Table 2
Differences in plasma serum concentrations between HF and control subjects.

	HF	Controls	Significance
Adiponectin	23.5 ± 15.9	16.7 ± 8.2	<0.05
NT-proBNP	1522.2 ± 1827.9	168.2 ± 398.5	<0.001
Leptin	12.4 ± 15.4	10.5 ± 11.4	NS
Insulin	37.0 ± 39.8	26.1 ± 31.8	NS
Glucose	120.2 ± 63	100.4 ± 23.5	NS

inverse relationship between adiponectin and body composition in HF patients require further evaluation. Furthermore, while previous studies have attributed this phenomenon to disease-related atrophy and cachexia, we show that even in patients with average physique, adiponectin levels remain elevated in patients with diagnosed HF. Future studies should seek correlations between prognosis and body composition, in order to determine if adiponectin could potentially be used as a prognosticator among this patient population.

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Comparing the value of BNP in predicting mortality among community-dwelling elderly with and without overweight/obesity: the Bambuí (Brazil) Cohort Study of Aging ☆

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The role of natriuretic peptides (NPs) as independent predictors of cardiovascular events, hospitalization and death [1,2] in older adults has been already demonstrated and is related to their hemodynamic actions (natriuresis, diuresis, vasodilatation and inhibition of the renin–angiotensin–aldosterone system) [3]. Besides these, NPs have metabolic and lipolytic actions [4]. Interestingly, lower plasmatic NPs levels are found in overweight and obese subjects when compared to lean ones in several clinical settings [4], which raise doubts concerning the usefulness of NPs as prognostic biomarkers in overweight/obese subjects. We aimed to investigate whether the ability of B-type NP (BNP) to predict 11-year mortality risk in community-dwelling elderly of the Bambuí (Brazil) Cohort Study of Aging (BHAS) differed in relation to overweight/obesity and abdominal obesity status.

The BHAS, a cohort study of elderly residents in the Bambuí City (Minas Gerais, southeast of Brazil) is described in detail elsewhere [5], and was approved by the ethics board of the Fundação Oswaldo Cruz, Belo Horizonte, Brazil. An informed consent form was obtained from all participants. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing.

The outcome of the present analysis was overall death from baseline (1997) to 2007. Anthropometric measures (AM) assessment, B-type natriuretic (BNP), *Trypanossoma cruzi* tests and definitions of other measurements performed were detailed previously [5]. We classified individuals in subgroups with (BMI ≥ 25 kg/m^2) or without (BMI < 25 kg/m^2) overweight/obesity and with (WC ≥ 88 cm for women and ≥102 cm for men) or without abdominal obesity (WC < 88 cm for women and <102 cm for men).

To deal with missing values, we performed multiple imputation [6]. This procedure generated five complete datasets, which were used to estimate crude and adjusted hazard ratios (HR) for death by Cox regression models. BNP was subsequently added to models adjusted for BMI (continuous and quadratic term) or WC (continuous), age (continuous), gender, Chagas disease (no, yes), current smoking (no, yes), diabetes (no, yes), total cholesterol (continuous), systolic blood pressure (continuous), major ECG abnormalities (no, yes), log-

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1
Baseline characteristics according to overweight/obesity and abdominal obesity groups.

Characteristics	Overweight/obesity*		p value†	Abdominal obesity*		p value†
	No (747; 51.5%)	Yes (703; 48.5%)		No (815; 56.1%)	Yes (639; 44.0%)	
Age, mean (SD)	70 (8)	68 (7)	<0.001	69 (7)	69 (7)	0.181
Female sex, n (%)	395 (52.9)	484 (68.8)	<0.001	314 (38.5)	566 (88.6)	<0.001
Chagas disease, n (%)	320 (43.8)	216 (31.3)	<0.001	309 (38.9)	229 (36.4)	<0.001
Diabetes, n (%)	69 (9.5)	138 (20.0)	<0.001	79 (10.0)	127 (20.2)	<0.001
Systolic blood pressure, mean (SD)	136 (24)	139 (21)	0.003	136 (23)	139 (22)	0.025
Cholesterol, mean (SD)	229 (49)	238 (49)	0.003	227 (48)	242 (49)	<0.001
Creatinine, median (IQR)	0.87 (0.76–1.00)	0.84 (0.74–0.98)	0.019	0.90 (0.78–1.04)	0.80 (0.72–0.92)	<0.001
Major ECG abnormalities, n (%)	328 (44.9)	246 (35.7)	<0.001	332 (41.8)	245 (39.0)	0.275
Smoking, n (%)	183 (25.1)	68 (9.9)	<0.001	203 (25.6)	50 (7.9)	0.332
Physically active‡, n (%)	140 (16.7)	190 (24.8)	<0.001	169 (20.7)	143 (22.4)	0.440
Household income§, n (%)						
Low/Intermediate	697 (93.9)	623 (89.4)	<0.001	743 (92.2)	580 (91.1)	
High	45 (6.1)	74 (10.6)		63 (7.8)	57 (8.9)	
Education‖, n (%)						
Low/Intermediate	791 (92.5)	600 (85.3)	<0.001	735 (95.3)	558 (87.3)	0.041
High	56 (7.5)	103 (14.7)		79 (9.7)	81 (12.7)	

*Overweight/obesity: body mass index ≥25 kg/m^2; abdominal obesity: waist circumference ≥88 cm for women and 102 cm for men† P value: Student's t test, Pearson's chi square test and the Mann–Whitney test for differences between means, frequencies and medians, respectively between the groups with and without obesity and abdominal obesity ‡Leisure physical activity (walking or any other physical exercise) for at least 20–30 min, ≥3–5 times/week § Monthly household income in minimum wages (lower category 1–4, intermediate category 4–10, higher category ≥10) ‖ Education: lower category-never studied, intermediate category - <4 school years, higher category - ≥4 school years) |.

transformed serum creatinine level (continuous), physical activity (no, yes), education (never studied (low), <4 school years (intermediate), ≥4 school years (high)), monthly household income (1–4 (low), 4–10 (intermediate), ≥10 minimum wage (high)). Additionally, we added product terms of interaction between BNP and BMI/WC to verify the effect modification of BMI and WC on the association between BNP and death.

The agreement between observed and predicted events (calibration) at the end of the follow-up (t = 11 years) was assessed for each model by a modified Hosmer–Lemeshow chi-square statistic with nine df, in which the observed incidence of the outcome was compared to the probabilities of events predicted by Cox models across ten groups yielded by the deciles of the predicted probabilities [7]. The incremental improvement of BNP to the ability of models in predicting death was assessed by means of discrimination, net reclassification improvement (NRI) and integrated discriminative improvement (IDI) for the whole population and for the subgroups with and without obesity or abdominal obesity. Discrimination (i.e., ability of the models to separate between individuals who had or did not have the event) was assessed by Harrell's C-statistics at t = 11 years, and compared by De Long et al. test for the models without and with BNP [8]. The impact of the addition of BNP to model the correct movement of cases across categories of risk for events and non-events was evaluated by NRI [9]. Categories of risk were based on the tertiles of the probabilities estimated by the model without BNP (<0.22, 0.22 to 0.43, ≥0.43). Differences in integrated sensitivity and integrated one minus specificity between the new and the model without BNP were tested by IDI [9].

Of the 1606 participants enrolled at baseline, 1450 (90.3%) had BMI, and 1454 (90.5%) had WC measurements, respectively. Mean follow-up time was 8.8 years, which led to 12, 971 person-years of follow-up. Deaths occurred among 523 participants along the follow-up time. Median BMI was 21.7 kg/m^2 (IQR 19.8–23.4) and 28.1 kg/m^2 (IQR 26.5–30.3) in the subgroups without and with overweight/obesity, respectively. BNP levels were higher in the subgroup without (90 pg/mL, IQR 50–163) than with (74 pg/mL, IQR 40–137; p < 0.001) overweight/obesity. Other characteristics of the participants at baseline, according to overweight/obesity and abdominal obesity are depicted in Table 1. BNP predicted mortality in models with BMI (HR 1.24; 95% CI 1.10–1.39) and WC (HR 1.22; 95% CI 1.09–1.38). Neither BMI nor WC modified the effect of BNP on mortality (p for interaction = 0.53 and 0.88, respectively). All models were well-calibrated (p > 0.05) and the addition of BNP yielded either a non significant or a modest improvement to the models with traditional risk factors (Table 2).

Keeping with previous studies, we found an independent prognostic value of BNP for death in older adults [1,2]. Regarding the findings of the lack of influence of obesity on the association between BNP and death, results in agreement [10,11] and contrary [12] to ours have been previously reported in diverse clinical settings.

The investigation of the incremental value of BNP as a prognostic marker, and not only of its statistical significance as a determinant of death adds contribution to the investigation of a critical issue to clinical application of BNP as a prognostic biomarker in community-dwelling elderly. The use of both WC and BMI as markers of obesity decreases the probability that the results are related to misclassification of obesity by

Table 2
Changes in discrimination (C-statistics), net reclassification improvement (NRI) and integrated discrimination improvement (IDI) after addition of BNP to the models.

Model	Model without BNP*	Model with BNP†
All subjects-model with BMI		
C-statistic	0.80 (0.76–0.81)	0.80 (0.79–0.82)
p value‡		0.25
NRI §	————	0.01
p value		0.58
IDI ‖	————	0.01
p value		<0.001
Participants with overweight/obesity-models with BMI		
C-statistic	0.78 (0.76–0.79)	0.78 (0.76–0.80)
p value‡		0.57
NRI §	————	0.07
p value		0.02
IDI ‖	————	0.02
p value		<0.001
Participants without overweight/obesity-models with BMI		
C-statistics	0.81 (0.77–0.81)	0.82 (0.80–0.84)
p value ‡		0.10
NRI §	————	0.01
p value		0.51
IDI ‖	————	0.01
p value		<0.001
All subjects-model with WC		
C-statistics	0.80 (0.77–0.81)	0.80 (0.79–0.81)
p value‡		0.25
NRI §	————	0.12
p value		<0.001
IDI ‖	————	0.05
p value		<0.001
Participants with abdominal obesity-model with WC		
C-statistics	0.77 (0.73–0.80)	0.77 (0.74–0.78)
p value‡		0.93
NRI §	————	0.02
p value		0.42
IDI ‖	————	0.01
p value		<0.001
Participants without abdominal obesity-model with WC		
C-statistics	0.80 (0.77–0.83)	0.82 (0.80–0.84)
p value ‡		0.02
NRI §	————	0.02
p value		0.39
IDI ‖	————	0.01
p value		<0.001

* Model without BNP: BMI (continuous and quadratic term) or WC (continuous), age (continuous), gender, Chagas disease (no, yes), current smoking (no, yes), diabetes (no, yes), total cholesterol (continuous), major ECG abnormalities (no, yes), log-transformed serum creatinine level (continuous), physical activity (no, yes), education (never studied (low), <4 school years (intermediate), ≥4 school years (high)), monthly household income (1–4 (low), 4–10 (intermediate), ≥10 minimum wage (high)).
† Model with BNP: Model without BNP plus log-BNP (continuous).
‡ p value refers to comparison of c-statistics between the models without and with BNP by De Long et al. method.
§ NRI quantifies the correct movement across categories of risk yielded by the addition of BNP to the model for events and non-events. The categories of risk were established according to the quartiles of the predicted probabilities of the model without BNP with BMI (<0.22, 0.22 to 0.43, ≥0.43).
‖ IDI refers to differences in integrated sensitivity and one minus specificity between the models with and without BNP.

BMI in the elderly. However, we might have lacked power to find an effect modification of BMI and WC on the association between BNP and death, and to extend our conclusions to the subgroup of subjects with BMI ≥ 40 kg/m^2 (n = 12; 1.1%).

In conclusion, BNP was associated with increased mortality among elderly with and without overall or abdominal obesity. Despite being an independent predictor of death, the rational use of BNP in the elderly must take into account that the biomarker led only to a modest incremental improvement in the prediction of long-term death compared to traditional cardiovascular, clinical and socioeconomic risk factors regardless of overall or abdominal obesity status.

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