Body Mass Index and Mortality Among Hospitalized Patients

Francesco Landi, MD, PhD; Graziano Onder, MD; Giovanni Gambassi, MD; Claudio Pedone, MD; PierUgo Carbonin, MD; Roberto Bernabei, MD; for the Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) Study Group

Background: Body mass index (weight in kilograms divided by the square of the height in meters [BMI]) is known to be associated with overall mortality. However, the effect of age on excess mortality from all causes associated with obesity is controversial. The aim of the present study is to determine the effect of age on the relationship between BMI and mortality.

Methods: We analyzed data from a large collaborative observational study group, the Italian Group of Pharmacoepidemiology in the Elderly (GIFA), that collected data on hospitalized patients. A total of 18316 patients consecutively admitted to 79 clinical centers during 5 different surveys in 1998, 1991, 1993, 1995, and 1997 were enrolled in the present study. The main outcome measure was the relative hazard ratio of death for different levels of BMI.

Results: Mortality rate was lowest among men and women with BMIs from 25.0 through 27.4 kg/m^2 (relative risk, 0.24; 95% confidence interval, 0.15-0.38). The graphed relationship between BMI and mortality in younger patients was hyperbolic, with increased death rates at the lowest and highest BMI rankings. On the contrary, the older patients showed an increased death rate at the lowest BMIs with only a slight elevation at the highest BMIs (>35 kg/m^2).

Conclusions: Our results suggest that BMI, a simple anthropometric measure of nutritional status, is an important predictor of mortality among young and old hospitalized patients. Even when controlling for clinical and functional variables, a low BMI remained a significant and independent predictor of shortened survival. Furthermore, the finding of the high BMI associated with minimum hazard in elderly subjects supports some past findings and opposes others and, if confirmed, has important implications for geriatric clinical guidelines.

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THE GRAPHED relationship of body weight to mortality throughout the range of body mass index (weight in kilograms divided by the square of the height in meters [BMI]) has been described as J-shaped, U-shaped, inverse, positive, and even absent.[1-6] In most population studies, the association between BMI and mortality is described by a U-shaped curve, with augmented risk in the lowest and highest percentiles of the distribution, even when controlling for comorbid disease, age, and smoking.[7] However, the association between body weight and mortality remains controversial.[8] In particular, important questions remain about the impact of age on the relationship between overweight conditions and mortality.[9-11] The third edition of the *Dietary Guidelines for Americans*[12] has recommended a higher BMI with increasing age. On the contrary, the last edition of analogous weight guidelines[13] did not include age-specific recommendations.

Recent studies supported the hypothesis that the relative risk of death associated with obesity is lower for older than for younger adults[10,11,14-17] and that optimal weight for longevity may be higher in older people.[18-20] To evaluate further the risk of death associated with weight and to investigate whether this risk varies according to age, we examined the relationship between BMI and death rates in a large cohort of hospitalized patients.

RESULTS

Table 1 gives the main sociodemographic, medical, and functional characteristics of the patients, according to sex and different age groups. On average, the women were older than the men (71.2±15.8 vs 66.9±16.5 years, respectively). Apart from smoking history and consumption of wine, men and women did not differ in regard to the prevalence of comorbidity and functional and cognitive impairment. On the contrary, among the older patients (>75 years) there was a higher prevalence of comorbidy and a higher level of functional impairment relative to those in the younger groups. The average BMI data are consistent with good nutritional status, and no age or sex differences. However, the stratified distribution of BMI reveals that a severe status of malnutrition (BMI<18.5 kg/m^2) oc-

From the Istituto di Medicina Interna e Geriatria, Universitá Cattolica del Sacro Cuore, Rome, Italy (Drs Landi, Onder, Gambassi, Pedone, Carbonin, and Bernabei); and the Center for Gerontology and Health Care Research, Brown University, Providence, RI (Dr Gambassi). A complete list of the Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) investigators has been published previously (Eur J Epidemiol. *1999;15:893-901*).

SUBJECTS AND METHODS

The present study uses data from a large collaborative observational study group, the Italian Group of Pharmacoepidemiology in the Elderly (Gruppo Italiano di Farmacoepidemiologia nell'Anziano [GIFA]). The methods of the GIFA have been described in detail elsewhere.[21] We considered all patients consecutively admitted in the 79 participating clinical centers during 5 different surveys in 1988, 1991, 1993, 1995, and 1997 for 13 months overall (N=20456). Subsequently, we excluded 1938 patients admitted to the hospital with explicit diagnosis of terminal illness and 202 patients with obesity-related diseases (ie, hypothyroidism, Cushing syndrome, and acromegaly). Procedures were in accordance with guidelines provided by the Catholic University ethical committee; the study was also approved and monitored by the steering committee of the National Research Council of Italy.

For each patient a questionnaire was completed at admission and updated daily by a study physician who received specific training for the study. Data recorded included sociodemographic characteristics such as age, sex, household composition, smoking status, and alcohol intake history; medical variables such as main and coexisting diseases, prescribed medications, physical findings, electrocardiography results, chest radiography findings, and complete blood count; neuropsychological variables; and physical function variables. Comorbidity was measured using the Charlson comorbidity index.[22] Cognitive status was assessed with the Hodkinson's Abbreviated Mental Test Examination.[23] Physical function was measured with a 6-item scale of activities of daily living ranging from 0 (independent) to 6 (total dependence).[24]

Weight and height were measured during the first day of hospitalization according to guidelines by de Groot and van Staveren[25] and each measure was repeated 3 times and averaged.[26] The BMI was then computed. We categorized BMI as lower than 18.5 kg/m^2, 18.5 to 21.7 kg/m^2, 21.8 to 24.9 kg/m^2, 25.0 to 27.4 kg/m^2, 27.5 to 29.9 kg/m^2, 30.0 to 34.9 kg/m^2, and 35.0 kg/m^2 or higher. Combinations of these 7 categories are in accordance with the cutoff points proposed by the World Health Organization: a BMI between 18.5 and 24.9 kg/m^2 defines the normal range; between 25.0 and 29.9 kg/m^2, mildly overweight; and 30.0 kg/m^2 or higher, moderately to severely overweight.[27]

Data were first analyzed by descriptive statistics. Continuous variables are presented as mean values ± SD. Differences in categorical parameters according to age and sex were tested using the Fisher exact test. Differences between continuous variables were assessed by analysis of variance comparisons for normally distributed parameters, or the Kruskal-Wallis test was adopted.

To address whether the relationship between different levels of BMI and mortality were homogeneous in the study population, we used a sex-adjusted Cox proportional hazards regression model stratifying the cohort according to age. Adjustments were made for all possible confounders. Cox models were adjusted for potential risk factors reported at admission: index of comorbidity, physical disability, cognitive impairment, smoking status, and alcohol abuse. Statistical analyses were performed using SPSS software (version 8; 1998, Chicago, Ill).

curred quite frequently, with higher prevalence among women than men (7.3% vs 3.8%, respectively).

The overall in-hospital mortality rates were 2.9% (n=260) and 3.2% (n=288) for men and women, respectively, and this was not statistically significant ($P=.22$). **Table 2** gives both the crude and adjusted relative risks of death for each of the BMI levels considered in the study. The graphed relationship was hyperbolic, with very little elevation in the highest level of BMI (>35.0 kg/m^2) for both men and women. Mortality was lowest among men and women with BMIs from 25.0 through 27.4 kg/m^2. Multivariate adjustment for other risk factors strengthened the association between severe malnutrition and mortality but did not substantially modify the results.

A comparison of the shapes of the curves for different classes of age is presented in the **Figure**. For younger patients (<65 years), the relationship between BMI and mortality was U-shaped, with increased death rates among both the leanest and the heaviest persons. On the contrary, the middle-aged and older patients showed only a slight elevation of death rates in the highest level of BMI (>35.0 kg/m^2).

COMMENT

The results of this large observational study suggest that a very low BMI has an important prognostic implication for patients in an acute care setting, independent of age, sex, and other nonnutritional risk factors. On the contrary, the excess mortality associated with highest levels of BMI in younger patients declined considerably with age in all degrees of obesity (BMI >30.0 kg/m^2). These data are consistent with previous studies in different settings[6,9-11,16,19] that evaluated mortality rates among geriatric populations as a function of BMI. Even when controlling for multiple other potential risk factors, such as comorbidity, smoking, alcohol consumption, and functional and cognitive impairment, the mortality rate among elderly patients was greatest at the lowest BMI and not at the highest BMI rankings.

Our findings suggest that obesity does not qualify as a risk factor in hospitalized older patients, assuming that an obesity-related disease has been excluded. However, the findings of some epidemiological surveys that compared death rates according to BMI across age groups support the hypothesis of important prognostic implications of obesity even in older people.[7,28,29] Recently, Calle and colleagues[7] have demonstrated that the risk of death from all causes increases throughout the range of moderately and severely overweight conditions for both men and women in all age groups. Disagreement in specific findings may be ascribed to differences in populations studied, exclusion criteria, risk factors controlled for in the analysis, and cutoff points for categories of BMI.

Some limitations of the present study must be acknowledged. Overall, results from the present study should be considered cautiously, given the relatively low number of events in the younger group (42 deaths) and among those with the highest level of BMI (12 deaths). Second, malnu-

Table 1. Descriptive Analysis of Baseline Sociodemographic, Functional, and Clinical Parameters According to Age and Sex*

	Age Group, y Men				Age Group, y Women			
Characteristic†	**Total (n = 9170)**	**<65 (n = 3272)**	**65-74 (n = 2418)**	**≥75 (n = 3480)**	**Total (n = 9145)**	**<65 (n = 2294)**	**65-74 (n = 2132)**	**≥75 (n = 4719)**
Mean ± SD age, y	66.9 ± 16.5	48.9 ± 13.3	70.0 ± 2.9	81.6 ± 4.5	71.2 ± 15.8	49.1 ± 13.6	70.2 ± 2.8	82.4 ± 5.0
Smokers, %	26.8	42.6	24.2	13.8	6.7	16.7	5.6	2.2
Consumption of wine, %‡	19.2	25.9	19.1	13.0	2.9	4.8	3.4	1.8
Mean ± SD ADL score	1.1 ± 2.1	0.4 ± 1.3	0.9 ± 1.9	1.9 ± 2.5	1.5 ± 2.3	0.4 ± 1.4	1.1 ± 2.0	2.2 ± 2.5
Mean ± SD AMT score	7.9 ± 2.8	9.0 ± 1.9	8.3 ± 2.4	6.7 ± 3.2	7.2 ± 3.0	9.0 ± 1.8	7.9 ± 2.4	6.1 ± 3.2
Index of comorbidity, %§	1.1 ± 1.2	0.8 ± 1.1	1.3 ± 1.2	1.4 ± 1.3	1.0 ± 1.2	0.5 ± 0.9	1.1 ± 1.2	1.2 ± 1.2
Mean ± SD No. of medications	5.9 ± 4.4	4.9 ± 4.3	6.3 ± 4.4	6.6 ± 4.4	6.0 ± 4.3	4.5 ± 4.0	6.2 ± 4.5	6.6 ± 1.2
Mean ± SD BMI, kg/m^2	24.9 ± 3.9	25.4 ± 4.1	25.3 ± 3.8	24.2 ± 3.7	24.9 ± 5.0	25.7 ± 5.6	25.9 ± 5.1	24.1 ± 4.5
BMI, %								
<18.5	3.8	2.9	2.8	5.4	7.3	6.4	4.4	9.0
18.5-21.7	15.0	12.7	12.0	19.2	20.0	16.7	14.4	24.2
21.8-24.9	34.9	35.0	34.6	34.9	27.7	27.7	28.1	27.5
25.0-27.4	23.9	24.2	25.0	23.0	19.1	17.4	20.7	19.3
27.5-29.9	12.7	13.1	14.3	11.1	11.2	12.2	14.0	9.5
30.0-34.9	8.2	9.7	9.8	5.7	10.6	12.8	12.9	8.5
>35.0	1.5	2.4	1.5	0.7	4.1	6.8	5.4	2.1

*The total number of patients (men and women) younger than 65 years is 5566; ages 65-74 years, 4550; 75 and older, 8199. The total number of patients overall is 18 315.

†ADL indicates activities of daily living; AMT, Hodkinson's Abbreviated Mental Test Examination (normal range, 0-6; a higher number indicates higher level of impairment); and BMI, body mass index.

‡More than 0.5 L/d.

§Charlson comorbidity index.

Table 2. Crude and Adjusted Relative Risks (RRs) of Mortality According to Body Mass Index (BMI) Levels*

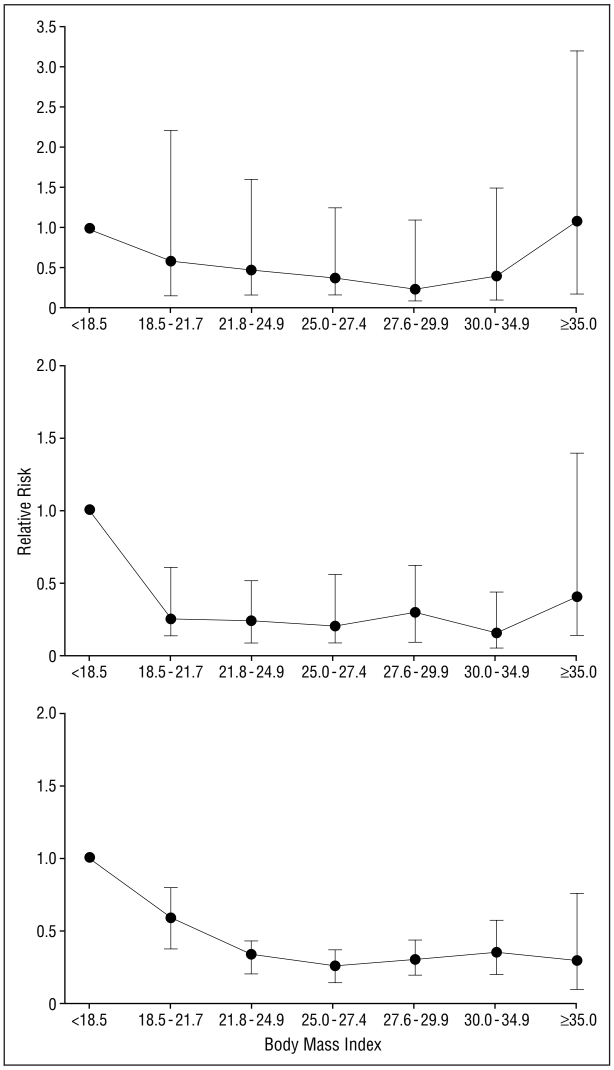
	Men			Women		
BMI, %	**Dead/Alive, No. of Patients**	**Crude Model, RR (95% CI)**	**Adjusted Model,† RR (95% CI)**	**Dead/Alive, No. of Patients**	**Crude Model, RR (95% CI)**	**Adjusted Model, RR (95% CI)**
<18.5	39/310	...	...	55/607	...	...
18.5-21.7	73/1296	0.44 (0.29-0.67)	0.50 (0.32-0.77)	80/1746	0.50 (0.35-0.72)	0.54 (0.37-0.79)
21.8-24.9	82/3102	0.21 (0.14-0.31)	0.29 (0.19-0.44)	51/2473	0.22 (0.15-0.33)	0.30 (0.20-0.45)
25.0-27.4	46/2143	0.17 (0.10-0.26)	0.24 (0.15-0.38)	31/1714	0.19 (0.12-0.31)	0.24 (0.15-0.38)
27.5-29.9	29/1129	0.20 (0.12-0.33)	0.28 (0.16-0.48)	18/1005	0.19 (0.11-0.33)	0.25 (0.14-0.44)
30.0-34.9	14/735	0.15 (0.08-0.28)	0.22 (0.11-0.42)	18/946	0.21 (0.12-0.36)	0.28 (0.16-0.49)
>35.0	5/137	0.29 (0.11-0.75)	0.45 (0.16-1.21)	7/364	0.21 (0.09-0.47)	0.30 (0.13-0.68)

*RR indicates relative risk; CI, confidence interval; and ellipses, not applicable.

†The Cox proportional hazards model was used, with adjustment for age, smoking, alcohol abuse, comorbidity, functional status, and cognitive impairment.

trition and obesity were quantified by a single measurement of BMI at only 1 time point. This cross-sectional approach to assess the relationship between BMI and mortality does not provide evidence for direct causality. In some patients, weight loss may be the result of an illness that is ultimately fatal, a circumstance that produces the appearance of higher mortality among those with lower BMIs. Furthermore, we had no direct measure of adiposity or of lean body mass, and we had no measure of central adiposity, such as the waist-to-hip ratio. The BMI cannot distinguish adequately between fat mass and lean tissue mass, and it may be a less useful indicator of adiposity among the older patients who have a greater amount of body fat at a given BMI than younger ones because of to age-related declines in muscle mass.[30] Finally, a more critical consideration is that patients studied were only those hospitalized, indicating that an acute problem existed. For this reason we are not authorized to extend the results to community-dwelling elderly individuals.

Despite these methodological problems, a comparison of present and previous analyses suggests that treating overweight conditions should be avoided in hospitalized older patients. On the contrary, our findings support the well-established increase in the risk of death associated with malnutrition in all age groups.[10,11,16,19,31] Indeed, overweight conditions and obesity are important determinants of mortality among younger and middle-aged patients but not in older patients. Our results complement previous studies indicating that the relative risk associated with greater body weight declines with age.[9] Obesity increases morbidity, impairs quality of life, and is one of the most important causes of mortality.[32,33] The evidence makes clear that obesity is a major public health problem in industrialized countries. However, the rela-



Multivariate relative risk of death from all causes according to age and body mass index. The top figure includes subjects younger than 65 years (42 deaths); center, 65-74 years (90 deaths); and bottom, 75 years and older (413 deaths). The reference category was made up of patients with body mass indexes lower than 18.5 kg/m^2. Analyses were adjusted for sex, index of comorbidity, physical disability, cognitive impairment, smoking, and alcohol abuse.

tionship between body weight and mortality remains controversial in the geriatric population. Our data and those of previous studies support the hypothesis that the optimal weight for longevity may be higher in older people.

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Corresponding author: Francesco Landi, MD, PhD, Istituto di Medicina Interna e Geriatria, Centro Medicina dell'Invecchiamento, Universitá Cattolica del Sacro Cuore, Largo Agostino Gemelli 8, 00168 Rome, Italy (e-mail: francesco_landi@rm.unicatt.it).

REFERENCES

1. Manson JE, Willett WC, Stampfer MJ, et al. Body weight and mortality among women. *N Engl J Med.* 1995;333:677-685.
2. Wannamethee G, Shaper AG. Body weight and mortality in middle-aged British men: impact on smoking. *BMJ.* 1989;299:1497-1502.
3. Lee IM, Manson JE, Henneken CH, et al. Body weight and mortality: a 27-year follow-up of middle-aged men. *JAMA.* 1993;270:2823-2828.
4. Stevens J, Keil JE, Rust PF, et al. Body mass index and body girth as predictors of mortality in black and white women. *Arch Intern Med.* 1992;152:1257-1262.
5. Wilcosky T, Hyde J, Anderson JJB, et al. Obesity and mortality in the Lipid Research Clinics Program Follow-up Study. *J Clin Epidemiol.* 1990;43:743-752.
6. Dorm JM, Schisterman EF, Winkelstein W, Trevisan M. Body mass index and mortality in a general population sample of men and women. *Am J Epidemiol.* 1997;146:919-931.
7. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med.* 1999;341:1097-1105.
8. Willet WC, Dietz WH, Colditz GA. Guidelines for healthy weight. *N Engl J Med.* 1999:341:427-434.
9. Bender R, Jockel KH, Trautner C, Spraul M, Berger M. *JAMA.* 1999:281:1498-1504.
10. Antonelli Incalzi R, Landi F, Ciprani L, et al. Nutritional assessment: a primary component of multidimensional geriatric assessment in the acute care setting. *J Am Geriatr Soc.* 1996;44:166-174.
11. Landi F, Zuccalà G, Gambassi G, et al. Body mass index and mortality among older people living in the community. *J Am Geriatr Soc.* 1999;47:1072-1076.
12. Department of Agriculture, Department of Health and Human Services. *Nutrition and Your Health: Dietary Guidelines For Americans.* 3rd ed. Washington, DC: Government Printing Office; 1990.
13. Department of Agriculture, Department of Health and Human Services. *Nutrition and Your Health: Dietary Guidelines for Americans.* 4th ed. Washington, DC: Government Printing Office; 1995.
14. Singh PN, Lindsted KD. Body mass and 26-year risk of mortality from specific diseases among women who never smoked. *Epidemiology.* 1998;9:246-254.
15. Diehr P, Bild DE, Harris TB, Duxbury A, Siscovick D, Rossi M. Body mass index and mortality in nonsmoking older adults: the Cardiovascular Health Study. *Am J Public Health.* 1998;88:623-629.
16. Lindsted KD, Singh PN. Body mass and 26-year risk of mortality among women who never smoked: findings from the Adventist Mortality Study. *Am J Epidemiol.* 1997;146:1-11.
17. Stevens J, Cai J, Pamuk E, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body mass index and mortality. *N Engl J Med.* 1998; 338:1-7.
18. Cornoni-Huntley JC, Harris TB, Everett DF, et al. An overview of body weight of older persons, including the impact on mortality: the National Health and Nutritional Examination Survey I—Epidemiologic Follow-up Study. *J Clin Epidemiol.* 1991;44:743-753.
19. Allison DB, Gallagher D, Heo M, Pi-Sunyer FX, Heymsfield SB. Body mass index and all cause mortality among people 70 and over: the Longitudinal Study of Aging. *Int J Obes Relat Metab Disord.* 1997;21:424-431.
20. Losonczy KG, Harris TB, Cornoni-Huntley JC, et al. Does weight loss from middle age to old age explain the inverse weight mortality relation in old age? *Am J Epidemiol.* 1995;141:312-321.
21. Carbonin PU, Pahor M, Bernabei R, Sgadari A. Is age an independent risk factor of adverse drug reactions in hospitalized medical patients? *J Am Geriatr Soc.* 1991;39:1093-1099.
22. Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-383.
23. Hodkinson HM. Evaluation of a mental test score for assessment of mental impairment in the elderly. *Age Ageing.* 1972;1:233-238.
24. Katz S, Ford AB, Moskowitz RW, et al. Studies of illness in the aged: the index of ADL—a standardized measure of biological and psychosocial function *JAMA.* 1963;185:94-101.
25. de Groot CPGM, van Staveren WA. Nutrition and the elderly: a European collaborative study in cooperation with the World Health Organization, Special Program for Research on Aging (WHO-SPRA) and the International Union of Nutritional Sciences (IUNS), Committee on Geriatric Nutrition—Manual of Operations, Euronut Report 11: Wageningen, the Netherlands: WHO; 1988.
26. Vir SC, Love AHG. Anthropometric measurements in the elderly. *Gerontology.* 1980;26:1-8.
27. Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. *WHO Tech Rep Ser.* 1995;854:1-452.
28. Waaler HT. Height, weight and mortality: the Norwegian experience. *Acta Med Scand (Suppl).* 1984;679:1-56.
29. Harris T, Cook EF, Garrison R, et al. Body mass index and mortality among nonsmoking older persons: The Framingham Heart Study. *JAMA.* 1988;259:1520-1524.
30. Borkan GA, Hults DE, Gerzof SG, Robbins AH, Silbert CK. Age changes in body composition revealed by computed tomography. *J Gerontol.* 1983;38:673-677.
31. Galanos AN, Pieper CF, Kussin PS, et al. Relationship of body mass index to subsequent mortality among seriously ill hospitalized patients. *Crit Care Med.* 1997; 25:1962-1968.
32. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991-1998. *JAMA.* 1999;282:1519-1522.
33. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA.* 1999;282:1530-1538.