IMAGING CARDIAC INNERVATION AND RECEPTORS

Ignasi Carrió, Barcelona
SPECT IMAGING OF CARDIAC NEUROTRANSMISSION

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myocardial $^{123}$I-MIBG study

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I-123 MIBG myocardial SPECT

early

delayed

early

delayed

Slides are not to be reproduced without the permission of the author
I-123 MIBG myocardial SPECT

early

delayed

washout

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Clinical Role of MIBG imaging

PRIMARY CARDIONEUROPATHIES

- Dysautonomias: may be useful in the clinical classification
- Idiopathic ventricular tachycardia: demonstration of impaired presynaptic reuptake
- Heart Transplantation: denervation and re-innervation can be assessed.
MIBG uptake of postganglionic cardiac neurons is reduced in stage I and severely in stages Hoehn and Yahr II or higher of Parkinson’s disease.

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MIBG IN THE DIFFERENTIAL DIAGNOSIS OF PARKINSONIAN SYNDROMES

• Meta-analysis of studies with 246 cases of Parkinson and 45 cases of multiple system atrophy

• Sensitivity to detect Parkinson of 89.7% with specificity of 94.6%

*Braune, Clin Auton Res 2001;11:351-355*
CLINICAL CORRELATES IN PARKINSON’S DISEASE
Akincioglu NMC 2003;24:267-271

early          delayed

CONTROL

PD: UPDRS score of 13

PD: UPDRS score of 5

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IDIOPATHIC VENTRICULAR TACHYCARDIA AND FIBRILLATION

Schafers et al JACC 1998;32:181-186

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CARDIAC AUTONOMIC DYSFUNCTION IN BRUGADA SYNDROME. *Witcher, Circulation* 2002;105:702-706
HEART TRANSPLANTATION

**MIBG**

**Pre-transplantation**

**MIBG**

**Post-transplantation**

*Estorch et al, JNM 1999;40:911-916*

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Role of MIBG imaging

SECONDARY CARDIONEUROPATHIES

- CAD: identification of vulnerability to arrhythmias
- Dilated cardiomyopathies: prognosis, assessment/prediction of response
- Diabetes mellitus: assessment of neuronal integrity
- Cardiotoxicity: assessment of neuronal damage
• Viable but denervated tissue is supersensitive to sympathetic stimulation and may precipitate ventricular arrhythmias

• ICDs may reduce sudden cardiac death in LV dysfunction (MADIT II, COMPANION, DEFINITE …)

• Identification of patients who are unlikely to benefit from ICD placement. High negative predictive value would be needed …..

MIBG and selection of patients for ICDs?
MIBG and selection of patients for ICDs

*No patient with H/M > 1.54 and 5-minute low frequency > 433 ms² had an ICD discharge*
PROGNOSTIC VALUE OF MIBG IMAGING IN HEART FAILURE

Survival rate vs. Elapsed time in months for DCM and IDCM.

- **DCM, n=90**
  - H/M<120%
  - Survival rate decreases over time.

- **IDCM, n=112**
  - H/M<120%
  - Survival rate decreases over time.

**Merlet et al. JNM 1992**

**Merlet et al. JNM 1998**

**Acar, Heart 2001;85(6):692-696 (Childhood DCM)**

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PROGNOSTIC VALUE OF MIBG IMAGING IN HEART FAILURE


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PREDICTION OF RESPONSE TO β-BLOCKER THERAPY

Suwa et al. Am Heart J, 1997
Yamazaki et al. Am Heart J, 2001

INITIAL

HM

DELAYED

HM

2.1±0.4
1.5±0.2

WASHOUT

HM

%
I-123 MIBG myocardial SPECT

early

delayed

washout

washout rate

LVEF

before
0.4 yrs.
3.3 yrs.
6.8 yrs.

56%
24%
19%
18%

28%
59%
65%
62%

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I-123 MIBG myocardial SPECT

early

delayed

washout

before 0.4 yrs. 2.0 yrs. 2.5 yrs.

washout rate 56% 56% 61% 57%

LVEF 41% 42% 38% 40%

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21.9% increase in mean MIBG uptake after 6 months of metoprolol. A randomized placebo-controlled study in CHF

De Milliano Am Heart J 2002;144:2:E3
Patients with relatively advanced impairment of baseline I-123 MIBG uptake are most likely to show evidence of improved cardiac sympathetic nervous system function in response to carvedilol therapy.

Gerson et al, J Nucl Cardiol 2002;9:608-15

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IMPACT OF CARVEDILOL ON CARDIAC ADRENERGIC FUNCTION IN CHILDREN WITH CDM

6 months of carvedilol

HMR: 1.62±26  
LVEF: 26±11%

2.23±49  
43±17%

Maunoury, EJNM 2003;12:1604-1611

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EFFICACY OF CARVEDILOL AND METOPROLOL ON CARDIAC FUNCTION AND SYMPATHETIC ACTIVITY. Toyama et al JNM 2003;44:1604-1611

Change in Total Defect Score and H/M ratio related to favorable response

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EFFICACY OF CARVEDILOL AND METOPROLOL ON CARDIAC FUNCTION AND SYMPATHETIC ACTIVITY.

Toyama et al. JNM 2003;44:1604-1611
ADDICTION OF VALSARTAN TO AN ANGIOTENSIN-CONVERTING ENZYME INHIBITOR IMPROVES SYMPATHETIC ACTIVITY AND LV FUNCTION IN CHF.


Addition of valsartan to ACE

ACE

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EFFICACY OF AMIODARONE TREATMENT ON CARDIAC SYMPTOM, FUNCTION AND SYMPATHETIC ACTIVITY IN DCM. Toyama et al J Nucl Cardiol 2004;11:131-141
CHEMOTHERAPY: MIBG IN PREDICTING SIGNIFICANT CARDIOTOXICITY

If impaired MIBG uptake at intermediate dose, consider: continuous infusion or cardioprotection

Carrió, JNM 2001;42:1062-1076
“STRESS” CARDIAC MIBG IMAGING

tyrosine

DOPA

dopamine

noradrenaline

NE NE NE

PRESYNAPSE

Tricyclic antidepressants

uptake 1

SYNAPTIC CLEFT

β receptors

G proteins

ATP

cAMP

MYOCYTE

123I-MIBG

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2 day protocol

- Patients studied to rule out Parkinson disease and normal MIBG scan
- day 1: Baseline MIBG study
- day 2: Oral dose of Amitriptyline (25 mg). “Stress” MIBG study
CHANGES IN MIBG ACTIVITY AFTER AMITRIPTYLINE CHALLENGE

- Patient n. 1
- Patient n. 2
- Patient n. 3
- Patient n. 4
- Patient n. 5
- Patient n. 6

Legend:
- White: no change
- Gray: 5-10% decrease
- Black: > 10% decrease

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IMPLICATIONS

• “stressing” the reuptake mechanism is feasible and may unmask subclinical neuronal abnormality

• changes in the global and regional MIBG uptake can be seen after a single dose of amitriptyline

• response to such pharmacologic stress could relate to outcome and may allow stratification of patients
FUTURE DIRECTIONS IN CARDIAC NEUROTRANSMISSION IMAGING

• Development of new radioligands for SPECT for new types of receptors

• Prediction and assessment of response to therapy (hypertension, ß-blockers, cardiotoxicity, etc.)

• Assessment of vulnerability to arrhythmias in denervated but viable myocardium

• Selection of patients for expensive devices

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