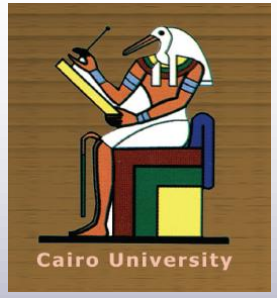
Obesity Paradox in Hypertension

Azza Farrag
Cairo University



- A 55 year old obese female patient with10 year history of T2DM
- Complaining of fatigue and difficulty in losing weight
- She stated that she has gained an enormous amount of weight since being placed on insulin 7 years ago
- Her weight has continued to increase over the past 5 years and she is presently at the highest weight she has ever been

- States that every time she tries to cut down on her eating, she got symptoms of diaphoresis and increased hunger ..

  So, she is so fearful of hypoglycemia and often eats extra snacks ..!
- Diabetologist has repeatedly advised weight loss and exercise to improve her health status,

  She complained that the pain in her knees and ankles make it difficult to perform any regular exercise

- **Past medical history is remarkable for hypertension, hypertriglyceridemia and degenerative arthritis**
- **Current medications:**
  - **Mixtard insulin, 45 U BB, 35 U BD**
  - **Regular insulin, 10 U BB, 20 U BD**
  - **Lisinopril 5 mg**
  - **Aspirin 81 mg**

- **Physical examination:**
  - **BP is 160/95 mmHg**
  - **BW is 85 Kg, Height is 162 cm, BMI is 32.4 Kg/m2**
  - **General and cardiac examination are unremarkable**

- **Laboratory testing:**
  - **Normal BUN, serum creatinine, liver function and thyroid profile**
  - **HbA1c is 8.7**
  - **Total cholesterol is 211 mg%, TGS is 205 mg% and HDL is 40 mg%**

- **After explanation that the increasing insulin dose was contributing to her weight gain,**
  - **Needs to decrease insulin dose together with reducing her food intake**
  - **Agreed, and reduce insulin dose to 30 U Mixtard and 10 U Regular insulin bid**
  - **Metformin was added 500 mg bid**

- **6 month later,**
  - **Lost 5 Kg, and her BMI was 30.5 kg/m2**
  - **Was happy with this result .. BUT**
  - **She asked about**

Obesity Paradox

Does obesity really bad ..?!

We are all different - part of the paradox!

Overweight: ✓✓✓

Drinker: ✓✓✓

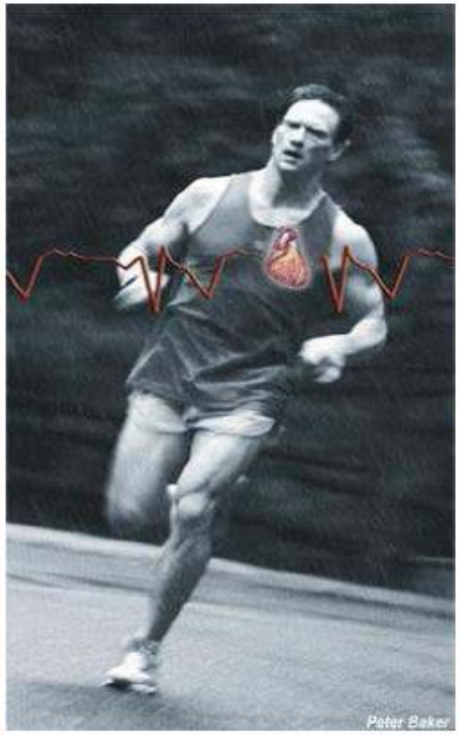
Smoker: ✓✓✓

Exercise: XXX

Healthy diet: XXX

Last job – British Prime Minister, Age 80

Died – Age 90



Jim Fixx

Author: *The Complete Book of Running*

Died, heart attack – Age 52

“One size does not fit all”

we are all genetically different in our response to diet and lifestyle .. but,
dietary recommendations are targeted to all populations

- **Obesity is a problem reaching epidemic proportions allover the world, but it still a major cause of preventable death**
- **Obesity, and mainly its abdominal form, is considered a major risk factor not only for T2DM, lipid disorders and hypertension, but also**
  - **Coronary artery disease**
  - **Certain cancers**

WHO Forecast

In 2020 70% of all diseases will be related to lifestyle

CHR HANSEN

6.5 bio people

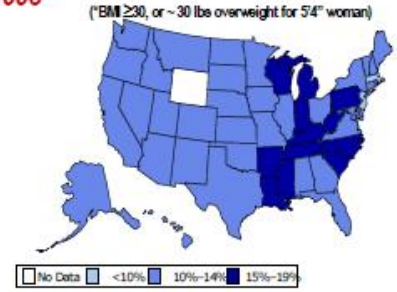
1 bio overweight

300 mio obese (min.)

Obesity* Trends Among U.S. Adults

1993

("BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)

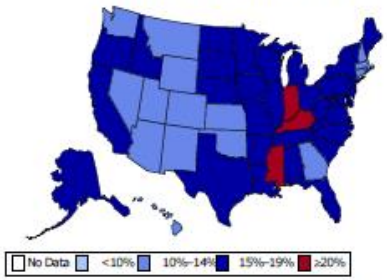


Source: Behavioral Risk Factor Surveillance System, CDC.

Obesity Trends Among U.S. Adults

1997

("BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)

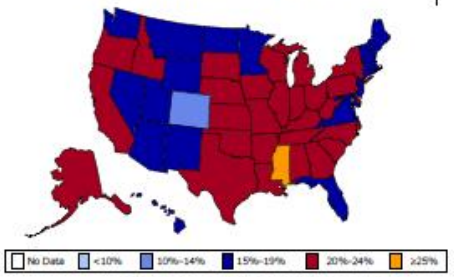


Source: Behavioral Risk Factor Surveillance System, CDC.

Obesity Trends Among U.S. Adults

2001

("BMI ≥30, or ~ 30 lbs overweight for 5'4" woman)



Source: Behavioral Risk Factor Surveillance System, CDC.

GAZETTE REVIEW

US World Business Entertainment Health Science Sports Technology

Home › World › Top 10 Fattest Countries In The World – 2016 List

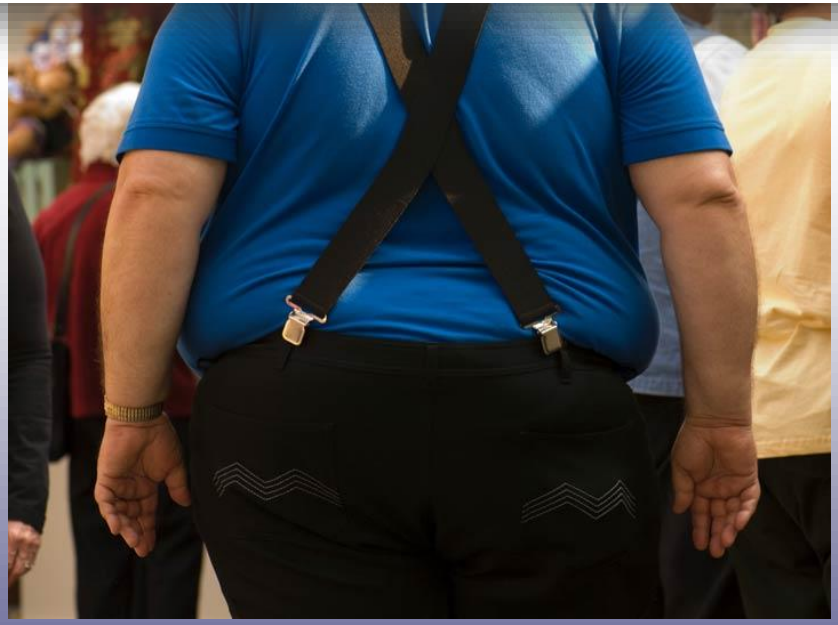
Top 10 Fattest Countries In The World – 2016 List

World Jun 17, 2016

Top 10 Fattest Countries in the World 2016

#4 – Egypt – 34.6%

Like many countries on this list of the fattest countries in the world, the problems in Egypt have been caused at least partially by rapid industrialization. In Egypt, the percentage of fat people in the cities is twice as big as the percentage of fat people in more rural areas. An abundance of cheap, fast food that isn't nourishing combined with a less active lifestyle is a dangerous mix. The results have been especially saddening in Egypt. Egypt has the highest diabetes rates in the world, and teenagers in the country drink an alarming amount of soda, making it the fattest country in Africa.



In the 1960s, Egypt produced enough food to feed its people a steady diet of red meat, poultry, lentils, maize and dairy products. But by the 1980s, the population had outgrown food production, leading to an increase in food imports that created poorer eating habits. Obesity among Egyptian women is particularly high, often attributed to cultural taboos on women exercising or playing sports.

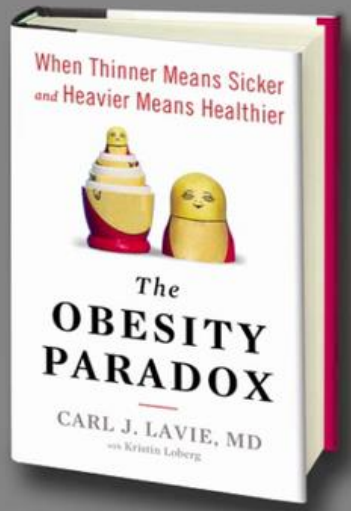
Classification of obesity

- BMI <18.5 kg/m^2 → underweight
- BMI 18.5-24.9 kg/m^2 → normal weight
- BMI 25-29.9 kg/m^2 → overweight
- BMI 30-34.9 kg/m^2 → class I obesity
- BMI 35-39.9 kg/m^2 → class II obesity
- BMI >40 kg/m^2 → class III obesity

When Thinner Means Sicker
and Heavier Means Healthier

The
OBESITY PARADOX

CARL J. LAVIE, MD
with Kristin Loberg



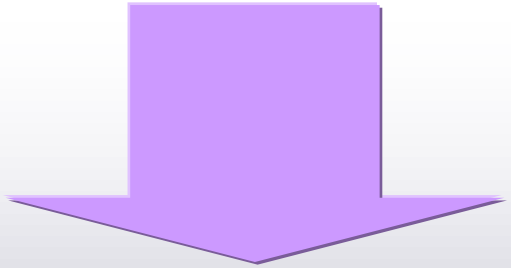
On sale
April 3, 2014.

HUDSON
STREET
PRESS

In 2014, Sorkin noted that these findings seriously challenged the existing dogma that increasing weight is necessarily associated with increasing mortality and that weight should remain unchanged throughout adult life

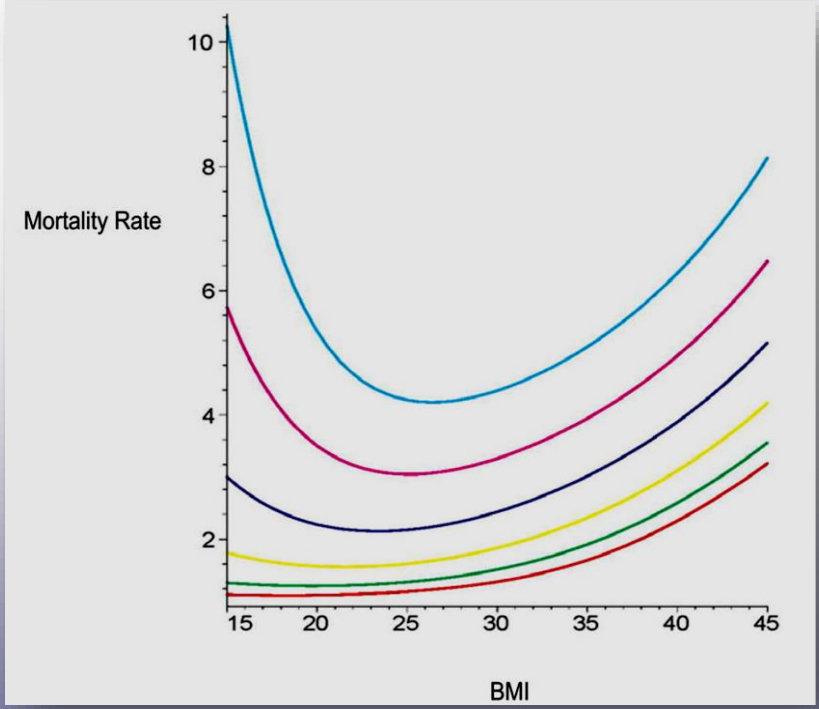
Skorin JD et al. Am J Clin Nutrition, 2014

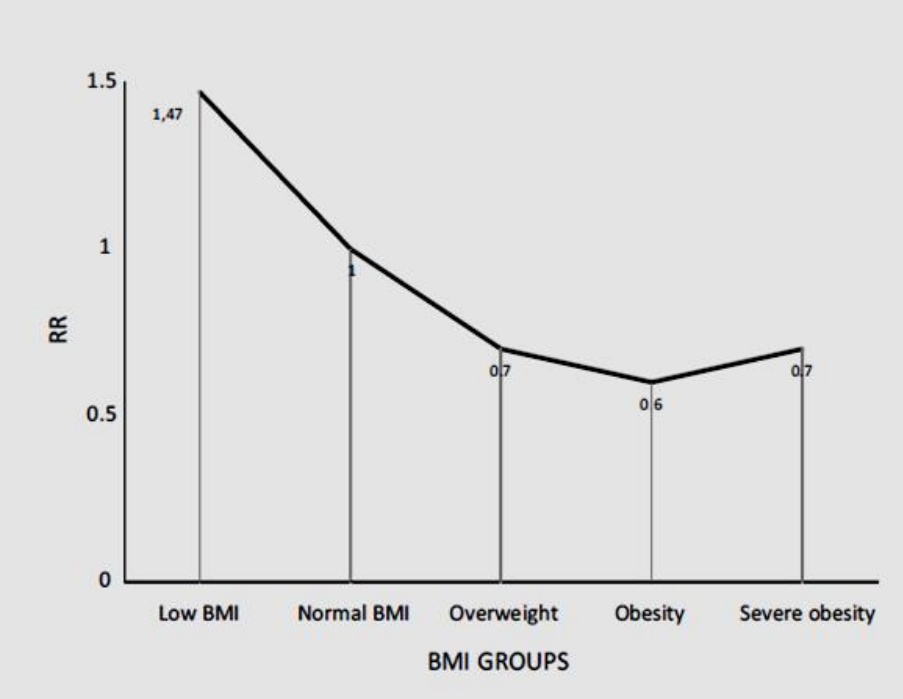
There is increasing evidence that **patients,** especially elderly, with several chronic diseases and elevated BMI, may demonstrate lower all-cause and cardiovascular mortality compared with patients of normal weight



Obesity Paradox

- **BMI is frequently used as a surrogate for assessment of excess body fat**
- **The relative risks (RR) of mortality and morbidity follows a U-shaped, or a J-shaped curve**





Obesity Paradox

Hypertension

- **Overweight and obese patients with hypertension had**
  - **Lower prevalence of non-fatal MI**
  - **Lower prevalence of non-fatal stroke**
  - **Lower prevalence of cardiovascular death**
  - **Decrease risk of all cause mortality**
  - **Lower prevalence of coronary artery calcification (calcification paradox)**

Obesity Paradox

Hypertension

- Connor and colleagues in 1985 were the first to suggest that hypertension was more benign when associated with obesity
- They studied 1727 men aged 50 to 79 years, age-adjusted all-cause and ischemic heart disease mortality was reduced in overweight and obese men, a finding which remained when those with a history of cigarette smoking were excluded

Connor E et al. Circulation, 1985

Obesity Paradox

Hypertension

- The ALLHAT study (The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) cohort of hypertensive patients without diabetes mellitus or manifest cardiovascular disease at entry, obesity was also found to be associated with lower all-cause mortality

Shah RV et al. J Clin Hypertension, 2014

Obesity Paradox

Hypertension

Hypertension

AHA Journals | Journal Information | All Issues | Subjects | Features | Resourc Educati

Home > Hypertension > Vol. 71, No. 1 > Obesity Paradox in Hypertension

FREE ACCESS

REVIEW ARTICLE

PDF/EPUB

Tools Share

Obesity Paradox in Hypertension

Is This Because Sympathetic Activation in Obesity-Hypertension Takes a Benign Form?

Murray Esler, Gavin Lambert, Markus Schlaich, John Dixon, Carolina Ika Sari, and Elisabeth Lambert

Originally published 20 Nov 2017 | https://doi.org/10.1161/HYPERTENSIONAHA.117.09790 | Hypertension. 2018;71:22–33

Obesity Paradox

Hypertension

Normal Weight	Obese
Cardiac sympathetic activity increased	Cardiac sympathetic activity normal or low
Single sympathetic fibers: increased firing rates, salvos of multiple firing	Single sympathetic fibers: recruitment of fibers which fire at normal rate, without salvos
Reduced norepinephrine reuptake	Neuronal norepinephrine reuptake normal
Sympathetic nerve epinephrine corelease	No sympathetic nerve epinephrine corelease

Esler M et al. Hypertension, 2018

Obesity Paradox

Hypertension

Regional Patterns of Sympathetic Activation in Essential Hypertension

		Lean	Obese
HEART		↑	↔
MSNA		↑	↑
KIDNEYS		↑	↑

Esler M et al. Hypertension, 2018

European Heart Journal Advance Access published September 4, 2012

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal
doi:10.1093/eurheartj/ehs217

CLINICAL RESEARCH

Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry

Oskar Angerås[1]*, Per Albertsson[1], Kristjan Karason[1], Truls Råmunddal[1], Göran Matejka[1], Stefan James[2], Bo Lagerqvist[2], Annika Rosengren[1], and Elmir Omerovic[1]

[1]Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; and [2]Uppsala Clinical Research Center, Department of Medical Sciences, Uppsala University, Uppsala, Sweden

Received 22 February 2012; revised 11 June 2012; accepted 27 June 2012

Obesity Paradox

coronary artery disease

- **Overweight and obese patients with CAD had**
  - **Better outcomes after PCI**
  - **lower incidence of major in-hospital complications including cardiac death**
  - **Lower 1-year mortality**
  - **Lower prevalence of left-main disease**
  - **Better outcome after CABG**
  - **Lower prevalence of complication after CABG (*re-intubation, re-exploration, stay in the ICU*)**

Am J Cardiol 2010

Obesity Paradox

coronary artery disease

Eur J Epidemiol (2014) 29:801–812
DOI 10.1007/s10654-014-9961-9

META-ANALYSIS

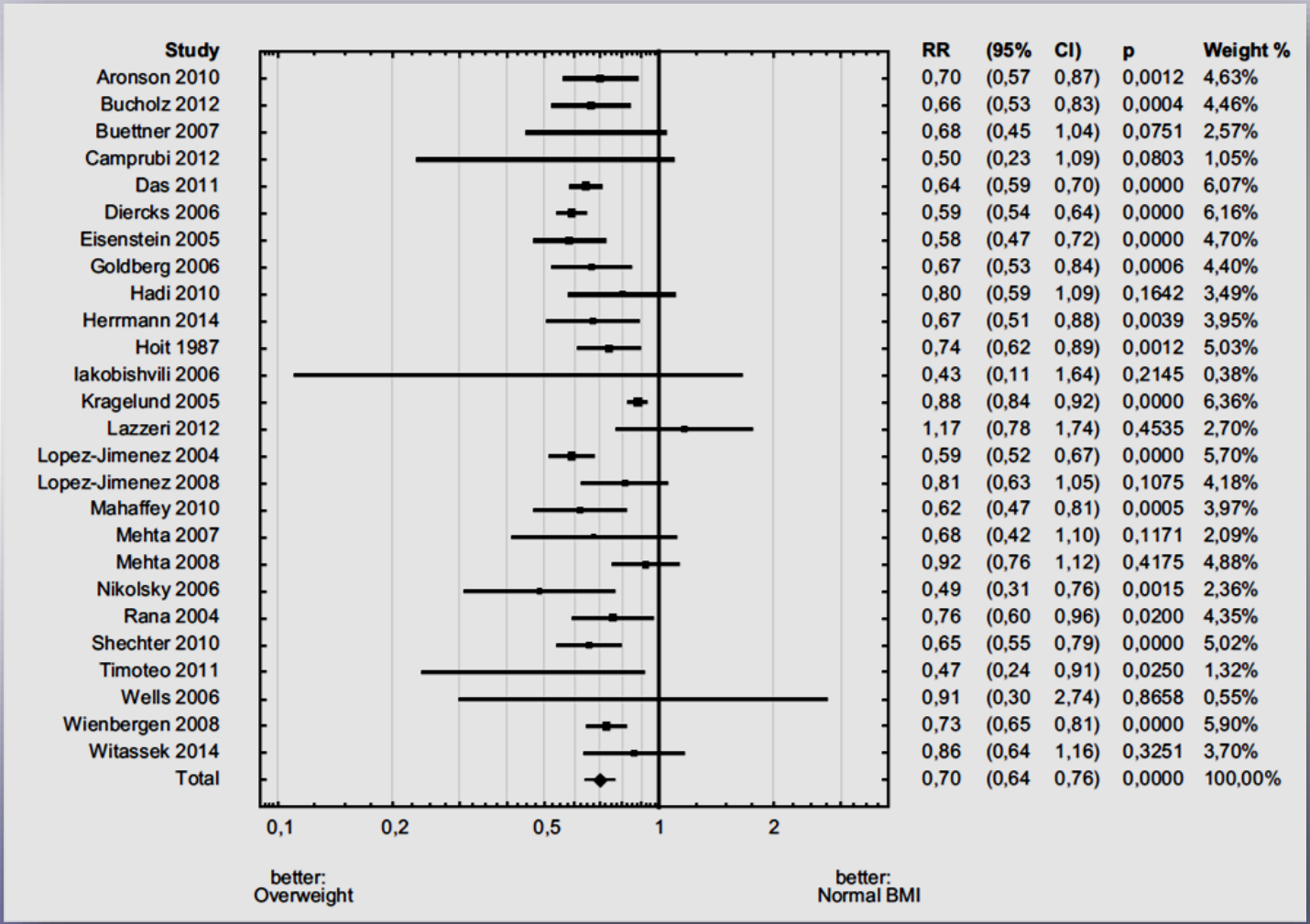
The obesity paradox in acute coronary syndrome: a meta-analysis

Jacek Niedziela · Bartosz Hudzik · Natalia Niedziela · Mariusz Gąsior · Marek Gierlotka · Jarosław Wasilewski · Krzysztof Myrda · Andrzej Lekston · Lech Poloński · Piotr Rozentryt

Received: 7 May 2014 / Accepted: 15 October 2014 / Published online: 30 October 2014
© The Author(s) 2014. This article is published with open access at Springerlink.com

Obesity Paradox

coronary artery disease



The American Journal of Medicine (2007) 120, 863-870

ELSEVIER

THE AMERICAN JOURNAL of MEDICINE®

CLINICAL RESEARCH STUDY

Obesity Paradox in Patients with Hypertension and Coronary Artery Disease

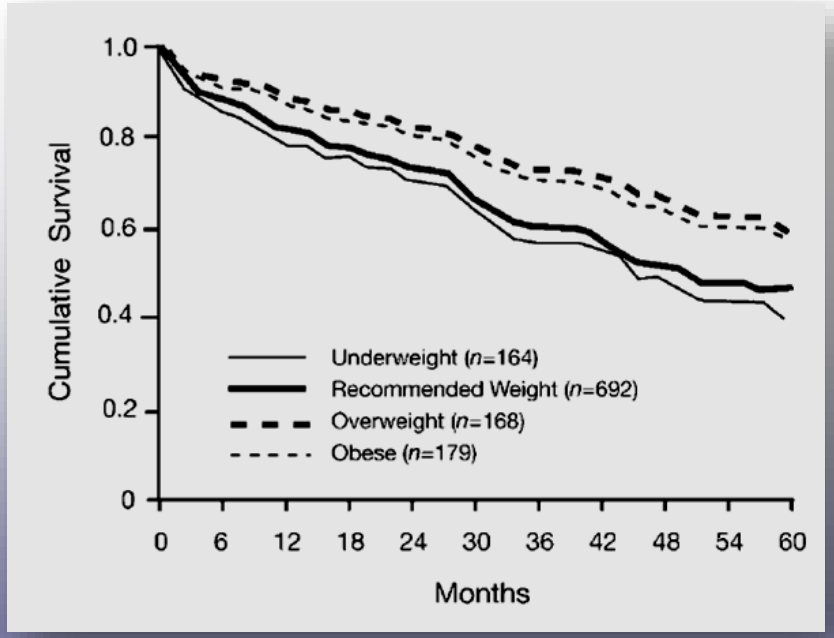
Seth Uretsky, MD,[a] Franz H. Messerli, MD,[a] Sripal Bangalore, MD, MHA,[a] Annette Champion, MBA,[b] Rhonda M. Cooper-DeHoff, PharmD,[c] Qian Zhou, PhD,[b] Carl J. Pepine, MD[c]

[a]Division of Cardiology, St Luke's-Roosevelt Hospital, New York, NY; [b]Abbott, Abbott Park, Ill; [c]Cardiovascular Medicine, University of Florida, Gainesville.

CONCLUSION: In a population with hypertension and coronary artery disease, overweight and obese patients had a decreased risk of primary outcome compared with patients of normal weight, which was driven primarily by a decreased risk of all-cause mortality. Our results further suggest a protective effect of obesity in patients with known cardiovascular disease in concordance with data in patients with heart failure and those undergoing percutaneous coronary intervention. © 2007 Elsevier Inc. All rights reserved.

Obesity Paradox
heart failure

- **Overweight and obese patients with CHF had**
  - **Lower prevalence mortality (reverse epidemiology)**
  - **Lower prevalence of in-hospital mortality**
  - **Decreased risk of death on follow up**
    (*Digitalis Investigation Group Trial*)



Obesity Paradox

stroke

- **Overweight and obese patients with CVS had**
  - **Better survival rate after stroke**
  - **Lower risk of stroke post carotid endarterectomy**

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

Obesity Paradox and Stroke: Noticing the (Fat) Man Behind the Curtain

Michael Katsnelson and Tatjana Rundek

Stroke. 2011;42:3331-3332; originally published online September 29, 2011;
doi: 10.1161/STROKEAHA.111.632471
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

How to Explain Obesity Paradox ..??

Obesity Paradox

Role of age

J Cachexia Sarcopenia Muscle (2012) 3:1–4
DOI 10.1007/s13539-012-0059-5

EDITORIAL

The obesity paradox in chronic disease: facts and numbers

Mitja Lainscak · Stephan von Haehling ·
Wolfram Doehner · Stefan D. Anker

Obesity Paradox

Role of age and risky obesity

- Obese aged patients with risk obesity (abdominal obesity) die earlier
- Obese patients with less risky (hip obesity) survive
- Late onset obesity, with its short duration did not exhibit the unhealthy complications
- MDCT studies showed decrease VAT accumulation with age

Condition and study/country	*N* (% men)	Age	Main finding
Heart failure			
Acute (ADHERE registry) [9]	108,927 (49%)	72±14 years	Inhospital mortality decreased from 5.0% to 2.2% per BMI quartiles The mortality OR for obese, overweight, and underweight vs healthy weight was 0.74 (95% CI 0.68–0.81), 0.83 (95% CI 0.76–0.90), and 1.34 (95% CI 1.15–1.58), respectively
Chronic (USA) [10]	7,767 (75%)	64±11 years	Higher BMI associated with lower mortality risk: adjusted HR for all-cause death for obese or overweight vs healthy weight patients was 0.81 (95% CI 0.72–0.92) and 0.88 (95% CI 0.80–0.96), respectively
Coronary artery disease			
Coronary artery disease and hypertension (INVEST) [11]	22,576 (NA)	66±10 years	With normal weight subjects as reference, overweight and obese patients had better (HR 0.52–0.66, $p<0.001$) and thin patients had worse survival (HR 1.85, $p<0.001$)
Percutaneous coronary intervention (Germany) [12]	4,880 (70%)	Median age 62 years	Patients with BMI 27.5–30 kg/m^2 had lowest adjusted HR for death (0.59, 95% CI 0.39–0.90)
Coronary artery bypass grafting (Germany) [13]	22,599 (72%)	63±10 years	Lowest RR for 30-day mortality in patients with BMI of 33 kg/m^2, patients with BMI<22 kg/m^2 had significantly higher RR for death
Stroke (Greece) [14]	2,785 (62%)	Mean age 70 years	Obese and overweight patients had significantly higher early (1 week and 1 month) and long-term (10 years) survival when compared to patients with normal BMI ($p<0.001$ for all)
Intensive care unit (Germany) [15]	9,935 (64%)	63±15 years	Overweight (HR 0.86, 95% CI 0.74–0.99) and obese (HR 0.83, 95% CI 0.69–0.99) patients had lower 30-day inhospital mortality.
Chronic obstructive pulmonary disease			
Acute exacerbation (Slovenia) [16]	968 (72%)	70±9 years	In an adjusted model, BMI per 1 kg/m^2 unit increase was associated with 5% less chance of death (hazard ratio 0.95, 95% confidence interval 0.93–0.97)
Stable disease (Copenhagen city heart study) [17]	2,132 (57%)	56±11 years	Adjusted RR for death in underweight vs normal weight patients was 1.64 (95% CI 1.20–2.23) in men and 1.42 (95% CI 1.07–1.89) in women
Chronic kidney disease (DaVita dialysis facilities, USA) [18]	121,762 (54%)	63±15 years	Higher BMI (optimal range 40–45) was independently associated with better survival after adjustment for available surrogates of nutritional status and inflammation
Diabetes plus cardiovascular disease PROactive Study [19]	5,202 (66)	62±7 years	Higher BMI (optimum range 30–35 kg/m^2) was associated with lower mortality and hospitalization. Weight loss but not weight gain was predictive of increased mortality.

BMI body mass index, *OR* odds ratio, *HR* hazard ratio; *RR* relative risk; *95% CI* 95% confidence interval

Obesity Paradox

Role of metabolic syndrome

- Obese insulin- sensitive, and obese insulin-resistant had similar BMI, but the formers had lower waist circumference, BP, FBG, TGs, fibrinogen and a higher HDL

- Subcutaneous fat accumulation in lower body is associated with lesser likelihood probability of insulin resistance

Cardiovascular and Metabolic Risk

ORIGINAL ARTICLE

Prevalence, Metabolic Features, and Prognosis of Metabolically Healthy Obese Italian Individuals

The Cremona Study

Giliola Calori, MD[1]
Guido Lattuada, PHD[1,2]
Lorenzo Piemonti, MD[3]
Maria Paola Garancini, MD[4]
Francesca Ragogna, PHD[1]
Marco Villa, MD[5]
Salvatore Mannino, MD[5]
Paolo Crosignani, MD[6]
Emanuele Bosi, MD[1]
Livio Luzi, MD[1,2]
Giacomo Ruotolo, MD[1,7]
Gianluca Perseghin, MD[1,2]

OBJECTIVE — Some obese individuals have normal insulin sensitivity. It is controversial whether this phenotype is associated with increased all-cause mortality risk.

RESEARCH DESIGN AND METHODS — Fifteen-year all-cause mortality data were obtained through the Regional Health Registry for 2,011 of 2,074 Caucasian middle-aged individuals of the Cremona Study, a population study on the prevalence of diabetes in Italy. Individuals were divided in four categories according to BMI (nonobese: <30 kg/m^2; obese: ≥30 kg/m^2) and estimated insulin resistance (insulin sensitive: homeostasis model assessment of insulin resistance <2.5; insulin resistant ≥2.5).

RESULTS — Obese insulin-sensitive subjects represented 11% (95% CI 8.1–14.5) of the obese population. This phenotype had similar BMI but lower waist circumference, blood pressure, fasting glucose, triglycerides, and fibrinogen and higher HDL cholesterol than obese insulin-resistant subjects. In the 15-year follow-up, 495 deaths (cardiovascular disease [CVD]: n = 221; cancer: n = 180) occurred. All-cause mortality adjusted for age and sex was higher in the obese insulin-resistant subjects (hazard ratio 1.40 [95% CI 1.08–1.81], P = 0.01) but not in the obese insulin-sensitive subjects (0.99 [0.46–2.11], P = 0.97) when compared with nonobese insulin-sensitive subjects. Also, mortality for CVD and cancer was higher in the obese insulin-resistant subjects but not in the obese insulin-sensitive subjects when compared with nonobese insulin-sensitive subjects.

CONCLUSIONS — In contrast to obese insulin-resistant subjects, metabolically healthy obese individuals are less common than previously thought and do not show increased all-cause, cancer, and CVD mortality risks in a 15-year follow-up study.

Diabetes Care 34:210–215, 2011

therapeutic approach with respect to obese individuals with metabolic abnormalities are currently debated (4,5). In the Framingham Offspring Study, Meigs et al. (6) found that MHO individuals do not have increased risk of incident diabetes and cardiovascular disease (CVD). Conversely, in the Third National Health and Nutrition Examination Survey (NHANES III), Kuk et al. (7) reported increased all-cause mortality associated with the MHO phenotype. Finally, in a Scandinavian study (8), middle-aged overweight/obese subjects without metabolic syndrome also had an increased risk of CVD when compared with normal-weight individuals without metabolic syndrome. The present study shows the prevalence of the MHO phenotype, its metabolic features, and 15-year all-cause, CVD, and cancer mortality rates in the Caucasian population of the Cremona Study (9,10).

RESEARCH DESIGN AND METHODS

Study cohort and follow-up

The Cremona Study is a population survey carried out in 1990–1991 in the health district of Cremona (Lombardia, Italy) to determine the prevalence of dia-

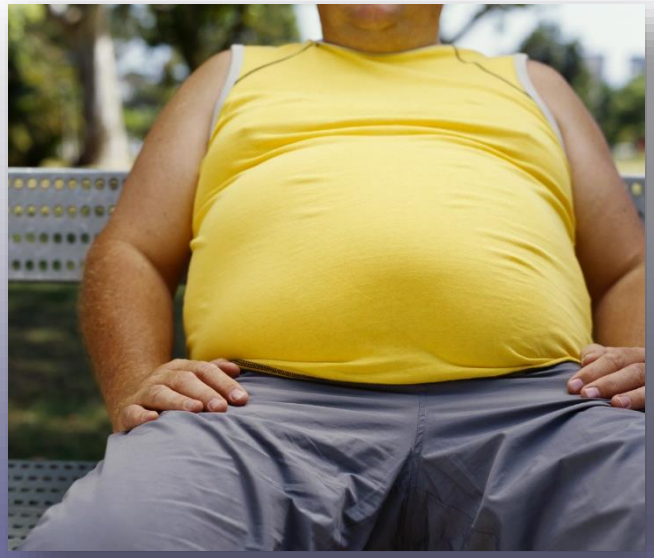
Obesity Paradox

Other parameters of obesity

Obesity Paradox

Other parameters of obesity

- Increased waist circumference is associated with all cardiovascular causes of morbidity and mortality
- Decreased hip circumference is associated with great progression of carotid artery atherosclerosis

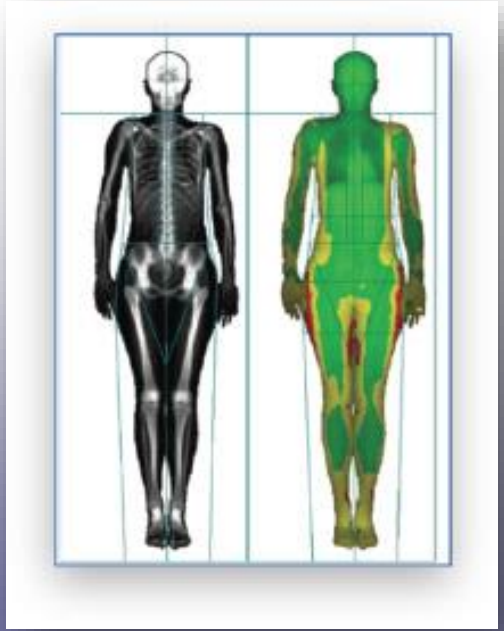


Diabetes Care 2013

Obesity Paradox

BMI is not enough

- Measurement of body composition using dual-energy X-ray absorptiometry, revealed that BMI misclassified body fat status
- BMI is a better indicator of lean body mass but not body fat



Obesity Paradox

Other possible hypothesis

- Level of cardiorespioratory fitness
- Greater mobilization of progenitor cells
- Deceased TNF-α level (due to production of soluble TNF-α receptors by SC tissue)

Obesity Paradox

Hypertension

Does weight loss in obesity-hypertension transform the patient into a normal-weight hypertensive patient, with all the accompanying sympathetic phenotype demerits?

Obesity Paradox

Hypertension

The 2 hypertension variants, obese and lean, are not interconvertible. Normal-weight essential hypertension must have its own unique origins

At this stage, she got disappointed, but tried to smile and gave me the impression that she is really convinced …!

Thank You