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Interpretation of the "obesity paradox": A 30-year study in patients with cardiovascular disease ☆

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ABSTRACT

Background: Several epidemiological reports indicate that the body mass index (BMI) is inversely related with mortality, in spite of the notion that obesity is a recognized cardio-metabolic risk factor. The aim of the study was to evaluate the independent impact of overweight and obesity on long-term mortality in a large cohort of patients with heart disease (HD).

Methods: The study included 10,446 patients hospitalized in the last three decades for ischemic (60%) or non-ischemic HD and followed-up for 10 years. The relationship between BMI and total or cardiovascular mortality was analyzed in the whole cohort, and in age-stratified categories (≤65 and >65 years). Considering that survival in HD patients has improved after the introduction of revascularization, beta-blockers, ACE inhibitors, and statins, the relationship was re-examined separately in patients hospitalized before and after 1990.

Results: Diabetes, hyperuricemia, hypertension, glycaemia, and triglyceridemia increased across BMI groups. During follow-up (73 ± 59 months) there were 1707 all-cause deaths (47% cardiac). Any relationship between BMI and mortality was lost in the ≤65 age category and in patients hospitalized before 1990, but it persisted in old patients hospitalized after 1990. Most significant independent predictors of mortality in all groups were hyperuricemia, diabetes and impaired ejection fraction.

Conclusions: No independent relationship was found between BMI and mortality in subjects ≤65 years of age. This neutral relationship seems to be partly counteracted by treatment, particularly in old patients. A different effect of obesity onset in old vs. young age cannot be ruled out.

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1. Introduction

Obesity has reached an epidemic prevalence, which continues to rise at an exponential rate [1,2]. Obesity is a confirmed cardiovascular risk factor, increasing the likelihood of developing coronary heart disease (CHD), likely due to an increased cardiac workload and to the prevalence of associated metabolic risk factors. In spite of this recognized causal role, there is epidemiological evidence that the mortality in CHD decreases as the body mass index (BMI) increases [3–6]. Opposite findings were reported by others [7–10] as well as the effect of confounders [11], which may not all be easy to fully correct for, by use of statistical tools [12]. The most important include age [3,4,9,10], healthier status at diagnosis [10,13–15], higher frequency of female gender [5,6,10,15], lesser frequency of smoking habits [9,15], and more extensive or efficacious treatment in the obese population [4,5,15,16], altogether justifying a reduced mortality in the face of a higher prevalence of diabetes, hypertension and other risk factors [3,4,9]. Large cohorts and long follow-up data are needed to select patients with similar disease severity, age, gender, co-morbidities, and treatment.

The current study evaluates the independent impact of overweight and obesity on the long-term, i.e. 10 year mortality in a large cohort of patients with HD who were hospitalized over the last thirty years, and compares the BMI related outcome between the last two and previous decades, the latter representing a historical time in which the best treatments for cardiovascular disease and dyslipidemia were not available or less in use [17]. Moreover the study describes the possible effect of age and treatment on the prognostic model.

2. Methods

2.1. Study population

The study included 10,446 consecutive patients hospitalized at the National Research Council Institute of Clinical Physiology of Pisa between January 1975 and October 2005, due to suspected or documented HD. During hospitalization, 69% underwent cardiac catheterization to exclude coronary artery disease. At discharge, all demographic, clinical and instrumental data were collected in the dedicated cardiovascular database of the Institute (IMAGE). For this study, data on coronary artery disease (defined as >50% stenosis in at least one major coronary branch), echocardiography measurements, risk factors: family history of CHD (one or more first-degree relatives with CHD at any age), arterial hypertension (systolic blood pressure >140 mm Hg and/or diastolic pressure >90 mm Hg out of

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treatment), hypercholesterolemia (fasting plasma total cholesterol >200 mg/dl out of treatment), diabetes mellitus (fasting plasma glucose >126 mg/dl out of treatment), smoking, hyperuricemia (uricemia >7.2 mg/dl at hospitalization), and survival follow-up were considered. Diagnosis of CHD was based on the history of myocardial infarction (MI) and/or of coronary revascularization and/or documentation of myocardial ischemia and/or documentation of at least one coronary vessel disease, as diagnosed during coronary angiography. The definition of obesity was based on the BMI, which is defined as weight in kilograms divided by height in meters squared (kg/m^2). Patients were categorized into four groups of BMI using the nomenclature proposed by the AHA (obesity: >30, overweight: >25 and ≤30, normal weight: >20 and ≤25; underweight: ≤20). Patients with documentation of cancer at enrollment were not included in the study.

The study was approved by the CNR Institutional Review Board. The study complies with the Declaration of Helsinki. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

2.2. Follow-up

For each patient, follow-up began at discharge and was planned for a maximum period of 10 years. Follow-up was closed in December 2010. Follow-up data were obtained in at least one of the following ways: from the patient's hospital record reviews; by contacting the patient's physician; by telephone interview conducted by trained personnel; during periodic scheduled visit at the outpatient clinic. The endpoints included all-cause and cardiac death. Cause of death was based on medical records or death certificates. The diagnosis of cardiac death required documentation of life threatening arrhythmias, cardiac arrest, death attributable to congestive heart failure or MI in the absence of any other precipitating factor. Sudden unexpected death was classified as cardiac death. When sufficient validation was not obtained, to avoid misclassification of the cause of death, overall mortality was considered.

2.3. Statistical analysis

Values are presented as mean ± standard deviation (SD). Continuous variables were compared among the different weight groups, by using Kruskal–Wallis tests. Discrete variables were compared by the continuity adjusted Chi square test with Yates correction, which adjusts the formula for Pearson's chi-squared test by subtracting 0.5 from the difference between each observed value and its expected value in a 2×2 contingency table. Bonferroni adjustment was employed for multiple comparisons. All tests were two-sided. A P-value of <0.05 was considered as statistically significant. The predictive value of BMI on survival was evaluated with the Cox proportional multivariable hazards regression model. Variables had initially been assessed as continuous variables. For ease of communication and for clinical use we dichotomized the variables when estimating their association with mortality. Cut-off values were based on the standard normal ranges given by the clinical reports: for left ventricular ejection fraction (EF) 50% was the cut-off value. Age was included as a continuous variable. To avoid bias due to the non-linear relationship linking BMI and mortality, we examined mortality in the predefined BMI categories, by using the "normal weight" category as the reference one. To eliminate possible confounding effects of age (residual bias) in the determination of survival [12,18], we evaluated different age groups, as based on the Italian and European age limit defining the elderly population (≤65 and >65 yrs), and we analyzed the groups separately in a Cox proportional hazards survival model. In addition, since we expected that epoch-related improvements in treatment (particularly a greater use of beta-blockade, revascularization, ACE inhibition, and statins) might affect the prognostic model, we compared the multivariable predictive model best suited for patients enrolled before 1990 with the one obtained in the group hospitalized after 1990. Due to the small number of old patients in the <1990 epoch (149/1508 patients, 10%), the analysis in this subgroup was not performed.

Interaction analysis was used to establish if the impact of BMI was different between the selected subgroups. Moreover, clinical variables with a well-recognized and significant prognostic impact, namely CHD history, EF, and other risk factors, were considered as covariates. More specifically, the analysis was performed while adjusting for diabetes mellitus, family history of CHD, arterial hypertension, hypercholesterolemia, smoking, sex, age, personal history of CHD, and EF. Subsequently, significant predictors of mortality in the multi-variable model were identified. Results were expressed as hazard ratio (HR) of all-cause death and cardiac death and 95% confidence intervals (CI). Kaplan–Meier survival curves were also constructed and BMI categories were compared with the log-rank test (Mantel–Cox). SPSS (SPSS Inc., Chicago, IL, USA) version 13 was used in all analyses.

3. Results

3.1. Patients

Baseline characteristics of the 10,446 patients enrolled are reported in Table 1. Mean age was similar in the four BMI categories. Males were prevalent, but females were overrepresented in the underweight category (349 pts, 62% females, P<0.001) and were older (in the whole population 65 ± 13 and 62 ± 12 years in females and males respectively, p<0.001). There was a significant increase in coronary risk factors, particular diabetes and hypertension, across the four BMI groups (Table 1). Overweight and obesity were more prevalent in the ≤65 than the >65 year old group (Table 2). As expected, the frequency of risk factors, except for smoking and family history, increased with age (Table 2).

Multiple cardiologic treatment associations were prevalent in overweight/obese patients compared to normal/underweight individuals (Table 3), and in older patients compared to younger ones, with the exception of revascularization and lipid-lowering drugs that were more commonly used by younger patients.

Table 1
Patient characteristics according to body mass index.

	Patients	BMI				P
	10,446	≤20	>20 ≤25	>25 ≤30	>30	
	group	(1)	(2)	(3)	(4)	
	no. (%)	349 (3)	3141 (30)	4802 (46)	2154 (21)	
BMI, kg/m2, mean ± SD	10446	18 ± 1	23 ± 1	27 ± 1	33 ± 3	
Age, yrs, mean ± SD	63 ± 13	64 ± 18	63 ± 14	63 ± 12	62 ± 12	NS
Male, no. (%)	7180 (69)	133 (38)	2130 (68)	3573 (74)	1344 (62)	**
CHD history, no. (%)	6248 (60)	154 (44)	1889 (60)	3045 (63)	1160 (54)	**
Coronary angiography, no. (%)	7254 (69)	156 (45)	2164 (69)	3512 (73)	1422 (66)	**, NS 1 vs. 2
≥1 vessel disease, no. (%)	5193 (71)	103 (66)	1544 (71)	2192 (62)	954 (67)	*
MI, no. (%)	3854 (37)	114 (33)	1185 (38)	1863 (39)	692 (32)	**, NS 1 and 3 vs. 4
EF, no. (%), mean ± (SD)	8459 (81)	51 (14)	51 (14)	52 (12)	52 (11)	**, NS 1 vs. 2
≤45%, no. (%)	2180 (26)	93 (30)	729 (29)	932 (25)	426 (23)	**, NS 1 vs. 2
Hypertension, no. (%)	5188 (50)	127 (36)	1256 (40)	2398 (50)	1407 (65)	**
Hyperuricemia, no. (%)	1248 (12)	32 (9)	311 (10)	598 (13)	307 (14)	*, NS 1 vs. 2
Diabetes, no. (%)	1894 (18)	39 (11)	436 (14)	840 (17)	579 (27)	**
Smokers, no. (%)	4743 (45)	120 (34)	1386 (44)	2284 (48)	953 (44)	*, NS 2 vs. 4
Family history, no. (%)	4384 (42)	111 (32)	1272 (40)	2072 (43)	929 (43)	*, NS 3 vs. 4
SAP, no. (%) mean (SD) (mm Hg)	10391 (99)	127 (23)	131 (22)	134 (21)	138 (22)	**
Cholesterol, no. (%), mean (SD) mg/dl	8509 (81)	181 (46)	193 (49)	198 (48)	198 (50)	*, NS 2 vs. 3
HDL, no. (%),mean (SD), mg/dl	5757 (55)	49 (19)	45 (14)	41 (13)	41 (13)	**, NS 3 vs. 4
Triglycerides, no. (%),mean (SD), mg/dl	8123 (78)	98 (59)	120 (85)	143 (87)	153 (98)	**
Fasting glycemia, no. (%),mean (SD), mg%	7990 (76)	102 (45)	101 (37)	105 (37)	114 (39)	**, NS 2 vs. 3
Uric acid, no. (%), mean (SD), mg/dl	4435 (42)	5.1 (1.8)	5.7 (1.8)	6.1 (1.7)	6.3 (1.5)	**

BMI = body mass index. % = percentage into the relative group. CHD = coronary heart disease. MI = myocardial infarction. EF = ejection fraction. SAP = systolic arterial pressure. HDL = high density lipoprotein.

* P≤0.05 for comparison among all groups;

** P≤0.001 for comparison among all groups.

Table 2
Patient characteristics according to age stratification.

	Patients	Age		P
	10,446	≤65	>65	
	no. (%)	5690 (54)	4756 (46)	
BMI >25 ≤30	4802 (46)	2662 (55)	2140 (45)	0.06
BMI >30	2154 (21)	1214 (56)	940 (44)	0.04
Male, no. (%)	7180 (69)	4206 (74)	2974 (42)	<0.001
CHD history, no. (%)	6248 (60)	3402 (54)	2846 (46)	0.958
LVMI,no (%), mean (SD)	6684 (64)	113 (35)	122 (37)	<0.001
EF, no. (%), mean (SD)	8459 (81)	52 (12)	50 (12)	<0.001
≤45%, no. (%)	2180 (26)	960 (44)	1220 (56)	<0.001
Hypertension, no. (%)	5188 (50)	2307 (44)	2881 (55)	<0.001
Hyperuricemia, no. (%)	1248 (12)	602 (48)	646 (52)	<0.001
Diabetes, no. (%)	1894 (18)	817 (43)	1077 (57)	<0.001
Smokers, no. (%)	4743 (45)	3165 (67)	1578 (33)	<0.001
Family history, no. (%)	4384 (42)	2677 (61)	1707 (39)	<0.001
SAP, no. (%) mean(SD) (mm Hg)	10392 (99)	130 (20)	139 (23)	<0.001
Cholesterol, no. (%), mean (SD) mg/dl	8509 (81)	202 (50)	188 (45)	<0.001
HDL, no. (%),mean (SD), mg/dl	5757 (55)	42 (12)	43 (14)	<0.001
Triglycerides, no. (%), mean (SD), mg/dl	8123 (78)	150 (102)	119 (68)	<0.001
Fasting glycemia, no. (%), mean(SD), mg/dl	7990 (76)	102 (39)	110 (39)	<0.001

Abbreviations as in Table 1.

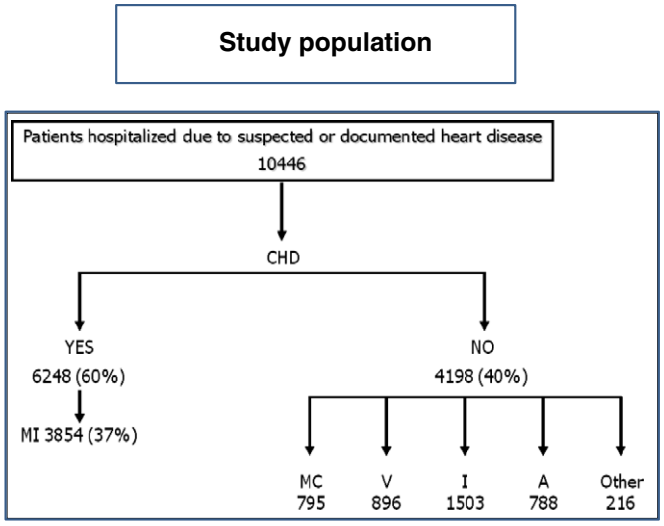

Fig. 1. Flowchart of population. CHD: coronary heart disease. MC: cardiomyopathy. V: valvular disease. I: arterial hypertension. A: arrhythmias. Other: other cardiac disease as pericarditis, miocarditis.

The final diagnosis is reported in Fig. 1. CHD was diagnosed in 60% of all patients, and in 54% of obese patients and showed the same prevalence in the two age groups.

3.2. Prognosis

During follow-up (73 ± 59 months), there were 1707 all-cause deaths, 808 cardiac deaths (17% sudden death, 27% due to acute MI, 51% to congestive heart failure and 5% to cardiac surgery), and 899 non-cardiac deaths were registered (276 cancer, 360 multiorgan failure, 105 peripheral vascular disease, 35 renal or liver failure, 27 traumatic, 96 surgical deaths). Seventeen patients were lost to follow-up. In the entire population, the most important predictors of total death by univariate analysis were age, sex, EF, CHD diagnosis, hyperuricemia, hypertension, diabetes, and smoking. In a multivariable analysis, independent and additive prognostic values persisted for age, diabetes, hypertension, hyperuricemia, EF and CHD diagnosis. The same predictors were found for cardiac death. Total mortality rate was significantly related to underweight, and in contrast both total and cardiac death were significantly inversely related to an increased BMI.

In the two hospitalization epochs, namely ≤1990> hazard ratios for death were evaluated in patients ≤65 years old while controlling for the impact of all the covariates described above. The analysis showed a higher mortality before 1990 compared to more recent years (total mortality HR 1.31, CI 1.03–1.68, P = 0.029; cardiac death HR 1.56, CI 1.12–2.20, P = 0.01), a positive, though not significant correlation between BMI and mortality in the first epoch and a tendency toward an inverse correlation in the second epoch (Table 4). A significant BMI protective effect appeared both for total and cardiac mortality in the older patients (>65 years) hospitalized in recent years (>1990) (Table 4).

Kaplan Meier survival curves confirmed the Cox findings both for age and for stratification period (Fig. 2).

4. Discussion

The main finding of the study was that the subdivision of subjects according to age categories and treatment epochs was identified as a key strategy to examine and to prove the inconsistency of the so defined obesity paradox in patients requiring hospitalization for HD of various origins (see Fig. 1).

The stratification of the population in age categories documented that overweight and obesity were not protective in the ≤65 age group (Fig. 2). Likewise, the relationship between BMI and cardiovascular mortality was neutral in the group hospitalized ≤1990, whereas the BMI showed a non-significant tendency towards a protective effect in the >1990 group. Only in the older patients, especially if hospitalized in the >1990 epoch the BMI was protective (Table 4) (Fig. 2).

Table 3
Medical therapy according to BMI, years of hospitalization and age.

Treatment %	BMI ≤25>		P	Time ≤1990>		P	Age ≤65>		P
Patients no.	*6956*	*2154*		*1508*	*8938*		*5690*	*4756*	
mean ± SD years							*54 ± 9*	*74 ± 6*	
Ca channel blockers	25	28	<0.001	69	20	<0.001	34	19	<0.001
Betablockers	32	35	<0.001	7	38	<0.001	29	39	<0.001
Nitrates	45	49	0.002	57	46	<0.001	45	51	<0.001
Antiplatelets	59	62	0.004	46	63	<0.001	58	63	<0.001
Anticoagulants				0	19	<0.001	11	24	<0.001
ACE inhibitors	26	28	0.017	0	31	<0.001	21	34	<0.001
Antilipid treatment	21	28	<0.001	1	47	<0.001	34	31	0.004
Statins				0	45	<0.001	32	29	<0.001
Antiarrhythmics	3	4	0.113	3	4	0.045	3	6	<0.001
Diuretics	32	31	0.281	24	32	<0.001	22	41	<0.001
Antidiabetics	10	15	<0.001	2	14	<0.001	11	17	<0.001
Revascularization procedure	35	39	<0.001	52	63	<0.001	39	36	0.001

BMI = body mass index. ACE = angiotensin converting enzyme.
P is <0.001 for all italicized data.

Table 4
Multivariable Cox proportional regression analyses.

	All cause death		Cardiac death	
Patients	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
≤65 yrs≤1990 (N.1359)				
Age	1.05 (1.03–1.52)	<0.001	1.08 (0.60–1.94)	<0.001
EF	0.95 (0.94–0.96)	<0.001	0.93 (0.91–0.94)	<0.001
BMI				
≤20	1.50 (0.35–6.33)	0.58	1.83 (0.23–14.23)	0.56
>25≤30	1.08 (0.72–1.62)	0.70	1.04 (0.60–1.79)	0.89
>30	1.53 (0.85–2.72)	0.15	1.83 (0.85–3.96)	0.12
≤65 yrs>1990 (N.4331)				
Diabetes mellitus	1.69 (1.28–2.24)	<0.001	1.84(1.25–2.69)	0.002
Hyperuricemia	1.56 (1.14–2.12)	0.005	1.63(1.08–2.46)	0.019
Age	1.03 (1.00–1.04)	0.002		
CHD history			1.79(1.21–2.64)	0.004
EF	0.95 (0.94–0.96)	<0.001	0.93(0.92–0.94)	<0.001
BMI				
≤20	1.60 (0.89–2.88)	0.11	1.24 (0.49–3.16)	0.65
>25≤30	0.80 (0.60–1.07)	0.13	0.85 (0.56–1.28)	0.43
>30	0.79 (0.56–1.10)	0.16	0.85 (0.53–1.36)	0.49
>65 yrs>1990 (N.4607)				
Diabetes mellitus	1.32 (1.13–1.54)	<0.001	1.26 (1.00–1.58)	0.047
Hyperuricemia	1.62 (1.38–1.90)	<0.001	1.66 (1.32–2.09)	<0.001
CHD history	1.32 (1.14–1.53)	<0.001	1.45 (1.16–1.80)	0.001
Age	1.07 (1.06–1.08)	<0.001	1.06(1.04–1.08)	<0.001
EF	0.97 (0.96–0.97)	<0.001	0.95 (0.94–0.96)	<0.001
BMI				
≤20	1.27 (0.97–1.67)	0.09	1.13 (0.75–1.69)	0.57
>25≤30	0.81 (0.69–0.95)	0.008	0.76 (0.61–0.96)	0.02
>30	0.81 (0.66–0.99)	0.040	0.74 (0.54–1.00)	0.05
>1990 (N.8938)				
Hyperuricemia	1.61 (1.39–1.86)	<0.001	1.65 (1.35–2.02)	<0.001
Diabetes mellitus	1.38 (1.21–1.58)	<0.001	1.36 (1.12–1.66)	0.002
CHD	1.28 (1.13–1.45)	<0.001	1.49 (1.23–1.80)	<0.001
Age	1.06 (1.05–1.07)	<0.001	1.05 (1.03–1.06)	<0.001
EF	0.96 (0.96–0.97)	<0.001	0.94 (0.94–0.95)	<0.001
BMI				
≤20	1.35 (1.05–1.73)	0.017	1.16 (0.90–1.69)	0.418
>25≤30	0.80 (0.70–0.92)	0.002	0.79 (0.65–0.96)	0.021
>30	0.80 (0.67–0.95)	0.010	0.77 (0.60–0.99)	0.042

Only the significant covariates were reported in the table.
CI = confidence interval. Other abbreviations as in Table 1.

Our findings are in agreement with, and extend to the long follow-up of chronic patients the recent observation of Wu in patients with acute MI documenting that matching for age is sufficient to debut the paradoxical effect of obesity on the 16-month post-event survival [18]. The work by Wu et al. [18] did not explore the possibility that BMI may intersect its confounders in a different manner in young patients with earlier onset of HD as compared with old patients, who are generally characterized by a later age of HD onset, and in patients exposed to a different intensiveness of treatment.

We observed that the relative proportion of overweight/obese subjects was not constant with advancing age, as reported in the literature [4–9,16]. More specifically, our younger individuals showed a greater prevalence of overweight/obesity, corresponding to almost twice that in the general national population of comparable age [2]. This led us to stratify the population according to age as well as according to treatment, with the hypothesis that the protective influence of obesity could be secondary to a confounding effect of age and therapy in these patients. We compared the outcome in the subgroups of patients hospitalized before and after 1990, because a dramatic change in treatment occurred between these two epochs (especially referring to a greater use of beta-blockade, ACE inhibition, and statins). The relationship of BMI and cardiovascular mortality was neutral in the patients hospitalized ≤1990, i.e. at a time in which the confounding effect of therapy was minimal. The evidence that the BMI was protective in older patients hospitalized after1990 (Table 4) supports the hypothesis that a more extensive cardiovascular and metabolic treatment contributes to explain the significant paradox in this age category. It is important to emphasize that the degree of overweight was tightly coupled with the number of medications (Table 2), and that multiple therapy associations were more common in older patients, who presented secondary diseases, such as diabetes and/or hypertension. On the other hand, we cannot refuse the hypothesis of different effects of late versus early onset obesity.

These observations reconcile the more recent literature on the obesity paradox [3–6], with the longitudinal studies published before 1990, which documented a detrimental influence of a growing BMI on mortality [7,8]. Our study, including both periods of observation, supports the hypothesis that the epochal change in treatment options in more recent years provokes the above mentioned epidemiological bias.

The strength of the current study was in the duration of the follow-up and broad size of the cohort, allowing stratification by age and treatment and evaluation of a number of confounders. Patients were fairly well characterized in terms of predictable confounding factors, since information on history, co-morbidities, cardiovascular disease and coronary involvement, therapy, including revascularization, and concomitant medications was available in all subjects. Hyperuricemia appeared as an important predictor of mortality, and our results are in agreement with the literature data [19], suggesting that the ischemic heart may cause hypoxia, which trigger xanthine oxidase and oxidative stress production leading to hyperuricemia.

On the other hand our study had some limitations. First, BMI was determined at the time of first hospitalization [16], and therefore we cannot exclude that patients may have shifted between BMI categories during the 10-year follow-up period. However, in the subset (n = 826) of patients who were hospitalized for a second time after 10 ± 4 years, the BMI did not significantly change on average (p = 0.58, data not shown), and only a minor group of patients (15%) experienced a shift towards a lower BMI category (from overweight to normal or obese to overweight). Second, we cannot exclude the effect of other changes in lifestyle, such as smoking cessation on mortality. Third, body weight and BMI are not always reliable indices of body composition [14,16], and the balance between fat and lean mass, i.e. adiposity and sarcopenia, may provide a more direct and physiological readout of the obesity paradox, especially in the elderly. Also, central adiposity has been related with the cardiometabolic risk more closely than the BMI [20,21], but unfortunately this evidence has become stronger in recent years, whereas the vast majority of our data collection was done more than ten years ago, thereby allowing to explore the 10-year mortality. Previous reports had indicated that abdominal adiposity does not differ from BMI in the association with mortality in cardiac patients [22,23], though a most recent publication supports the measurement of waist circumference as a better indicator of mortality, as compared with the BMI [24].

In conclusion, no independent relationship was found between BMI and mortality in subjects of ≤65 years of age. This neutral relationship seems to be partly counteracted by treatment, particularly in old patients. A different effect of obesity onset in old vs. young age cannot be ruled out.

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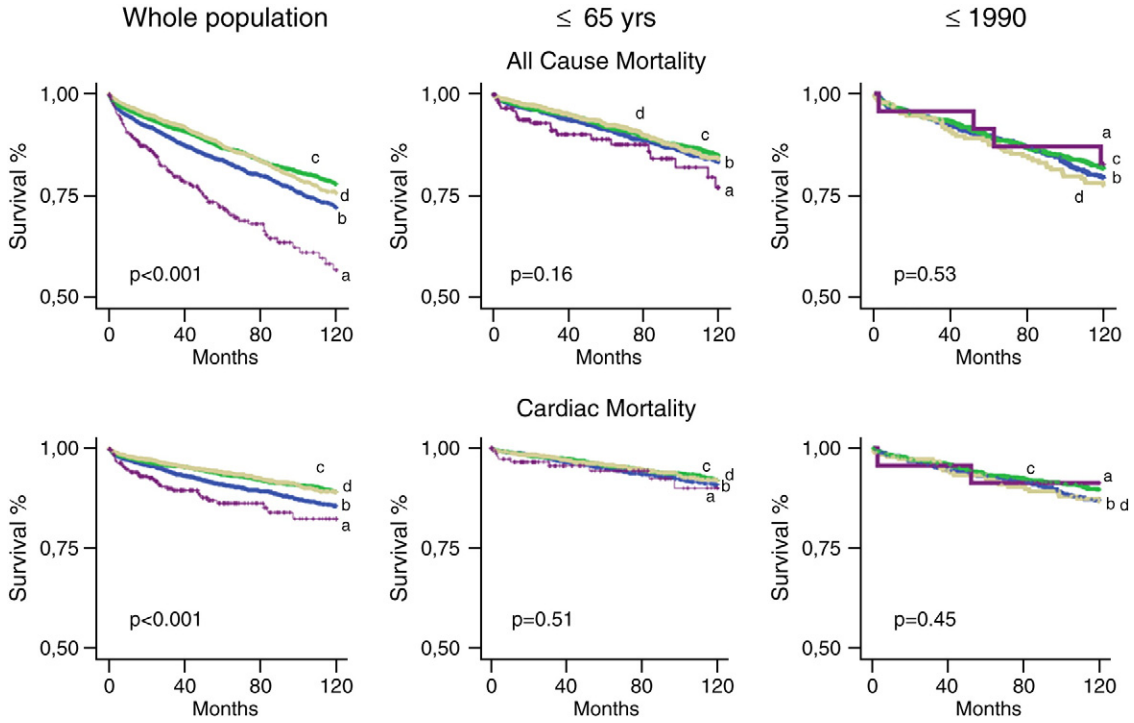

Fig. 2. Mortality in all population and in age and hospitalization period subgroups. In the upper panel Kaplan Meier survival plots are reported for all cause death. Curves show the obesity paradox as it was found in the whole population (left) and the absence of the phenomenon in younger patients (in the center) and in the subgroup of patients hospitalized before 1990 (right). In the lower panel similar results are shown for cardiac death. Log rank indicates comparison between obesity and normal categories. BMI = body mass index. BMI categories: a = ≤20; b > 20 ≤25; c > 25 ≤30; d > 30.

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