The Change in Body Weight During Hospitalization Predicts Mortality in Patients With Acute Decompensated Heart Failure

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Abstract

Background: In our experience, the change in body weight (BW) during hospitalization varies greatly in patients with acute decompensated heart failure (HF). Since the clinical significance of a change in BW is not clear, we investigated whether a change in BW could predict mortality.

Methods: We retrospectively enrolled 130 patients (72 males; aged 68 ± 10 years) who were hospitalized due to acute decompensated HF and followed for 2 years after discharge. The change in the BW index during hospitalization (ΔBWI) was calculated as (BW at hospital admission minus BW at hospital discharge)/body surface area at hospital discharge.

Results: The patients were divided into quartiles according to ΔBWI, and the 2-year mortality rates in the quartiles with the lowest, second, third and highest ΔBWI were 18.8%, 12.1%, 3.1% and 9.1%, respectively. In a multivariate Cox proportional hazards analysis after adjusting for variables with a P value less than 0.05, ΔBWI was independently associated with 2-year mortality ($P = 0.0002$), and the quartile with the lowest ΔBWI had a higher relative risk (RR) for 2-year mortality than the quartile with the highest ΔBWI (RR: 7.46, 95% confidence interval: 1.03 - 53.99, $P = 0.04$).

Conclusion: In conclusion, ΔBWI was significantly associated with 2-year mortality after discharge, which indicates that ΔBWI might be a simple predictor of prognosis in acute decompensated HF.

Keywords: Predictor of prognosis; Change in body weight index; Acute decompensated heart failure

Introduction

Heart failure (HF) is a clinical syndrome that occurs in patients who, because of an inherited or acquired abnormality of cardiac structure and/or function, develop a constellation of clinical symptoms (dyspnea and fatigue) and signs (edema and rales). Patients with HF are repeatedly hospitalized and experience a poor quality of life and a shortened life expectancy. Although long-term mortality rates for patients with HF are gradually improving through the application of various therapies [1-7], they are still unacceptably high [8]. In recent years, there has been an increase in the number of biomarkers in HF, such as troponin [9], estimated glomerular filtration rate [10], cystatin C [11], serum uric acid [12], and anemia [13], in addition to B-type natriuretic peptide (BNP) and amino acid N-terminal pro-BNP [14, 15]. The ultimate clinical role of these novel biomarkers is not clear. Since patients with HF often show fluid retention with leg edema regardless of the etiology of HF, an important goal in the acute phase of HF is fluid control by diuretics. When we treated patients with HF in clinical practice, we noted that the change in body weight (BW) during hospitalization varied greatly in patients with acute decompensated HF. We considered that the change in BW during hospitalization may be a simple predictor of the prognosis in HF. There have been no previous reports on the association between changes in BW due to treatment and the prognosis of HF. The patients with greater changes in BW may have a wide range of therapeutic responses, compared to those with smaller changes who exhibit a narrow range of responses. Therefore, we hypothesized that patients with greater changes in BW might have a better prognosis than those with smaller changes.

In this study, we investigated the associations between the change in BW during hospitalization and the prognosis in patients with acute decompensated HF.

Methods

Study population

We retrospectively investigated the association between the change in BW during hospitalization and the prognosis of HF.

Table 1. Patient Characteristics in the Survival and Death Groups

	Survival group (n = 116)	Death group (n = 14)	Survival vs. death P value
Age, years	67 ± 10	81 ± 5	0.0007
Male, n (%)	72 (62)	7 (50)	0.38
DM, n (%)	26 (22)	8 (43)	0.09
HTN, n (%)	69 (59)	7 (50)	0.53
SBP, mm Hg	127 ± 19	119 ± 18	0.03
NYHA functional class			
II, n (%)	23 (19)	2 (14)	0.61
III, n (%)	25 (22)	6 (42)	0.08
IV, n (%)	65 (56)	6 (42)	0.34
The cause of HF			
IHD, n (%)	34 (29)	3 (21)	0.53
HTCM, n (%)	11 (9)	1 (7)	0.77
Valvular disease, n (%)	22 (18)	3 (21)	0.82
DCM, n (%)	21 (18)	5 (35)	0.11
Arrythmia, n (%)	13 (11)	1 (7)	0.64
Unknown, n (%)	15 (12)	1 (7)	0.53
ICD, n (%)	16 (13)	6 (42)	0.006
LVEF, %	43 ± 18	39 ± 16	0.38
Medications			
Diuretics, n (%)	92 (79)	13 (92)	0.22
ACEI/ARB, n (%)	87 (75)	8 (57)	0.15
Digitalis, n (%)	11 (9)	2 (14)	0.57
Oral anticoagulant, n (%)	56 (48)	7 (50)	0.90
Nitrates, n (%)	11 (9)	2 (14)	0.57
Spironolactone, n (%)	68 (58)	9 (64)	0.68
β-blockers, n (%)	70 (60)	8 (57)	0.81
Antiplatelets, n (%)	61 (52)	5 (35)	0.23
Laboratory test			
BNP, pg/mL	370.0 ± 274.2	842.5 ± 292.5	0.006
Na, mEq/L	141.0 ± 2.0	137.0 ± 2.0	0.001
BUN, mg/dL	18.0 ± 4.0	37.5 ± 12.5	0.00003
Hb, g/dL	13.5 ± 2.5	11.6 ± 1.4	0.008
CCr, ml/min	54.9 ± 17.4	26.5 ± 7.1	0.00002
Duration of hospitalization, days	21.0 ± 8.5	36.0 ± 16.5	0.01
SFA at discharge, m^2	1.57 ± 0.19	1.48 ± 0.22	0.12
BW at hospitalization, kg	61.0 ± 8.9	52.5 ± 12.6	0.13
BW at discharge, kg	54.9 ± 8.3	48.3 ± 8.6	0.19
BMI at admission, kg/m^2	23.9 ± 2.4	23.2 ± 3.2	0.59
BMI at discharge, kg/m^2	21.8 ± 2.2	21.1 ± 1.8	0.89
ΔBWI, kg/m^2	3.18 ± 1.69	2.14 ± 1.42	0.13
Lowest Q, n (%)	26 (22)	6 (42)	0.09
Second Q, n (%)	29 (25)	4 (28)	0.77
Third Q, n (%)	31 (26)	1 (7)	0.10
Highest Q, n (%)	30 (25)	3 (21)	0.71

DM: diabetes mellitus; HTN: hypertension; SBP: systolic blood pressure; NYHA: New York Heart Association; HF: heart failure; IHD: ischemic heart disease; HTCM: hypertensive cardiomyopathy; DCM: dilated cardiomyopathy; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin II type 1 receptor blocker; BNP: brain natriuretic peptide; Na: sodium; BUN: blood urea nitrogen; Hb: hemoglobin; CCr: creatinine clearance; SFA: surface area; BW: body weight; BMI: body mass index; ΔBWI: changes in body weight index; Q: quartile.

We enrolled 130 consecutive patients who were initially hospitalized due to acute decompensated HF at Fukuoka University Hospital from 2001 to 2013 and followed for 2 years after discharge. The diagnosis of HF was established by the simultaneous presence of at least two major Framingham criteria or one major criterion in conjunction with two minor criteria. The primary end-point was 2-year mortality after discharge. We excluded patients with end-stage renal disease under maintenance dialysis. This study was approved by the Ethics Committee of Fukuoka University Hospital (#16-1-21). We collected and analyzed all data using the database of Fukuoka University Hospital.

Clinical parameters

Data on age, gender, BW at admission and discharge, body mass index (BMI) at admission and discharge, systolic blood pressure (SBP) at admission, body surface area (SFA) at discharge calculated by the formula of DuBois, duration of hospitalization, New York Heart Association (NYHA) functional class at hospitalization, the etiology of HF, the presence or absence of diabetes mellitus (DM) and hypertension (HTN), medications, left ventricular ejection fraction (LVEF) using Simpson's method, BNP, hemoglobin (Hb), serum sodium, blood urea nitrogen (BUN), creatinine clearance (CCr) calculated by the formula of Cockcroft-Gault, and the presence of an implantable cardioverter defibrillator (ICD) were collected. In the measurement of BW at admission, a weighing scale was used for mobile patients with acceptable dyspnea, while a weighing and lifting scale was used in immobile patients with severe dyspnea. The change in the BW index (ΔBWI) during hospitalization was calculated as (BW at hospital admission minus BW at hospital discharge)/(SFA at hospital discharge).

The cause of HF was classified as ischemic heart disease (IHD), hypertensive cardiomyopathy (HTCM), valvular heart disease, dilated cardiomyopathy (DCM), arrhythmia, or unknown. When there were multiple causes of HF, the main cause of HF was assumed based on the patient's medical history. Patients who had a current SBP and DBP $\geq$ 140 and 90 mm Hg, respectively, or who were receiving antihypertensive therapy were considered to have HTN. DM was defined using the Japan Diabetes Society criteria.

Statistical analysis

All statistical analyses were performed using StatFlex V6 (Artech Co., Ltd., Osaka, Japan). Date were expressed as the mean ± standard deviation (SD) or median ± quartile deviation (QD) for continuous variables and as a percentage (%) for categorical variables. Subjects were classified into two groups according to 2-year mortality (survival and death groups) after discharge. In addition, subjects were categorized into quartiles according to ΔBWI as follows: < 1.3 kg/m^2 (lowest ΔBWI), 1.3 - 2.9 kg/m^2 (second ΔBWI), 3 - 4.7 kg/m^2 (third ΔBWI) and $\geq$ 4.8 kg/m^2 (highest ΔBWI). Categorical and continuous variables were compared between two groups by a

Chi-square analysis and Student's *t*-test, respectively. When continuous variables did not show a normal distribution, we performed a Mann-Whitney U test. Categorical and continuous variables were compared among the quartile ΔBWI groups by a Chi-square analysis and one-way analysis of variance, respectively. When continuous variables did not show a normal distribution, we performed a Kruskal-Wallis test. The univariate relationship between ΔBWI and 2-year mortality was evaluated using a Kaplan-Meier analysis. Differences in 2-year mortality across the quartiles of ΔBWI were evaluated using the log-rank test. The association between ΔBWI and 2-year mortality was evaluated by Cox proportional hazards regression. Before the multivariate analysis, the duration of hospitalization, age, CCr, BW at admission and discharge, BMI at admission and discharge, SBP at admission, BUN, serum sodium, BNP and ΔBWI were normalized by a power transformation to correct for a skewed distribution. A backward-stepwise Cox proportional hazards model was used to identify the independent predictors of mortality, retaining variables with P < 0.05. Significant factors included the etiology of HTCM, DM, CCr, SBP at admission, BNP, β-blockers, duration of hospitalization, and ΔBWI. Additional covariates were not considered to be independent predictors of mortality, including age, gender, HTN, DM, NYHA functional class, Hb, serum sodium, BUN, the etiology of IHD, valvular cardiac disease and arrhythmia, LVEF, the use of diuretics, angiotensin converting enzyme inhibitors (ACEI) or angiotensin II type 1 receptor blocker (ARB), digitalis, oral anticoagulants, nitrates, spironolactone and antiplatelets, BW at admission and discharge, BMI at admission and discharge, and the presence of ICD implantation. A multivariate Cox proportional hazards analysis was then conducted, and the above variables were combined with the categorized ΔBWI. The reference group was defined as ΔBWI $\geq$ 4.8 kg/m^2, which was the quartile with the highest ΔBWI. P < 0.05 was considered to be statistically significant.

Results

Patient characteristics in the survival and death groups

The mean age of the 130 patients was 68 ± 10 years, and 79 of them were male (60%). Fourteen patients died during the 2-year follow-up period (11%). The cause of death was progressive pump failure in 13 patients and sudden death in one and six of these patients were implanted with an ICD (42%). Table 1 shows the patient characteristics in the survival (n = 116) and death (n = 14) groups. The patients in the death group were significantly older and had lower SBP at admission, lower CCr, Hb and serum sodium, higher BNP and BUN, a longer duration of hospitalization and more frequent ICD implantation than those in the survival group.

Mortality rates in quartiles according to ΔBWI

The mortality rates in quartiles according to ΔBWI were 19%
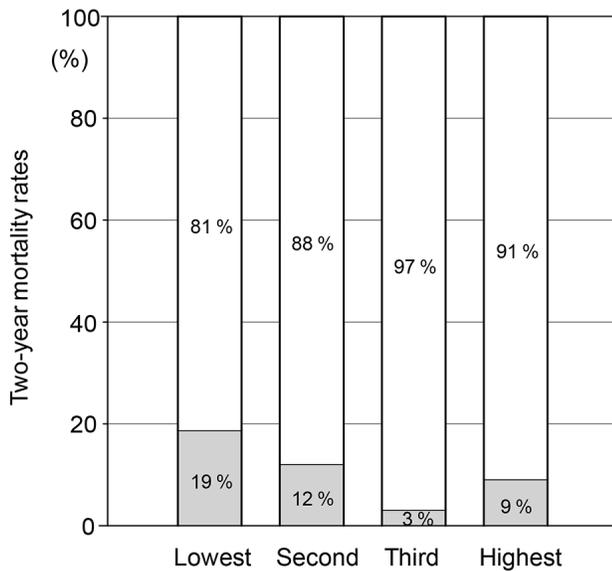
Figure 1. Mortality rates in quartiles (lowest, second, third and highest) according to ΔBWI.

(n = 6), 12% (n = 4), 3% (n = 1), and 9% (n = 3) in the quartiles with the lowest, second, third and highest ΔBWI, respectively (Fig. 1).

Patient characteristics in quartiles according to ΔBWI

The patient characteristics in the quartiles of ΔBWI are shown in Table 2. In a comparative analysis, age, gender, NYHA functional class II and IV, LVEF, BW at admission and duration of hospitalization significantly differed among the quartiles of ΔBWI.

Kaplan-Meier analysis of survival in the quartiles of ΔBWI

Figure 2 shows the Kaplan-Meier curves of survival in the quartiles of ΔBWI. Patients were categorized into quartiles according to ΔBWI. In unadjusted comparisons, the third-quartile ΔBWI group had the best survival, while the quartile with the lowest ΔBWI had the worst survival. A log-rank test showed that the difference between the quartiles with the third and lowest ΔBWI was statistically significant (P = 0.045).

Cox proportional hazards analyses to identify independent predictors of mortality

In the adjusted Cox proportional hazards analyses, as shown in Table 3, a decrease in ΔBWI was found to be a statistically significant predictor of 2-year mortality, as were other variables including SBP at admission, BNP, DM, CCr, duration of hospitalization, use of β-blocker and the etiology of HTCM.

A multivariate Cox proportional hazards analysis combined with categorized ΔBWI

In the quartiles according to ΔBWI, the quartile with the lowest ΔBWI showed a much higher risk of 2-year mortality than the quartile with the highest ΔBWI (Table 4) (relative risk: 7.46, 95% CI: 1.03 - 53.99, P = 0.04).

Discussion

The main finding in this study was that ΔBWI in hospitalized patients with acute decompensated HF was significantly associated with 2-year mortality after discharge independent of various covariates. The quartile with the lowest ΔBWI showed a much higher risk of 2-year mortality than that with the highest ΔBWI as assessed by a multivariate Cox proportional hazards analysis. Therefore, we should reinforce the treatment of HF to the patients with low ΔBWI, such as with additional medications, cardiac rehabilitation, Waon therapy, the introduction of supplemental oxygen therapy, and cardiac resynchronization therapy.

In this study, we first hypothesized that patients with a greater change in BW may have a better prognosis. Our findings support this hypothesis. Many previous reports have identified univariate predictors of reduced survival, including NYHA functional class, reduced LVEF [16], renal insufficiency, and comorbid factors, such as DM [17] and IHD. Predictive models that consider comorbidities and HF-related factors, such as the EFFECT model [18], the HF survival score [19], and the Seattle Heart Failure Model [20] have also been shown to be associated with the prognosis. However, these previous predictors and models have been insufficient: the former are limited in their ability to predict survival in individual patients, and the latter are complicated and are not performed in all institutions because of multiple factors, including the need for invasive tests. Since ΔBWI reflects the cardio-renal connection, it can be used in individual patients. Additionally, it can be used in all institutions because it is simple, inexpensive and easy to measure.

Longer period of hospitalization, lower SBP at admission, higher BNP, lower CCr and % β-blockers were also associated with 2-year mortality, as shown in Table 3, and these associations were consistent with previous reports [7, 8, 15, 21, 22]. Thus, the results indicated that the patients in this study did not represent any specific patient group.

This study has several limitations. First, this study was limited by its retrospective design. Although this study considered only a small number of patients, we collected data that we could follow for up to 2 years in as many patients as possible in our hospital from 2001 to 2013. The medication strategies in patients with HF, such as with respect to the use of human atrial natriuretic peptide and β-blockers, in the 1990s were much different from those used presently. Thus, the use of older data may directly influence the mortality. Second, the analysis was performed under conditions of various etiologies of HF and various medications. To confirm the clinical significance of the relationship between ΔBWI and 2-year mortality, we performed a multivariate Cox proportional hazards analysis. Prospective studies will be needed to clarify these limitations.

Table 2. Patient Characteristics in Quartiles According to ΔBWI

	Lowest Q (n = 32)	Second Q (n = 33)	Third Q (n = 32)	Highest Q (n = 33)	P value
Age, years	74 ± 9	65 ± 11	68 ± 7	63 ± 10	0.008
Male, n (%)	15 (47)	16 (49)	22 (69)	26 (79)	0.02
DM	8 (25)	13 (39)	5 (15)	6 (18)	0.11
HTN	24 (75)	19 (57)	17 (53)	15 (45)	0.10
SBP, mm Hg	124.5 ± 10.0	122.0 ± 22.9	130.0 ± 15.0	124.0 ± 28.5	0.83
NYHA functional class					
II, n (%)	9 (28)	8 (24)	7 (21)	1 (3)	0.048
III, n (%)	13 (40)	7 (21)	7 (21)	4 (12)	0.05
IV, n (%)	9 (28)	18 (54)	16 (50)	28 (84)	<0.0001
The cause of HF					
IHD, n (%)	7 (21)	7 (21)	9 (28)	14 (42)	0.19
HTCM, n (%)	3 (9)	2 (6)	3 (9)	4 (12)	0.86
Valvular disease, n (%)	9 (28)	7 (21)	7 (21)	2 (6)	0.13
DCM, n (%)	4 (12)	8 (24)	6 (18)	8 (24)	0.59
Arrythmia, n (%)	6 (18)	4 (12)	2 (6)	2 (6)	0.30
Unknown, n (%)	3 (9)	5 (15)	5 (15)	3 (9)	0.77
ICD, n (%)	3 (9)	8 (24)	5 (15)	6 (18)	0.45
LVEF, %	51 ± 18	42 ± 17	42 ± 19	36 ± 13	0.01
Medications					
Diuretics, n (%)	24 (75)	26 (78)	26 (81)	29 (87)	0.60
ACEI/ARB, n (%)	25 (78)	24 (72)	27 (84)	19 (57)	0.09
Digitalis, n (%)	0 (0)	5 (15)	2 (6)	6 (18)	0.06
Oral anticoagulant, n (%)	15 (46)	17 (51)	17 (53)	14 (42)	0.82
Nitrates, n (%)	4 (12)	4 (12)	4 (12)	1 (3)	0.49
Spironolactone, n (%)	15 (46)	22 (66)	21 (65)	19 (57)	0.33
β-blockers, n (%)	23 (71)	14 (42)	22 (68)	19 (57)	0.06
Antiplatelets, n (%)	17 (53)	15 (45)	14 (43)	20 (60)	0.50
Laboratory test					
BNP, pg/mL	262.5 ± 267.7	473.0 ± 333.3	370.0 ± 190.2	588.0 ± 533.2	0.10
Na, mEq/L	140.0 ± 2.0	141.0 ± 2.6	140.0 ± 2.0	141.0 ± 1.5	0.17
BUN, mg/dL	19.5 ± 4.3	19.0 ± 6.0	17.0 ± 4.8	19.0 ± 5.1	0.88
Hb, g/dL	12.5 ± 2.4	13.5 ± 2.4	13.1 ± 2.8	14.0 ± 2.2	0.08
BW at admission, kg	55.3 ± 8.3	58.7 ± 9.8	58.5 ± 8.6	65.0 ± 8.5	0.03
BW at discharge, kg	54.6 ± 8.7	55.9 ± 9.5	53.3 ± 8.3	53.4 ± 7.2	0.78
BMI at admission, kg/m^2	22.8 ± 2.5	24.3 ± 2.6	24.0 ± 2.3	24.9 ± 2.1	0.14
BMI at discharge, kg/m^2	22.5 ± 2.4	22.6 ± 2.4	21.4 ± 2.3	20.8 ± 2.0	0.07
Duration of hospitalization, days	18.5 ± 7.0	20.0 ± 8.3	23.5 ± 9.8	28.0 ± 11.8	0.006
CCr, mL/min	46.4 ± 18.5	63.0 ± 21.0	53.5 ± 19.6	52.9 ± 15.5	0.09
SFA at discharge, m^2	1.52 ± 0.21	1.59 ± 0.20	1.54 ± 0.17	1.58 ± 0.19	0.45
Two-year mortality rates, n (%)	6 (18)	4 (12)	1 (3)	3 (9)	0.23

ΔBWI: changes in body weight index; Q: quartile; DM: diabetes mellitus; HYN; hypertension; SBP: systolic blood pressure; NYHA: New York Heart Association; HF; heart failure; IHD: ischemic heart disease; HTCM: hypertensive cardiomyopathy; DCM: dilated cardiomyopathy; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin II type 1 receptor blocker; BNP: brain natriuretic peptide; Na: sodium; BUN: blood urea nitrogen; Hb: hemoglobin; BW: body weight; BMI: body mass index; CCr: creatinine clearance; SFA: surface area.
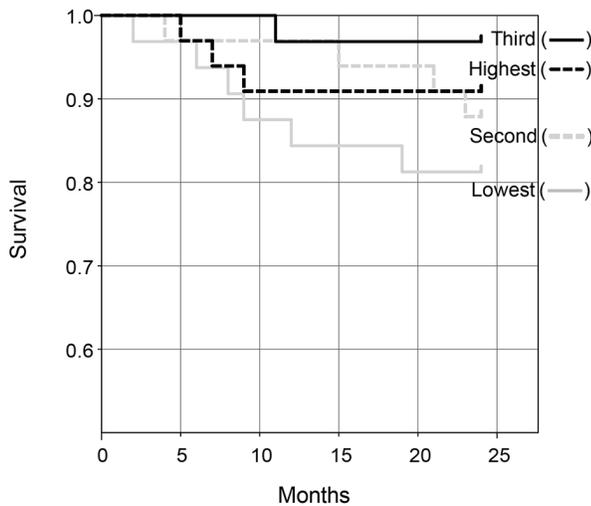
Figure 2. Kaplan-Meier curves of survival in quartiles (lowest, second, third and highest) according to ΔBWI.

In conclusion, ΔBWI was significantly associated with 2-year mortality after discharge, which indicates that ΔBWI might be a simple predictor of prognosis in acute decompensated HF.

Conflicts of Interest

KS is a Chief Director and SM is a Director of NPO Clinical and Applied Science, Fukuoka, Japan. KS has an Endowed "Department of Molecular Cardiovascular Therapeutics" supported by MSD, Co. LTD. SM belongs to the Department of Molecular Cardiovascular Therapeutics, which is supported by MSD, Co. LTD.

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Table 3. Cox Proportional Hazards Analyses to Identify Independent Predictors of Mortality

	β	z value	P value
DM	2.51	3.05	0.0023
Duration of hospitalization	0.99	3.38	0.0007
CCr	-1.01	3.7	0.0002
ΔBWI	-3.53	3.72	0.0002
β-blockers	-3.66	2.97	0.0029
HTCM	5.53	3.06	0.0022
BNP	0.52	3.44	0.0006
SBP	-1.29	3.67	0.0002

DM: diabetes mellitus; CCr: creatinine clearance; ΔBWI: changes in body weight index; HTCM: hypertensive cardiomyopathy; BNP: brain natriuretic peptide; SBP: systolic blood pressure.

Table 4. A Multivariate Cox Proportional Hazards Analysis Combined With Categorized ΔBWI

	β	z value	P value	RR (95% CI)
ΔBWI				
Lowest Q	2	1.99	0.04	7.46 (1.03 - 53.99)
Second Q	1.39	1.6	0.1	4.02 (0.73 - 22.04)
Third Q	-0.1	0.08	0.93	0.89 (0.07 - 11.16)
Highest Q				1.00

ΔBWI: changes in body weight index; Q: quartile; RR: relative risk; CI: confidence interval.

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