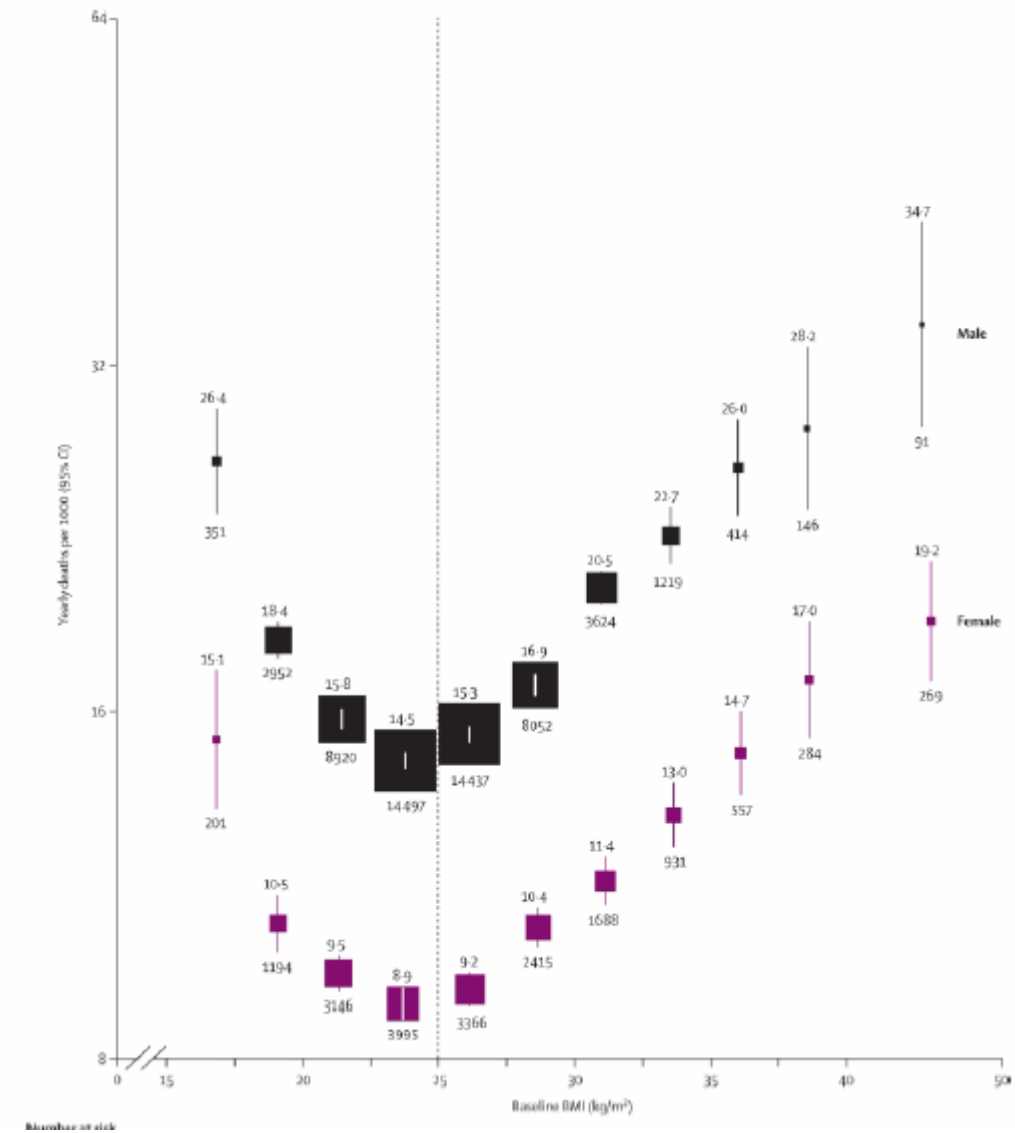
¿DEBEMOS INSISTIR EN UN CONTROL ESTRICTO DEL PESO EN EL PACIENTE CON INSUFICIENCIA CARDÍACA?

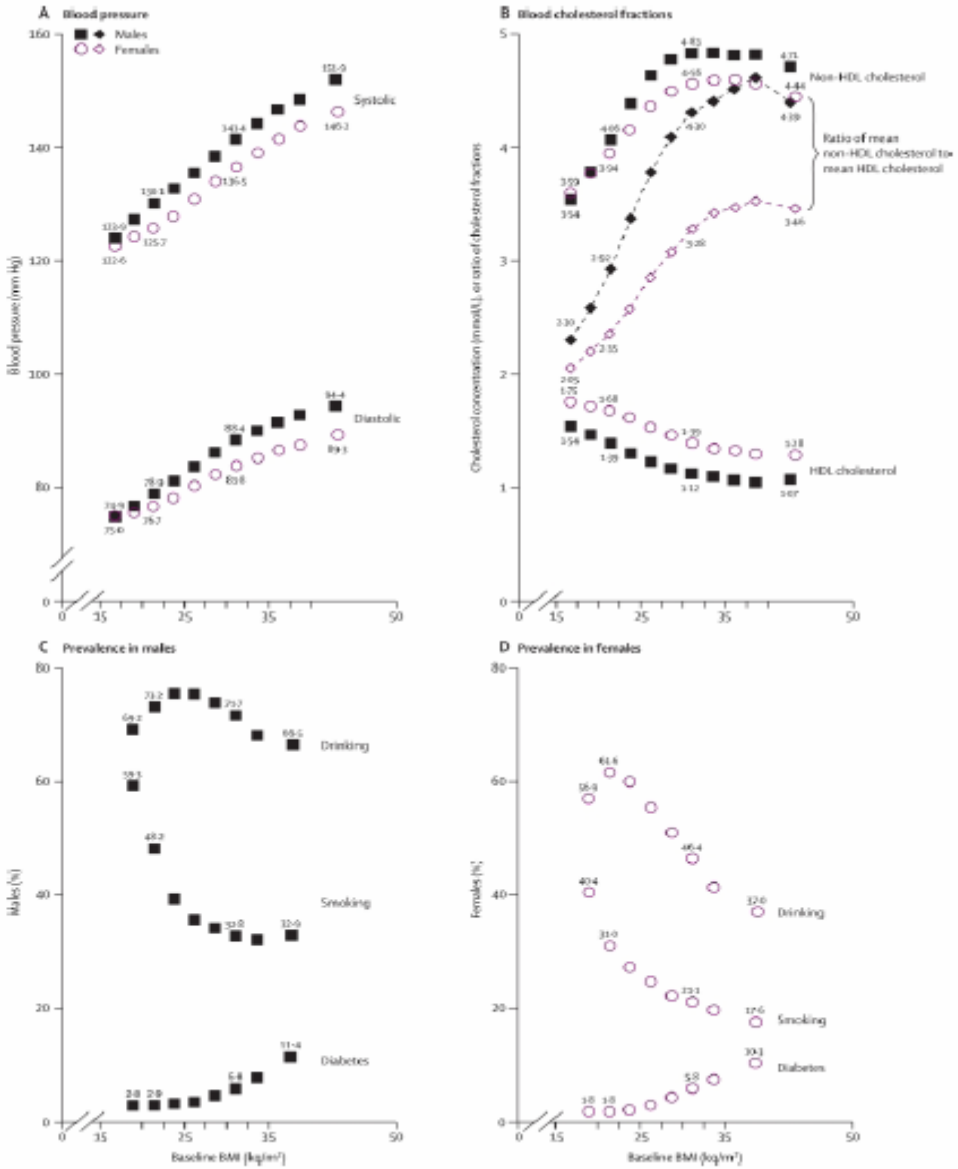
Ibiza, 7 de Mayo 2010

La obesidad reduce la expectativa de vida.

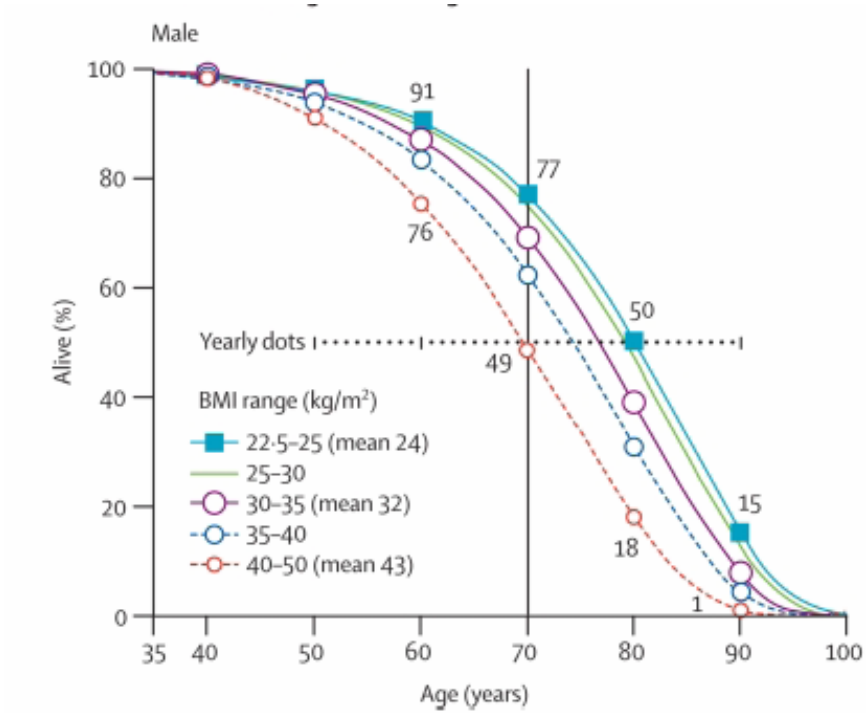


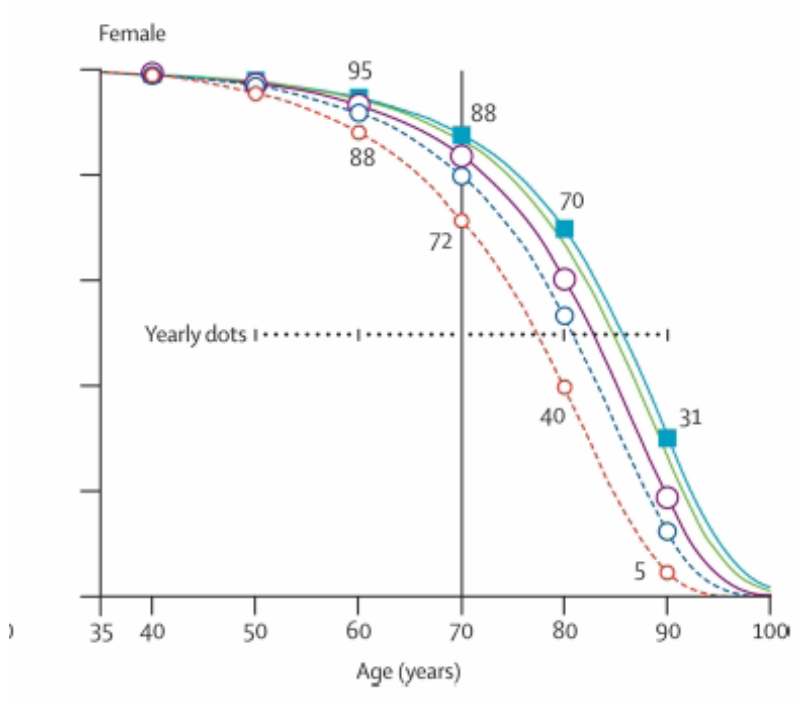
Prospective Studies Collaboration
Lancet 2009 28;373:1083-96

900.000 pacientes seguidos 8 años tras desestimar los primeros 5 años.



Prospective Studies Collaboration
Lancet 2009 28;373:1083-96



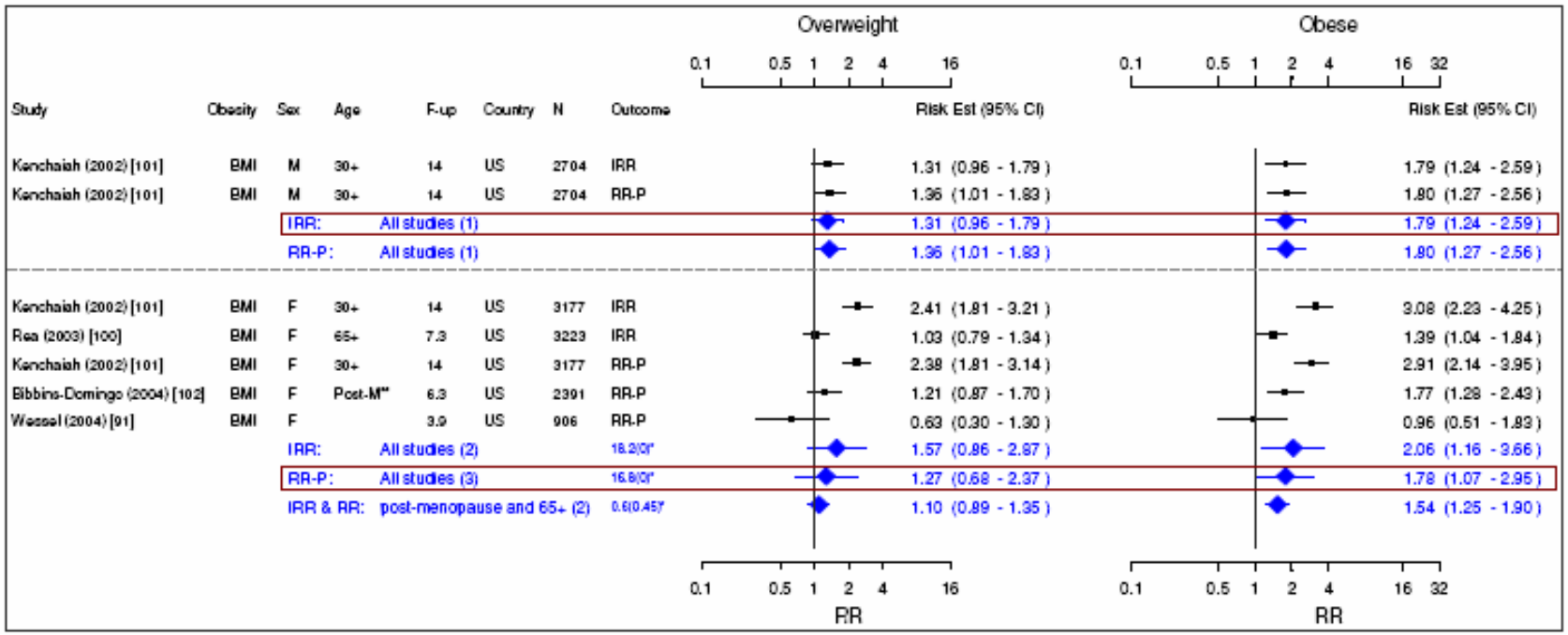


Arnlöv J. Circulation 2010 19;121(2):30-6

Incluso si no hay factores de riesgo asociados (1758 pacientes seguidos 30 años).

La obesidad es un factor de riesgo independiente en la incidencia de IC

Framingham: Por cada kg/m^2 de aumento del IMC,
aumenta la incidencia de IC en un 5% en hombres y 7% en mujeres



Meta-analysis of studies for congestive heart failure. *Q-statistic(p-value); **post-menopause; square shape: study- and gender- specific risk estimates; diamond shape: pooled risk estimates.

Guh et al. BMC Public Health 2009;9-88

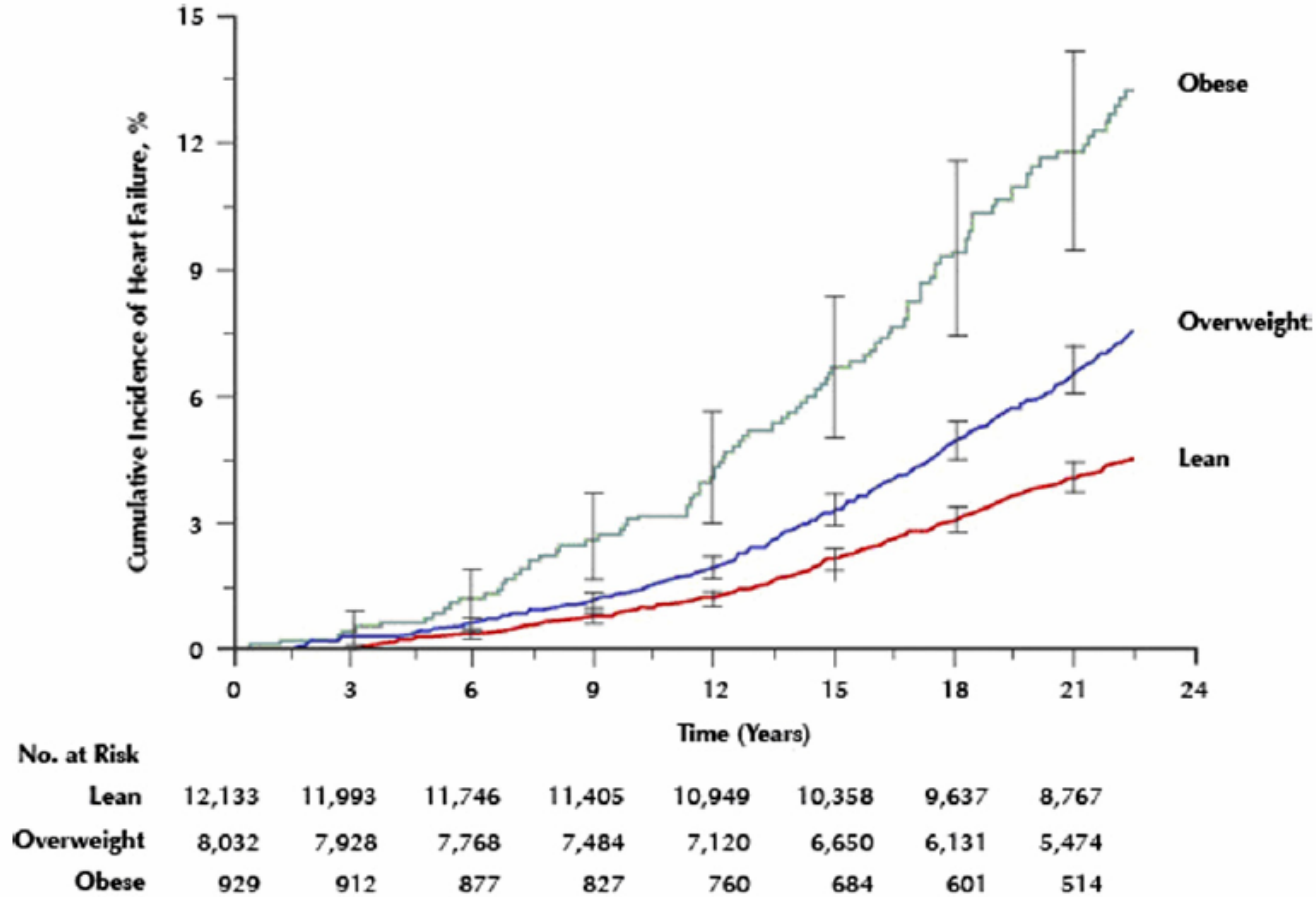


Figure 3 Cumulative Incidence of Heart Failure According to Categories of Body Mass Index

Horwich TB et al J Am Coll Cardiol 2010 Jan 26(4):283-93.

Comorbilidades asociadas

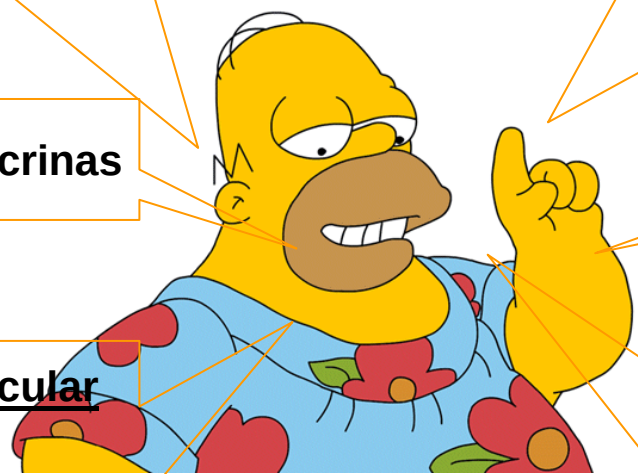
- Síndrome Apneas del sueño
- Insuficiencia venosa
- Hipertensión pulmonar
- Estado protrombótico

Factores de riesgo cardiovascular

- Síndrome metabólico
- Diabetes
- Hipertensión arterial
- Dislipemia

Alteraciones neuroendocrinas

Alteraciones inflamatorias



Alteración función ventricular

- HVI excéntrica
- Disfunción diastólica
- Disfunción sistólica
- Lipotoxicidad

Repercusiones hemodinámicas

- Descenso perfusión/adipocito
- Aumento volumen total
- Aumento volumen minuto
- Aumento resistencias periféricas

AHA Scientific Statement. Circulation 2006;113:898-918

Beneficios de la pérdida de peso en el sistema cardiovascular

TABLE 3. Benefits of Weight Reduction on the Cardiovascular System

↓ blood volume
↓ stroke volume
↓ cardiac output
↓ pulmonary capillary wedge pressure
↓ left ventricular mass
Improvement of left ventricular diastolic dysfunction
Improvement of left ventricular systolic dysfunction
↓ Resting oxygen consumption
↓ Systemic arterial pressure
↓ Filling pressures of the right and the left side of the heart
↓ or no change in systemic arterial resistance
↓ resting heart rate
↓ QT_c interval
↑ HRV

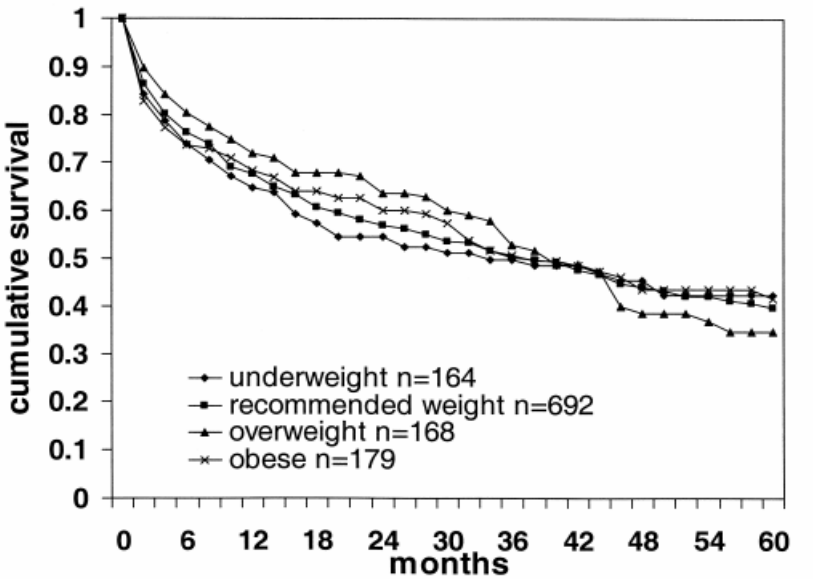
HRV indicates heart rate variability.

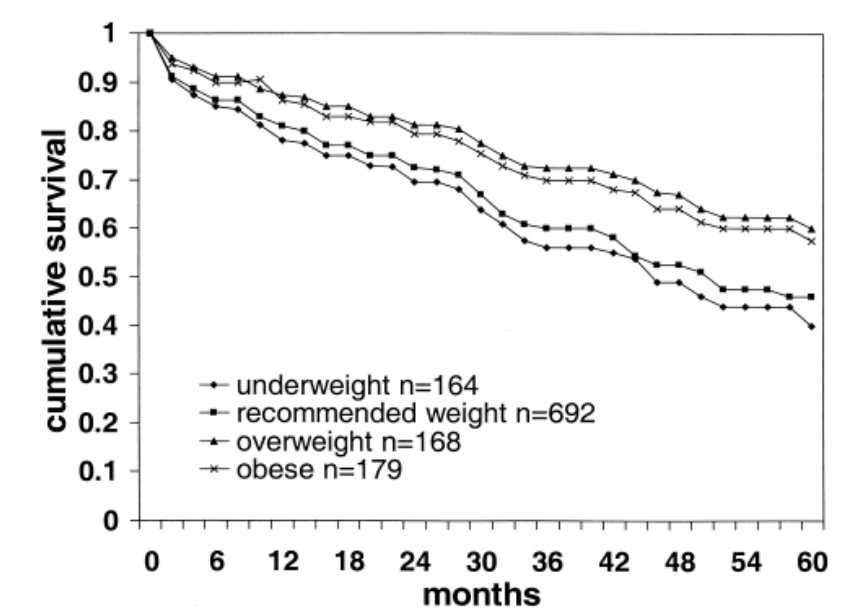
AHA Scientific Statement. Circulation 2006;113:898-918

¿Beneficios de la pérdida de peso en la incidencia de Insuficiencia cardiaca?

¡Ninguna evidencia!

Hipótesis:
Los obesos tienen peor pronóstico que los pacientes con normopeso

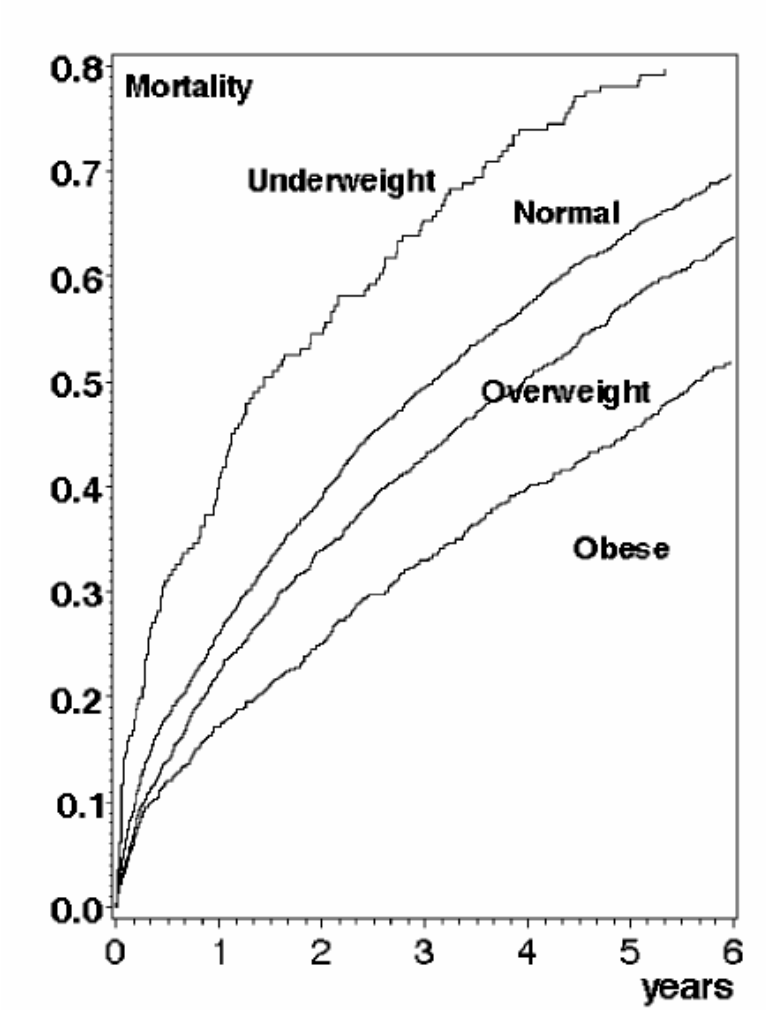




Los obesos no tienen peor supervivencia (1.203 pacientes pretrasplante) a 5 años. Tras ajustar por conocidas variables que afectan al pronóstico, la supervivencia fue mayor en los pacientes con obesidad y sobrepeso.

Horwich et al. ACC 2001;38:789-95

Los pacientes con obesidad y sobrepeso tienen mayor supervivencia



Guftansson et al. Eur Heart J 2005,26:58-64

4.700 hospitalizados. Si FE normal, obesos y sobrepeso mejor. Si baja, curva en u

Table 1
Summary of published reports relating body mass index to outcomes in patients with established heart failure

Authors	Year	Journal	n	CHF Diagnosis	Primary End Point	Follow-Up (yrs)	Main Findings
Mosterd et al[3]	2001	*EHJ*	181	Clinical	Mortality	6.1	Small BMI associated with decreased survival
Horwich et al[4]	2001	*JACC*	1,734	Clinical, echocardiographic, hemodynamic	Mortality	5	Obese patients had better survival at 1 and 2 yrs but not at 5 yrs
Lissin et al[5]	2002	*JCF*	522	Clinical	Mortality	6	BMI inversely related to outcome
Davos et al[6]	2003	*JCF*	589	Clinical and echocardiographic or RNA	Mortality	1	BMI inversely related to outcome; thinnest patients had worst outcomes
Lavie et al[7]	2003	*AJC*	209	Not explicitly defined, but patients had depressed EFs	CV death or urgent transplantation	2	Percentage body fat was multivariate predictor of outcome; no significant difference in survival among BMI quintiles
Curtis et al[8]	2005	*AIM*	7,767	Clinical, echocardiographic, and RNA	Mortality	3.5	Better survival among overweight and obese patients
Gustafsson et al[9]	2005	*EHJ*	4,700	Clinical and echocardiographic	Mortality	6.5	Obese patients had worse survival in depressed EF but better survival in preserved EF
Bozkurt and Deswal[10]	2005	*AHJ*	7,627	Clinical, echocardiographic, and RNA	Mortality	3.5	Better survival among overweight and obese patients

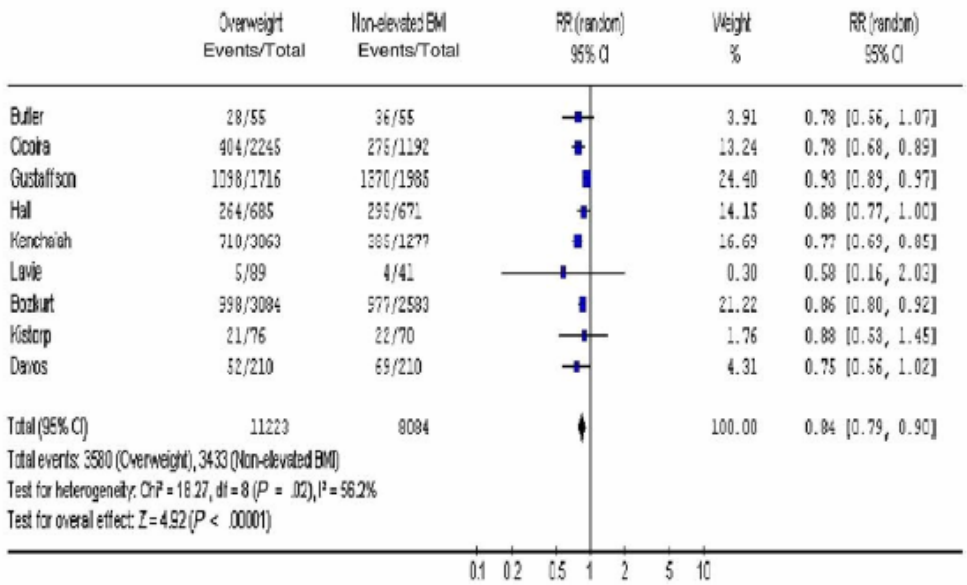
AJC = American Journal of Cardiology; *AHJ = American Heart Journal*; *AIM = Archives of Internal Medicine*; CV = cardiovascular; EF = ejection fraction; *EHJ = European Heart Journal*; *JACC = Journal of the American College of Cardiology*; *JCF = Journal of Cardiac Failure*; RNA = radionuclide angiography.

Habbu et al (Am J Cardiol 2006;98:944 –948)

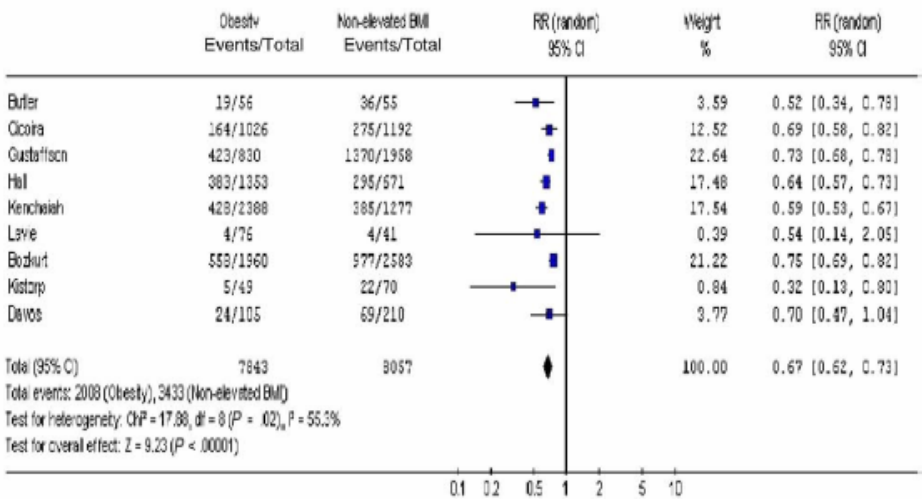
Study, y	Population	NYHA class	Sample size	Mean age, % female	BMI categories reported (kg/m^2)	Ottawa-Newcastle Quality Assessment Score (max total 9)	Mean follow-up
Bozkurt et al,[15] 2005 (USA)	Post hoc analysis of the DIG database	I-IV	7788	63, 24%	Normal 18.5-24.9, overweight 25.0-29.9, obese ≥30	8	3
Butler et al,[18] 2005 (USA)	Post hoc analysis of 2 FDA-approved clinical trials for LVAD placement	IV	222	51, 13%	Underweight/low-normal <23.0, normal 23.0-26.3, overweight 26.4-29.4, Obese ≥29.4	8	1
Cicoira et al,[17] 2007 (Italy)	Post hoc analysis of the Val-HeFT Study	II-IV	4463	63, 18%	Underweight/low-normal <22.0, normal 22.0-24.9, overweight 25.0-29.9, Obese ≥30	9	1
Davos et al,[12] 2003 (UK)	Retrospective, single-center cohort; NYHA class I-IV	I-IV	525	61, 17%	Nonelevated BMI ~<25.0, overweight ~25.0-29.0, obese ≥29-34.0, moderately/severely obese ≥34.0	9	3
Gustafsson et al,[16] 2005 (Denmark)	Post hoc analysis of the DIAMOND-CHF study	III-IV	4504	72, 39%	Underweight <18.5, normal 18.5-24.9, overweight 25.0-29.9, obese ≥30	9	6
Kenchaiah et al,[13] 2007 (USA)	Post hoc analysis of the CHARM study	II-IV	7599	66, 32%	Underweight/low-normal <22.5, normal 22.5-24.9, overweight 25.0-29.9, obese 30.0-34.9, moderately/severely obese ≥35.0	9	3
Hall et al,[10] 2005 (USA)	Retrospective, 20-hospital integrated health care system; NYHA class not given	Not given	2707	Age and sex not reported	Nonelevated BMI <24.3, overweight 24.4-28.5, obese 28.6-34.1, moderately/severely obese ≥34.2	8	3
Kristorp et al,[11] 2005 (Denmark)	Prospective, single-center	I-III (1 patient had IV)	195	69, 28%	Nonelevated BMI <25, overweight 25-29.9, obese ≥30	9	2.5
Lavie et al,[19] 2003 (USA)	Retrospective, single-center cohort	I-III	206	54, 19%	Normal 18.5-24.9, overweight 25.0-29.9, obese ≥30	8	1.5

DIG, Digitalis Investigation Group; *FDA*, Food and Drug Administration; *LVAD*, Left ventricular assist device; *DIAMOND*, Danish Investigations of Arrhythmia and Mortality.

Oreopulus et al.Am Heart J 2008;156:13-22.



Overweight vs nonelevated BMI: all-cause mortality.



Obese vs nonelevated BMI: all-cause mortality.

Oreopulus et al.Am Heart J 2008;156:13-22.

Body mass index and mortality in heart failure: A meta-analysis

Antigone Oreopoulos, MSc,[a] Raj Padwal, MD, MSc,[b] Kamyar Kalantar-Zadeh, MD, MPH, PhD,[c] Gregg C. Fonarow, MD, FACC,[d] Colleen M. Norris, PhD,[e] and Finlay A. McAlister, MD, MSc[b]
Alberta, Canada; Torrance, and Los Angeles, CA

Background In patients with chronic heart failure (CHF), previous studies have reported reduced mortality rates in patients with increased body mass index (BMI). The potentially protective effect of increased BMI in CHF has been termed the *obesity paradox* or *reverse epidemiology*. This meta-analysis was conducted to examine the relationship between increased BMI and mortality in patients with CHF.

Methods We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Scopus, and Web of Science to identify studies with contemporaneous control groups (cohort, case-control, or randomized controlled trials) that examined the effect of obesity on all-cause and cardiovascular mortality. Two reviewers independently assessed studies for inclusion and performed data extraction.

Results Nine observational studies met final inclusion criteria (total n = 28,209). Mean length of follow-up was 2.7 years. Compared to individuals without elevated BMI levels, both overweight (BMI ~25.0-29.9 kg/m^2, RR 0.84, 95% CI 0.79-0.90) and obesity (BMI ~≥30 kg/m^2, RR 0.67, 95% CI 0.62-0.73) were associated with lower all-cause mortality. Overweight (RR 0.81, 95% CI 0.72-0.92) and obesity (RR 0.60, 95% CI 0.53-0.69) were also associated with lower cardiovascular mortality. In a risk-adjusted sensitivity analysis, both obesity (adjusted HR 0.88, 95% CI 0.83-0.93) and overweight (adjusted HR 0.93,

Conclusions Overweight and obesity were associated with lower all-cause and cardiovascular mortality rates in patients with CHF and were not associated with increased mortality in any study. There is a need for prospective studies to elucidate mechanisms for this relationship. (Am Heart J 2008;156:13-22.)

Por cada 5 unidades de aumento del IMC disminuye un 10% el riesgo de mortalidad

¿Eran iguales los pacientes?

Más jóvenes

Con mayor FE

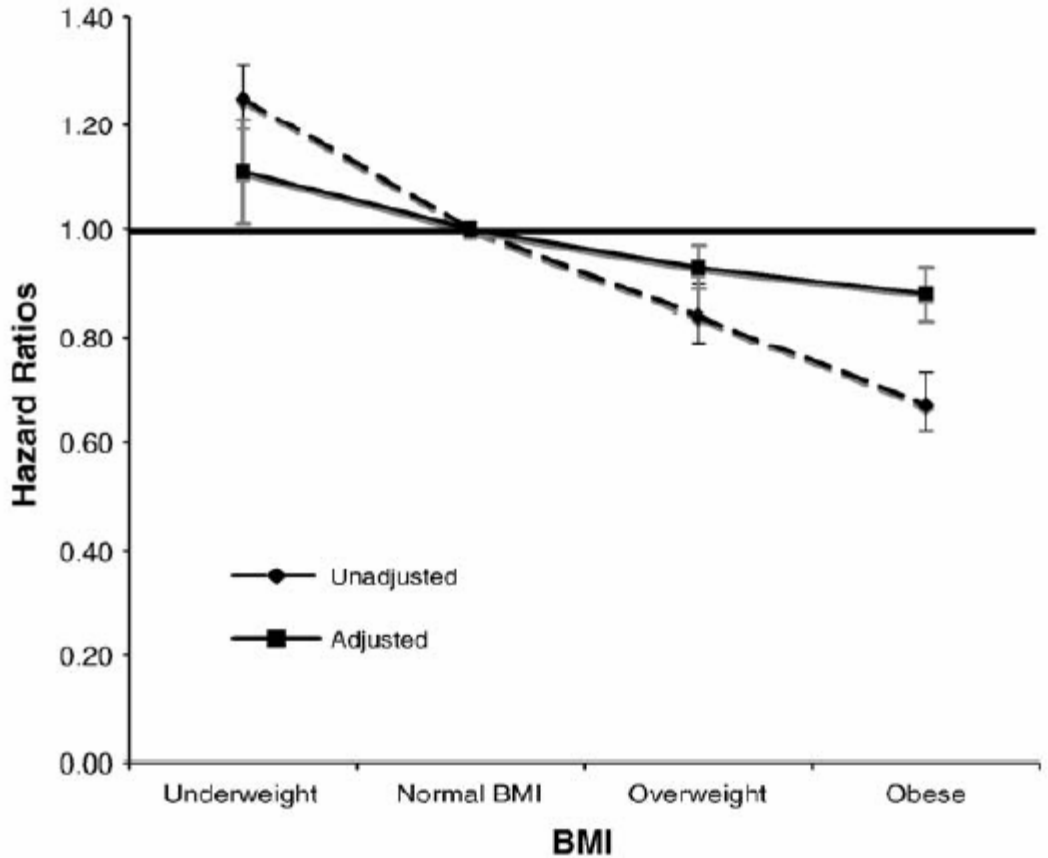
Mayor clínica de IC

Mayor % hipertensos

Mayor % diabéticos

Mayor % IAM previo

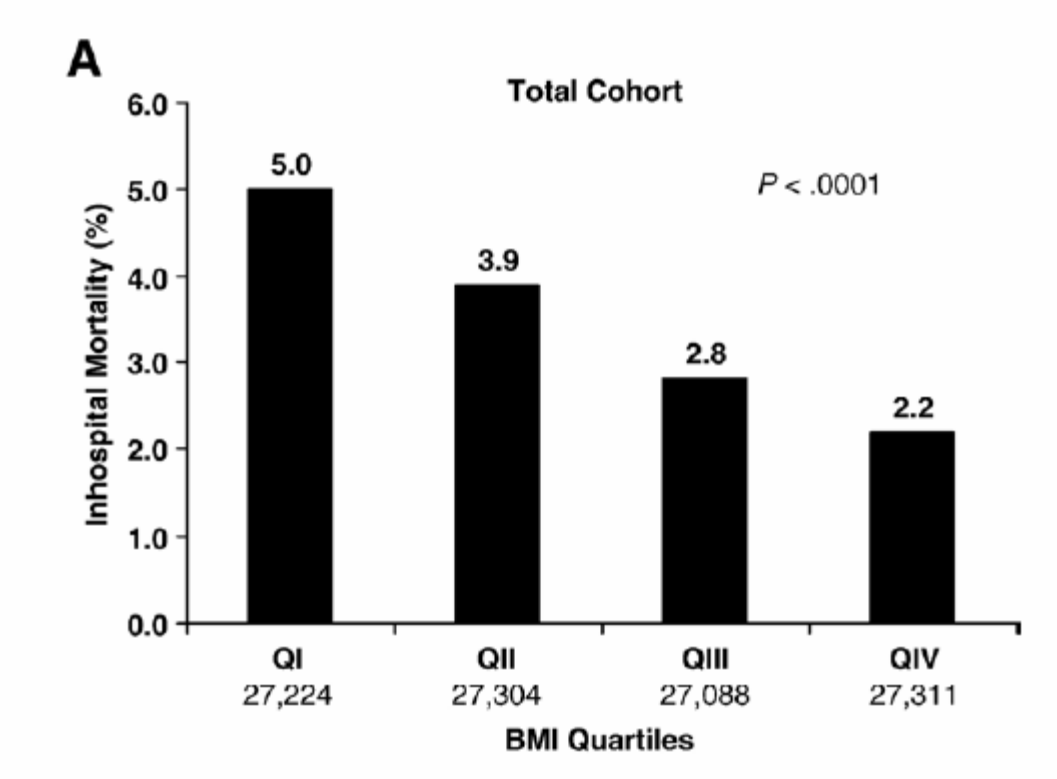
Menor % fumadores



Differences between unadjusted and adjusted results.

Oreopulus et al.Am Heart J 2008;156:13-22.

Mortalidad intrahospitalaria en 108.927 pacientes ingresados por descompensación de IC en 263 hospitales de EEUU



Fonarow et al (Am Heart J 2007;153:74281.)

Mortalidad intrahospitalaria en 3.722 pacientes ingresados en 11 centros de EEUU por descompensación de IC: la obesidad se asoció con aumento de la supervivencia.

Fitzibbons et al. Coron Artery Dis 2009 20(8):536-43.

¿Es el diagnóstico de IC fiable en los obesos?

Es difícil creer que…

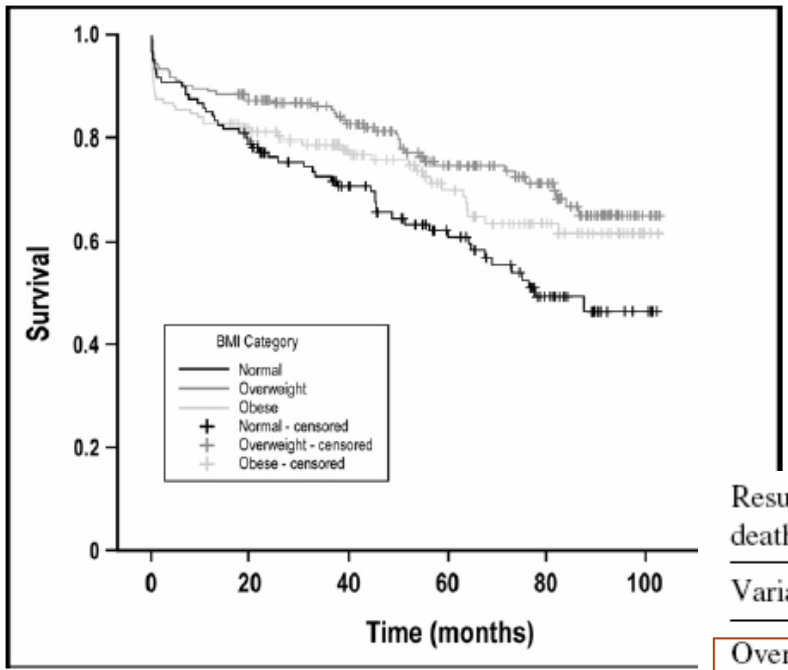
Los obesos remitidos a valoración de trasplante (**Horwich, 2001**) estuvieran incorrectamente diagnosticados.

Aunque…

El IMC influye en los resultados de los test de función cardiaca considerados el patrón oro en la valoración de la gravedad en la IC . El consumo de O2 es mayor aunque es comparable cuando se ajusta al peso magro.
La eficiencia ventilatoria es peor en los obesos.

(Horwich et al. Am Heart J 2009;158:S31-S36).

¿Estarán diagnosticados en estadíos más iniciales que los más delgados?



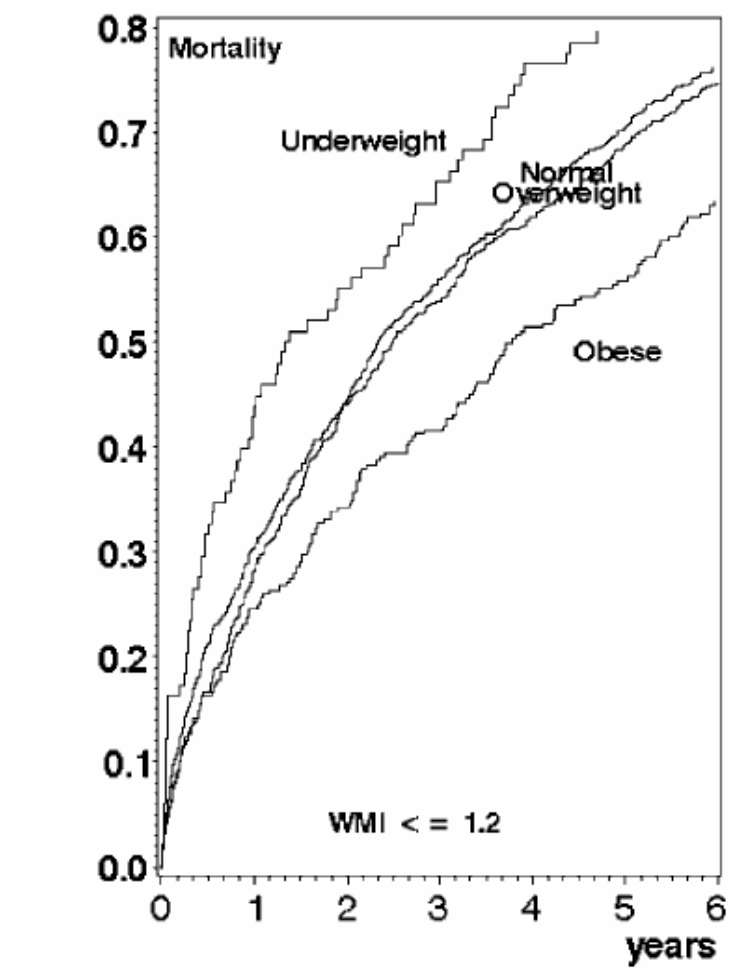
446 pacientes que desarrollaron IC tras un evento coronario, con FE deprimida.
Excluido IMC<18

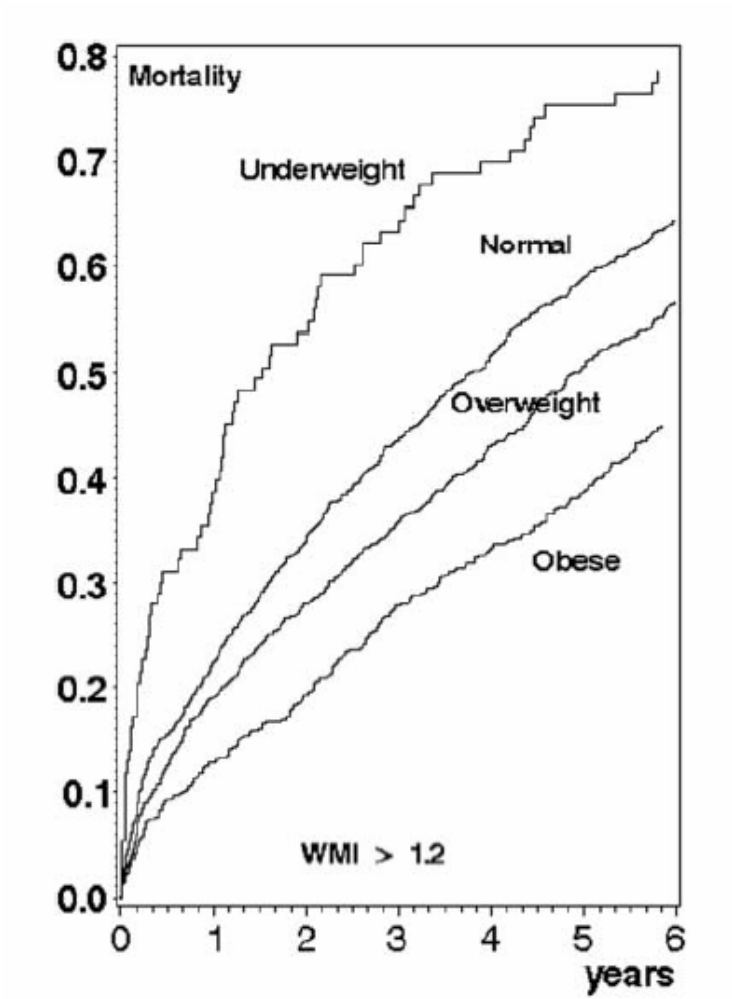
Results of Cox regression model with outcome of combined all-cause death

Variable	HR	95% CI	p Value
Overweight BMI (25 to <30 kg/m^2) vs normal BMI (18.5 to <25 kg/m^2)	0.63	0.42–0.94	0.02
Obese BMI (≥30 kg/m^2) vs normal BMI	1.06	0.69–1.64	0.8
Male gender	0.95	0.65–1.37	0.8
Age (per 1-yr increase)	1.04	1.03–1.06	<0.0001
Diabetes	1.47	1.04–2.09	0.03
Left ventricular ejection fraction (per 1% unit increase)	0.96	0.94–0.98	<0.0001
ACE inhibitor/ARB at discharge	0.54	0.37–0.78	0.001
Creatinine (per 1 mg/dl increase)	1.33	1.17–1.51	<0.0001

Wu et al. Am J Cardiol 2009;103:1736 –1740

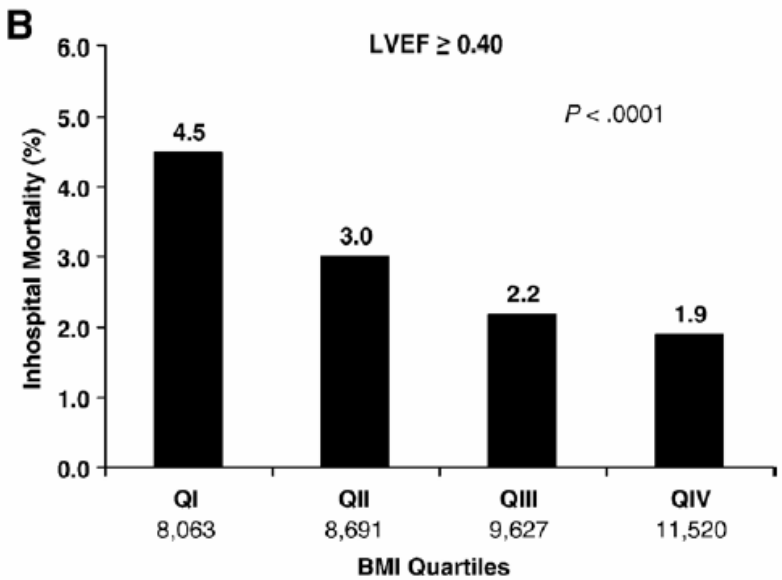
¿Influirá la función sistólica?

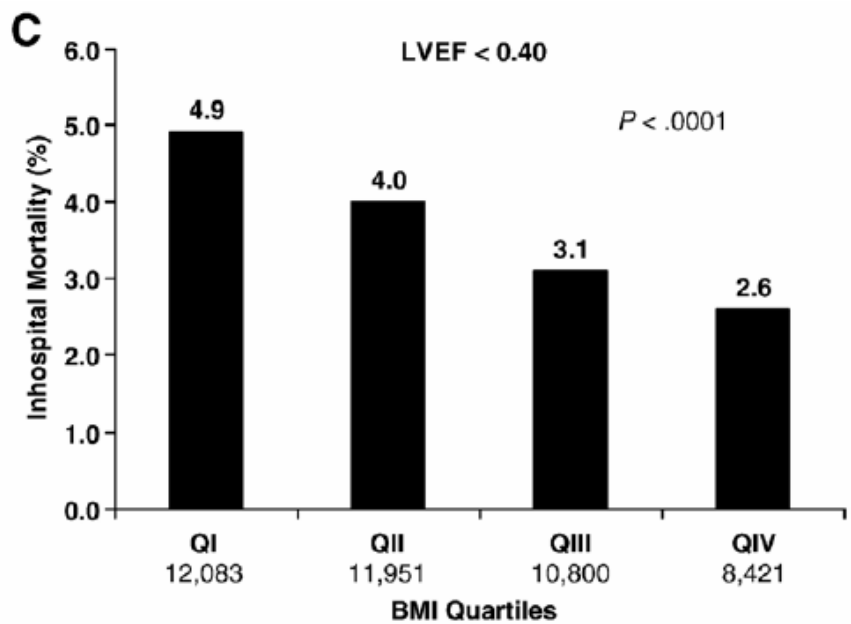




Guftansson et al. Eur Heart J 2005,26:58-64

¿Influirá la función sistólica?

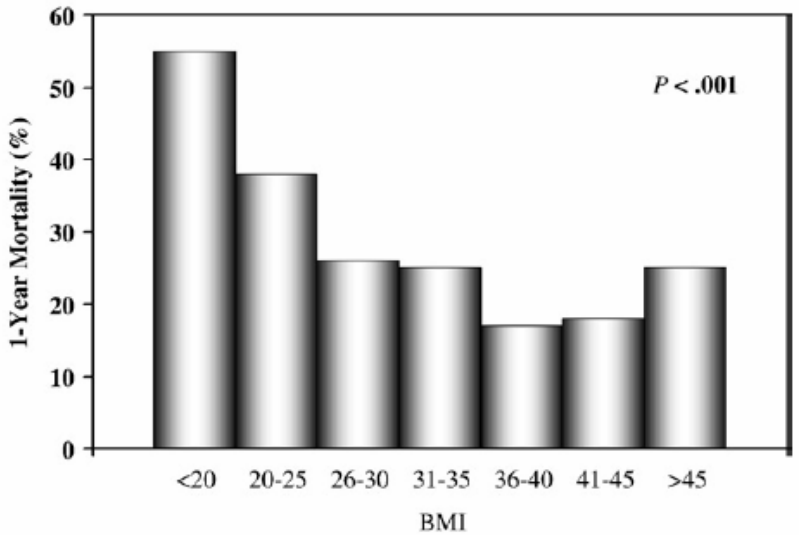




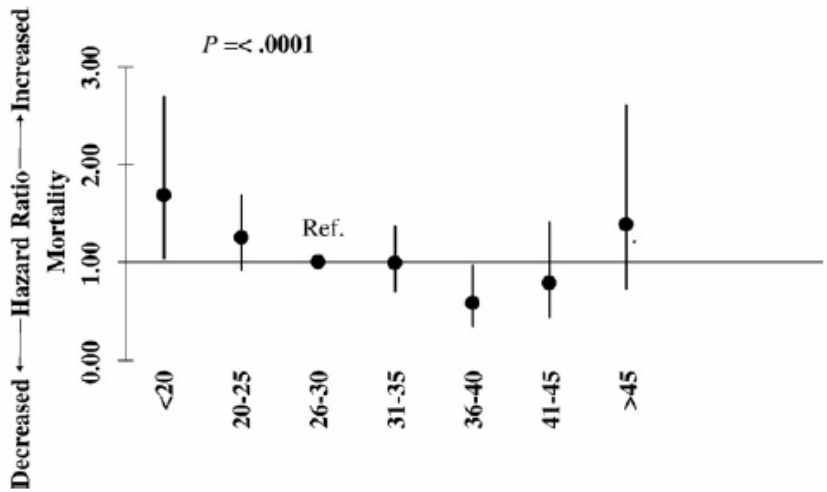
108.927 pacientes ingresados por descompensación de IC en 263 hospitales de EEUU

Fonarow et al (Am Heart J 2007;153:74281.)

¿Influirá la función sistólica?



Bar graph showing an increase in mortality a BMI of >45 kg/m^2, raising the possibility of a U-shaped relationship between unadjusted all-cause mortality and BMI.



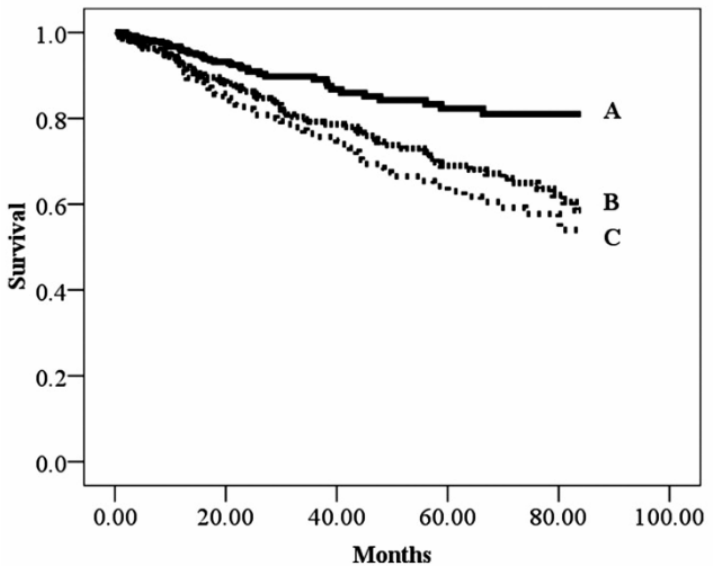
Hazard ratios for mortality by BMI after adjustment for age, history, labs, medications and echocardiographic findings (all $P < .0001$). A U-shape relationship persists between BMI and mortality.

1.236 pacientes con FE conservada, varios centros

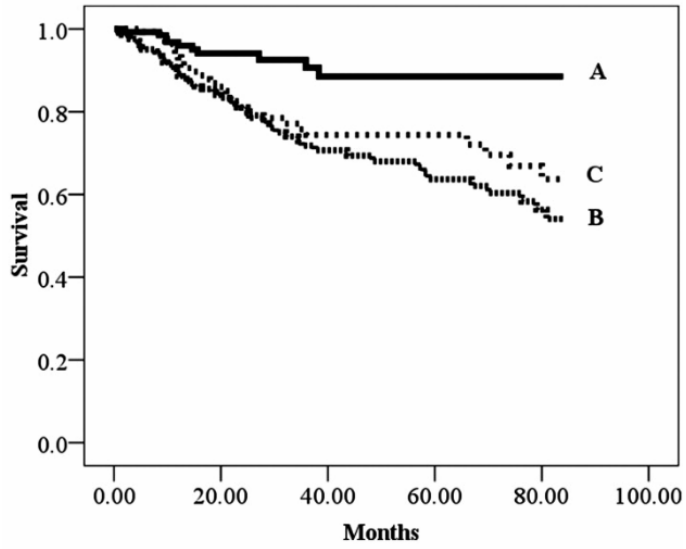
Kopoor et al. Am Heart J 2010;159:75-80.)

¿Dependerá de la etiología?

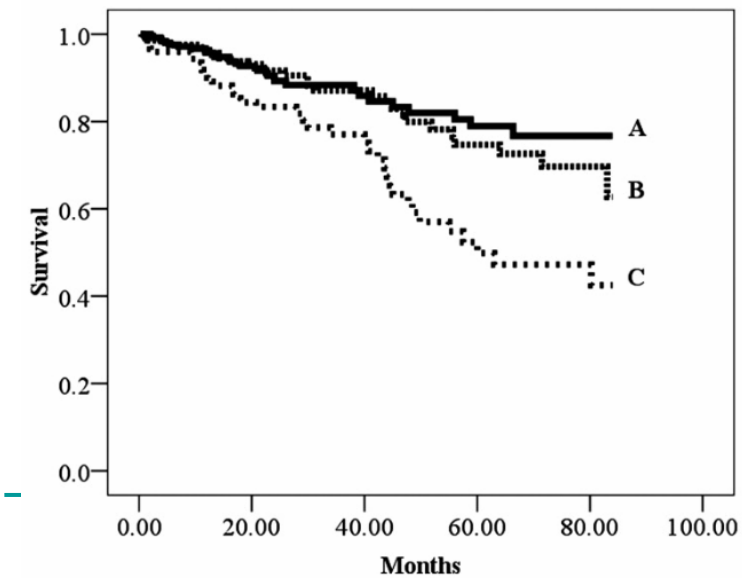
Todos



Isquémicos



No isquémicos



1160 pacientes, estudio multicéntrico, con FE deprimida.

A: IMC>30
B: IMC 25-29,9
C: IMC 18,5-24,9

Arena et al. Am J Cardiol 2009 Oct 15, 104(8):1116-21.

Los obesos tienen mayor presencia de edemas. ¿Puede ser un factor de confusión?

TABLE 3. Results of Multivariable Cox Proportional Hazards Models Examining the Relation of BMI to the Risk of All-Cause Death and Hospitalization for Worsening HF According to Left Ventricular Ejection Fraction and Edema Status at Baseline Examination

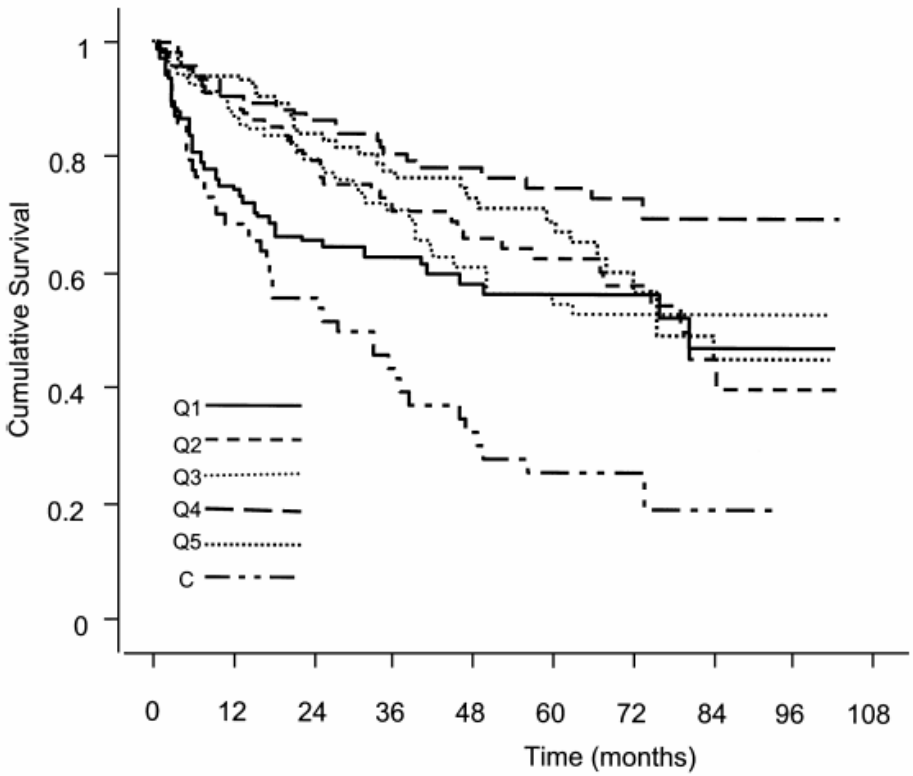
	BMI Categories, kg/m²				
	<22.5	22.5 to 24.9	25 to 29.9	30 to 34.9	≥35
All-cause death					
Left ventricular ejection fraction ≤40					
No. of events/at risk (%), rate/100 py	258/641 (40.2), 15.5	274/818 (33.5), 12.4	527/1876 (28.1), 10.0	201/878 (22.9), 7.8	90/363 (24.8), 8.6
Multivariable HR (95% CI), *P**	1.69 (1.39 to 2.06), <0.0001	1.44 (1.19 to 1.74), 0.0001	1.20 (1.02 to 1.41), 0.032	1.00 (referent)	1.19 (0.92 to 1.53), 0.18
Left ventricular ejection fraction >40					
No. of events/at risk (%), rate/100 py	70/248 (28.2), 10.4	91/459 (19.8), 6.9	183/1187 (15.4), 5.3	79/701 (11.3), 3.8	58/428 (13.6), 4.7
Multivariable HR (95% CI), *P**	1.99 (1.42 to 2.80), <0.0001	1.67 (1.23 to 2.29), 0.001	1.33 (1.01 to 1.74), 0.039	1.00 (referent)	1.25 (0.88 to 1.77), 0.21
Without edema					
No. of events/at risk (%), rate/100 py	272/753 (36.1), 13.6	285/1074 (26.5), 9.5	493/2409 (20.5), 7.0	174/1117 (15.6), 5.2	56/392 (14.3), 4.7
Multivariable HR (95% CI), *P**	1.92 (1.57 to 2.34), <0.0001	1.56 (1.29 to 1.89), <0.0001	1.22 (1.03 to 1.46), 0.024	1.00 (referent)	1.09 (0.80 to 1.47), 0.60
With edema					
No. of events/at risk (%), rate/100 py	56/136 (41.2), 16.3	80/203 (39.4), 15.2	217/654 (33.2), 12.5	106/462 (22.9), 8.1	92/399 (23.1), 8.3
Multivariable HR (95% CI), *P**	1.10 (0.78 to 1.56), 0.57	1.21 (0.89 to 1.64), 0.22	1.25 (0.99 to 1.59), 0.060	1.00 (referent)	1.24 (0.93 to 1.64), 0.14

7.599 pacientes clase II-IV NYHA con distinta FE.

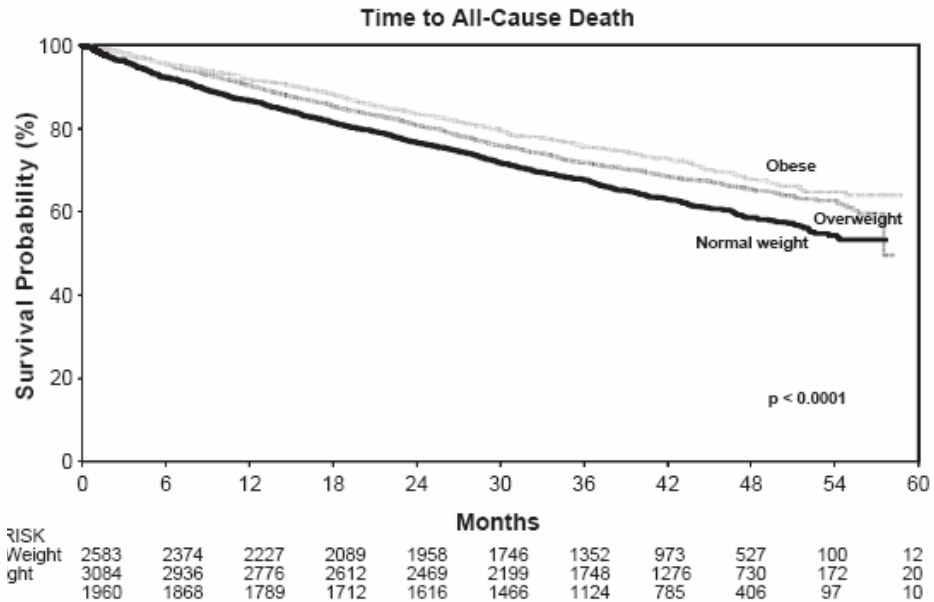
***Kenchaiach et al. Circulation*. 2007;116:627-636.**

La caquexia comporta mal pronóstico en todas las enfermedades

¿Existe el sesgo de los pacientes caquécticos?



Davos et al. J Car Fail 2003,9 (1):29-35.



Bozkurt et al. Am Heart J 2005,150:1233-9

Table II. Risk-adjusted death and hospitalization by BMI group

	Overweight		Obese	
Outcome	**HR* (95% CI)**	***P***	**HR* (95% CI)**	***P***
All-cause mortality	0.87 (0.79-0.95)	.0019	0.82 (0.73-0.92)	.0005
HF mortality	0.76 (0.65-0.88)	.0003	0.79 (0.65-0.95)	.014
Other cardiac mortality	0.96 (0.83-1.10)	.531	0.88 (0.74-1.04)	.128
HF hospitalizations	0.92 (0.83-1.01)	.084	0.96 (0.86-1.08)	.510
CV hospitalizations	0.96 (0.89-1.03)	.238	0.96 (0.88-1.05)	.373
Any hospitalization	0.97 (0.90-1.03)	.309	1.0 (0.92-1.08)	.947

*HR of the outcome relative to the normal BMI group.

¿Qué sucede cuando se pierde peso a lo largo del tiempo?

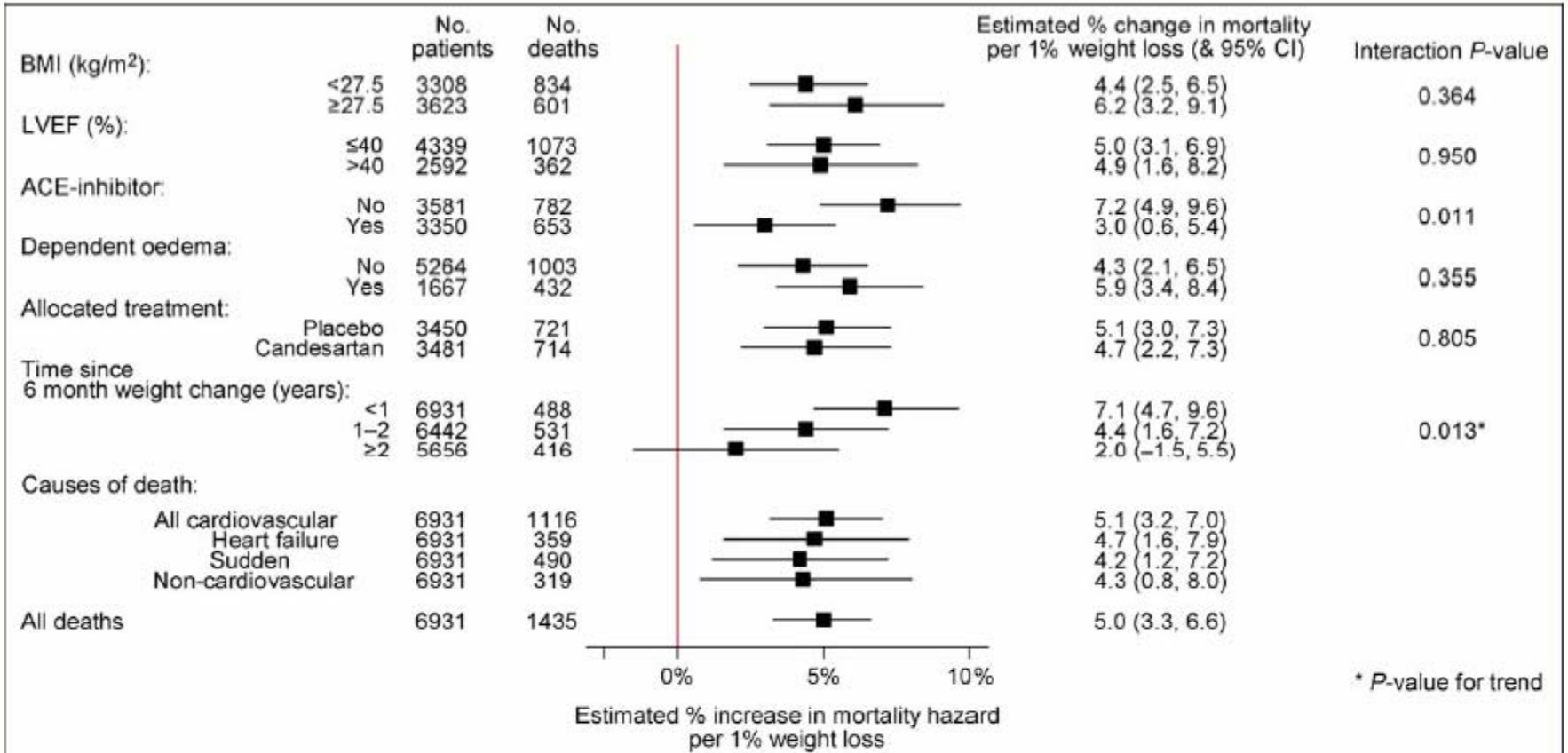
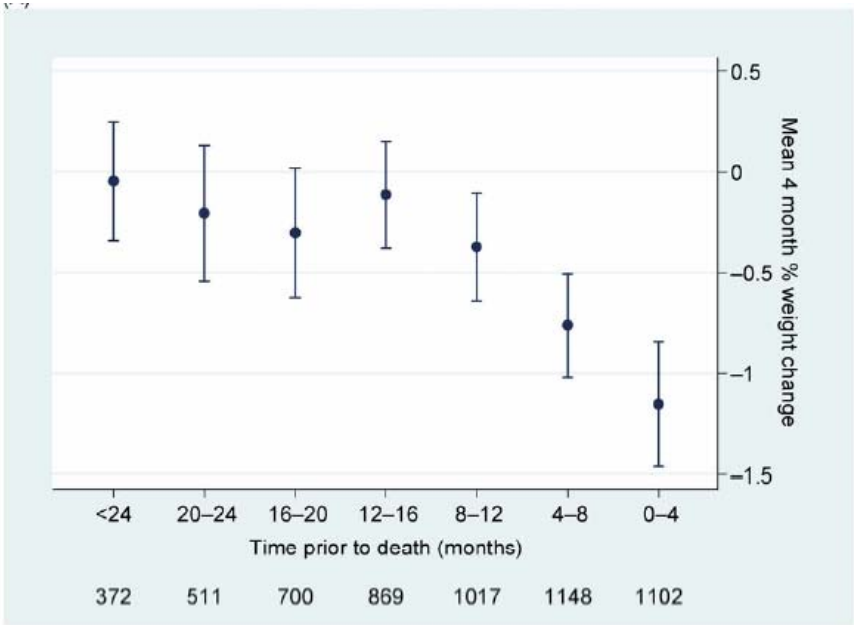
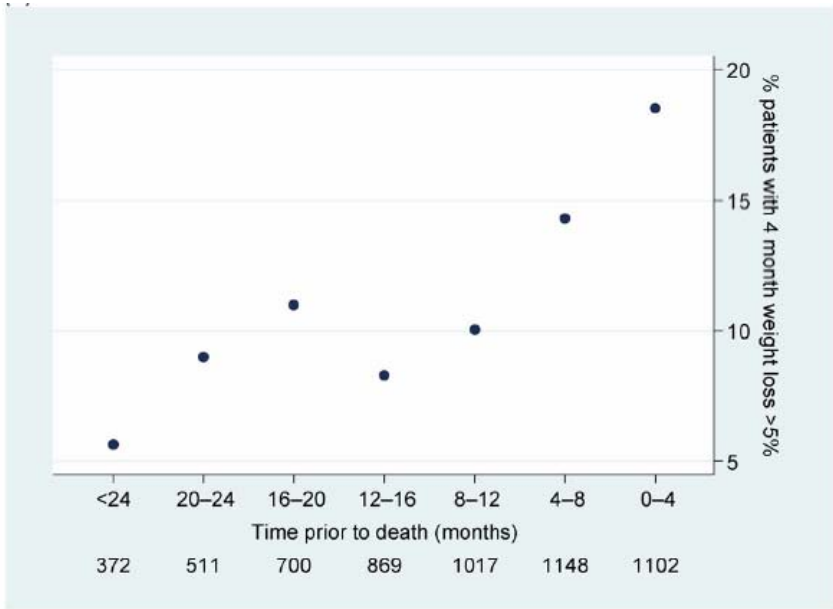


Figure 2 Estimated percentage increase in mortality per 1% weight loss in 6 months (and 95% CIs), for various subgroups, time intervals, and causes of death.

Pocock et al. European Heart Journal (2008) 29, 2641–2650





Se ha propuesto definir caquexia en IC como pérdida del 6% del peso. Afecta al músculo, grasa y hueso.

Alteración catabolismo/anabolismo; aumento de citoquinas inflamatorias y neurohormonales; aumento adiponectina; anemia.

No está demostrado que sea causa específica de muerte pero es un marcador de peores resultados.

¿Es el IMC el mejor parámetro para cuantificar el tejido adiposo?

Cohorte de 14.641 individuos, ambos sexos, blancos y negros.
PC y cintura/cadera no superiores al IMC en predecir IC.

Loehr et al. Circ Heart Fail 2009; Jan 2 (1) 18-24

Cohorte de 59.178 individuos finlandeses.
PC y cintura/cadera no superiores al IMC en predecir IC.
El ejercicio físico es protector a cualquier nivel de IMC.

Hu et al. Circulation 2010; Jan 19, 121 (2) 237-44

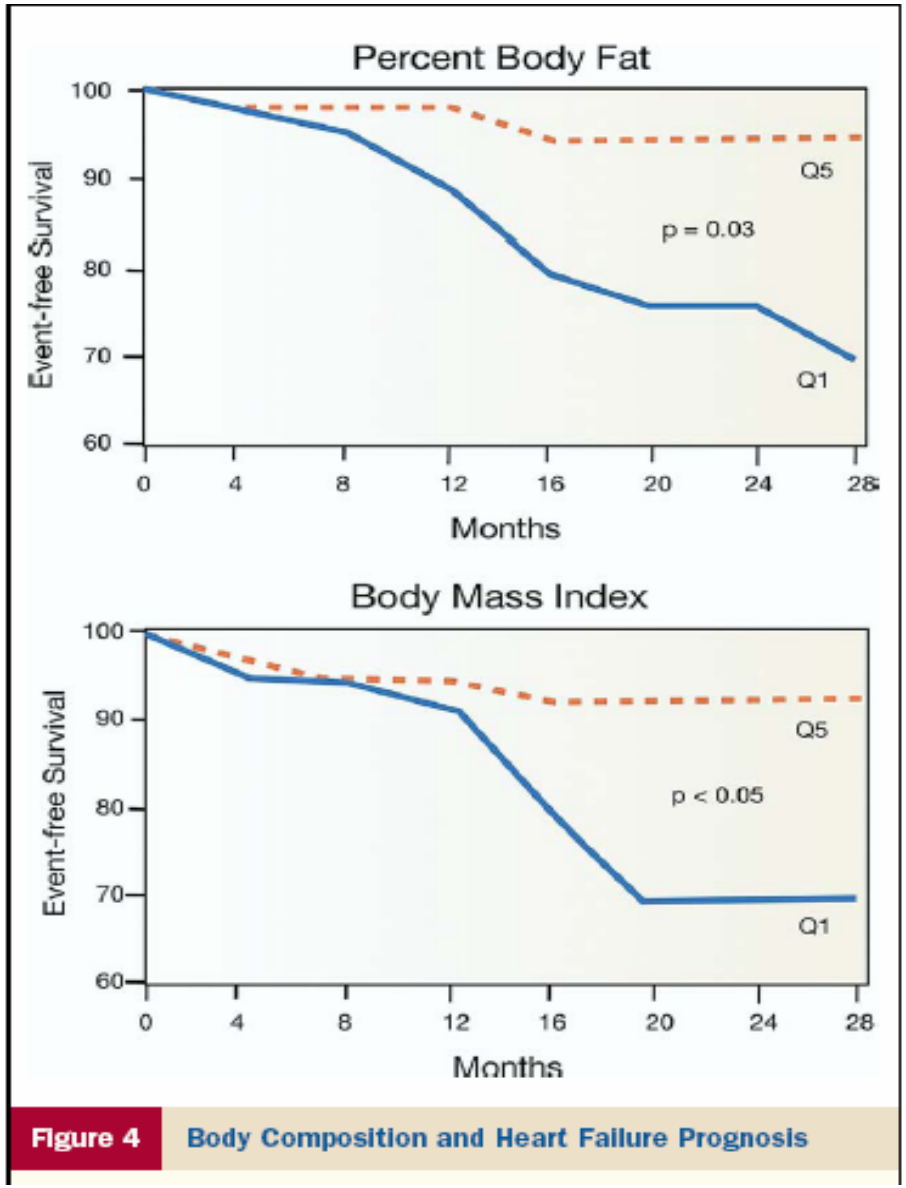


Figure 4 Body Composition and Heart Failure Prognosis

Lavie et al. (J Am Coll Cardiol 2009;53:1925–32)

¿Influye el tipo de estudio? ¿Cuál sería el más adecuado?

Smith et al. BMJ 2009;339-b543

- **Deben excluirse los primeros años de observación.**
- **Deben ajustarse posibles sesgos: tabaco, nivel socioeconómico etc**
- **La propia enfermedad puede contribuir al peso.**
- **Los ensayos clínicos no son los apropiados para establecer causalidad entre IMC y mortalidad.**
- **Lo mejor es utilizar variables instrumentales que no se vean afectados por la enfermedad.**

Utilizando el peso de los descendientes en >1.000.000 sujetos, demuestra que la obesidad aumenta la mortalidad por causa cardiovascular, diabetes y algunos cánceres

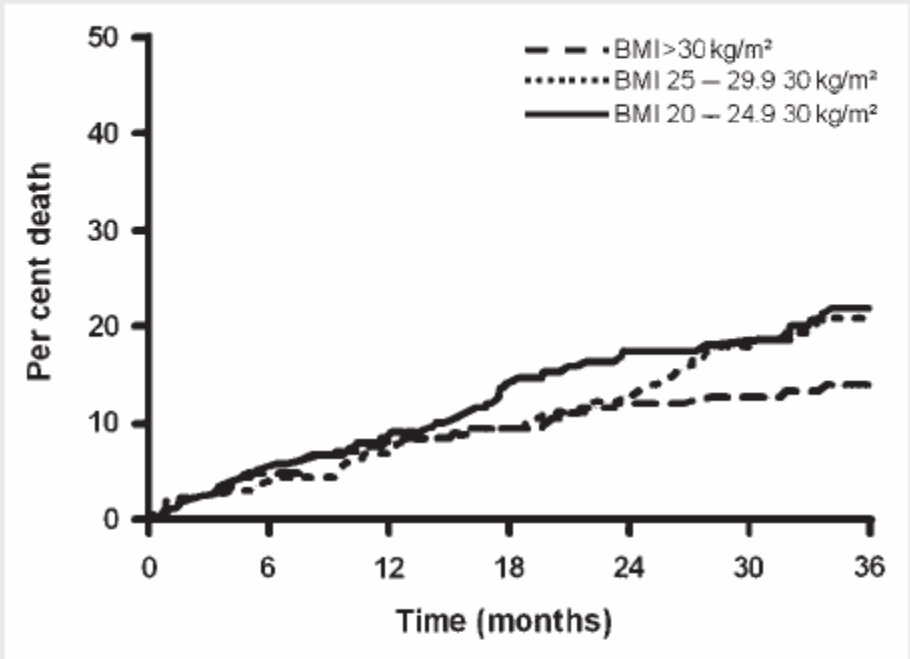
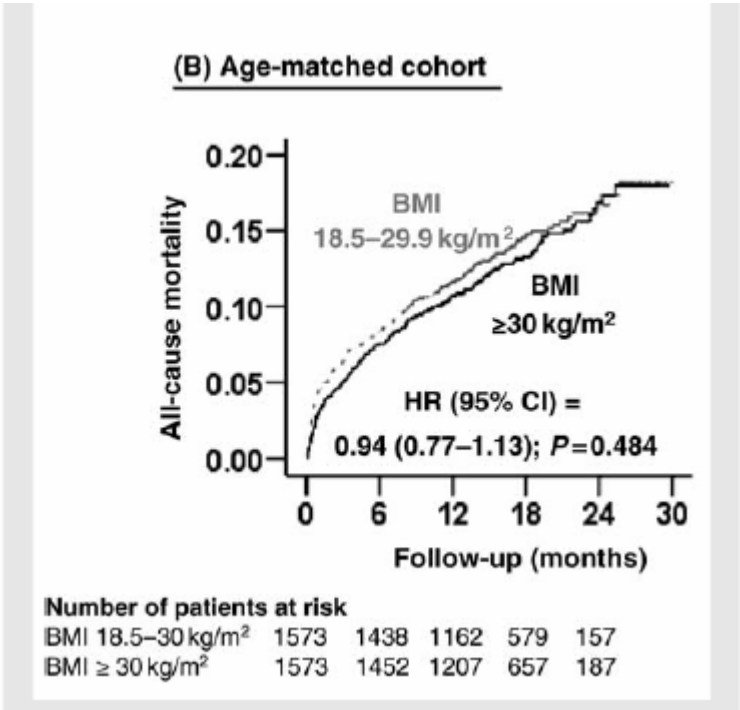


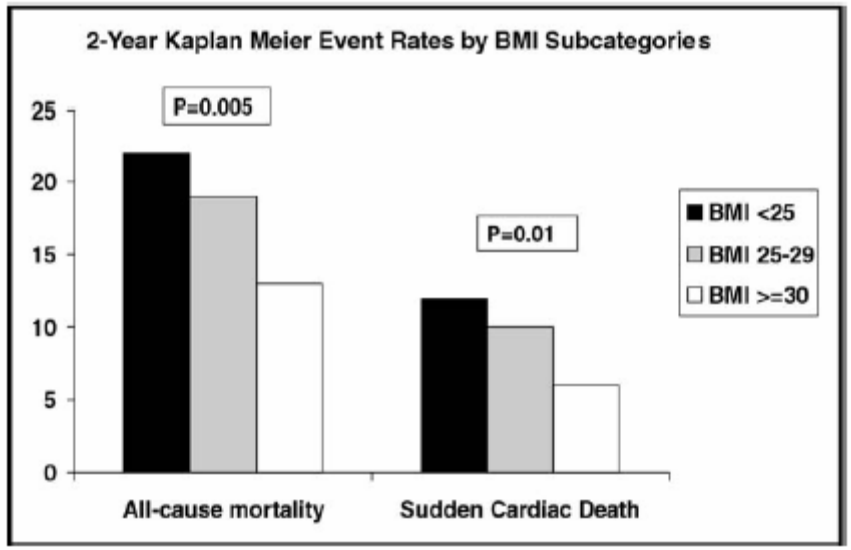
Figure 1 Kaplan–Meier curves (non-adjusted) for the matched cohort, $n = 690$. At 3-year follow-up, no significant differences in all-cause mortality were found between the BMI groups (log-rank χ^2: 0.23, $P = 0.63$ for Group 1 vs. Group 2; log-rank χ^2: 1.81, $P = 0.18$ for Group 2 vs. Group 3; log-rank χ^2: 3.35, $P = 0.07$ for Group 1 vs. Group 3).

1790 pacientes apareados
en grupos de 230. Un solo centro.
BNP fue el único factor predictor

Frankestein et al. European Journal of Heart Failure (2009) 11, 1189–1194

IC tras Infarto miocardio. Resultados contradictorios





Wu et al.European Journal of Heart Failure.doi:10.1093/eurjhf/hfq043 (Estudio Ephesus)

Choy et al. Am J Cardiol 2010;105:581–586 (Estudio Madit II)

Table 2 Obesity Paradox* in Cardiovascular and Noncardiovascular Patients

Cardiovascular
A. Hypertension
B. Heart failure
C. Coronary heart disease
1) Percutaneous revascularization
2) Coronary artery bypass graft surgery
3) Treadmill referrals
D. Peripheral arterial disease
E. Echocardiography referrals
Noncardiovascular
A. Elderly
B. End-stage renal disease and dialysis
C. Advanced cancers
D. Chronic obstructive lung disease
E. Rheumatoid arthritis
F. Human immunodeficiency virus/acquired immune deficiency syndrome

*Conditions in which obesity has been associated with a more favorable prognosis compared with that in nonobese patients.

TA más alta

Mayor número de fármacos

Mayor dosis

Colesterol más alto

Tampón y limpieza LPS
(descenso citoquinas inflamatorias)

Factores neurohormonales

Menor TNF circulante

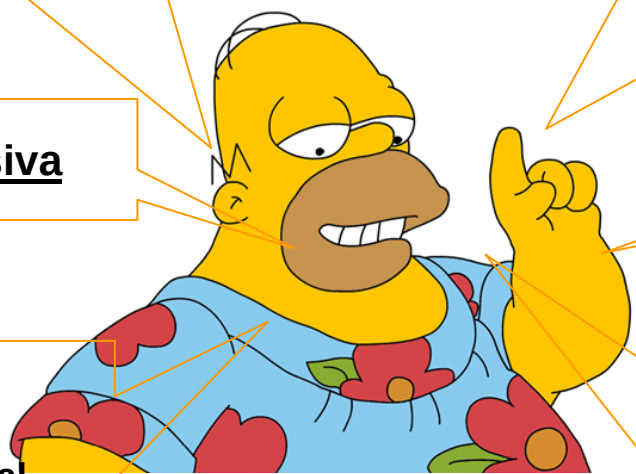
Menor respuesta adrenérgica

Menor respuesta SRA

Menor BNP

Menor adiponectina

Mayor % de IC hipertensiva



Mayor tolerancia a fármacos

Mayor reserva metabólica

Mejor estado nutricional

Mayor tolerancia a procesos agudos y crónicos

Síntomas más temprano

Disnea de esfuerzo

Edemas

Factores de riesgo

Menos BNP: más volumen

tion and epidemiological data. The perception that obesity is a plague of modern society, injurious to health, has become translated into an omnipresent appeal to achieve leanness regardless of potential co-existing conditions such as chronic disease or advanced age. We should recognize that in patients with some diseases, both acute and chronic, being overweight and even obese may be protective rather than harmful.

Whilst aiming for a lean body composition and preventing (and reversing) obesity are repeated like a Hindu mantra, it may be the time to consider a more differentiated strategy towards weight recommendations in patients with chronic ailments such as cardiovascular disease. Current data as confirmed again by Hastie *et al.* suggest that being overweight might not be the most important factor of concern in many patients.

Doehner et al. European Heart Journal (2010) 31, 146–148

ESC Guidelines **Eur J Heart Fail 10 2008: 933-989**

Class of recommendation I, level of evidence C

Weight reduction

Weight reduction in obese [body mass index (BMI) >30 kg/m^2] persons with HF should be considered in order to prevent the progression of HF, decrease symptoms, and improve well-being.

Class of recommendation IIa, level of evidence C

In moderate to severe HF, weight reduction should not routinely be recommended since unintentional weight loss and anorexia are common problems.

Unintentional weight loss

Clinical or subclinical malnutrition is common in patients with severe HF. The pathophysiology of cardiac cachexia in heart failure is complex and not completely understood, but altered metabolism, insufficient food intake, decreased nutritional uptake, gut congestion and inflammatory mechanisms may be important factors. Cardiac cachexia is an important predictor of reduced survival.[80]

- If weight loss during the last 6 months is >6% of previous stable weight without evidence of fluid retention, the patient is defined as cachectic.[81] The patient's nutritional status should be carefully assessed.

ACC-AHA 2009

Sólo menciona el beneficio de la reducción del peso para los factores de riesgo cardiovascular.
- No se pronuncia en IC-

Chronic heart failure: national clinical guideline for diagnosis and management **NICE 2003**

- Weight reduction may be appropriate in some people with heart failure.
- Fluid restriction is commonly advocated for those with heart failure, but this may cause dehydration in some, and may exacerbate confusion in the elderly.
- Salt reduction is also commonly recommended by physicians to help control fluid status, but may make food less palatable.

Further research in this area is required.

شكرا جزيلا !!!