Does Weight Loss Increase the Risk of Death from and Incidence of Cardiovascular Disease even among Individuals with Overweight or Obesity at 20 Years of Age?

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In the current issue of the Journal of Atherosclerosis and Thrombosis, the association between weight change from 20 years of age to middle age or older and death from cardiovascular disease (CVD) was reported from a large and longitudinal Japanese cohort study, the Japan Collaborative Cohort (JACC) Study1). In that report, participants were classified as follows into exclusive categories based on weight change (in kg) from 20 years of age to baseline (age range, 40–79 years): –12.5 or more, –10.0 to –12.4, –7.5 to –9.9, –5.0 to –7.4, –2.5 to –4.9, –2.4 to +2.4 (reference), +2.5 to +4.9, +5.0 to +7.4, +7.5 to +9.9, +10.0 to +12.4, and +12.5 or more. During the follow-up period (median, 19.1 years), a significantly linearly increased risk of total CVD mortality was observed for all weight loss groups. The hazard ratio (HR) was 1.50 for the –12.5 kg or more weight loss group. Cause-specific HRs among this group were 1.48 for ischemic stroke and 1.74 for intracerebral hemorrhage. On the other hand, among all weight gain groups, only the +12.5 kg or more group had a significantly linearly increased risk for total CVD and ischemic heart disease, with HRs of 1.21 and 1.62, respectively. During the follow-up period, a significantly linearly increased risk of total CVD mortality was observed for all weight loss groups. The hazard ratio (HR) was 1.50 for the –12.5 kg or more weight loss group. Cause-specific HRs among this group were 1.48 for ischemic stroke and 1.74 for intracerebral hemorrhage. On the other hand, among all weight gain groups, only the +12.5 kg or more group had a significantly linearly increased risk for total CVD and ischemic heart disease, with HRs of 1.21 and 1.62, respectively.

Studies carried out in Japan1-3), Sweden4), and Norway5) have reported an association between weight change from around 20 years of age to middle age or older and subsequent CVD mortality, and studies in Japan6), Norway7), and the USA8) have reported an association with CVD incidence. Many of these studies have observed an increased risk of CVD among individuals following weight loss1-7). Although the degree of risk and CVD type differed among these studies, none reported that weight loss reduced the risk of CVD incidence and mortality. The participants with weight loss in these studies had relatively high weight, overweight, or obesity at around 20 years of age. Therefore, they might have been advised to lose weight to help prevent lifestyle diseases and CVD. Unfortunately, the Ohsaki Cohort Study reported that those with overweight at 20 years of age who lost weight until middle age or older were at a slightly increased risk of CVD mortality compared with those with overweight at 20 years of age who maintained a stable weight until middle age or older2).

Why did those who lost weight have an increased risk of CVD mortality? Would it have been better not to lose weight? In a study involving White women in the USA, intentional weight loss reduced the risk of CVD mortality9), which conflicts with previous studies. One possible explanation for this was an inverse cause-and-effect relation, in which weight loss might have predicted CVD death and incidence. However, this hypothesis is likely not valid because several studies that have excluded CVD incidence and mortality in the first several years of follow-up from their analyses reported similar results. A second reason could be that weight change during the follow-up period subsequent to a previous weight change might have affected CVD incidence and mortality. In our previous study investigating the association between change in waist circumference over a 5–10-year period and the subsequent incidence of type 2 diabetes, those who lost waist circumference gained waist circumference during the subsequent follow-up period10). A similar rebound in body weight might have increased the risk of CVD mortality and incidence. A third reason could be that the weight loss was the result of frailty and sarcopenia, which are risk factors for CVD, as discussed in the JACC Study.

The strengths of the JACC Study described in...
Table 1.

| Study name or First author, year published | n     | Men (%) | Baseline year | Follow-up years | Age at baseline | Outcome | Weight change categories | Body weight at 18-25 years old | Hazard ratios or relative risks (95% Confidence intervals) |
|-------------------------------------------|-------|---------|---------------|-----------------|-----------------|---------|----------------------------|-------------------------------|------------------------------------------------------------|
| JACC Study, 2020 | 69,681 | 42.5    | 1988-1990     | median: 19.1    | 40-79           | Death from CVD | Loss ≥ 12.5kg               | 27.2 (kg/m²)                  | 1.50 (1.30-1.72), 1.45 (1.28-1.66), 1.20 (1.03-1.39)             |
|                |       |         |               |                 |                 |                     | Loss 10-12.4               | 24.7                           | 1.15 (1.04-1.28)                           |
|                |       |         |               |                 |                 |                     | Loss 7.5-9.9               | 24.0                           | 1.14 (1.02-1.29)                           |
|                |       |         |               |                 |                 |                     | Loss 5.0-7.4               | 23.4                           | reference                                  |
|                |       |         |               |                 |                 |                     | Loss 2.5-4.9               | 22.8                           | reference                                  |
|                |       |         |               |                 |                 | Stable ±2.4            | 21.9                           | reference                                  |
|                |       |         |               |                 |                 | Gain 2.5-4.9            | 21.4                           | 0.92 (0.80-1.06)                           |
|                |       |         |               |                 |                 | Gain 5.0-7.4            | 21.1                           | 0.98 (0.87-1.10)                           |
|                |       |         |               |                 |                 | Gain 7.5-9.9            | 20.9                           | 0.91 (0.77-1.07)                           |
|                |       |         |               |                 |                 | Gain 10-12.4            | 20.6                           | 1.05 (0.92-1.21)                           |
|                |       |         |               |                 |                 | Gain ≥ 12.5             | 20.0                           | 1.21 (1.07-1.36)                           |
| Ohsaki Cohort Study, 2013 | 41,364 | 48.6    | 1994          | 13.3            | 40-79           | Death from CVD | Loss ≥ 10.0kg               | 26.1 (26.5 (kg/m²))           | 1.52 (1.25-1.85), 1.62 (1.25-2.11)             |
|                |       |         |               |                 |                 |                     | Loss 5.0-9.9                | 24.2, 24.4                      | reference                                  |
|                |       |         |               |                 |                 | Stable ±4.9            | 22.5, 22.4                    | 0.95 (0.78-1.16)                           |
|                |       |         |               |                 |                 | Gain 5.0-9.9            | 21.7, 21.5                    | 0.98 (0.80-1.21), 1.36 (1.09-1.69)             |
|                |       |         |               |                 |                 | Gain ≥ 10.0             | 21.1, 20.7                    | reference                                  |
| JPHC, 2009 | 88,419 | 47.8    | 1990-1993     | median: 12.9    | 40-69           | Death from CVD | Loss ≥ 5kg                  | 24.4, 24.1                      | men, women                                  |
|                |       |         |               |                 |                 |                     | Stable ±4.9                | 21.8, 21.3                      | 1.34 (1.09-1.66), 1.22 (0.87-1.71)             |
|                |       |         |               |                 |                 | Gain ≥ 5                | 21.0, 20.3                    | reference                                  |
| Rosengren A, 1999 | 6,874  | 100     | 1970-1973     | mean: 19.7      | 47-55           | Death from coronary disease | Loss >4% Stable ±4 | 24.1 (kg/m²) | 1.84 (1.27-2.68) reference |
|                |       |         |               |                 |                 |                     | Gain 4-10                   | 23.1                           | 1.43 (1.04-1.97)                           |
|                |       |         |               |                 |                 | Stable ±4.9            | 22.7                           | 1.62 (1.18-2.22)                           |
|                |       |         |               |                 |                 | Gain 5-10               | 22.5                           | 1.36 (1.00-1.84)                           |
|                |       |         |               |                 |                 | Gain 15-25              | 22.2                           | 1.73 (1.24-2.42)                           |
|                |       |         |               |                 |                 | Gain 25-35              | 21.6                           | 1.86 (1.32-2.62)                           |
|                |       |         |               |                 |                 | Gain >35                | 20.6                           | reference                                  |
| Kjøllesdal MKR, 2020 | 148,021 | 78.4    | 1985-2003     | mean: 19        | 40-50           | Death from CVD | Loss ≥ 5.0kg               | Not described                  | 1.33 (0.87-2.03) reference |
|                |       |         |               |                 |                 |                     | Loss 2.5-5.0               | 23.8                           | 1.14 (0.74-1.76)                           |
|                |       |         |               |                 |                 | Stable ±2.4            | 21.9                           | 1.17 (0.88-1.55)                           |
|                |       |         |               |                 |                 | Gain 2.5-4.9            | 21.4                           | 1.03 (0.81-1.30)                           |
|                |       |         |               |                 |                 | Gain 5.0-9.9            | 20.9                           | 0.96 (0.76-1.22)                           |
|                |       |         |               |                 |                 | Gain 10.0-14.9           | 26.2 (kg/m²)                  | 1.8 (0.9-3.5) reference               |
| JPHC, 2008 | 90,679 | 47.7    | 1990-1993     | mean: 9.7       | 40-69           | Incidence of CHD | Loss ≥ 10.0kg               | 23.8                           | 0.9 (0.5-1.8) reference |
|                |       |         |               |                 |                 |                     | Loss 5-10                  | 21.9                           | 1.0 (0.6-1.8) reference               |
|                |       |         |               |                 |                 | Stable ±5.0             | 21.4                           | 1.3 (0.7-2.3) reference               |
|                |       |         |               |                 |                 | Gain 5-10               | 20.9                           | reference                                  |
| Prestgaard E, 2020 | 2,014  | 100     | 1972-1975     | median: 30.1    | 40-59           | Incidence of stroke | Loss Gain 0-4.9 kg         | Not described                  | 1.46 (0.99-2.11) reference |
|                |       |         |               |                 |                 |                     | Gain 5.0-9.9kg             | 1.86 (1.39-2.53) reference |
|                |       |         |               |                 |                 | Stable ≥ 10             | 1.09 (0.53-2.21) reference |
| Willett WC, 1995 | 115,818 | 0       | 1976          | 14              | 30-55           | Incidence of CHD | Loss ≥ 20kg                 | Not described                  | 1.15 (0.77-1.71) reference |
|                |       |         |               |                 |                 |                     | Loss 11-19.9               | 0.78 (0.57-1.06) reference |
|                |       |         |               |                 |                 | Stable ≥ 10             | 1.25 (1.01-1.55) reference |
|                |       |         |               |                 |                 | Gain 4.9-Gain 4.9       | 1.65 (1.33-2.05) reference |
|                |       |         |               |                 |                 | Gain 5-7.9               | 1.92 (1.61-2.29) reference |
|                |       |         |               |                 |                 | Gain 8-10.9              | 2.65 (2.17-3.22) reference |

CHD, coronary heart disease; CVD, cardiovascular disease.
the current issue were the exclusive weight change categories, the large sample size, and the information on cause-specific CVD mortality. However, a notable limitation was the non-adjustment for lipid profiles, unlike the adjustment for hypertension. In the “metabolic domino” concept, which involves the progression of lifestyle-related diseases to CVD, both hypertension and dyslipidemia are in middle stream. It is well known that hypertension and dyslipidemia are strongly associated with ischemic stroke and ischemic heart disease, respectively. Therefore, to compare the impact of weight change on each CVD type, it is important to adjust for both hypertension and dyslipidemia, or neither. A previous study in the Sweden investigated the association between weight change from 20 years of age to middle age and subsequent mortality from coronary heart disease (CHD), adjusting for serum cholesterol levels, and reported a significantly higher risk of mortality from CHD due to both weight loss and weight gain4. A multivariable model was used, so estimates of the attenuation of risk by adjusting for serum cholesterol levels could not be made; however, it is speculated that the risks of weight loss and gain remained significantly high after adjusting for lipid profiles in the JACC Study.

The association between weight loss and CVD mortality and incidence remains unclear. Therefore, further studies are needed that observe weight change until specified end points, measure body composition, and investigate the causes, methods, and processes of weight loss.

Conflicts of Interests

None.

References

1) Okada C, Kubota Y, Eshak ES, Renche C, Tamakoshi A, Iso H; and the JACC Study Group. Weight Change and Mortality from Cardiovascular Diseases: The Japan Collaborative Cohort Study. J Atheroscler Thromb, 2020 May 2. doi: 10.5551/jat.54114.
2) Chou WT, Kakizaki M, Tomata Y, Nagai M, Sugawara Y, Kuriyama S, Tsuji I. Impact of weight change since age 20 and cardiovascular disease mortality risk: the Ohsaki Cohort Study. Circ J, 2013; 77: 679-686
3) Saito I, Konishi M, Iso H, Inoue M, Tsugane S. Impact of weight change on specific-cause mortality among middle-aged Japanese individuals. J Epidemiol Community Health, 2009; 63: 447-454
4) Rosengren A, Wedel H, Wilhelmsen L. Body weight and weight gain during adult life in men in relation to coronary heart disease and mortality. A prospective population study. Eur Heart J, 1999; 20: 269-277
5) Kjøllesdal MKR, Ariansen I, Næss ØE. Early adulthood weight, subsequent midlife weight change and risk of cardiovascular disease mortality: an analysis of Norwegian cardiovascular surveys. Int J Obes (Lond), 2020; 44: 399-408
6) Chel CI, Iso H, Yamagishi K, Inoue M, Tsugane S. Body mass index and weight change since 20 years of age and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based Study. Int J Obes (Lond), 2008; 32: 144-151
7) Prestgaard E, Mariampillai J, Engeseth K, Eriksen J, Bodegård J, Liestøl K, Kjeldsen S, Grundvold I, Berge E. Change in Body Weight and Long-Term Risk of Stroke and Death in Healthy Men. Stroke, 2020; 51: 1435-1441
8) Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, Hennekens CH. Weight, weight change, and coronary heart disease in women. Risk within the ‘normal’ weight range. JAMA, 1995; 273: 461-465
9) Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C. Prospective study of intentional weight loss and mortality in never-smoking overweight US white women aged 40-64 years. Am J Epidemiol, 1995; 141: 1128-1141
10) Tatsumi Y, Watanabe M, Nakai M, Kokubo Y, Higashiyama A, Nishimura K, Kobayashi T, Takegami M, Nakao YM, Watanabe T, Okayama A, Okamura T, Miyamoto Y. Changes in Waist Circumference and the Incidence of Type 2 Diabetes in Community-Dwelling Men and Women: The Suita Study. J Epidemiol, 2015; 25: 489-495