Manejo clínico del paciente con miocarditis

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Patogénesis Miocarditis

Dennert el al. Eur Heart J 2008; 29:2073

Patogénesis Miocarditis

Table I Causes of myocarditis

Infectious causes	Non-infectious causes
RNA viruses: picornaviruses (coxsackie A + B, echovirus, poliovirus, hepatitis virus), orthomyxovirus (influenza), paramyxoviruses (respiratory syncitial virus, mumps), togaviruses (rubella), flaviviruses (dengue fever, yellow fever)	Autoimmune diseases: dematomyositis, inflammatory bowel disease, rheumatoid arthritis, sjögren syndrome, systemic lupus erythematodes, Wegener's granulomatosis, giant cell myocarditis
DNA viruses: adenovirus (A 1, 2 ,3, and 5), erythrovirus [1 (B19V) and 2], herpesviruses (human herpes virus 6 A/B, cytomegalievirus, Epstein-Barr virus, varicella-zoster virus), retrovirus (HIV)	Drugs: aminophyllin, amphetamine, anthracyclin, catecholamines, chloramphenicol, cocain cyclophosphamid, doxorubicin, 5-fluoruracil, mesylate, methylsergit, phenytoin, trastuzumab, zidovudine
Bacteria: chlamydia (*C. pneumonia*/psittacosis) haemophilus influence, legionella, pneumophilia, brucella clostridium, francisella tularensis, neisseria meningitis, mycobacterium (tuberculosis), salmonella, staphylococcus, streptococcus A, S. pneumonia, tularemia, tetanus, syphilis, *Vibrio cholera*	Hypersensitivity reactions (drugs): azitromycin, benzodiazepines, clozapine, cephalosporins, dapsone, dobutamin, lithium, diuretics, thiazide, methyldopa, mexiletine, Streptomycin, sulfonamides, non-steroidal anti-inflammational drugs, tetanus toxoid, tetracycline, tricyclic antidepressiva
Spirocheta: *Borrelia recurrentis*, leptospira, *Treponema pallidum*	Hypersensitivity reactions (venomes): bee, wasp, black widow spider, scorpion, snakes
Reckettsia: *Coxiella burnetii*, *R. rickettsii/prowazekii*	Systemic diseases: Churg-Strauss syndrome, collagen diseases, sarcoidosis, Kawasaki disease, scleroderma
Fungi: actinomyces, aspergillus, candida, cryptococcus, histoplasma, nocardia	Others: heart stroke, hypothermia, transplant rejection, radiation injury
Protozoa: *Entamoeba histolytica*, leishmania, *Plasmodium falciparum*, *Trypanosoma cruzi*, *Trypanosoma brucei*, *Toxoplasma gondii*	
Helmintic: ascaris, *Echinococcus granulosus*, Schistosoma, *Trichinella spiralis*, *Wuchereria bancrofti*	

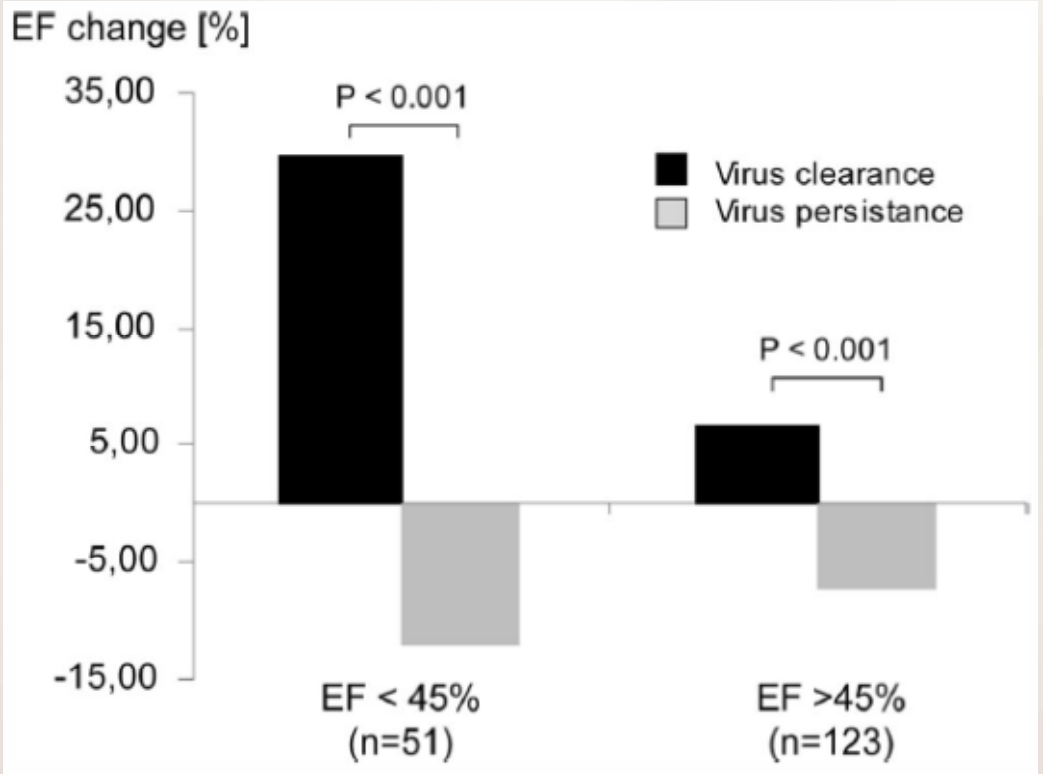
Schultheiss et al. Eur Heart J 2011;32:2616

Infección viral

TABLE 3. Distribution of Virus Genomes at Baseline and Follow-Up

	No. of Subjects (N=172)	Virus Clearance
PVB19	63 (36.6)	14/63 (22.2)
EV	56 (32.6)	28/56) (50.0)
HHV6	18 (10.5)	8/18 (44.4)
ADV	14 (8.1)	5/14 (35.7)
PVB19+HHV6	21 (12.1)	9/21 (42.8)

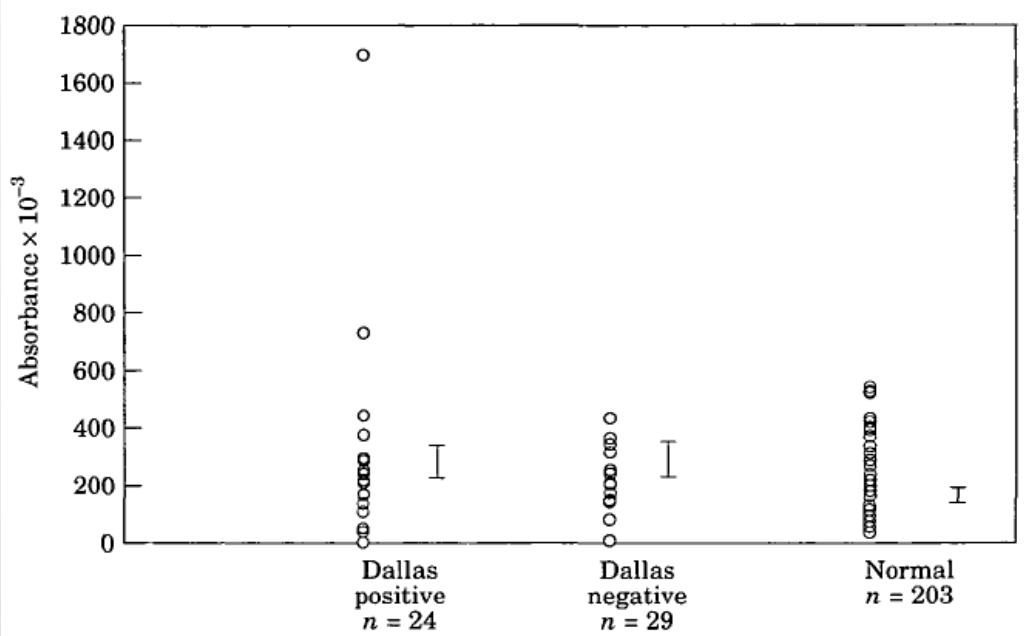
Data are presented as No. (%) of subjects.



Kühl et al. Circulation 2005;112:1965

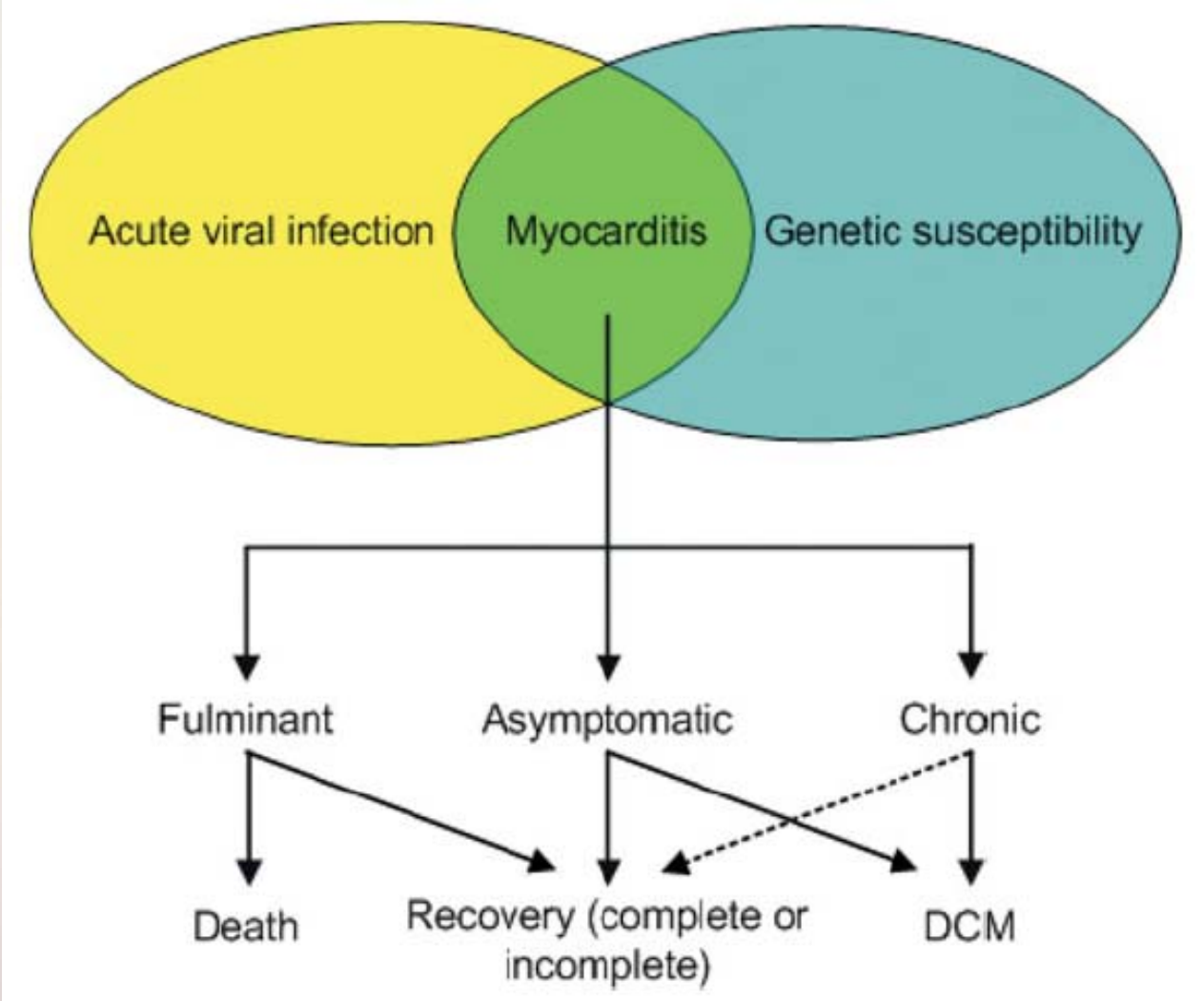
Autoanticuerpos en miocarditis

- Presentes en hasta el 50% de pacientes con miocarditis en BEM
- Anticuerpos anti-α-myosina



Caforio et al Eur Heart J 2007; 28:1326-1333
Caforio et al. NEJM 1997; 18:270

Clínica Miocarditis

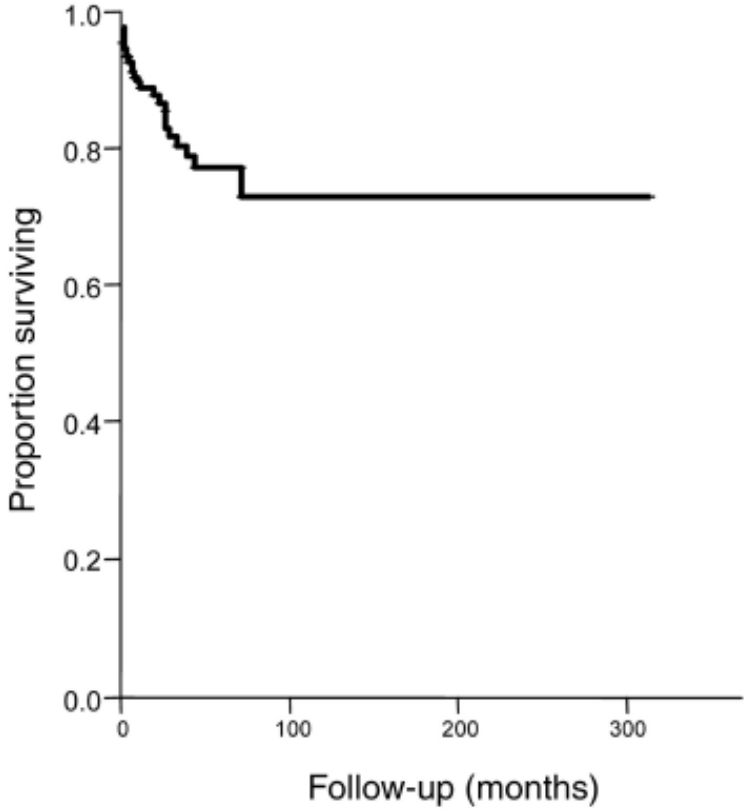


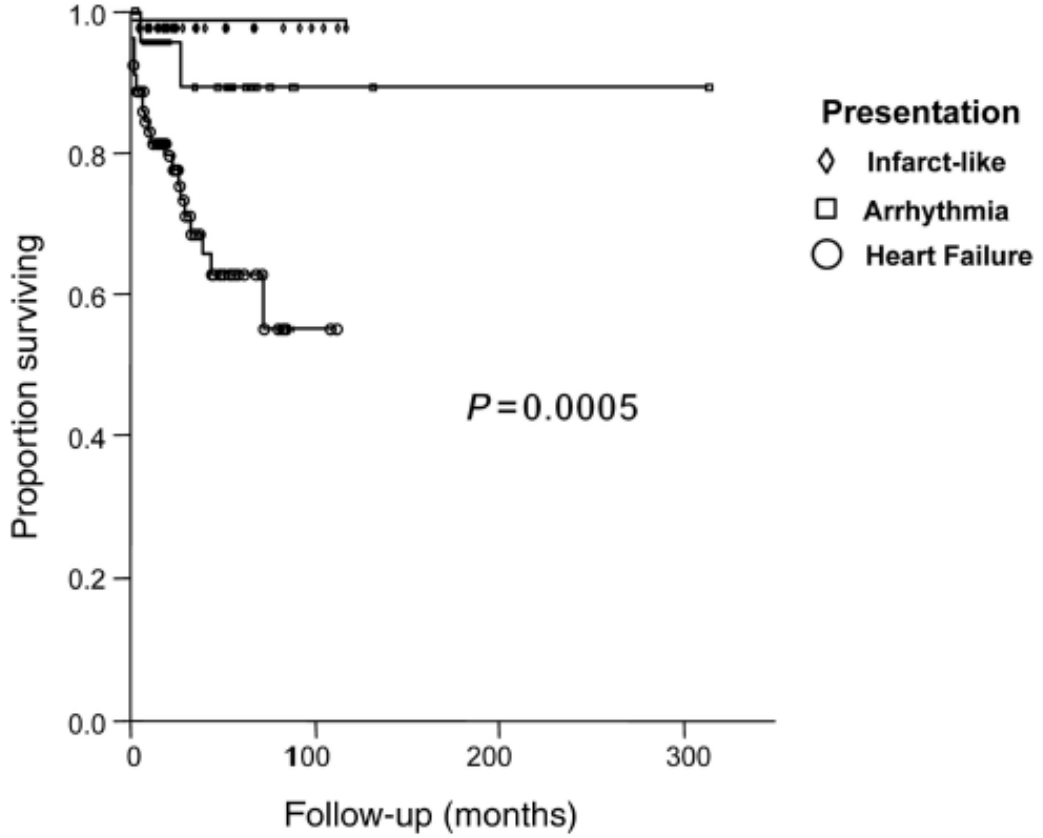
Dennert el al. Eur Heart J 2008; 29:2073

Diagnóstico clínico de miocarditis

- ¿Cuándo pensar en miocarditis?
  - Miocardiopatía rápidamente progresiva
  - Arritmias ventriculares idiopáticas
  - Shock cardiogénico no explicado
  - SCA con arterias coronarias normales
- Diagnóstico diferencial:
  - Otras causas infecciosas: Lyme
  - Miocarditis autoinmune o farmacológica
  - Miocarditis células gigantes
  - Miocarditis eosinofílica
  - Miocardiopatía periparto
  - Sarcoidosis cardíaca

Pronóstico miocarditis

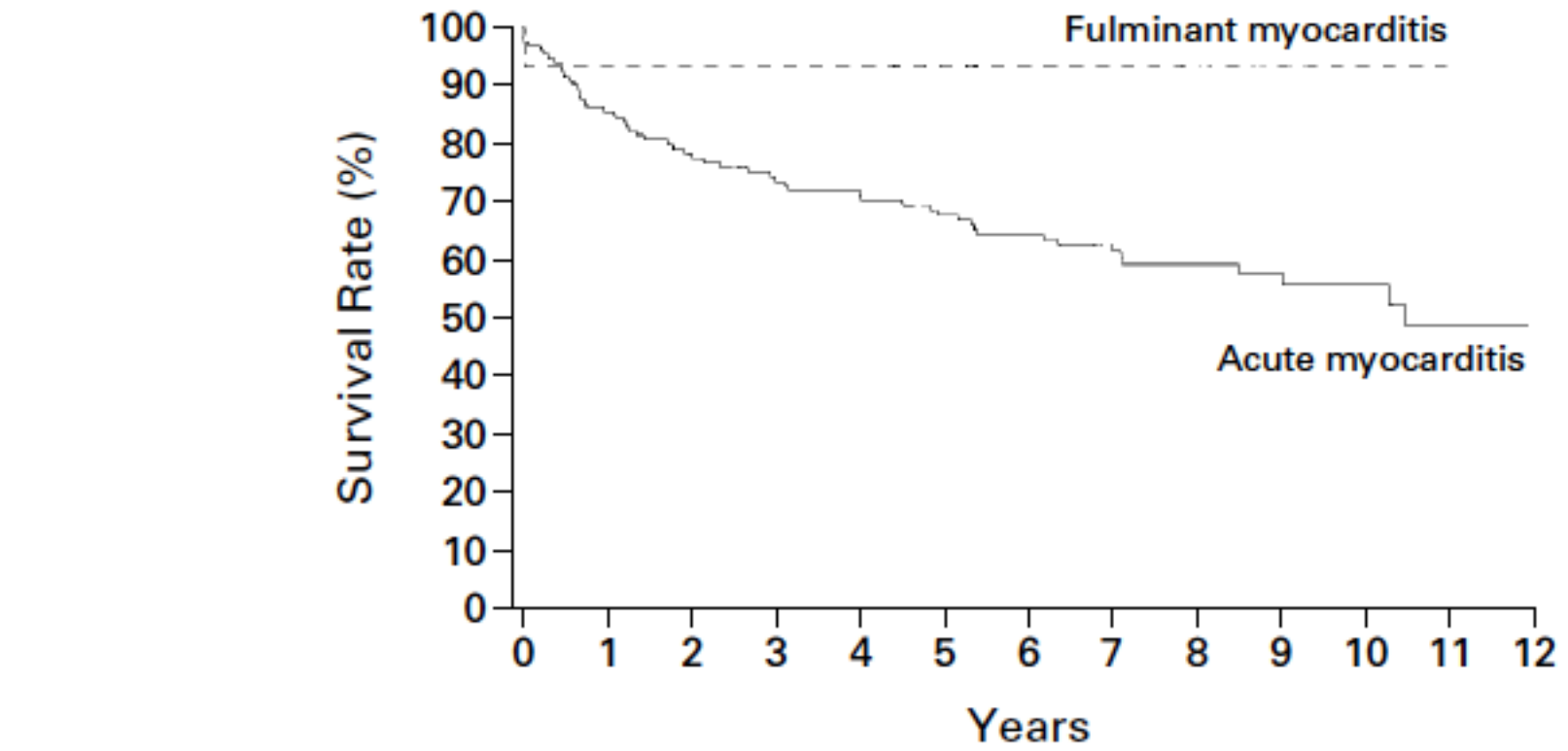




- N=174 pacientes con miocarditis por BEM

Caforio et al. Eur Heart J 2007; 28:1326

Pronóstico Miocarditis



No. at Risk												
Acute myocarditis	132	110	98	91	84	79	73	59	41	28	18	3	0
Fulminant myocarditis	15	12	12	10	10	9	7	5	4	3	2	0	0

McCarthy III et al. NEJM 2000; 342:690

Diagnóstico: Indicación de BEM Clase I

- VI normal o dilatado con:
  - Síntomas de IC de < 2 semanas de duración
  - Compromiso hemodinámico
- VI dilatado con:
  - Síntomas de IC de 2 semanas a 3 meses
  - Nuevas arritmias ventriculares o BAV 2º grado Mobitz 2 o BAV 3er grado
  - No respuesta a tto médico habitual en 1-2 semanas

Cooper LT et al. J Am Coll Cardiol 2007;50:1914

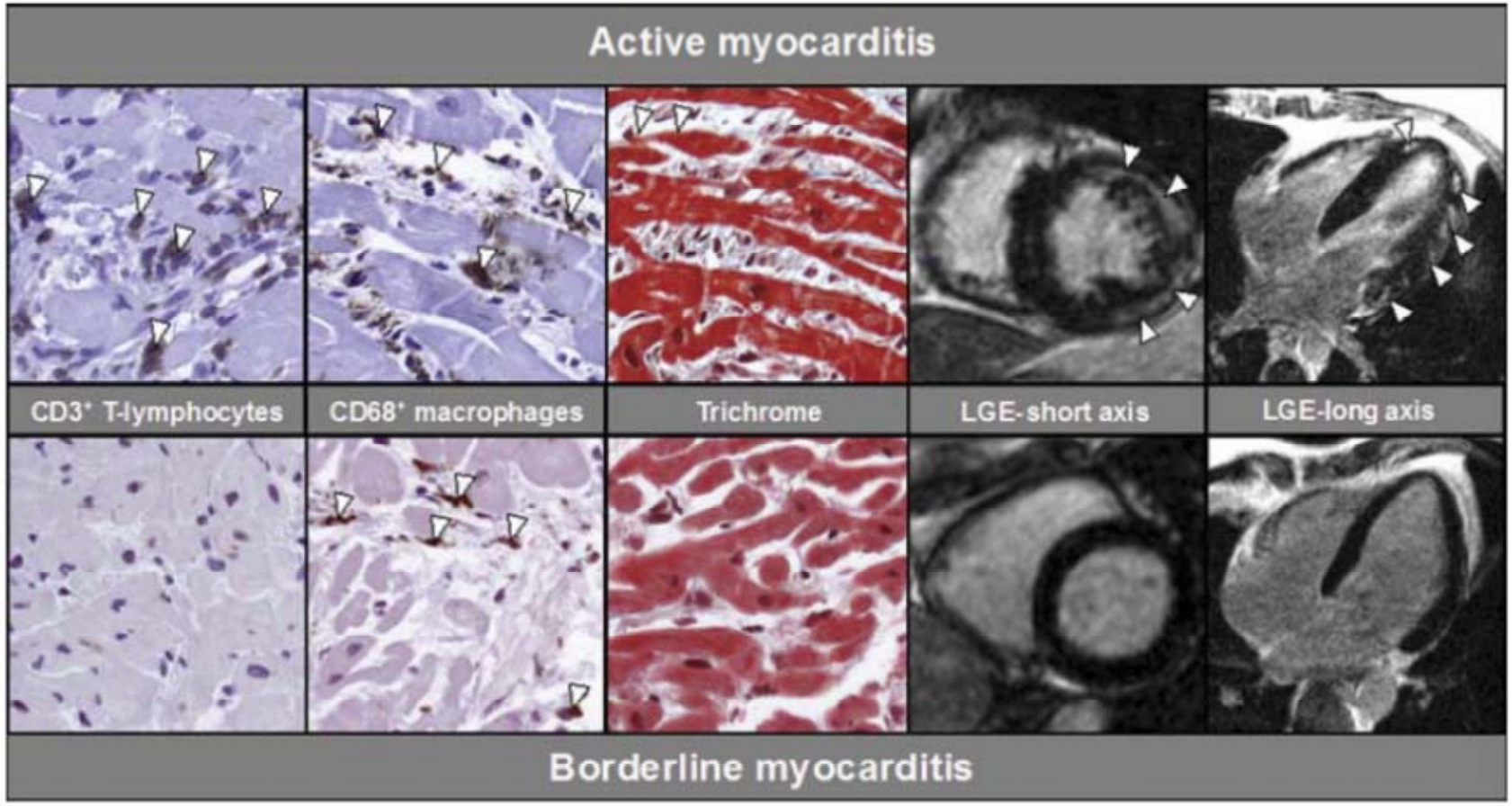
Complicaciones BEM

- BEM en VD o VI o ambos guiada por RMN cardiaca en 755 pacientes
- 4 – 6 muestras por ventrículo en 2 – 3 zonas.
- Complicación mayor: 0,64% en VI y 0,82% en VD
  - Taponamiento cardiaco
  - Hemo o neumopericardio
  - BAV permanente
  - IAM
  - AIT o AVC
  - Daño valvular
  - Muerte
- Rendimiento diagnóstico de BEM del 70%

Yilmaz A et al. Circulation 2010;122:900

Diagnóstico Miocarditis

- Enfermedad inflamatoria del miocardio con

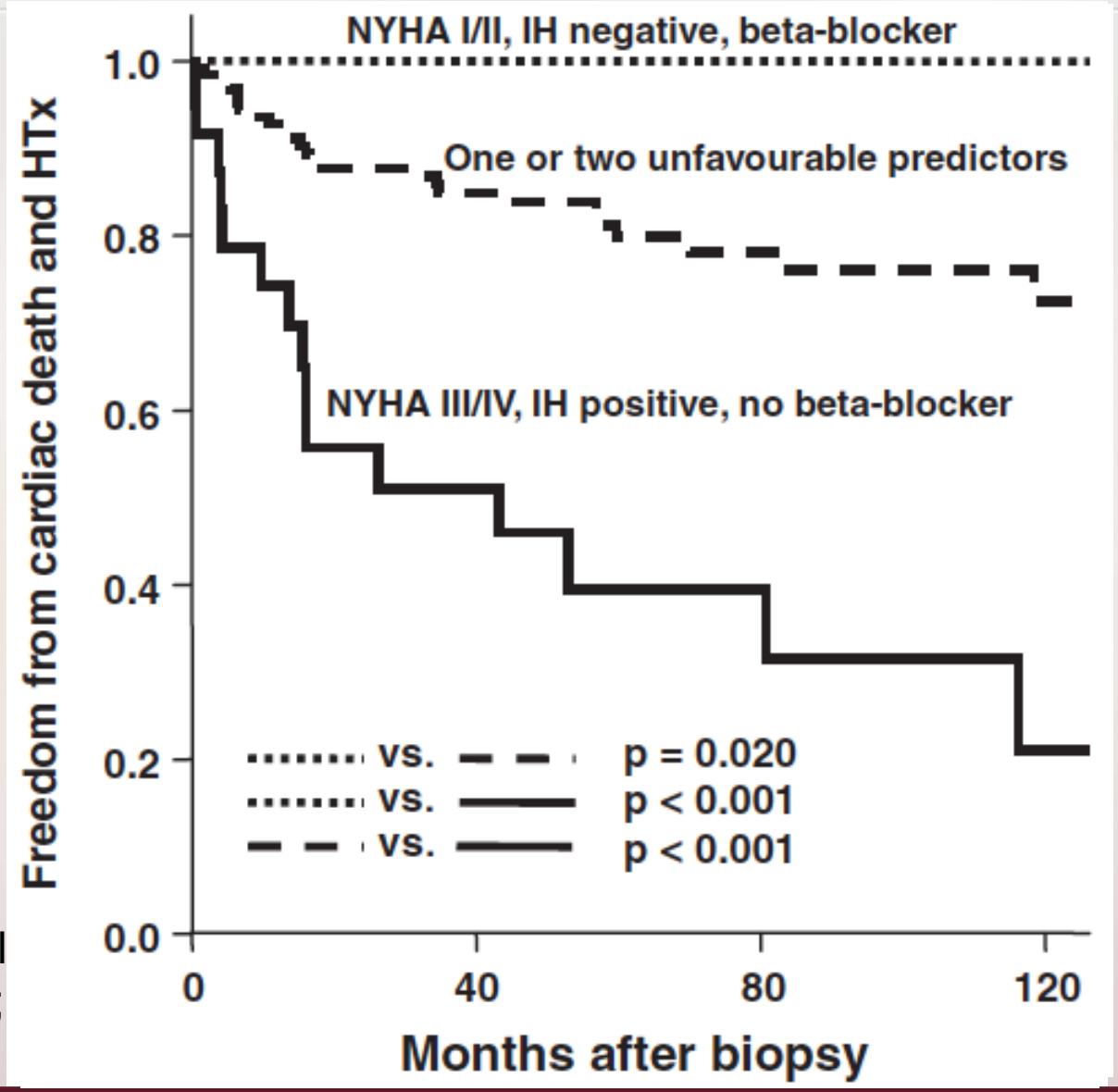


sis

  - PCR viral

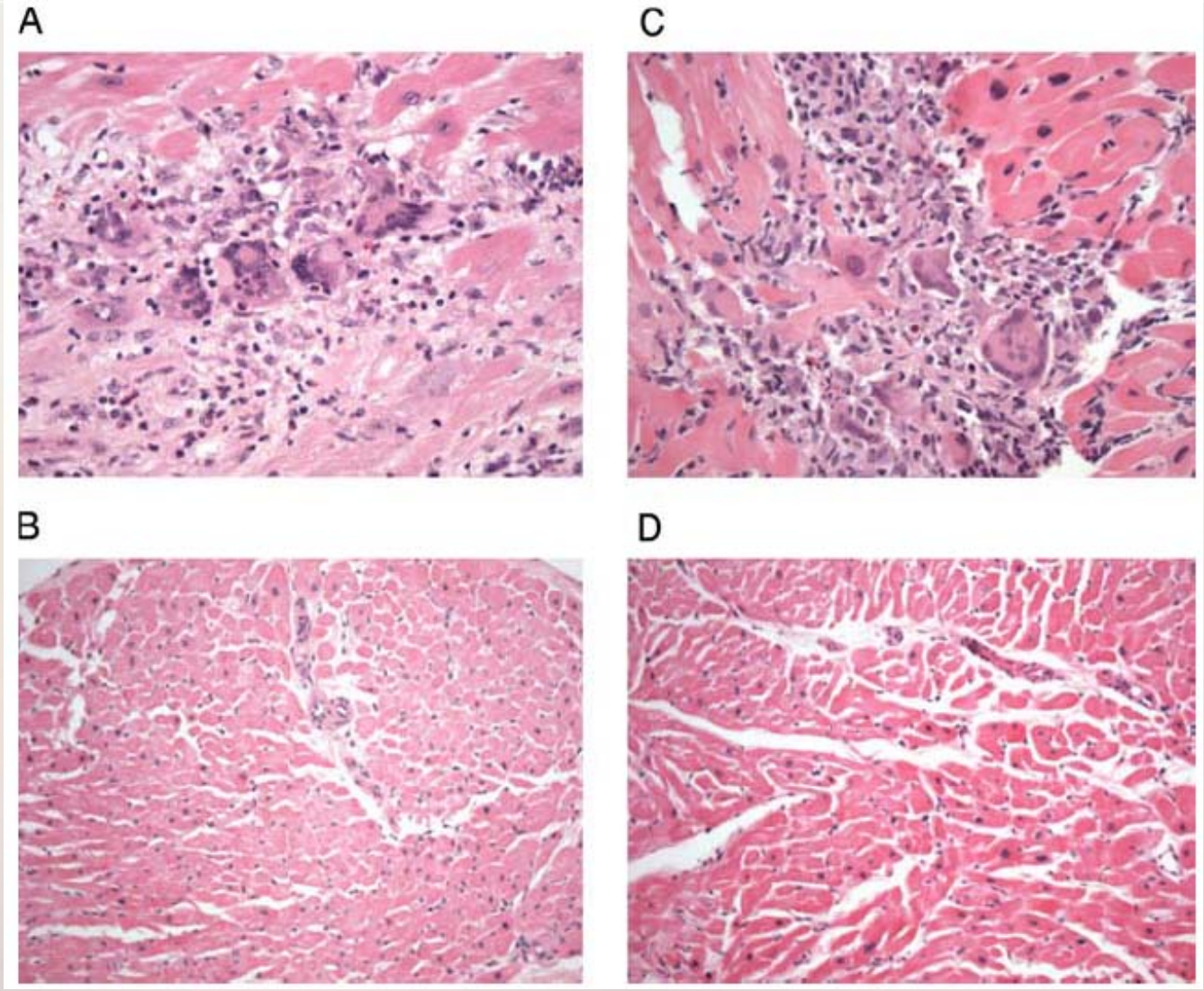
Richardson P et al. Circulation 1996;93:841

Utilidad pronóstica de la BEM



Kindermann et al
Circulation 2008;
118:639

¿Por qué hacer BEM?



Murray L, González-Costello et al. Eur J Heart Fail. 2012;14:312

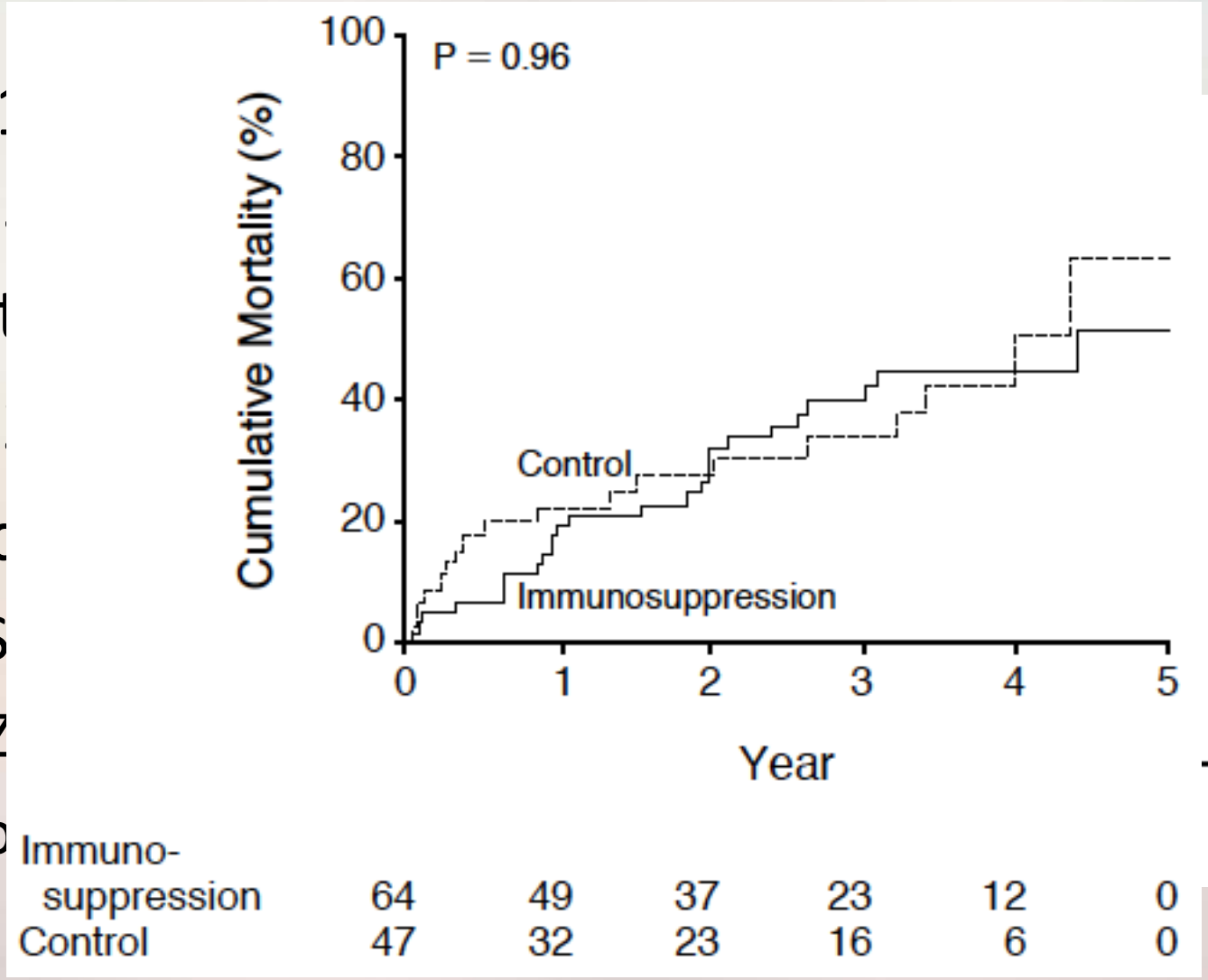
Tratamiento Miocarditis

- Limitar ejercicio físico: Puede aumentar replicación viral
- Tratamiento estándar de la IC: IECAs/BBloq
- Soporte mecánico con BCIAo o AV si precisa
- AINES a dosis mínimas para control de dolor en pacientes con cuadro de miopericarditis y FEVI normal

Schultheiss et al. Eur Heart J 2011; 32:2616

Tratamiento Miocarditis

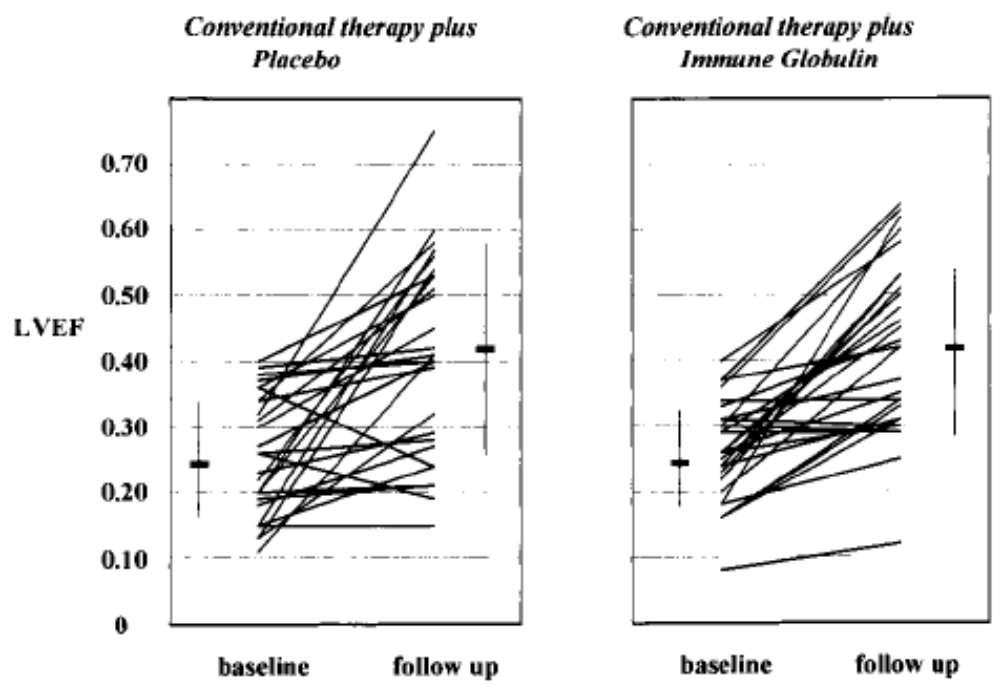
- N=1
- FEVI
  posit
- IC <
- Rand
  - CS
  - AZ
  - Co



Mason et al. N Engl J Med 1995;333:269

Tratamiento Miocarditis

- N = 62
- FEVI<40%
- IC < 6 meses duración
- Randomizado:
  - Inmunoglobulina ev
  - Control

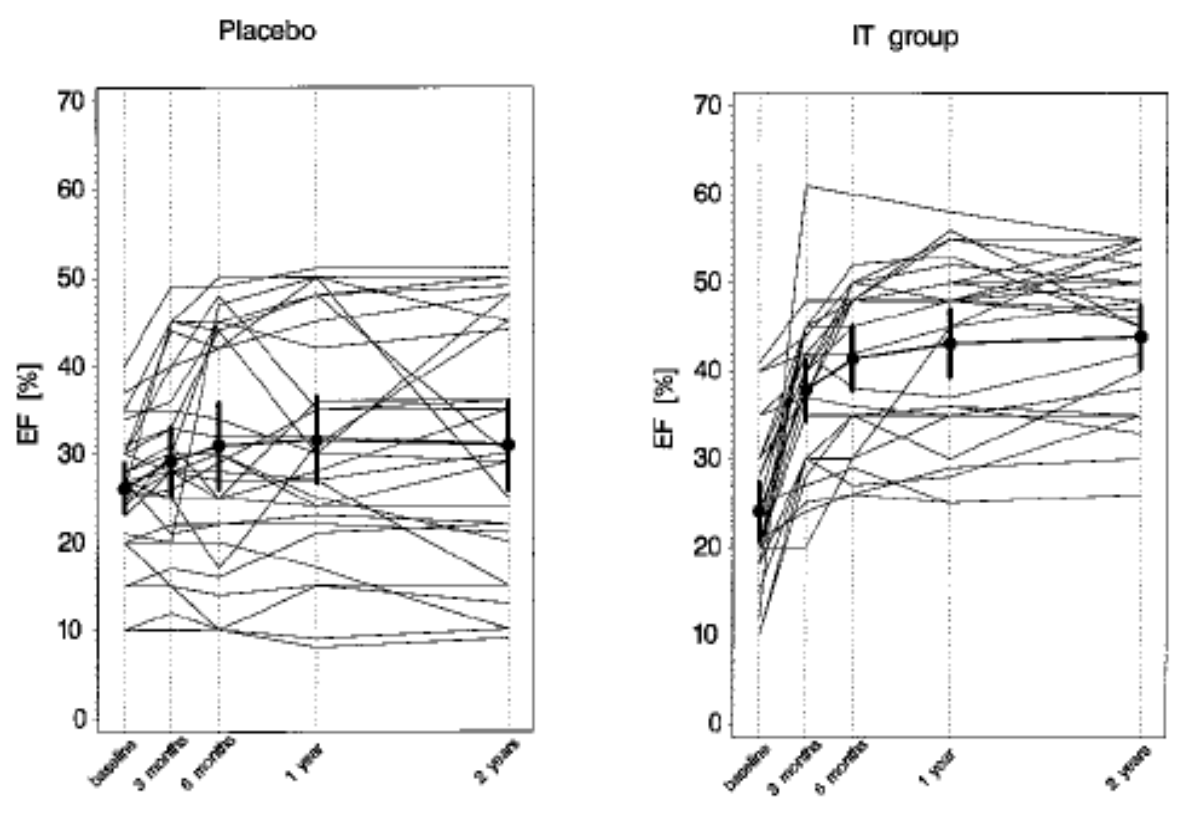


16% con BEM positiva (Criterios de Dallas)

McNamara DM et al. Circulation 2001:103:2254

Tratamiento Miocarditis

- N = 84
- Miocardiopatía dilatada
- >6 meses duración
- Aumento expresión HLA en BEM
- Randomizado:
  - Prednisona + AZA
  - Control



Wojnicz et al. Circulation 2001;104:39

- N
- En
- Es

		Baseline					After 6 Month IT	
Pt	Age/Sex	EF, %	NYHA Class	Viral Agent	Cardiac AutoAb	Months Since Disease Onset	EF, %	NYHA Class
1	55/M	21	IV	–	–	8	16	IV
2	62/F	23	IV	EBV	–	9	22	IV
3	29/F	33	IV	INFA	–	10	29	IV
4	37/M	30	III	PVB19	–	11	24	III
5	50/M	25	IV	EBV	–	12	20	IV
6	52/M	26	IV	EBV	–	8	24	IV
7	59/M	25	IV	–	–	9	17	III
8	54/M	33	IV	AV	–	7	32	IV*
9	49/M	28	IV	–	–	10	27	III
10	37/M	32	III	EV	–	11	28	IV*
11	59/M	30	III	AV	–	9	15	IV*
12	25/M	21	IV	AV+EV	–	9	20	IV†
13	51/M	24	IV	EV	–	8	24	IV*
14	41/M	31	III	AV	–	10	26	IV*
15	48/M	31	IV	EV	–	8	28	IV†
16	26/M	19	IV	EBV	–	9	18	III
17	34/M	25	IV	EV	–	8	24	IV†
18	27/M	29	III	EV	–	10	20	IV
19	57/F	32	III	EBV	–	10	28	III
20	56/M	27	IV	AV	–	9	24	III

Tratamiento antiviral con IFN-β

- N = 2

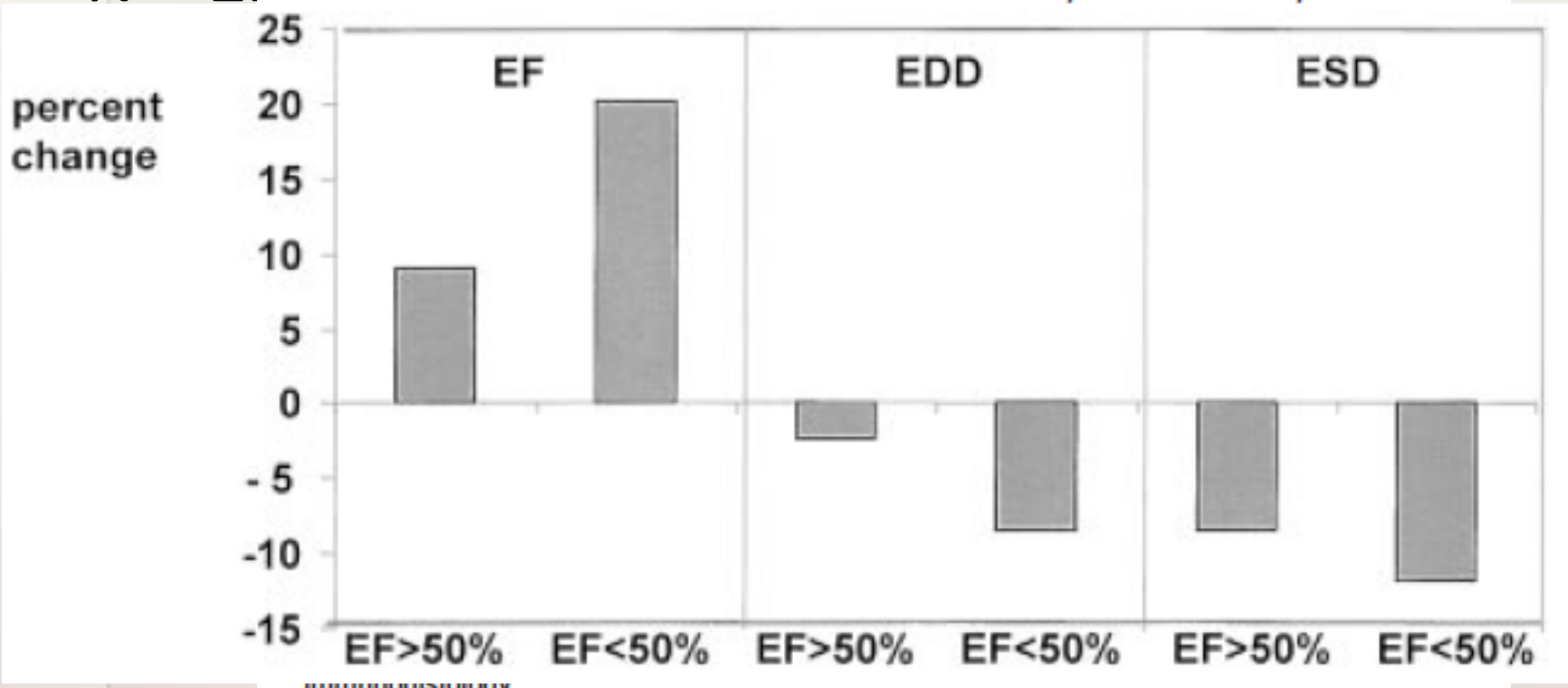
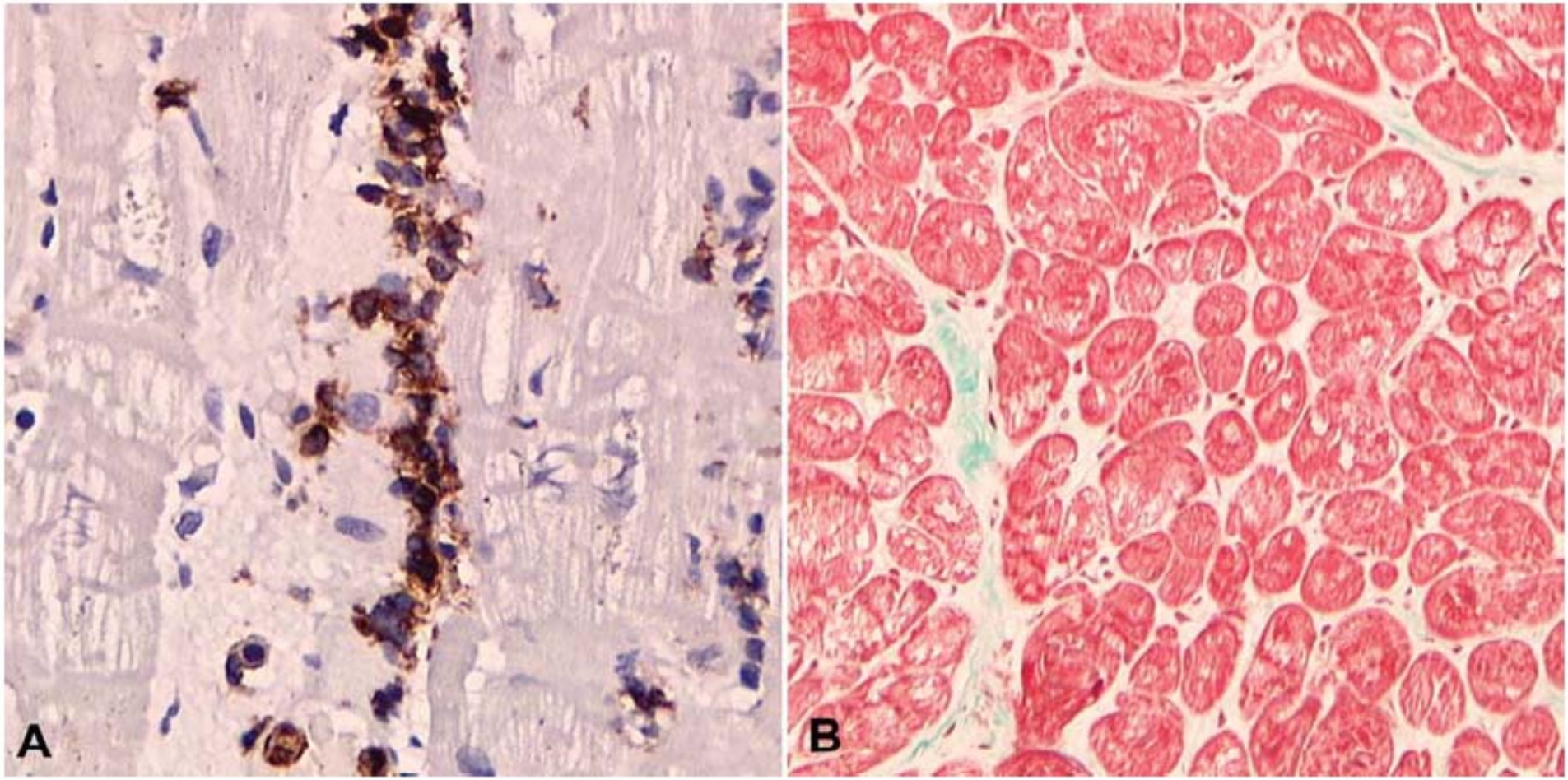


TABLE 2. Clinical, Hemodynamic, Virological, and Immunohistological Data of Patients Before and After IFN-β Treatment

	Before IFN-β	After IFN-β	P
Immunohistology			
Inflammation (n=7) CD3, cells/mm^2	19.2±4.8*	6.0±4.6*	<0.05
No inflammation (n=15) CD3, cells/mm^2	2.6±1.8*	2.9±3.1*	NS
NYHA	2.5±0.6*	1.7±0.7*	<0.05

Kuhl et al. Circulation 2003; 107:2793

Tratamiento Miocarditis



meses + Azatioprina 2 mg/kg/día 6 meses

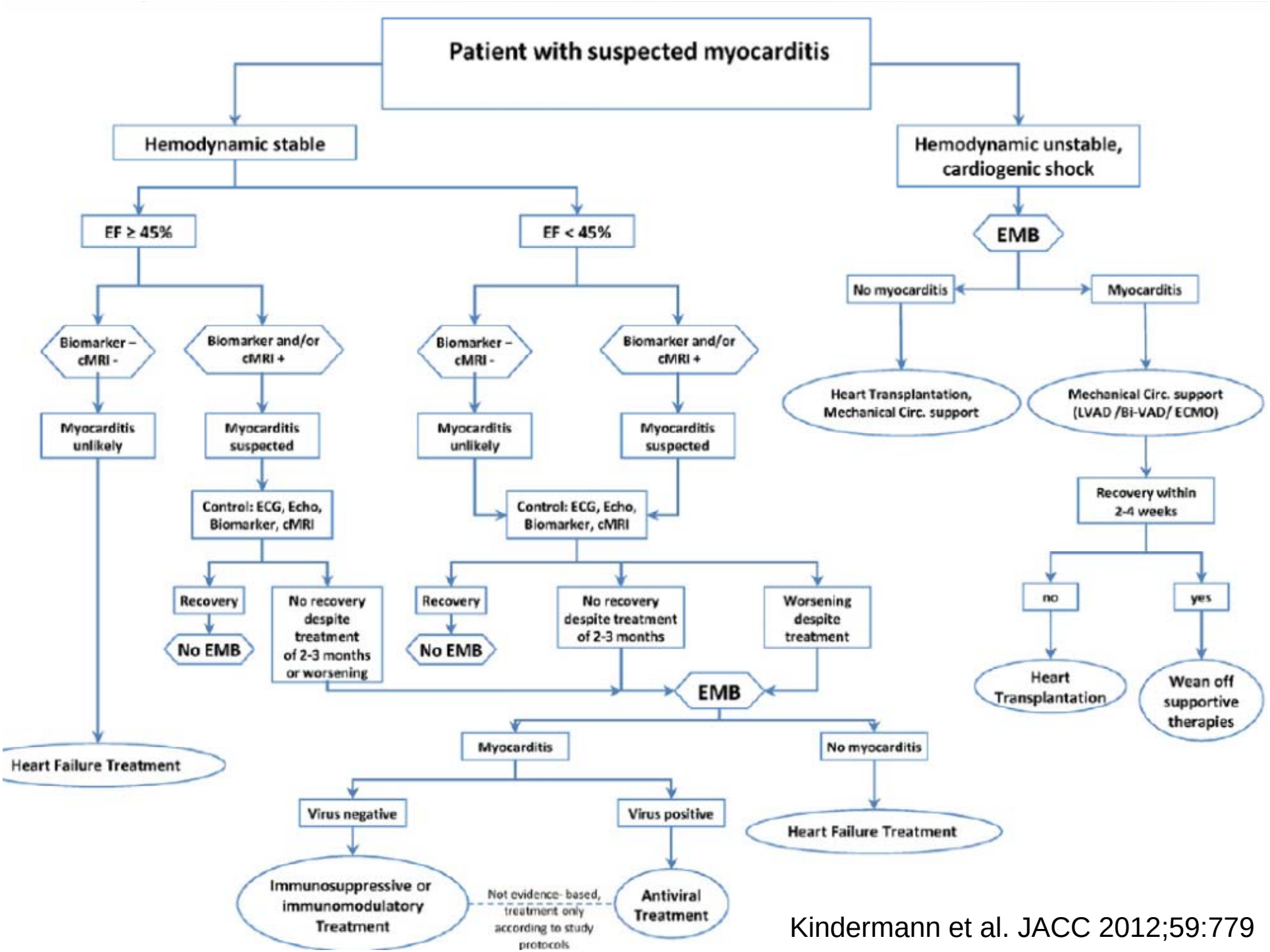
– Placebo

Frustaci et al. Eur Heart J 2009;30:1995

Tratamiento miocarditis

Immunoadsorption and subsequent immunoglobulin G substitution in patients with DCM, 2010, Herda et al. (86)	Single center university hospital-based case-control; 60 patients with DCM (NYHA II–IV, LVEF ≤45%); therapy with or without IA/IgG.	LVEF improved significantly in IA/IgG-treated group from 33.0 ± 1.2% to 40.1 ± 1.5% ($p < 0.001$).	Benefit
Removal of cardiodepressant antibodies in DCM by immunoadsorption (IA) (87), 2002, Felix et al. (84)	Multicenter, double-blind, prospective; 11 patients with DCM; IA on 3 consecutive days; IA also conducted on 500 ml blood from 9 healthy donors (control subjects).	IgG plasma level decreased from 10.7 ± 0.6 g/l to 2.4 ± 0.1 g/l and the cardiac index increased from 2.2 ± 0.1 l/min/m^2 to 2.7 ± 0.2 l/min/m^2 ($p < 0.01$).	Benefit
Immunoadsorption (IA) in DCM, 2006, Staudt et al. (100)	Randomized, uncontrolled; 22 patients with heart failure (LVEF <35%) due to DCM; group 1 ($n = 11$) treated with 4 IA courses at monthly intervals; group 2 ($n = 11$) received 1 IA course only without repetition.	Group 1, improved LVEF after 6 months, from 28.1 ± 1.5% to 37.0 ± 1.6% ($p < 0.01$); cardiac index increased from 2.2 ± 0.1 l/min/m^2 to 2.8 ± 0.2 l/min/m^2 after 6 months ($p < 0.01$); group 2, comparably improved LVEF at 6 months, from 26.5 ± 2.2% to 34.8 ± 2.9% ($p < 0.01$). Cardiac index increased from 2.1 ± 0.1 l/min/m^2 to 2.7 ± 0.2 l/min/m^2.	Benefit
Effects of protein A immunoadsorption in patients with advanced chronic DCM, 2009, Doesch et al. (85)	Single center; 27 patients with DCM, congestive heart failure NYHA class ≥II, LVEF <40%; therapy with IA.	Mean LVEF not significantly improved at 6 months (24.1 ± 7.8% to 25.4 ± 10.4%, $p = 0.38$); LVEF improved (≥5% absolute) in 9 of 27 (33%) patients; bicycle spiroergometry showed significant increase in exercise capacity from 73.7 ± 29.4 W to 88.8 ± 31.1 W ($p = 0.003$) after 6 months; VO_2max increased from 13.7 ± 3.8 ml/min/kg to 14.9 ± 3.0 ml/min/kg ($p = 0.09$).	No benefit in LVEF, but in exercise capacity

Kindermann et al. JACC 2012;59:779



Kindermann et al. JACC 2012;59:779

Experiencia HUB (2006-2011)

- Realización de RFM en pacientes con sospecha cl
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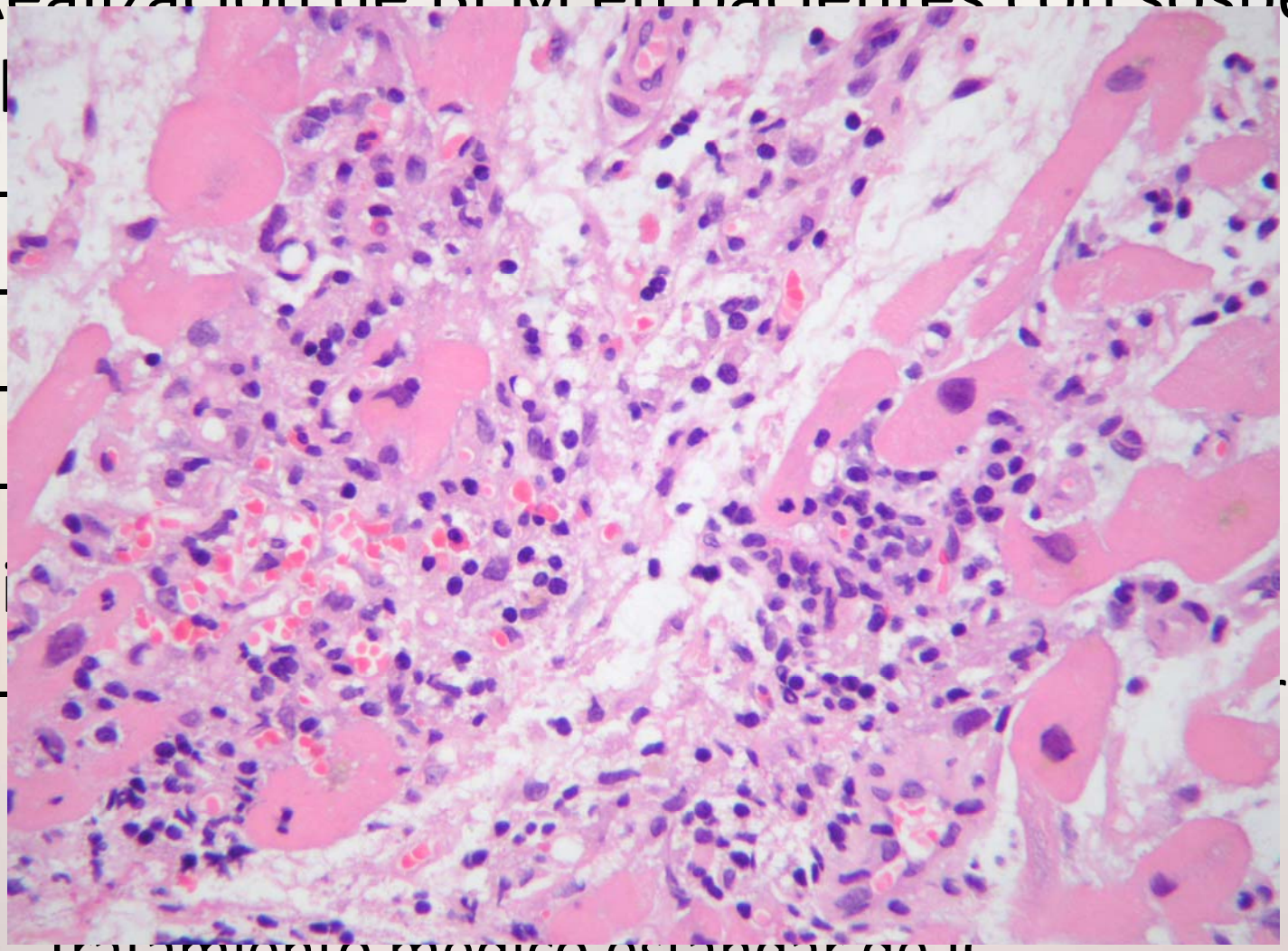
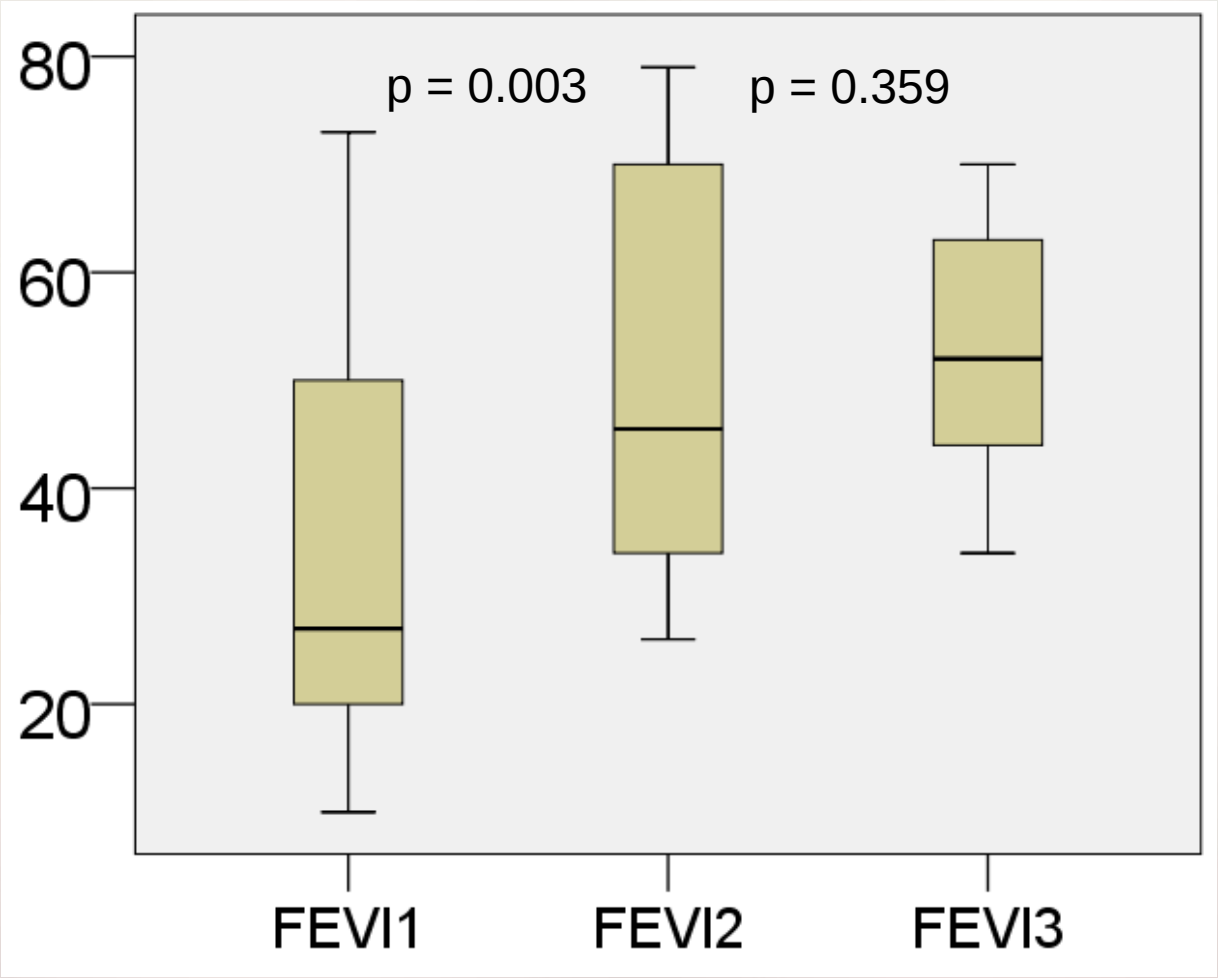
  -
  -
  -
- Si
  - ante
    y
  - Tratamiento médico estándar de IC



Experiencia HUB

Variables	**N = 15**
Edad (años)	38±10
Cuadro viral previo	10
BAV / TV	2 / 5
Tiempo inicio IC a BEM (días)	5,5 (3-11)
Infiltrado linfocitario lig/mod/sev	5 / 3 / 7
Inotropos / BCIAo / AV	10 / 8 / 3
VMK no invasiva / invasiva	2 / 5
Dilatación VI	8
Disfunción VD	8
Tratamiento con corticoides	12
Etiología Viral / Idiopática /Auto / Farmac	4 / 8 / 2 / 1

Experiencia HUB



Experiencia HUB

- Mediana de seguimiento de 11 meses
- Necesidad de MCP definitivo (2) o DAI (3)
- Infección herida quirúrgica: 1
- Exitus: 1 por sangrado alveolar con AV
- Trasplante cardiaco: 1 por 3er episodio de miocarditis

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