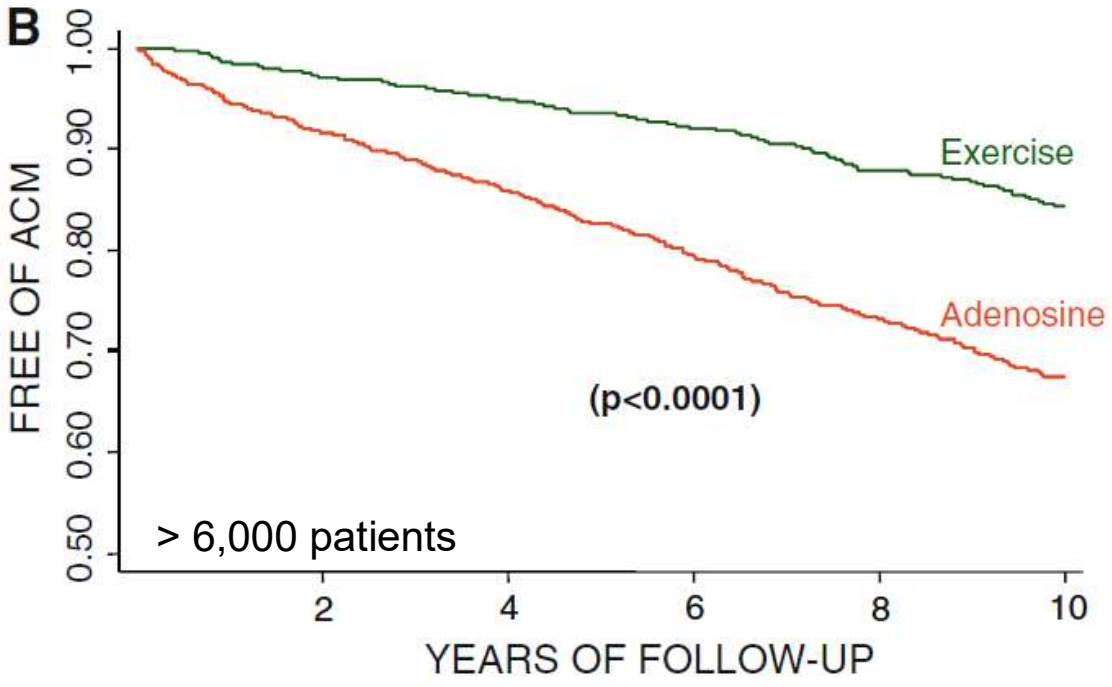
Exercise *vs.* Pharmacologic stress

Valeur prédictive négative

7376 patients, follow-up 665±200 days



Hachamovitch et al., J Am Coll Cardiol 2003



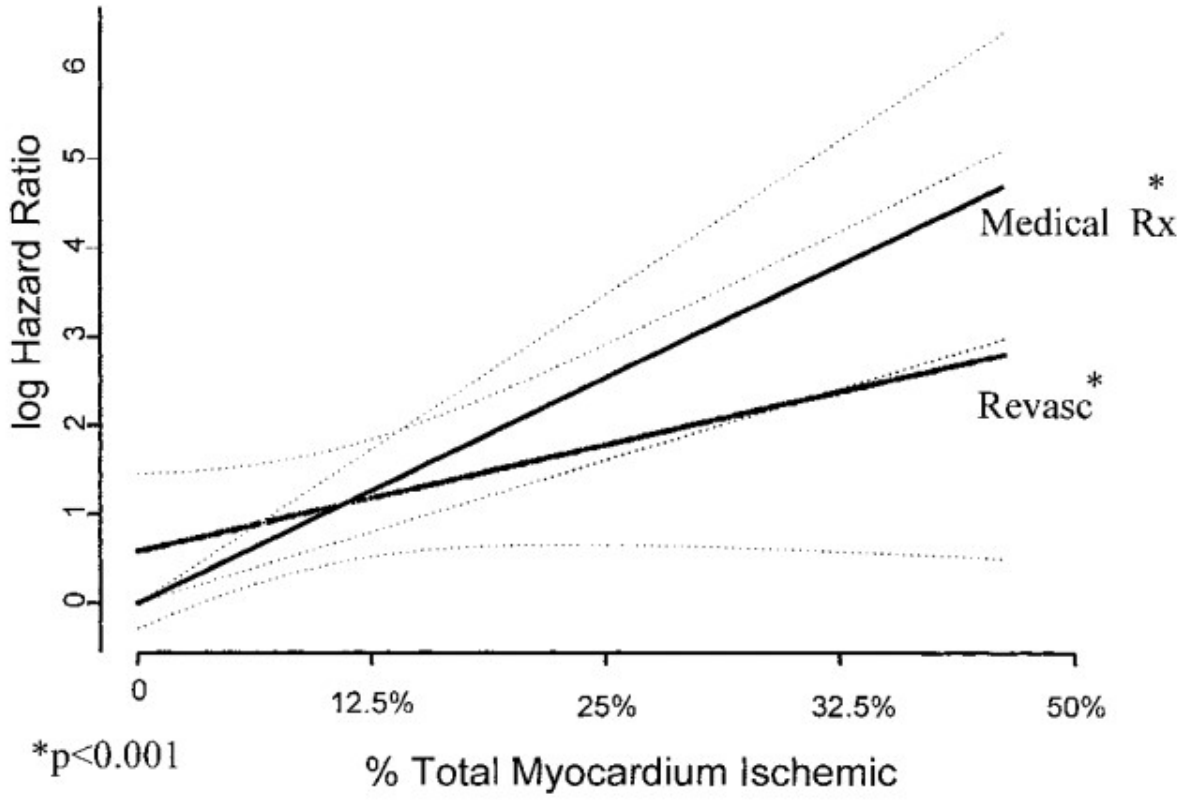
Comparative survival in exercise and adenosine patients following propensity-matching based on age, gender, chest pain symptom, and CAD risk factors.
ACM, All-cause mortality.

Rozanski et al., J Nucl Cardiol 2010

Valeur pronostique de la SPECT

Therapeutic benefit of revascularization

10 627 patients (without prior CAD), mean follow-up 2 years

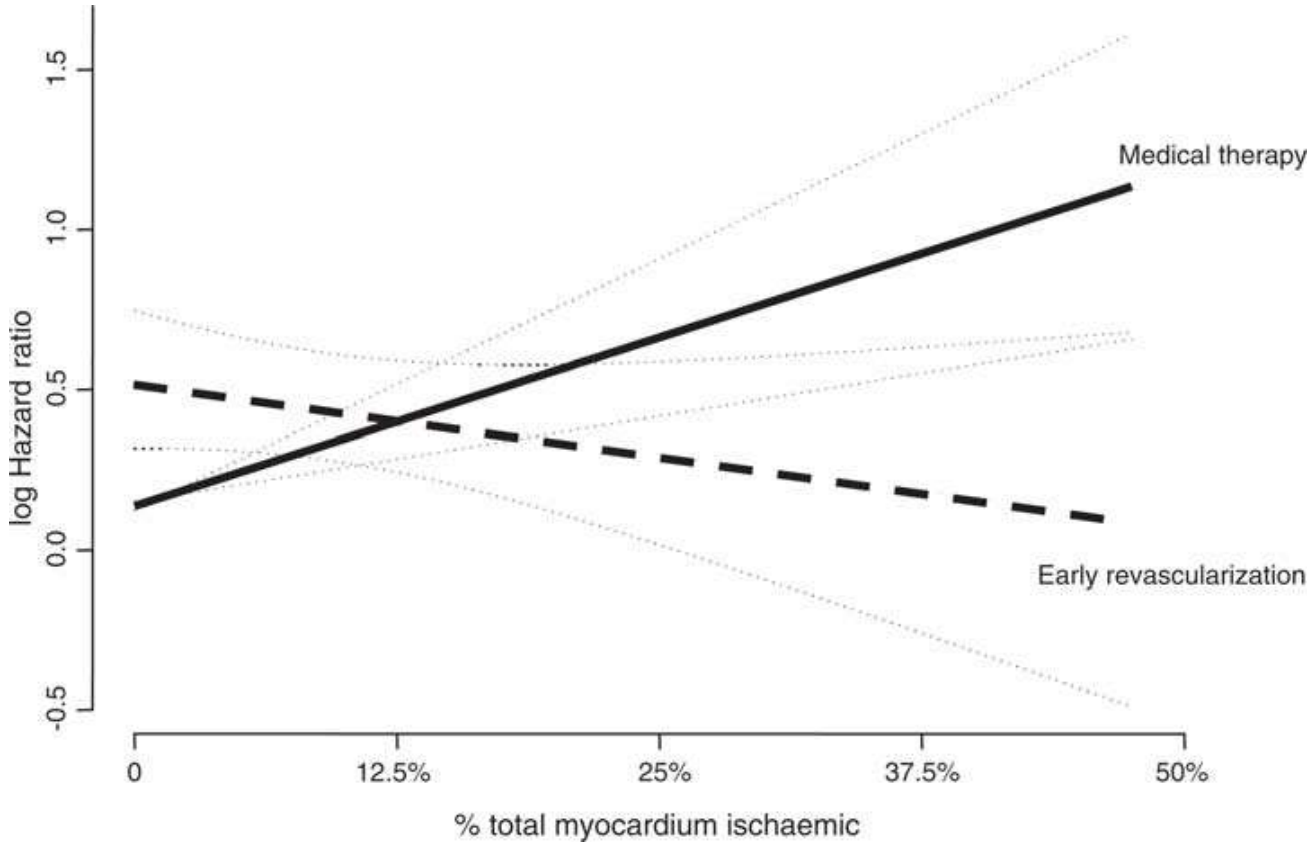


Hachamovitch et al., Circulation 2003

Valeur pronostique de la SPECT

Therapeutic benefit of revascularization

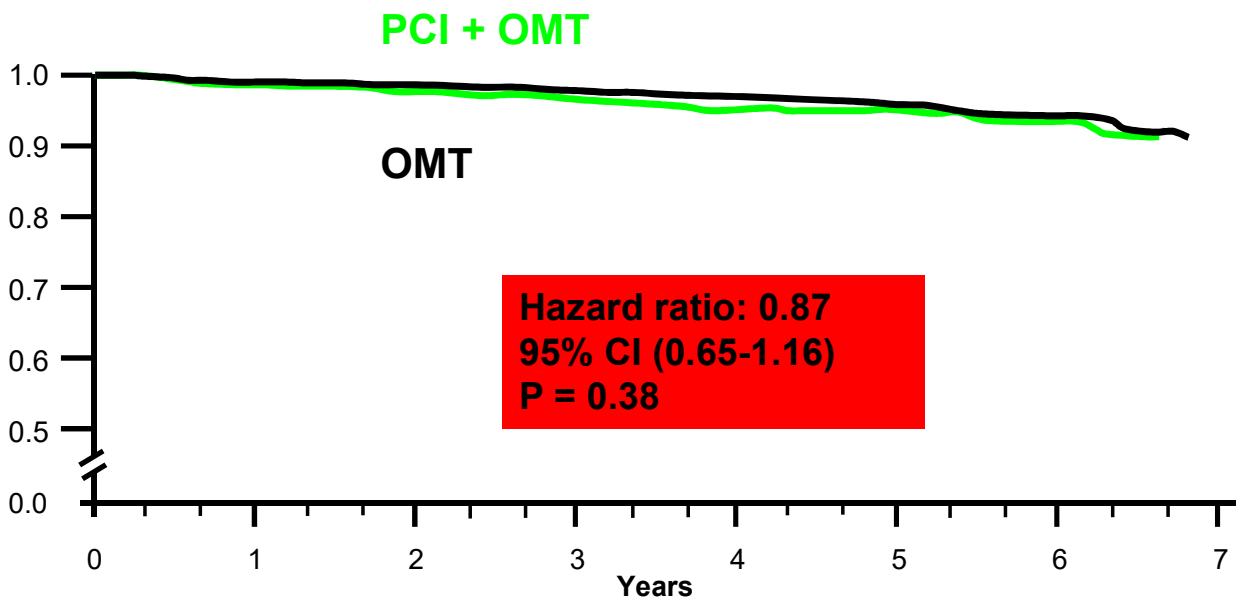
13 555 patients , mean follow-up 8 years



Hachamovitch et al., Eur Heart J 2013

Etude COURAGE

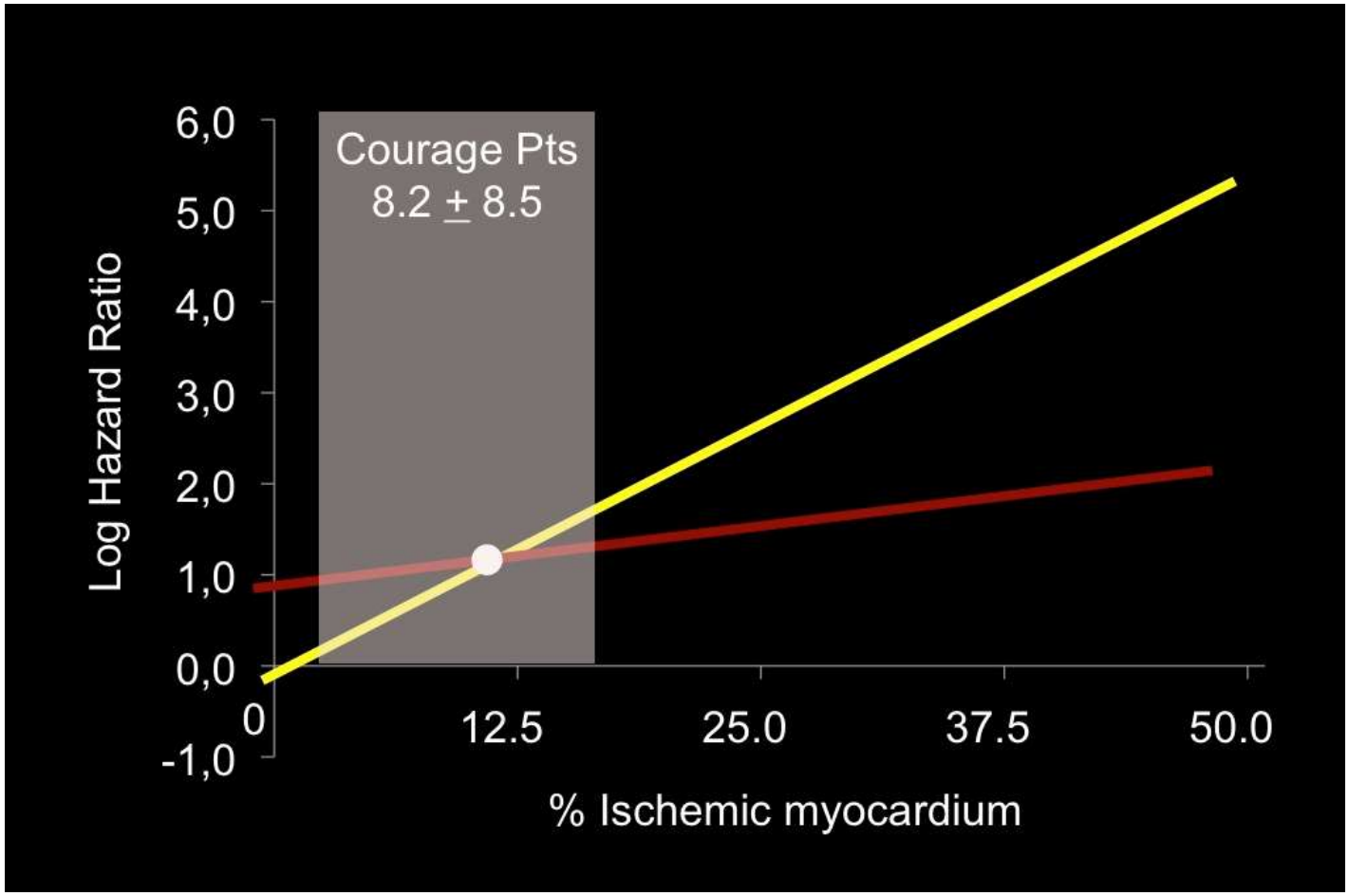
Stable CAD: benefit of revascularization



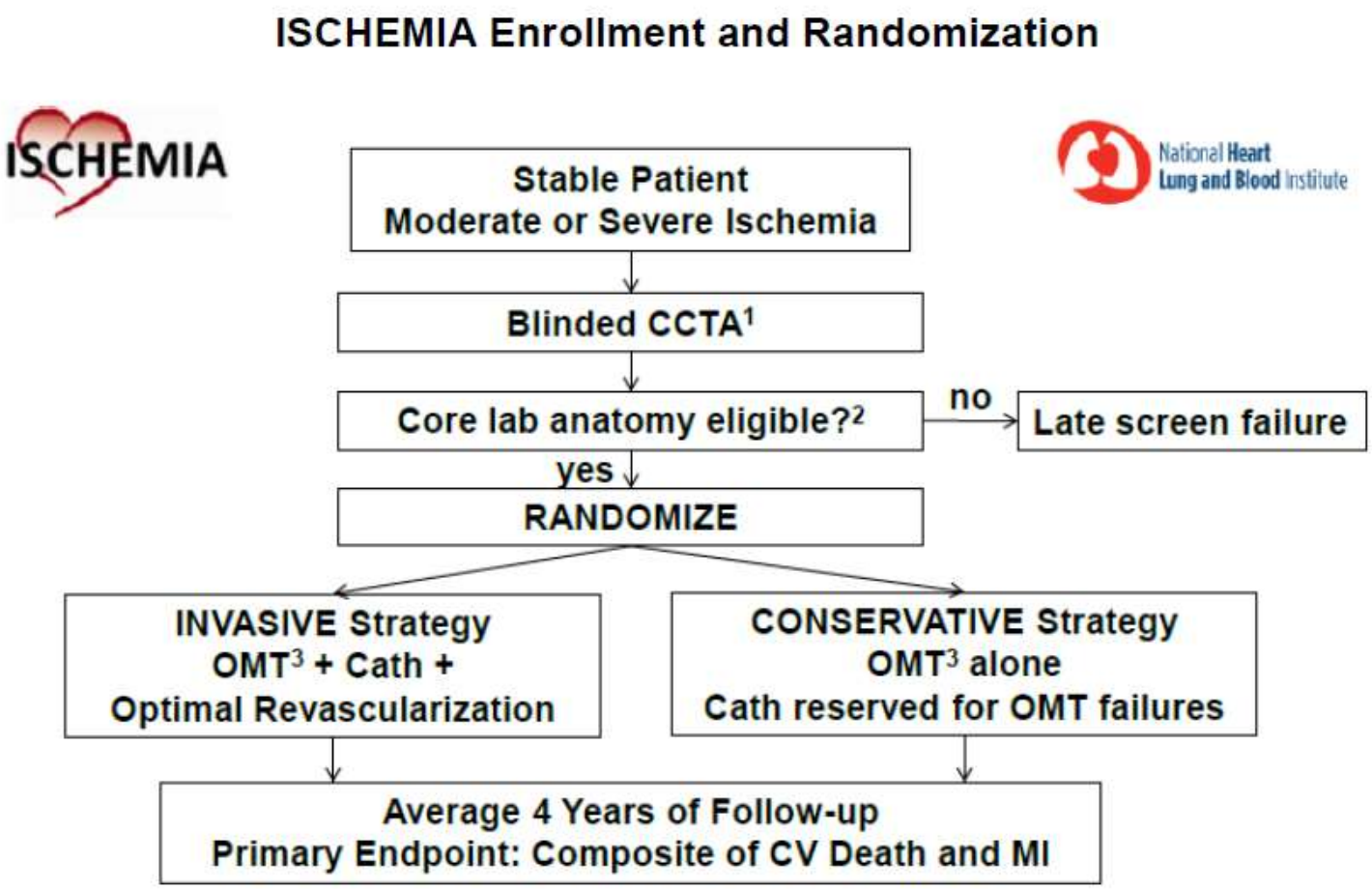
Number at Risk

Medical Therapy	1138	1073	1029	917	717	468	302	38
PCI	1149	1094	1051	929	733	488	312	44

Etude COURAGE



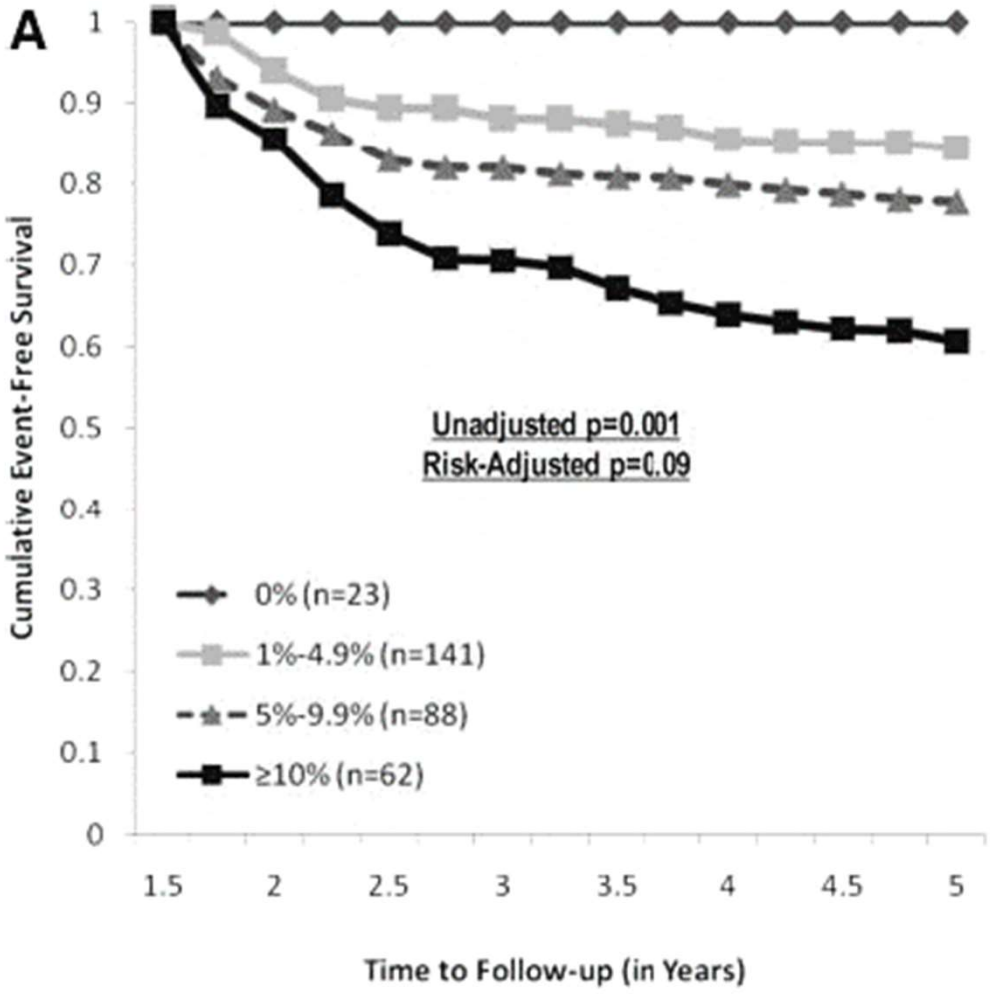
Étendue de l'ischémie >10%



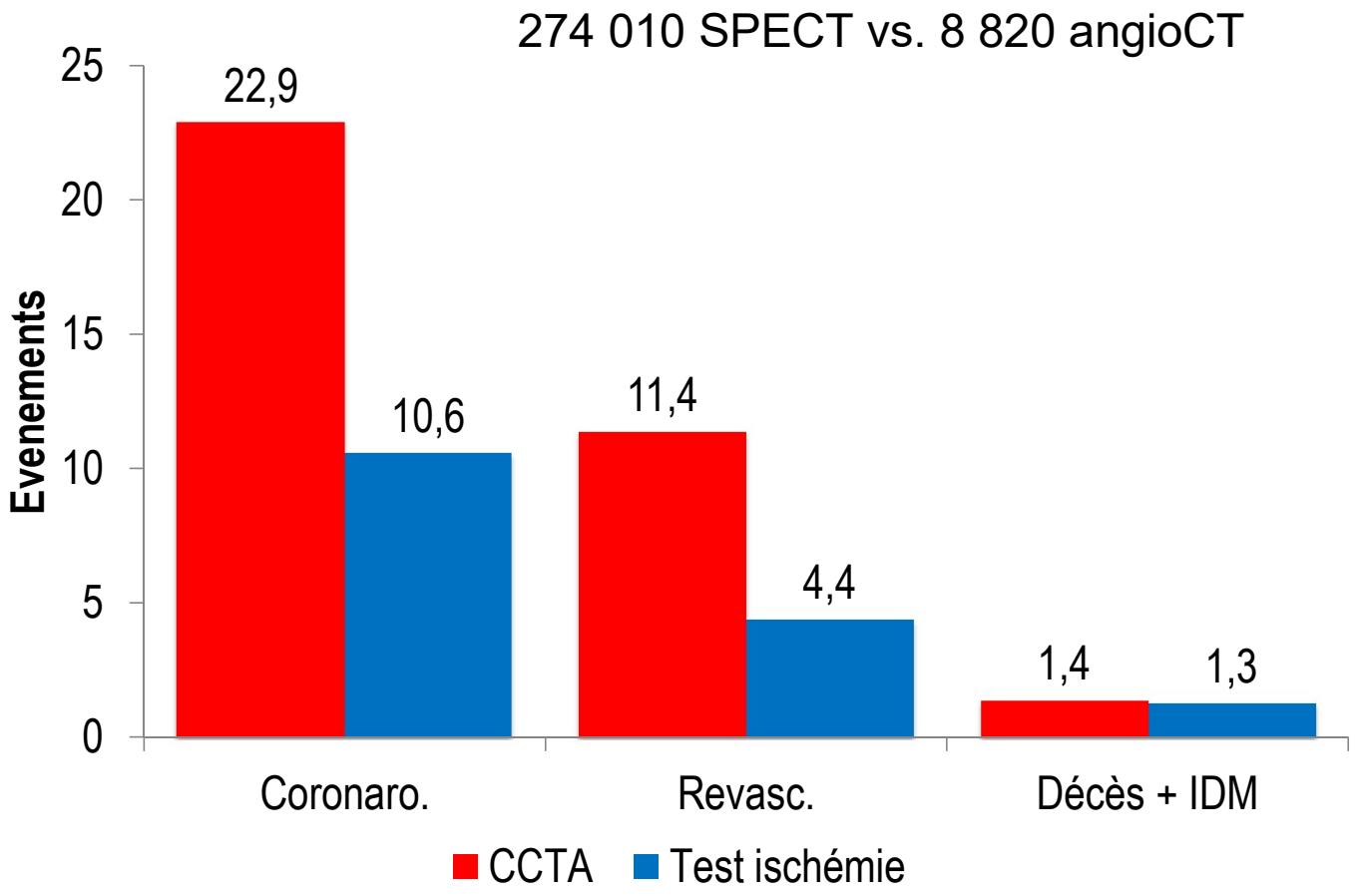
Ischémie résiduelle

COURAGE –
Nuclear substudy

Shaw L et al.,
Circulation 2008



Registre Medicare



Baras Shreibati & al. JAMA 2011;306:2128-36

Flux sanguin myocardique

Microcirculation

Résistances circulation coronaire

Camici PG, Rimoldi OE, J Nucl Med 2009

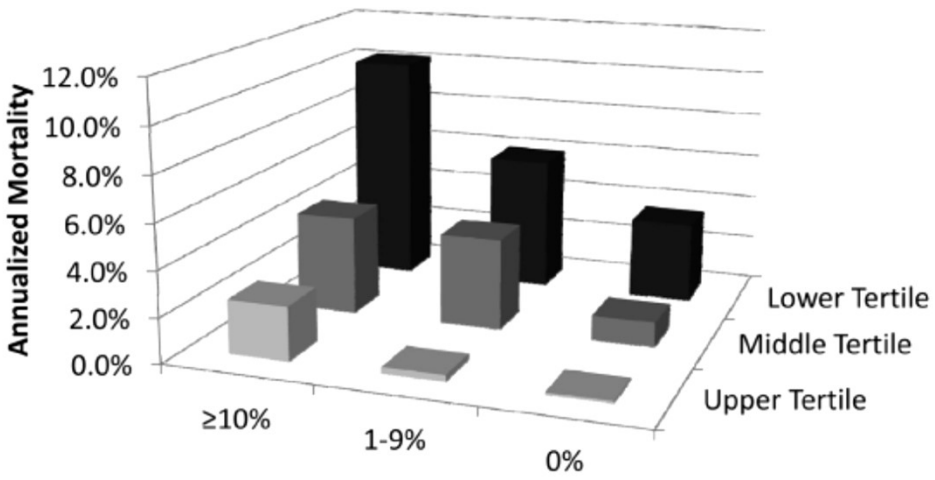
MBF: large-scale validation

Hypothesis: incremental prognostic value of coronary flow reserve (CFR), beyond clinical risk factors and semi-quantitative assessment of myocardial ischemia and left ventricular function.

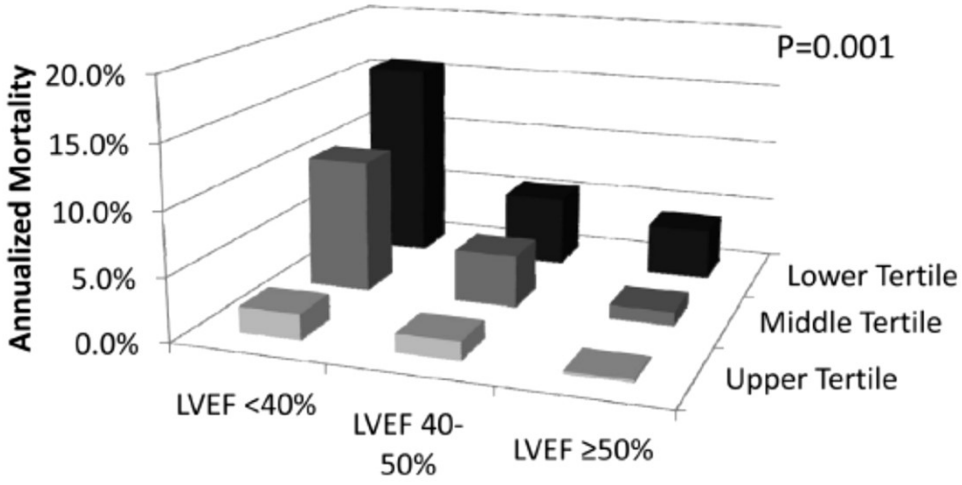
Murthy et al, Circulation 2011

- Single-centre, non-randomized, observational study
- 2783 consecutive patients
- Perfusion analysis: **^{82}Rubidium PET**
- Median follow-up: 1.4 years [0.7 – 3.2]

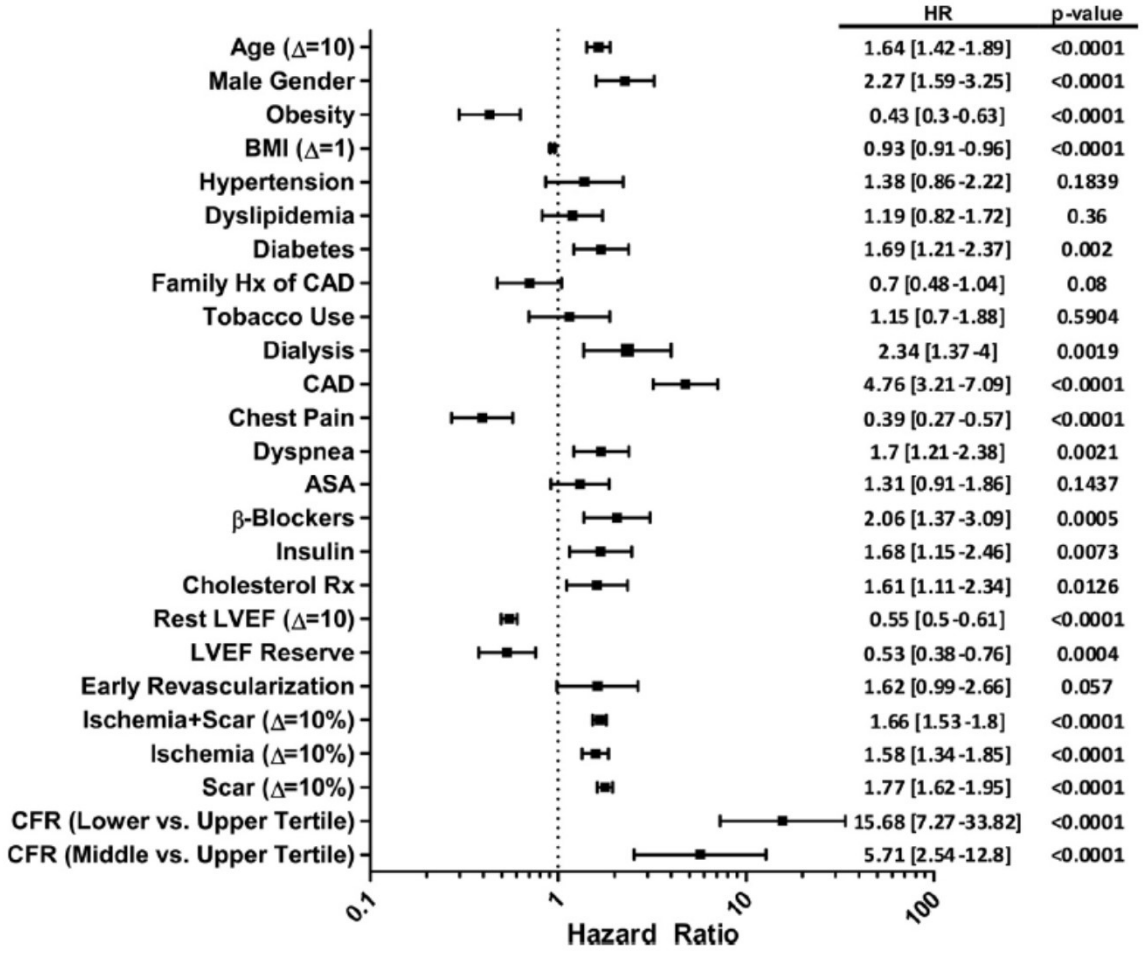
Extent of ischemia + scar



Left ventricular ejection fraction

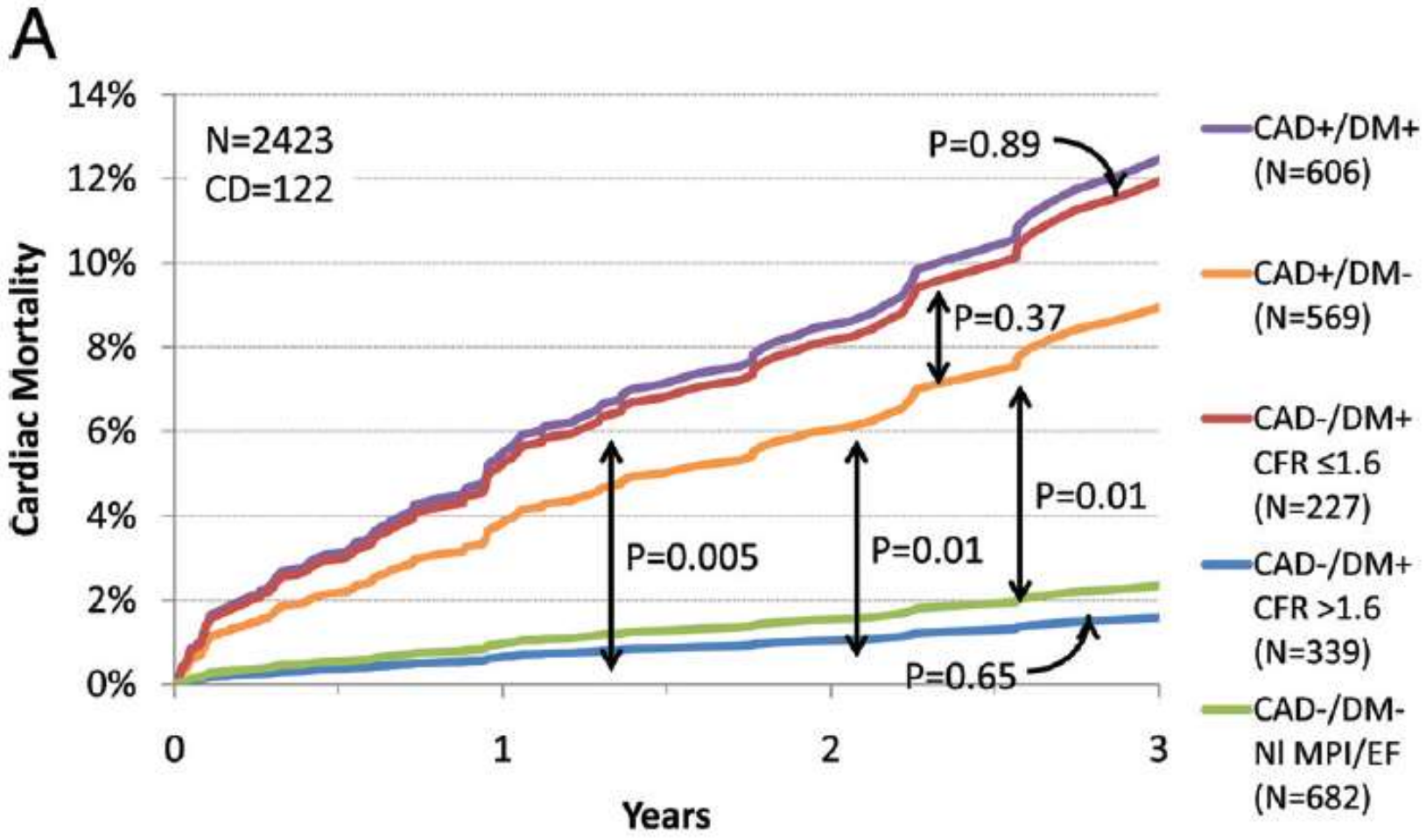


MBF: integration of risk profile



Murthy et al, Circulation 2011

Diabétiques



Murthy et al, Circulation 2012

Stratification du risque

Recommendations	Class [a]	Level [b]
Risk stratification is recommended based on clinical assessment and the result of the stress test initially employed for making a diagnosis of SCAD.	I	B
Stress imaging for risk stratification is recommended in patients with a non-conclusive exercise ECG[d]	I	B
Risk stratification using stress ECG (unless they cannot exercise or display ECG changes which make the ECG non evaluable) or preferably stress imaging if local expertise and availability permit is recommended in patients with stable coronary disease after a significant change in symptom level.	I	B
Stress imaging is recommended for risk stratification in patients with known SCAD and a deterioration in symptoms if the site and extent of ischaemia would influence clinical decision making.	I	B
Pharmacological stress with echocardiography or SPECT should be considered in patients with LBBB.	IIa	B
Stress echocardiography or SPECT should be considered in patients with paced rhythm.	IIa	B

Ischaemia imaging	High risk	Area of ischaemia >10% (>10% for SPECT; limited quantitative data for CMR – probably ≥2/16 segments with new perfusion defects or ≥3 dobutamine-induced dysfunctional segments; ≥ 3 segments of LV by stress echo).
	Intermediate risk	Area of ischaemia between 1 to 10% or any ischaemia less than high risk by CMR or stress echo.
	Low risk	No ischaemia.

2014 ESC/EACTS Guidelines on myocardial revascularization

Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class[b]	Level[c]	References
For prognosis	Left main disease with stenosis >50%[a]	I	A	108,134,135
	Any proximal LAD stenosis >50%[a]	I	A	94,108,135,136
	Two-vessel or three-vessel disease with stenosis > 50%[a] with impaired LV function (LVEF<40%)[a]	I	A	93,94,108,112, 121,135,137–142
	Large area of ischaemia (>10% LV)	I	B	54,91,97,99,143,144
	Single remaining patent coronary artery with stenosis >50%[a]	I	C	
For symptoms	Any coronary stenosis >50%[a] in the presence of limiting angina or angina equivalent, unresponsive to medical therapy	I	A	54,96,105,108, 118–120,145

CAD = coronary artery disease; FFR = fractional flow reserve; LAD = left anterior descending coronary artery; LV = left ventricular.
[a]With documented ischaemia or FFR $\leq$ 0.80 for diameter stenosis <90%.
[b]Class of recommendation.
[c]Level of evidence.

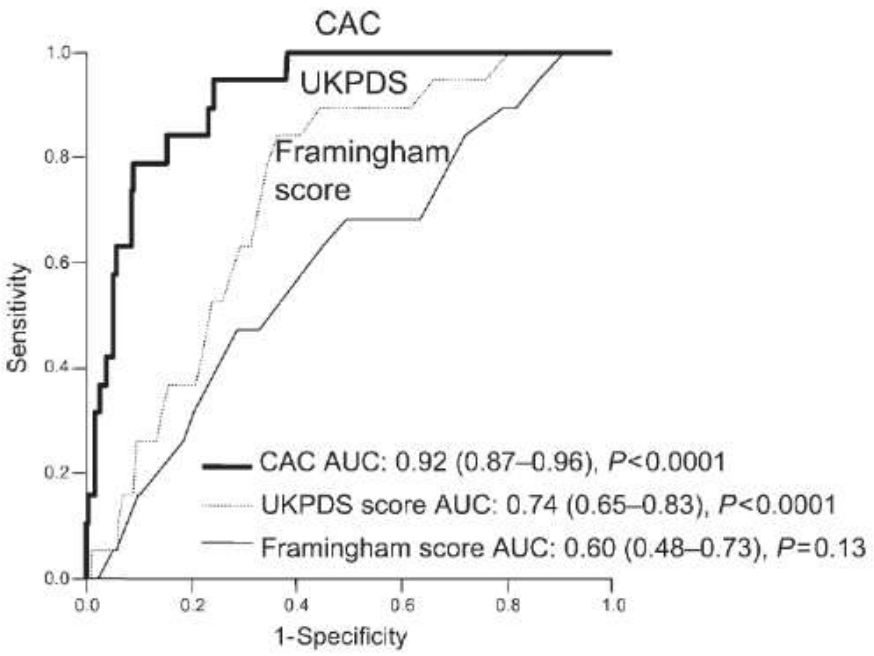
2014 ESC/EACTS Guidelines on myocardial revascularization

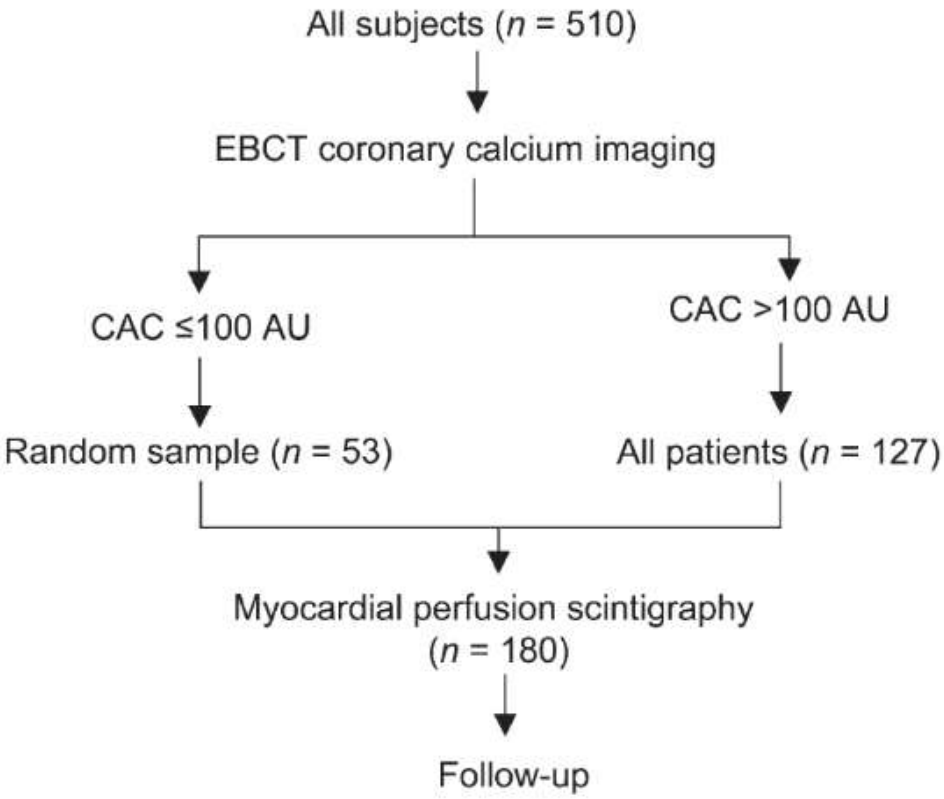
Strategies for follow-up and management in patients after myocardial revascularization

Recommendations	Class[a]	Level[b]	Ref[c]
Asymptomatic patients			
Early imaging testing should be considered in specific patient subsets.[d]	IIa	C	
Routine stress testing may be considered >2 years after PCI and >5 years after CABG.	IIb	C	
After high-risk PCI (e.g. unprotected LM stenosis) late (3–12 months) control angiography may be considered, irrespective of symptoms.	IIb	C	
Symptomatic patients			
It is recommended to reinforce medical therapy and lifestyle changes in patients with low-risk findings[d] at stress testing.	I	C	
With intermediate- to high-risk findings[e] at stress testing, coronary angiography is recommended.	I	C	

[d]Specific patient subsets indicated for early stress testing with imaging:
– patients with safety-critical professions (e.g. pilots, drivers, divers) and competitive athletes;
– patients engaging in recreational activities for which high oxygen consumption is required;
– patients resuscitated from sudden death;
– patients with incomplete or suboptimal revascularization, even if asymptomatic;
– patients with a complicated course during revascularization (perioperative myocardial infarction, extensive dissection during PCI, endarterectomy during CABG, etc.);
– patients with diabetes (especially those requiring insulin);
– patients with multivessel disease and residual intermediate lesions, or with silent ischaemia.

Stratification du risque dans le diabète de type 2 non compliqué





Anand DV et al, Eur Heart J 2006

Stratification du risque dans le diabète de type 2 non compliqué

Table 4 Interaction between CAC scores and the extent of myocardial perfusion abnormality for prediction of event-free survival ($P = 0.003$)

% Myocardium	CAC 0–100	CAC 101–400	CAC 401–1000	CAC >1000
0%	100%	98%	96%	90%
1–5%	100%	92%	83%	77%, RR = 9.20 (1.48, 57.19), $P = 0.017$
>5%	100%	80%, RR = 8.30 (1.35, 50.99), $P = 0.022$	64%, RR = 12.64 (2.97, 53.84), $P = 0.001$	48%, RR = 24.43 (5.59, >100), $P < 0.0001$

Interaction $P = 0.003$ (unadjusted) and <0.0001 (adjusted for UKPDS risk score). Event-free survival estimates are from a stratified Cox model.

- **Synergie entre CAC et SPECT** pour la prediction des événements

Anand DV et al, Eur Heart J 2006

Événement après CAC et scintigraphie de perfusion myocardique

- Objective: to assess the prognosis in patients undergoing both coronary artery calcium (CAC) scanning and exercise myocardial perfusion scintigraphy (MPS).

- Methods: assessment of the frequency of cardiac death and myocardial infarction over a mean follow-up of 32 months in 1,153 patients undergoing both CAC scanning and MPS.

Rozanski A et al, JACC 2007

Table 2 Frequency of Revascularization Procedures and Cardiac Events During Follow-Up Results in the CAC Cohort

Groups	CAC Grouping						p Value*
	0	1–9	10–99	100–399	400–999	≥1000	
All CAC patients (n = 1,153)							
Patients (n)	252	52	205	274	230	140	
% ischemia	1.2%	1.9%	1.5%	4.0%	7.8%	20.0%	<0.0001

Rozanski A et al, JACC 2007

Prevalence de l'ischémie en fonction du CAC score

TABLE 2 Pooled Prevalence and Odds Ratio for Ischemia by CAC Categories From 6 Major Studies*

CAC Categories	Patients (n)	Pooled Prevalence of Ischemia (%)	Range of Ischemia (%)	Pooled Odds Ratio (95% CI)
0	487	6.6	0.0-24.1	Reference
1-100	529	8.5	2.1-50.0	1.7 (1.04-2.2)
101-399	513	10.5	4.0-63.6	3.3 (1.4-8.2)
≥400	594	23.6	12.4-57.1	6.9 (3.5-13.4)

- wide variance in the frequency of ischemia among patients with intermediate to high CAC scores

Bavishi C et al, JACC imaging 2016

Table 2 Frequency of Revascularization Procedures and Cardiac Events During Follow-Up Results in the CAC Cohort

Groups	CAC Grouping						p Value*
	0	1–9	10–99	100–399	400–999	≥1000	
All CAC patients (n = 1,153)							
Patients (n)	252	52	205	274	230	140	
% ischemia	1.2%	1.9%	1.5%	4.0%	7.8%	20.0%	<0.0001
Ischemic (n = 64)							
Ischemic patients (n)	3	1	3	11	18	28	
Early cath (<60 days)	1 (33%)	1 (100%)	1 (33%)	6 (55%)	11 (61%)	13 (46%)	0.99
Revascularized <60 days	0 (0%)	0 (0%)	0 (0%)	5 (46%)	9 (50%)	13 (46%)	0.06
Revascularized ≥60 days	0 (0%)	0 (0%)	0 (0%)	1 (9.1%)	1 (5.6%)	3 (10.7%)	0.41
CD/MI*	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (7.1%)	0.23
Annualized CD/MI rate	0%/yr	0%/yr	0%/yr	0%/yr	0%/yr	2.7%/yr	0.88
Nonischemic (n = 1,089)							
Nonischemic patients (n)	249	51	202	263	212	112	
Early cath (<60 days)	2 (0.8%)	1 (2.0%)	0 (0%)	5 (1.9%)	3 (1.4%)	6 (5.4%)	0.01
Revascularized <60 days	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (2.7%)	0.007
Revascularized ≥60 days	2 (0.8%)	0 (0%)	6 (3.0%)	6 (2.3%)	11 (5.2%)	7 (6.3%)	0.001
CD/MI*	1 (0.4%)	0 (0%)	0 (0%)	2 (0.8%)	6 (2.8%)	2 (1.8%)	0.02
Annualized CD/MI rate	0.2%/yr	0%/yr	0%/yr	0.3%/yr	1.0%/yr	0.6%/yr	0.10

CAC élevé sans ischémie documentée

- La presence d'un CAC élevé est plus fréquemment suivie d'une coronarographie ± angioplastie coronaire, y compris en l'absence d'ischémie documentée

- Le taux d'événements reste <1%/an, c'est-à-dire un risque faible

- à l'inverse le taux d'événements global est élevé lorsque CAC>1000

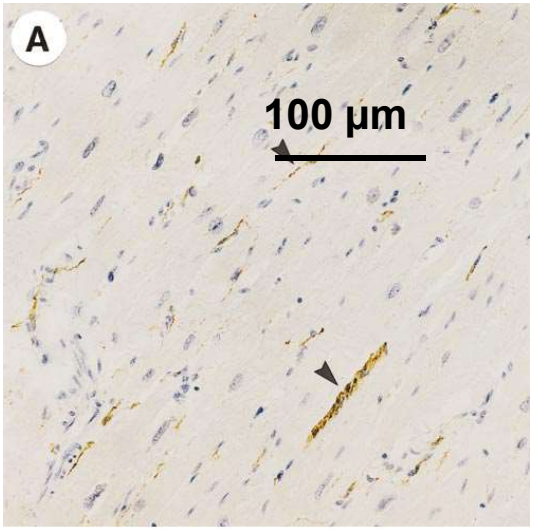
Rozanski A et al, JACC 2007

Innervation sympathique

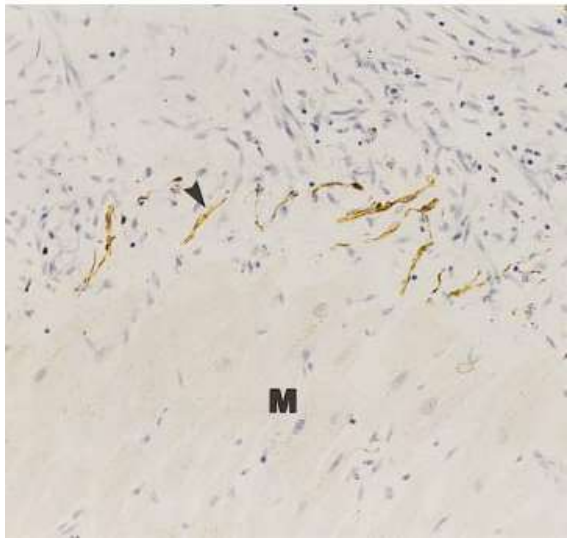
Innervation sympathique et insuffisance cardiaque (1)

Facteur anatomique : dénervation

- Dégénérescence myocytaire, fibrose
- Lésion des terminaisons nerveuses
- hétérogénéité de la réinnervation sympathique



Normal



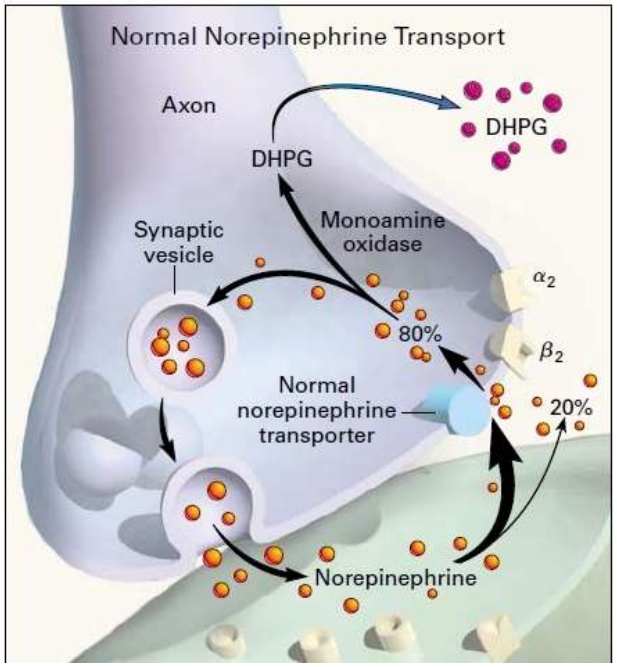
TV ischémique

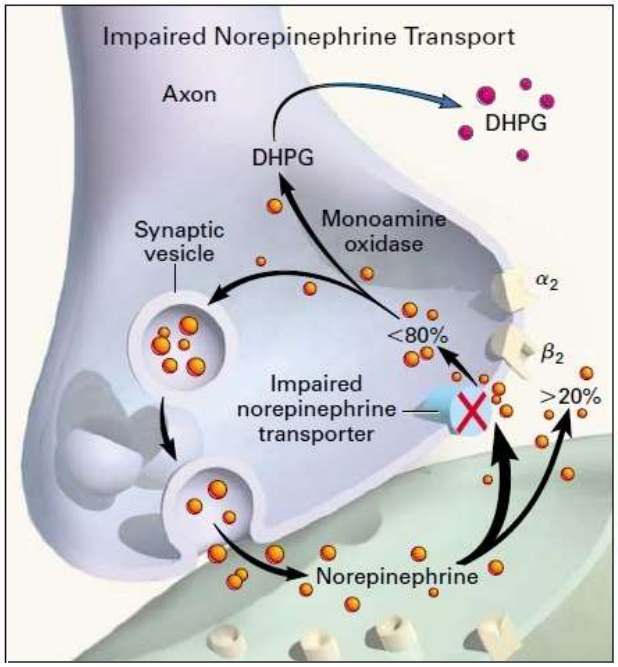
Immunomarquage protéine S100

Cao et al, Circulation 2000

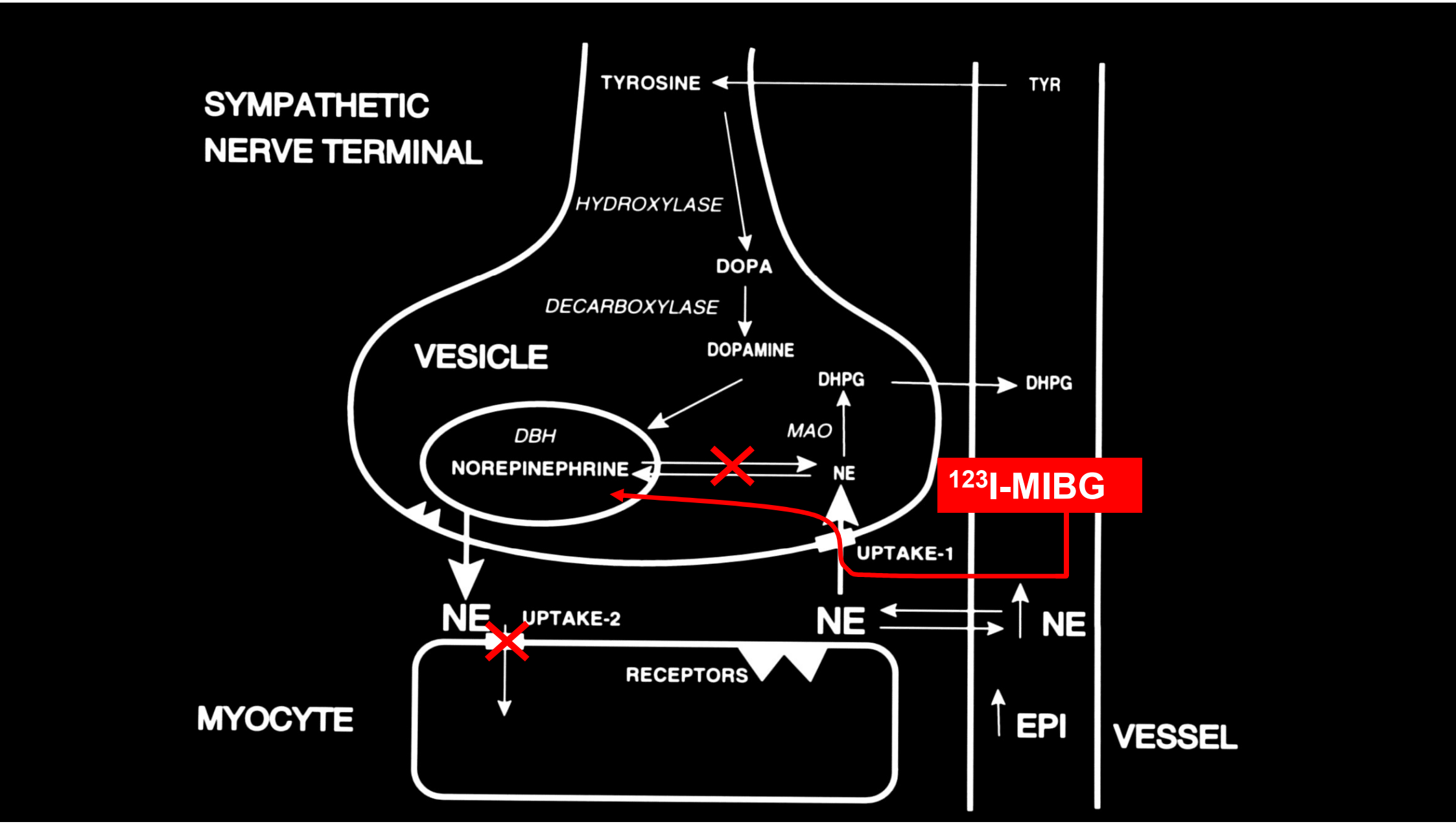
Innervation sympathique et insuffisance cardiaque (2)

Facteur fonctionnel : diminution de la recapture et du stockage vésiculaire de la NA

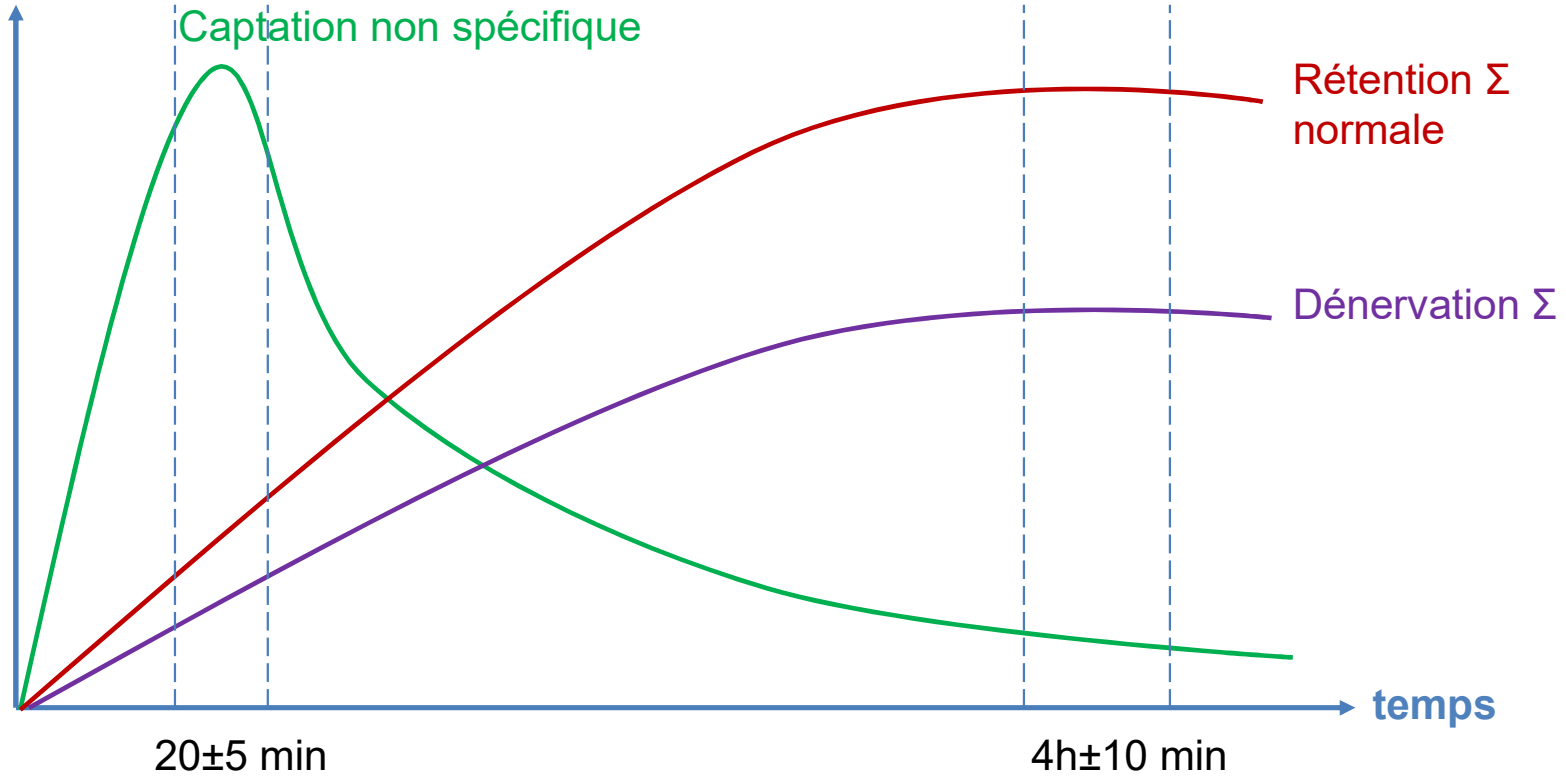




Shannon et al, NEJM 2000


SYMPATHETIC
NERVE TERMINAL
TYROSINE
TYR
HYDROXYLASE
DOPA
DECARBOXYLASE
DOPAMINE
VESICLE
DHPG
DHPG
DBH
MAO
NOREPINEPHRINE
NE
123I-MIBG
UPTAKE-1
NE
UPTAKE-2
NE
NE
RECEPTORS
MYOCYTE
EPI
VESSEL

Cinétique de captation de la MIBG



Interactions médicamenteuses

Diminution de la captation et/ou de la rétention lors de l'administration des produits suivants :

- réserpine,
- labétalol,
- les inhibiteurs calciques (diltiazem, nifédipine, vérapamil),
- les **antidépresseurs tricycliques** (amitryptiline, imipramine et leurs dérivés),
- les **agents sympathomimétiques** (présents dans les décongestionnants nasaux, telles que phényléphrine, éphédrine ou phénylpropanolamine),
- la cocaïne,
- les phénothiazines.

Déroulement de l'examen

- Explication du déroulement de l'examen au patient, interrogatoire
- Mise en place d'une voie veineuse périphérique
- Ensuite, patient au repos strict (supprimer les stimulations adrénergiques)
- Blocage thyroïdien : iodure de potassium (130 mg)
- 1 heure après le blocage de la thyroïde : Injection IV lente de 185 MBq de ^{123}I-MIBG
- 20 min post IV : acquisition planaire du thorax en face antérieure, décubitus dorsal, bras le long du corps

Déroulement de l'examen

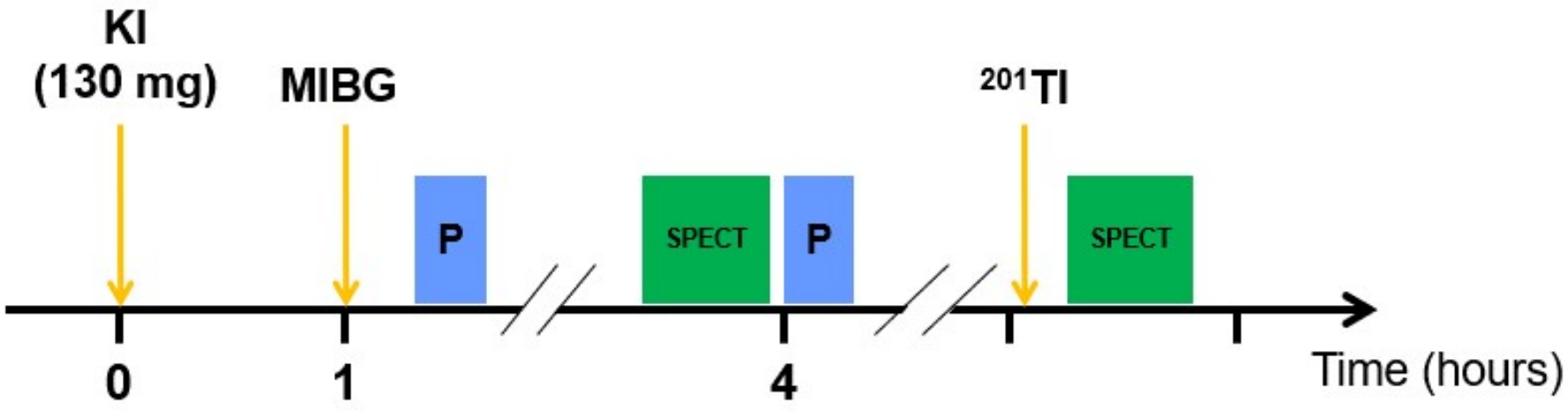
- 4h post IV : acquisition planaire du thorax en face antérieure, décubitus dorsal, bras le long du corps.

➢ Respect impératif du délai 20 min / 4 heures car permet de calculer la clairance (WOR) de la MIBG

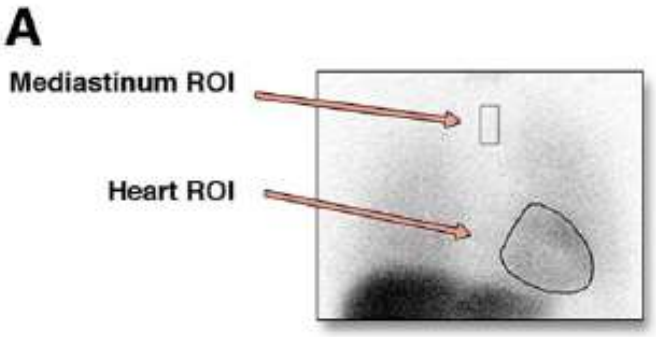
- 3h30 post IV ou après l'acquisition planaire tardive (4h) : TEMP thorax, décubitus dorsal, bras gauche relevé

- Si nécessaire : exploration de la perfusion myocardique au repos au ^{201}Tl (111 MBq; T=73 h; E=75 et 135 keV) ou traceur technétié sur caméra CZT

Déroulement de l’examen



Quantification en planaire

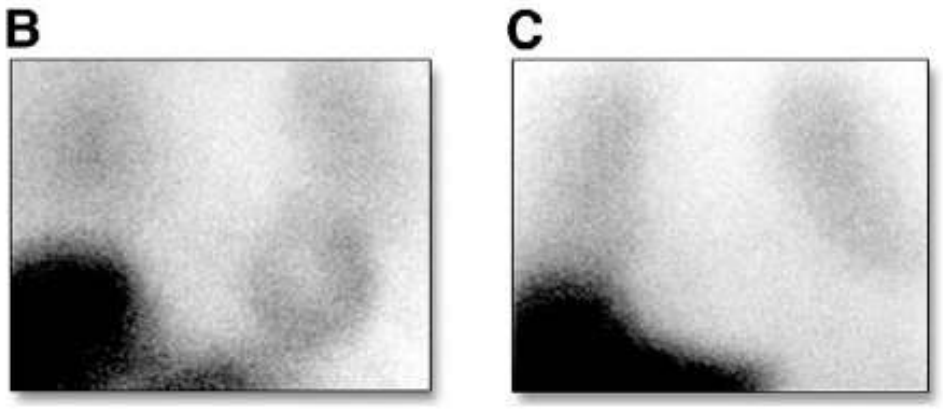


Heart ROI Mean Count: H

Mediastinum Mean Count: M

$$\text{H/M Ratio} = \frac{H}{M}$$

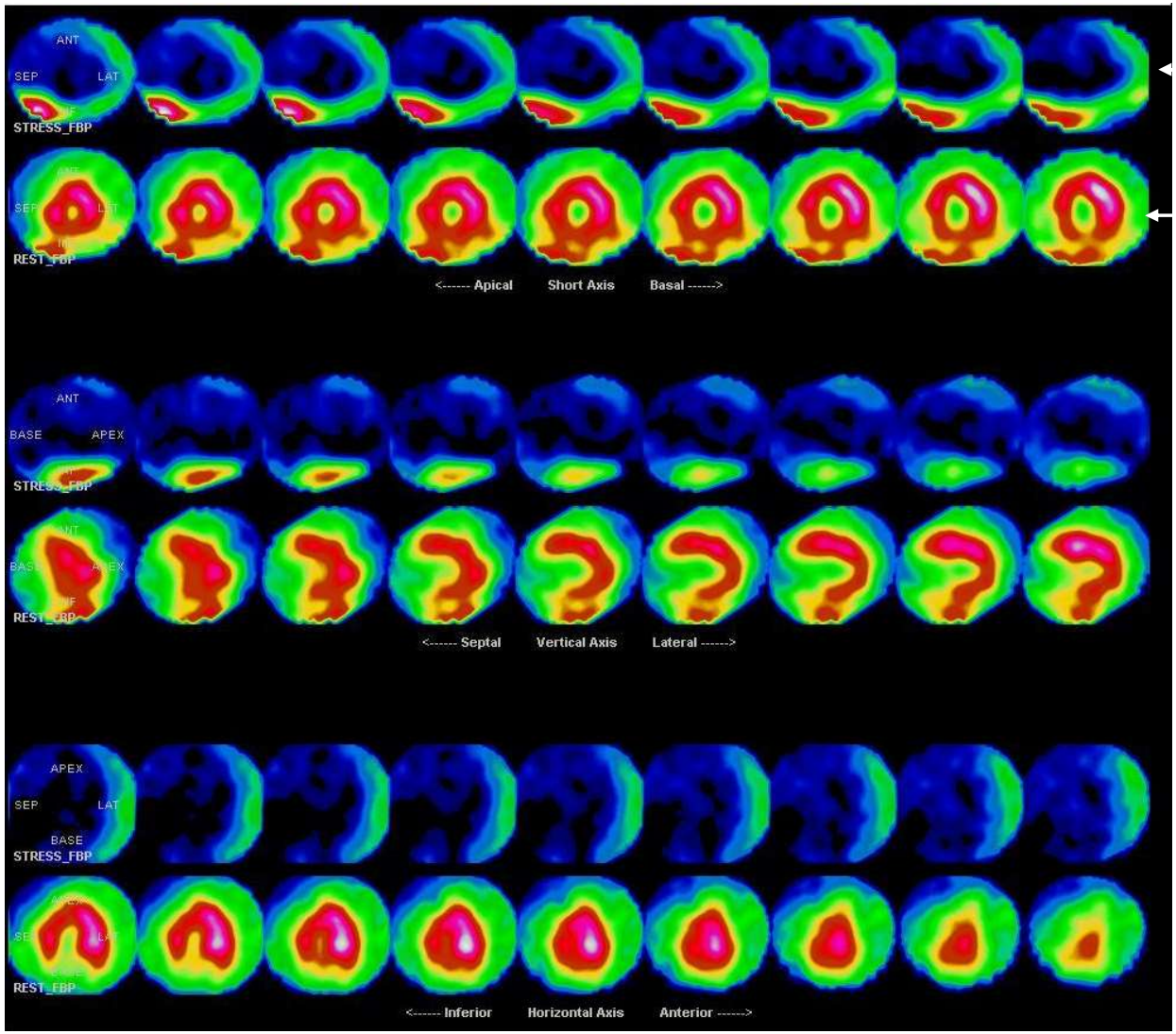
$$\text{Washout Rate} = \frac{\text{Early Image (H – M)} - \text{Delayed Image (H – M)}}{\text{Early Image (H – M)}} \times 100\ (\%)$$



Valeurs normales (LEHR)

- H/M à 4 heures ≥1,85

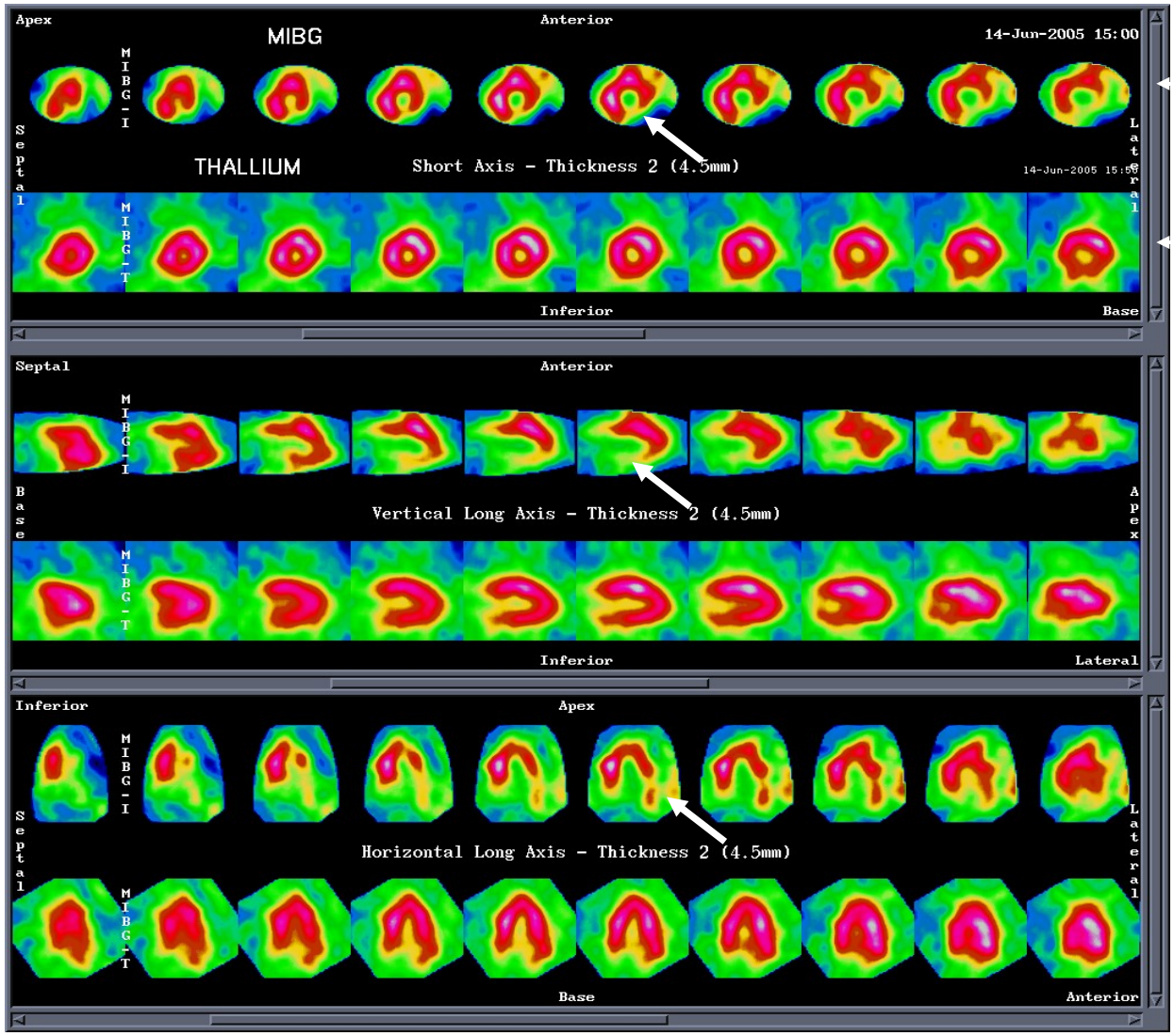
- WOR <40%



TEMP ^{123}I-MIBG

TEMP ^{201}TI

Dénervation myocardique globale

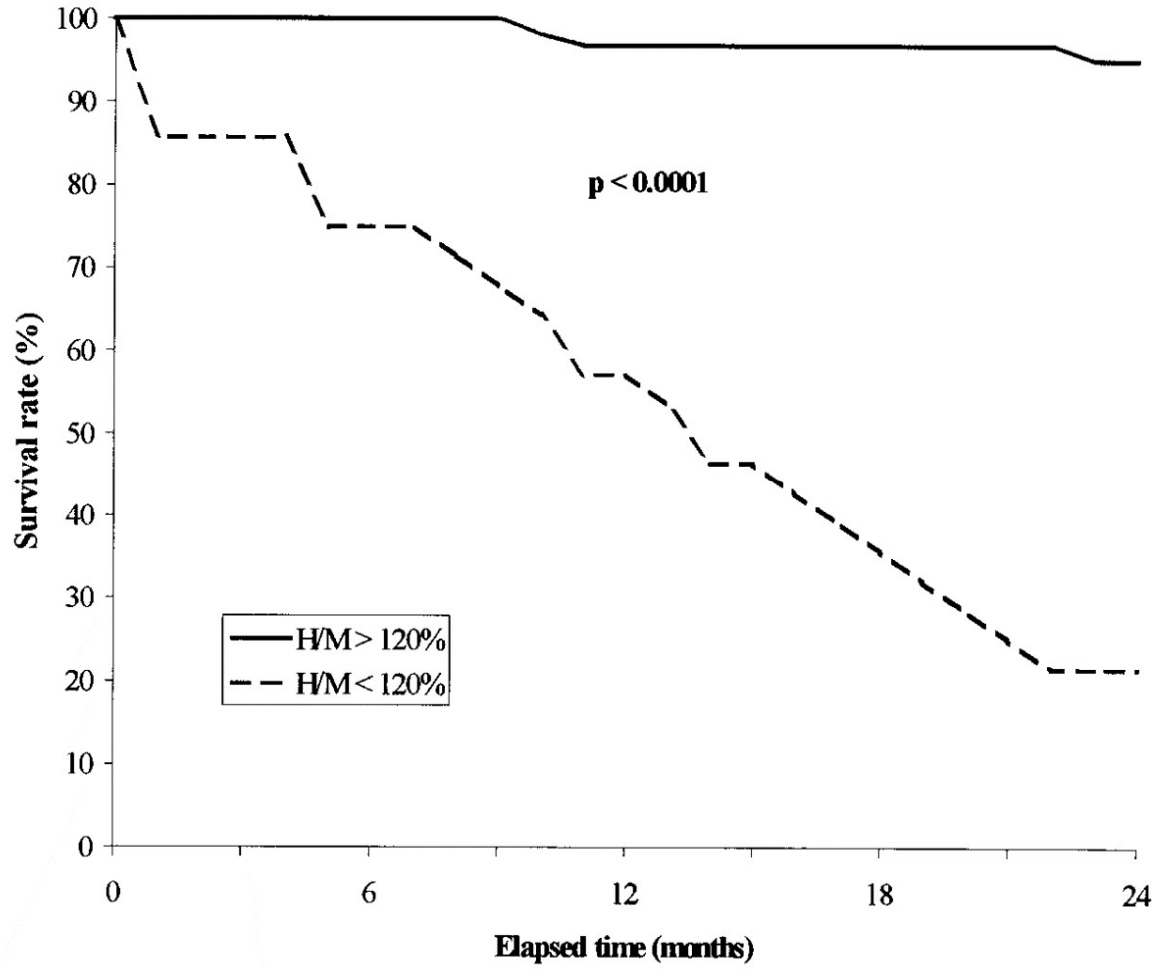


TEMP ^{123}I-MIBG

TEMP ^{201}TI

Dénervation segmentaire

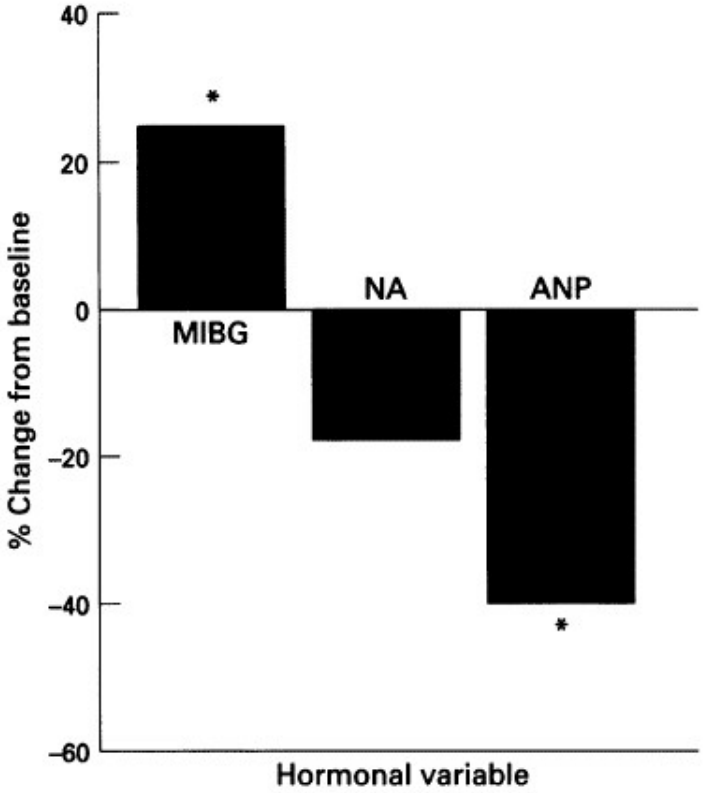
Valeur pronostique de la MIBG dans l'insuffisance cardiaque



Merlet et al, J Nucl Med 1999

Évolution sous IEC

Evolution après 6 semaines de traitement



23 patients
NYHA II (52%)
Ischémique (65%)

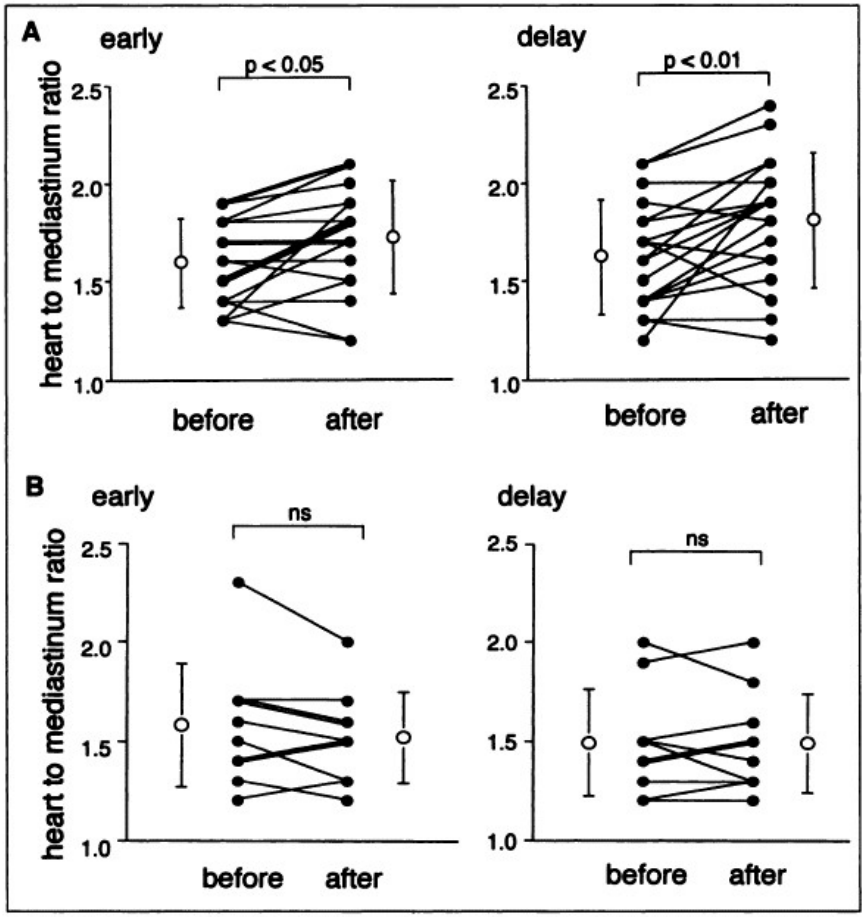
Somsen GA et al., Heart 1996

Évolution sous IEC

Evolution après 9 (± 3) mois de traitement

IEC+

IEC-

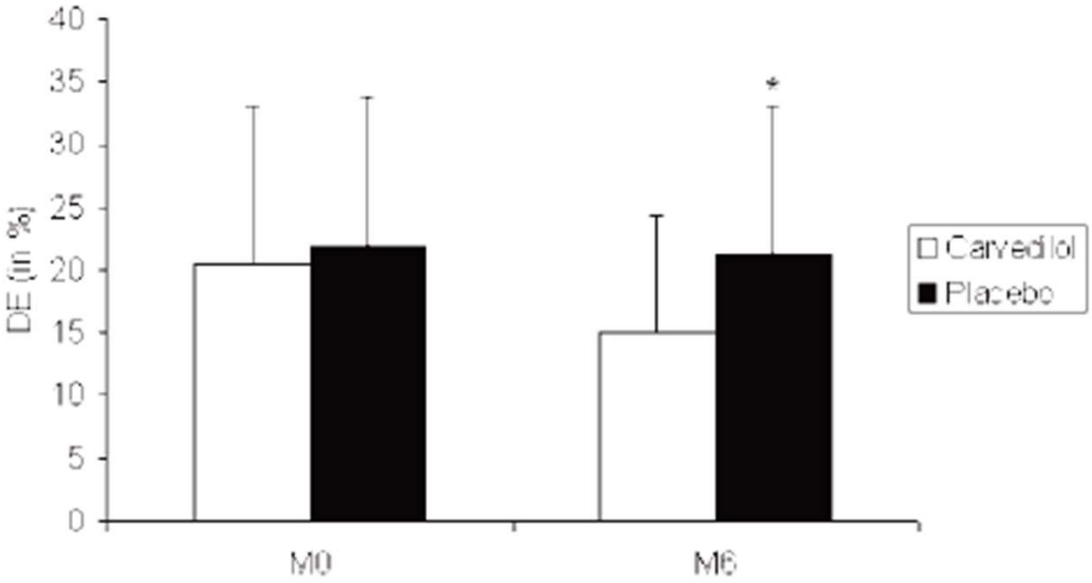


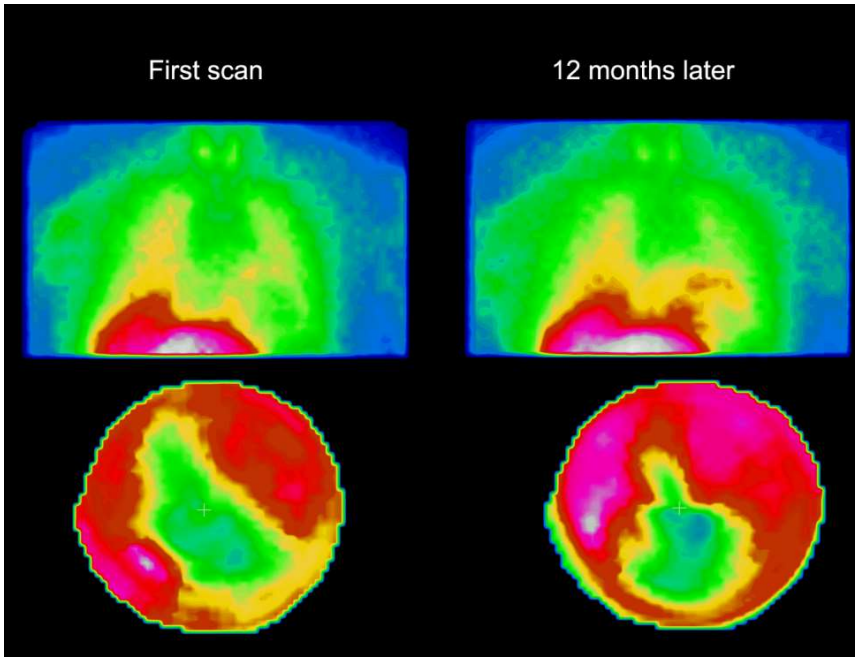
- 19 patients (IEC+)
- 10 témoins (IEC-)
- B-bloquants : 10%

Takeishi et al., JNM 1997

Evolution sous β–bloquant

- Étude multicentrique, contrôlée (placebo), double-aveugle
- 64 pts NYHA classe II/III; FEVG <40%





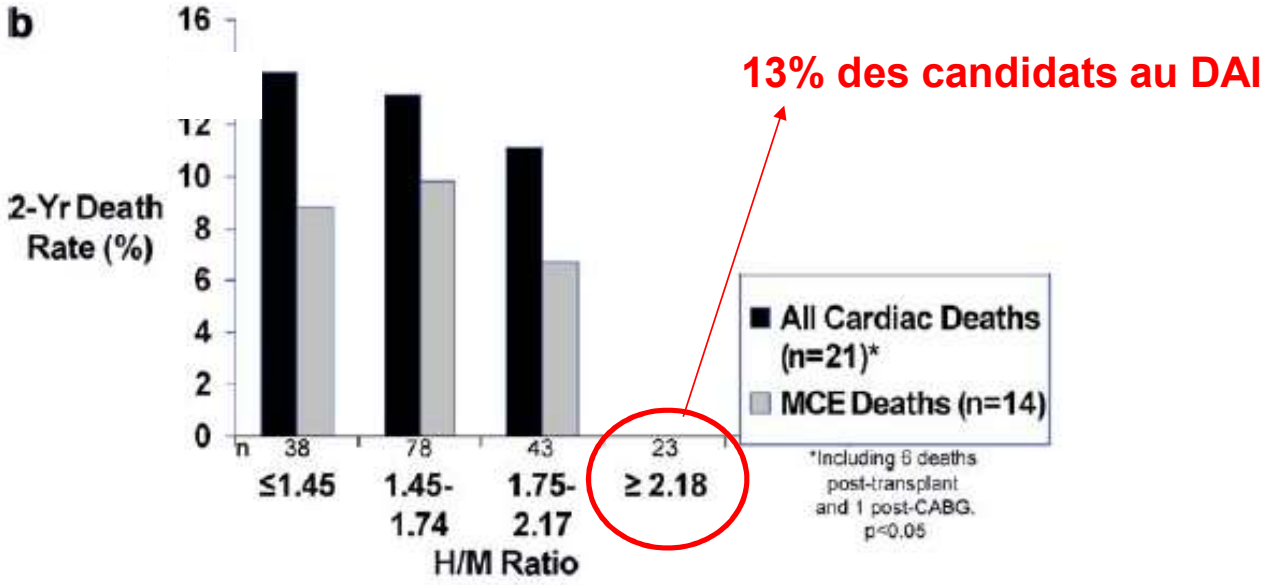
Cohen-Solal et al., J Nucl Med 05

Valeur prédictive négative

H/M	Number of patients	Transplants (row %)	SCD and arrhythmic events[a] (row %)	HF and other cardiac deaths[b] (row %)	Total MCEs (row %)	2-year event-free survival (%)
≤1.45	71	25 (35)	1 (1)	8 (11)	34 (48)	52
1.46–1.74	74	12 (16)	7 (9)	2 (3)	21 (28)	72
1.75–2.17	72	6 (8)	2 (3)	3 (4)	11 (15)	85
≥2.18	73	1 (1)	0 (0)	0 (0)	1 (1)	99
Total	290	44 (15)	10 (3)	13 (8)	67 (23)	–

Critères de sélection :

- LVEF ≤35%
- NYHA II-III
- N=182



Agostini et al, EJNM 2007

ADMIRE-HF

- Objectifs
  - ***Primaire :*** valeur pronostique de la MIBG (C/M < 1,6) dans l'insuffisance cardiaque
  - ***Secondaire :***
    - progression de l'insuffisance cardiaque
    - événements rythmiques
    - mortalité

- Critères d'inclusion
  - Insuffisance cardiaque NYHA II/III (ischémique ou non)
  - FEVG ≤35%
  - Traitement médical optimal

Jacobson et al, JACC 2010

ADMIRE-HF

Subject Demographics and Clinical Characteristics

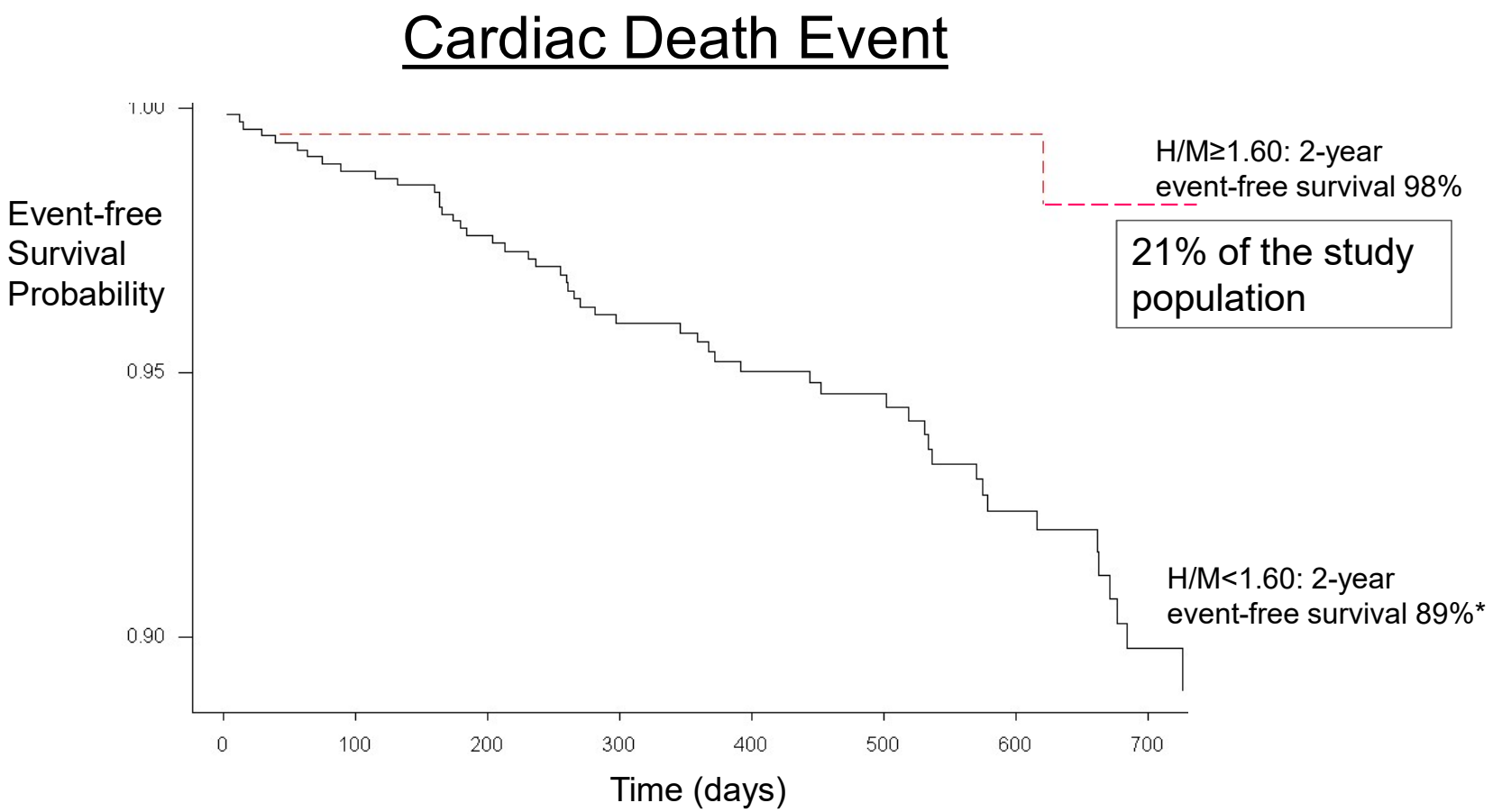
964 HF subjects were evaluable for efficacy.

Variable	Data	Range
Mean Age (yr)	62.4	20-90
Gender (M/F) (%)	80/20	-
Race (W/B/O) (%)	75/14/11	-
NYHA II/III (%)	83/17	-
HF Etiology (I/NI*) (%)	66/34	-
Mean LVEF (%)	27	5-35
Median Follow-up (mo)	17	0.1-27
2-year mortality rate (%)	12.8	-

*I=Ischemic; NI=Non-ischemic

Jacobson et al, JACC 2010

ADMIRE-HF: mortalité globale

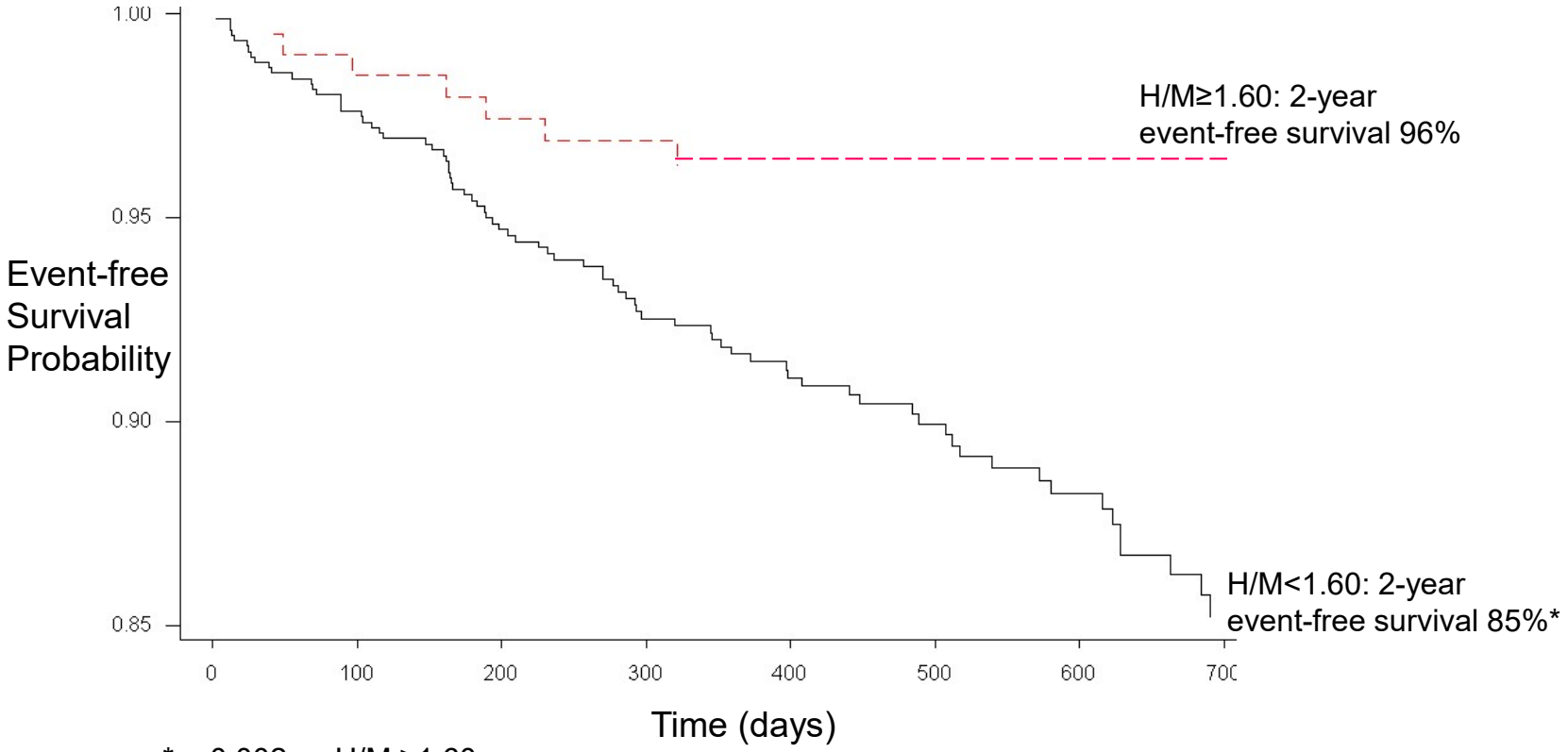


*p=0.002 vs H/M ≥1.60

Jacobson et al, JACC 2010

ADMIRE-HF: événements rythmiques

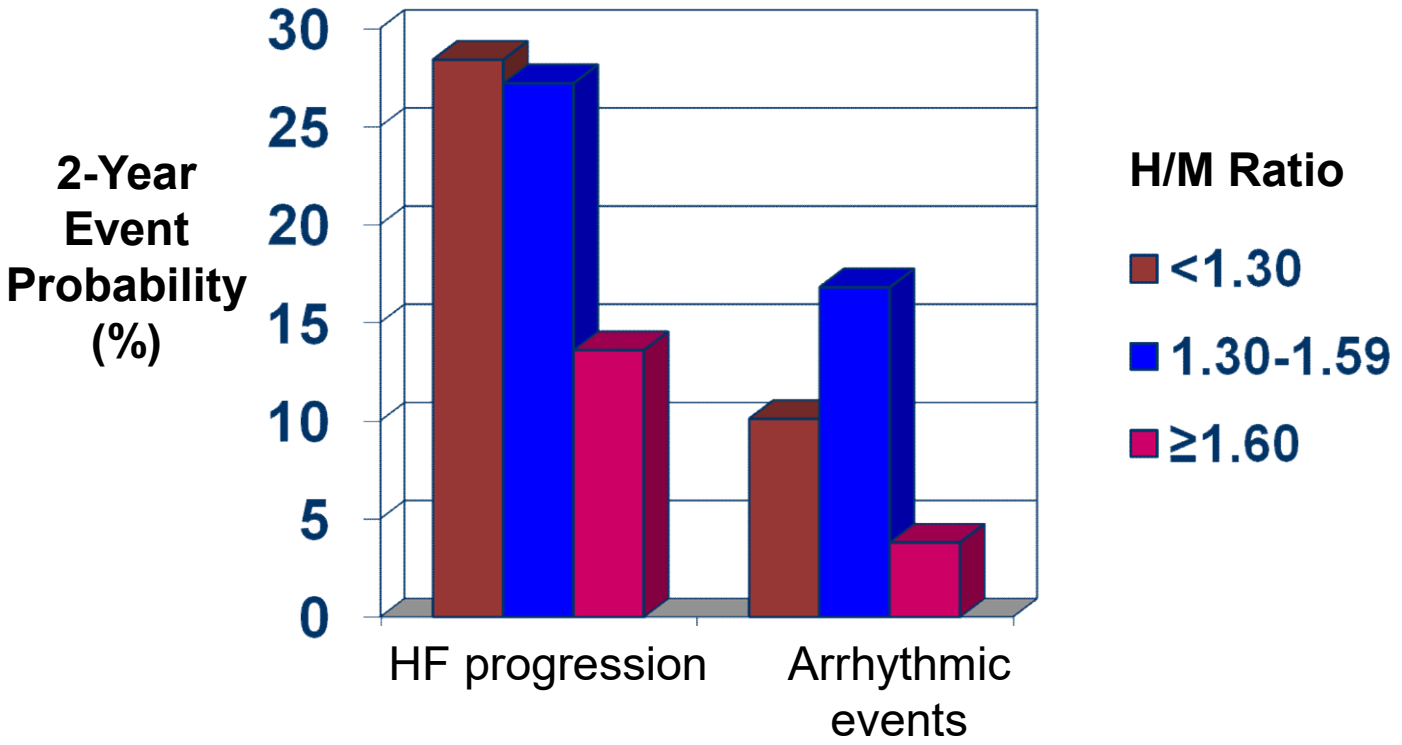
Arrhythmic Event



*p=0.002 vs H/M ≥1.60

Jacobson et al, JACC 2010

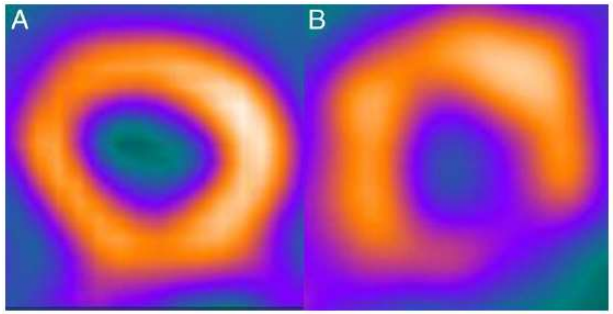
Insuffisance cardiaque : ADMIRE-HF



Differences between H/M≥1.60 and other groups are all significant ($p<0.05$).
Differences between H/M<1.30 and 1.30-1.59 are both $p>0.05$.

Jacobson et al, JACC 2010

Étude de Leiden



Perfusion **Innervation**

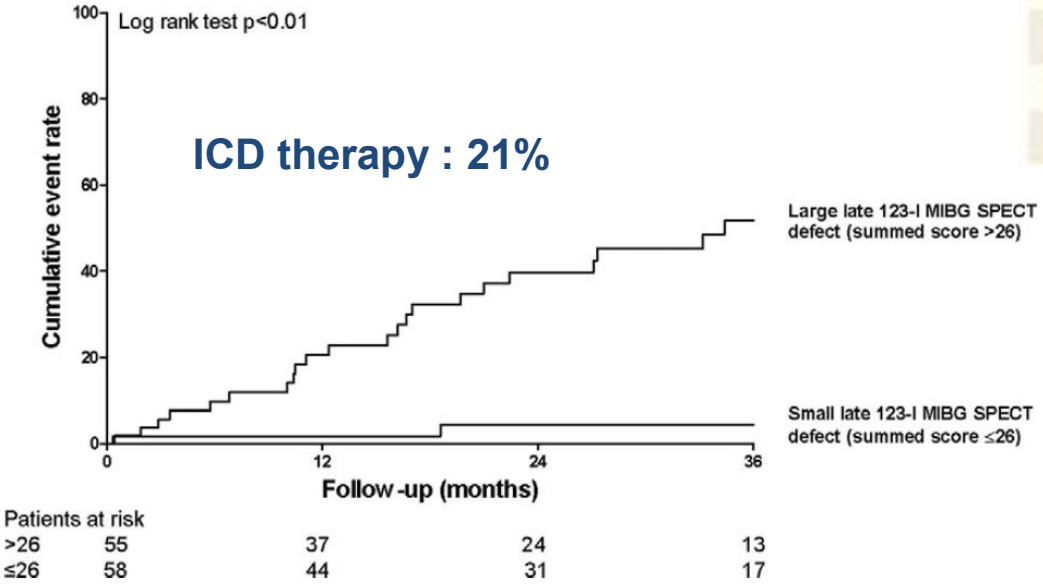
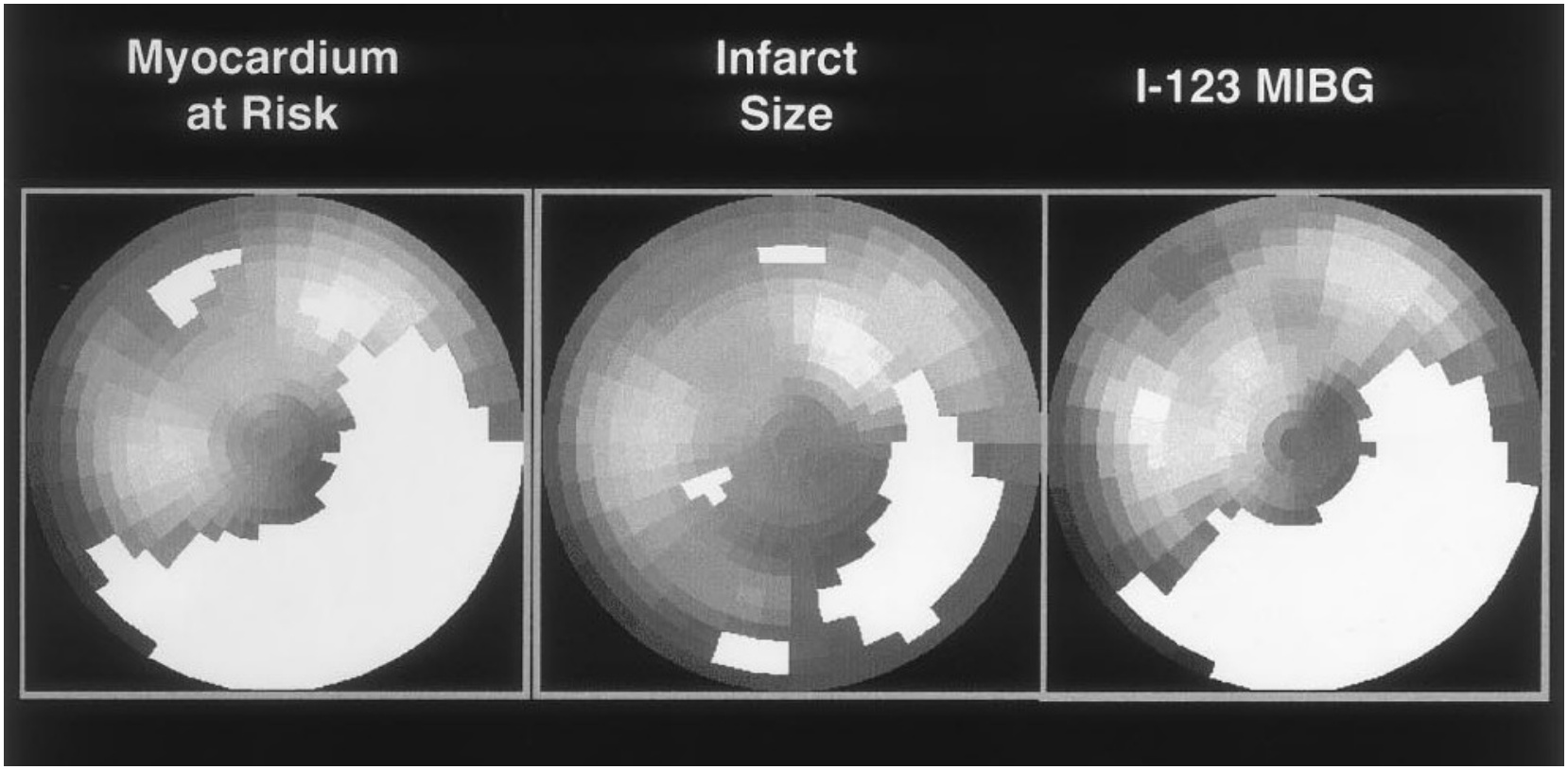


Table 1 Baseline Characteristics of the Study Population (n = 116)

Characteristics	Values
Age (yrs)	65 ± 9
Male sex	80 (69)
CRT-D	101 (87)
ICD indication	
Primary prevention	103 (89)
Secondary prevention	13 (11)
Ischemic cardiomyopathy	86 (74)
NYHA functional class	2.9 ± 0.6
LVEF (%)	28 ± 8

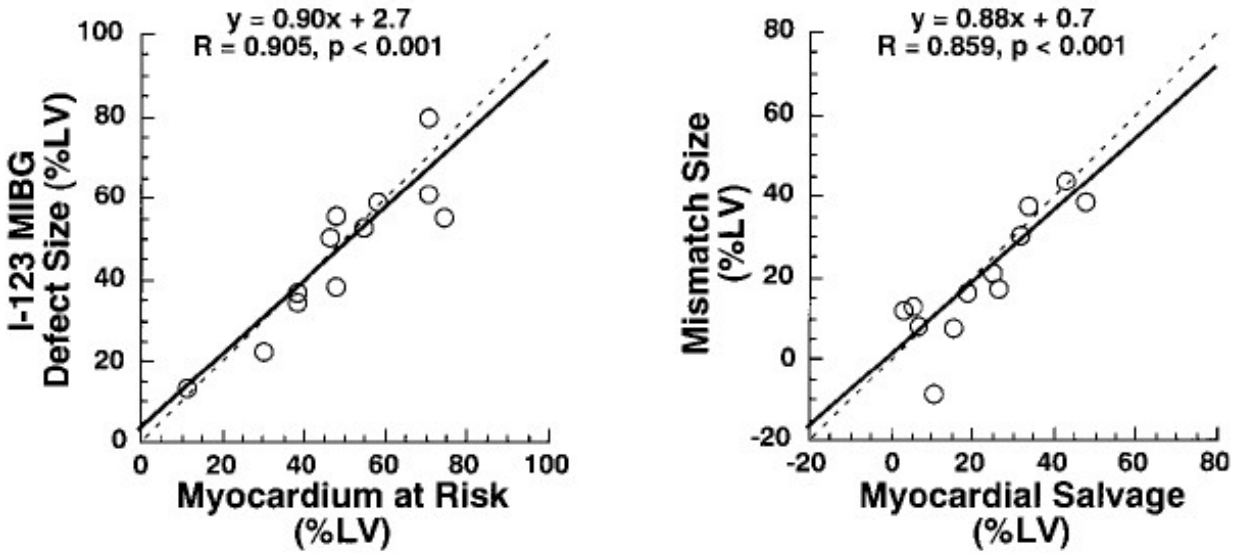
Boogers et al, JACC 2010

Après un SCA : l'étendue de la dénervation sympathique cardiaque est déterminée par le territoire à risque (ischémique)



Matsunari, Circulation 2000

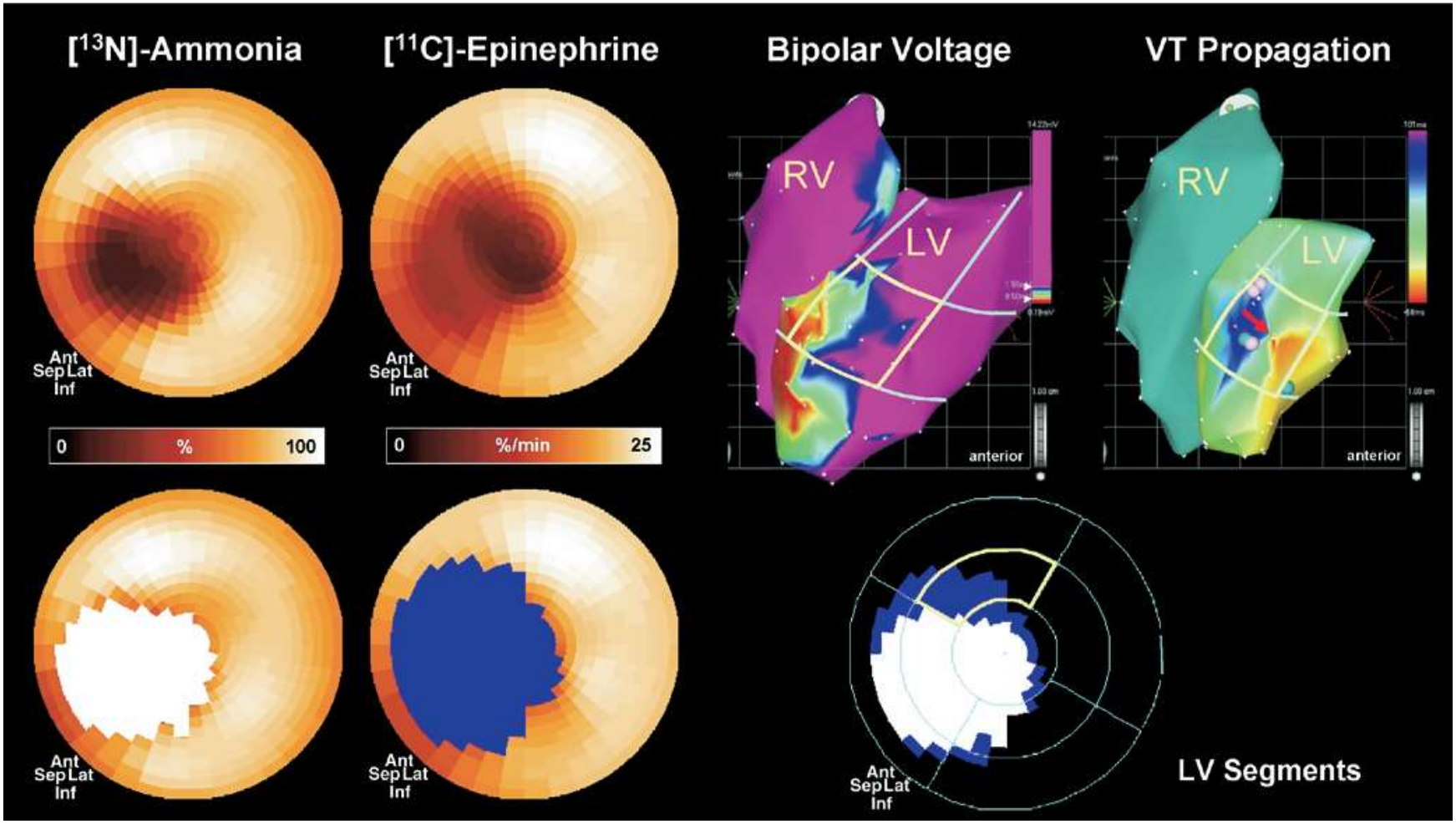
Après un SCA : l'étendue de la dénervation sympathique cardiaque est déterminée par le territoire à risque (ischémique)



- Les fibres sympathiques sont plus sensibles à l'ischémie que les cardiomyocytes
- Dans le post-infarctus, la ***dénervation sympathique*** se superpose au ***territoire à risque***

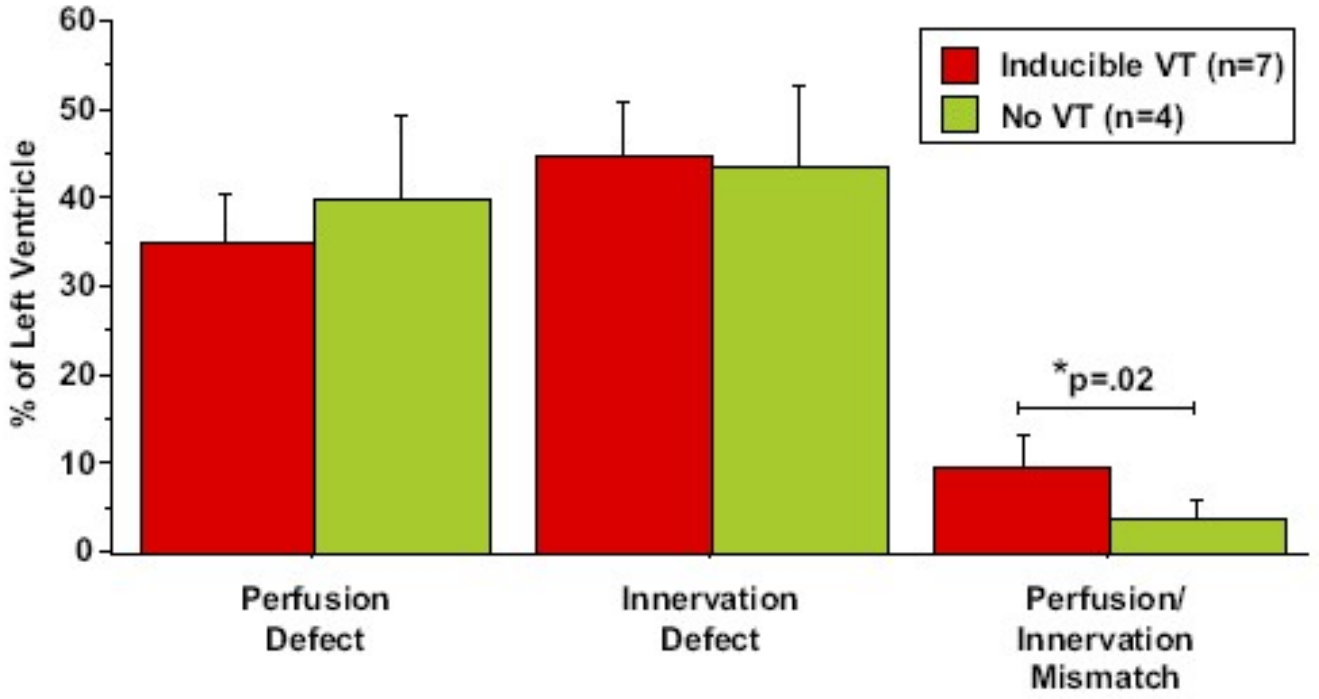
Matsunari, Circulation 2000

Discordance perfusion/innervation



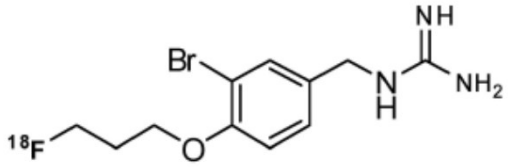
Perfusion **Innervation**

Abnormal Sympathetic Innervation of Viable Myocardium and the Substrate of Ventricular Tachycardia After Myocardial Infarction

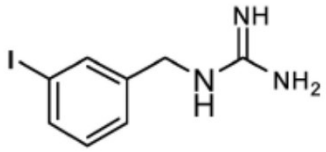


Sasano et al, JACC 08

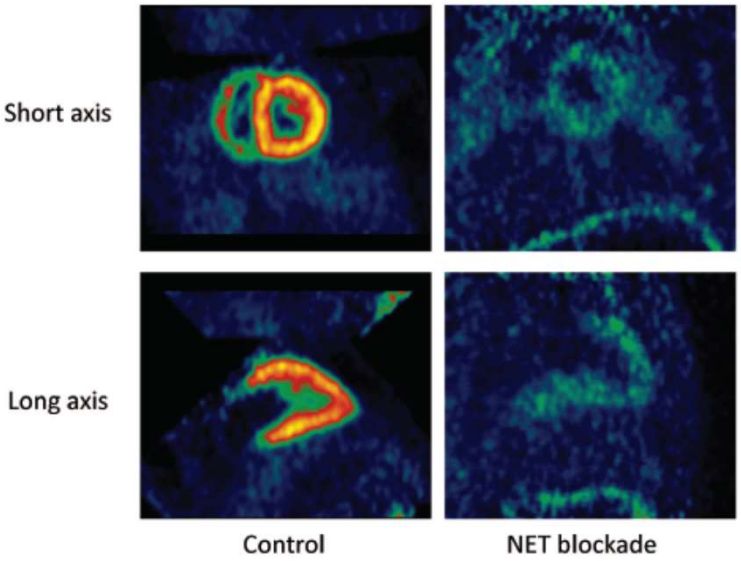
Perspectives : LMI 1195

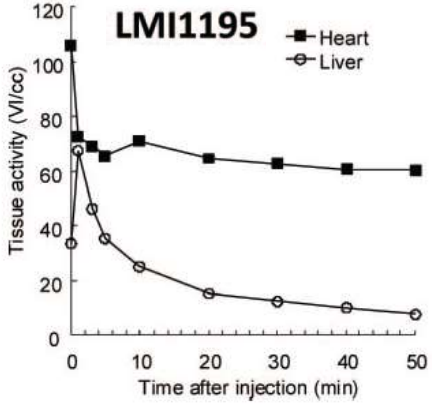


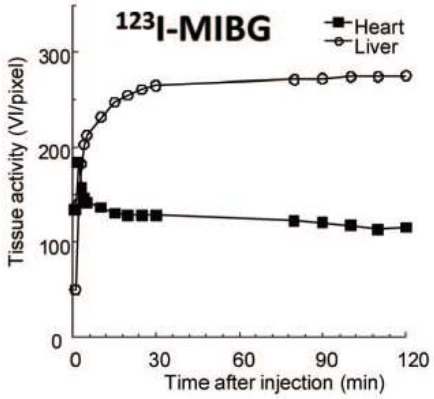
LMI1195



MIBG

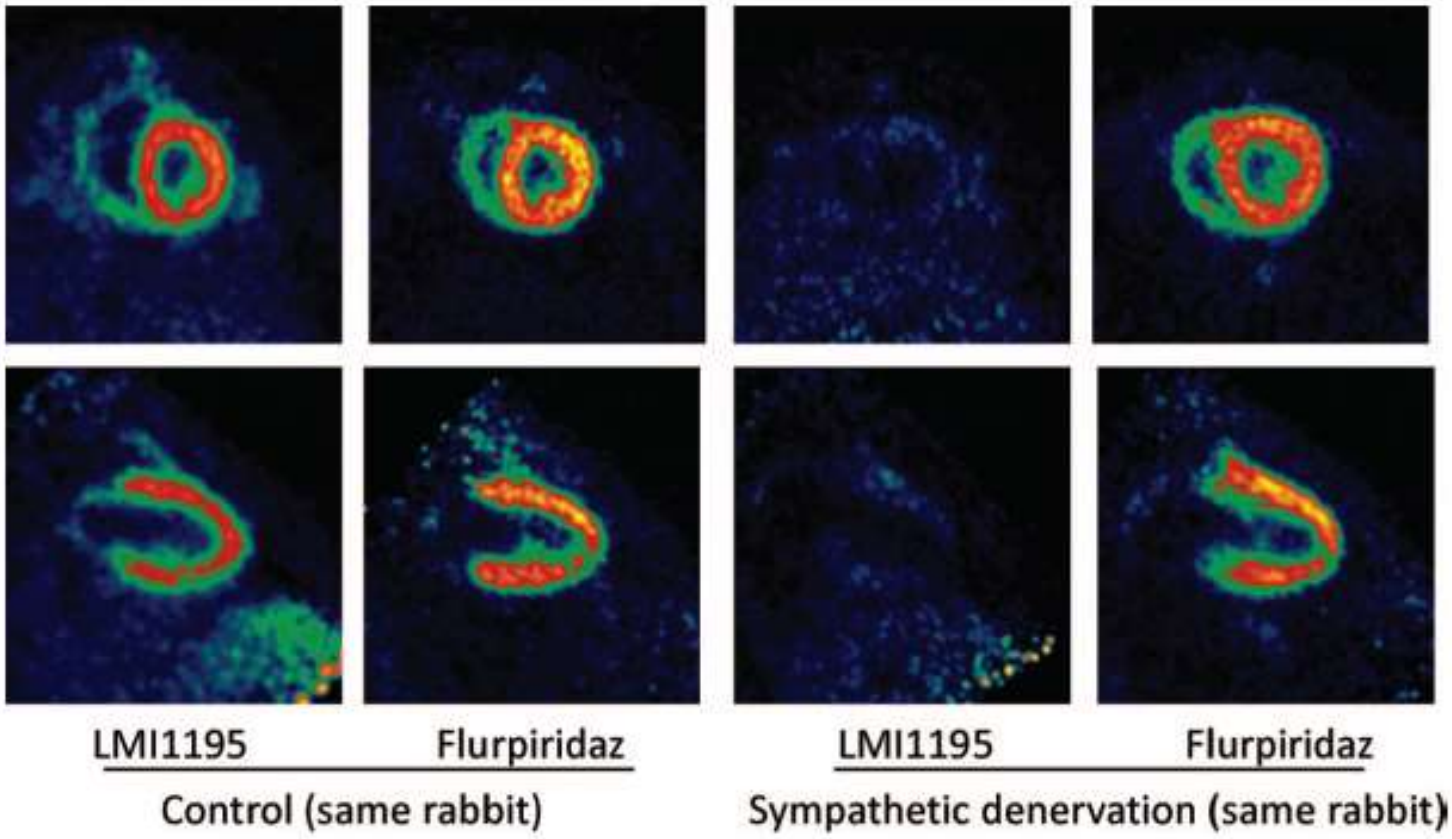






Yu et al, Circ Imaging 2011

Perspectives : LMI 1195



Yu et al, Circ Imaging 2011

En résumé

- La MIBG est un marqueur robuste de la dénervation sympathique cardiaque
- Elle possède une excellente valeur pronostique dans l'insuffisance cardiaque
- Des études sont en cours pour évaluer son rôle potentiel dans la sélection des patients candidats à un DAI