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ORIGINAL ARTICLE

Combined aerobic and resistance training, and incidence of diabetes: A retrospective cohort study in Japanese older women

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ABSTRACT

Aims/Introduction: To investigate the relationship between combined aerobic and resistance training, and the incidence of type 2 diabetes mellitus.

Materials and Methods: The present study included 10,680 Japanese women. Participants enrolled between 2005 and 2010, and were followed up until 2014. The frequency of combined training was counted for the first 3 months, the 6th month and the 9th month. In 2014, women reported whether or not they had diabetes, as well as the year of developing diabetes. Hazard ratios and 95% confidence intervals (CI) for the incidence of type 2 diabetes were obtained using Cox proportional hazard models.

Results: The median duration of follow up was 5 years, with 166 women developing type 2 diabetes. Using the lowest frequency of training group (1st quartile) as the reference, the hazard ratios for the second through fourth quartiles was as follows: 0.95 (95% CI 0.64–1.41), 0.73 (95% CI 0.48–1.13) and 0.69 (95% CI 0.44–1.07), respectively (*P* for trend = 0.116). After adjustment for age, body mass index and thigh circumference, the hazard ratios were: 0.84 (95% CI 0.56–1.26), 0.69 (95% CI 0.45–1.06) and 0.61 (95% CI 0.39–0.95), respectively (*P* for trend = 0.040).

Conclusions: A higher frequency of combined aerobic and resistance training is associated with a lower risk of developing type 2 diabetes in Japanese women.

INTRODUCTION

The World Health Organization announced that the number of patients with diabetes mellitus increased to 422 million in 2014, an approximately fourfold increase since 1980 when the number of patients with diabetes was 108 million[1]. Unless effective measures are taken, the Non-Communicable Disease Risk Factor Collaboration predicts that the number of patients with diabetes in the world will reach 700 million by 2025[2]. This increasing trend is mostly represented by patients with type 2 diabetes mellitus. The onset of type 2 diabetes is not only related to genetic factors, but also to environmental factors, especially lifestyle, and proper diet and physical activity are critical to delay and/or prevent its onset. Hence, it is important, in the consideration of effective measures, to identify the necessary components of diet and physical activity for the prevention of type 2 diabetes.

Several epidemiological studies have reported a negative dose–response relationship between regular physical activity and the incidence of type 2 diabetes[3,4]. Physical activity can be classified into two groups: (i) aerobic exercise, which enhances cardiorespiratory functional capacity; and (ii) resistance training, which enhances muscle strength. The American College of Sports Medicine and the American Diabetes Association report that combined aerobic and resistance training exerts superior glycemic control effects than independently practiced aerobic exercise or resistance training among patients with diabetes[5]. To our knowledge, randomized controlled trials studying the influences of a structured combined aerobic and resistance training on the incidence of type 2 diabetes have not yet been undertaken. However, recent cohort studies showed that people practicing resistance

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training in addition to aerobic exercise had a lower risk of developing type 2 diabetes as compared with people practicing aerobic exercise or resistance training independently[6,7]. These studies indicate that combined aerobic and resistance training is likely to be highly effective in delaying and/or preventing the onset of type 2 diabetes. However, these cohort studies that investigated the relationship between resistance training and the incidence of type 2 diabetes in people practicing aerobic exercise did not investigate the dose–response relationship between combined training and the incidence of type 2 diabetes. Therefore, we longitudinally evaluated the dose–response relationship between structured combined aerobic and resistance training, and the incidence of type 2 diabetes in >10,000 Japanese women who had been practicing a structured combined training for a long period by a retrospective cohort study.

METHODS

Participants

The present study is part of the Curves Japan Study examining the effects of exercise programs combining aerobic and resistance training on Japanese women[8]. The structured combined exercise training facilities (Curves Japan Co., Ltd.), to which the participants of the study belonged, were opened in 2005 as fitness facilities to hold 30-min combined exercise sessions exclusively for women. The present study was a retrospective study. Study participants were those who became members of these facilities between 4 July 2005 and 31 July 2010. From August to October 2014, self-administered questionnaires on medical history at enrollment year and current date were given to 16,241 members of 102 facilities in Tokyo or surrounding areas. Responses to participate in the study were obtained from 12,940 (response rate 79.7%).

For the present analysis, the exclusion criteria were as follows: participants aged <20 years on enrollment (n = 17); the presence of diabetes or thyroid disease on enrollment based on responses to a self-administered questionnaire, the question of diabetes was "Did you have diabetes or thyroid disease presently or in the past?", and there were two choices, "yes" or "no", on the health conditions carried out at that time (n = 1,008); not responding or responding "Unclear" to the above-mentioned questionnaire (n = 1,139); unavailability of values representing the height, weight, and waist and thigh circumferences measured on enrollment, errors in such measurement or clear entry errors (n = 95); and no training at the baseline period (n = 1). Consequently, 10,680 were included in the present study (Figure 1).

We obtained written informed consent from all participants according to the Declaration of Helsinki. The present study was approved by the Research Ethics Committee of the National Institutes of Biomedical Innovation, Health and Nutrition (Ikikenhatsu-198-3).

Anthropometric Measurement

On enrollment in the fitness facilities, the participants underwent height and weight measurements while wearing light

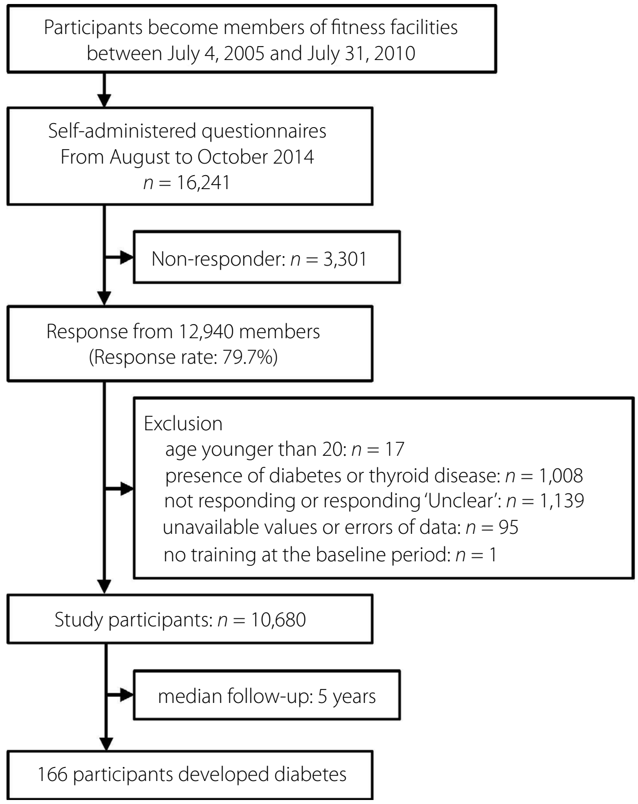

Figure 1 | Flow diagram of enrolled participants.

clothes without shoes, and the obtained values were used to calculate the body mass index (BMI) as a fatness index. As another fatness index, their waist circumferences (2 fingerbreadths above the level of the navel) were also measured. Their thigh circumferences (at the top of the thigh) were measured as a muscle mass index.

Combined Exercise Training

The number of admissions to the fitness facilities, recorded using an electronic admission management system, was examined for the first 3 months (day of enrollment to day 90), the 6th month (days 151–180) and the 9th month (day 241–270). As the number of admissions represents the training sessions in each facility, the former was defined as the combined exercise training frequency. The structured combined exercise training program provided by the fitness facilities consists of a 24-min training session (combining aerobic and resistance training using 12 different devices, each of which lasts for 30 s) and 6-min stretching. The aerobic exercise is stepping on a step board while executing the resistance training, using 12 different hydraulic devices (chest press/seated row, squat, shoulder press/lateral pull, leg extension/leg curl, abdominal crunch/back extension, lateral lift, elbow flexion/extension, horizontal leg press, pectoral deck, oblique, hip abductor/adductor, gluteus) developed for women to increase their muscle strength. All participants carried out both aerobic and resistance training in the same manner. During this program, the participants measured their heart rates once every 8 min based on the instructor's guidance to maintain them at 60–80% of their maximal heart rates throughout training by adjusting training intensity levels. From 10 November 2007 to 5 April 2008, a randomized controlled trial was carried out for 16 weeks, involving 41 women aged in their 40s to 60s, to confirm the effects of the exercise program[9]. The structured combined exercise program was shown to significantly reduce the waist circumference, systolic blood pressure, fasting blood glucose and brachial-ankle pulse wave velocity, with marked increases in the knee extension strength and flexibility.

Assessment of Type 2 Diabetes Mellitus

Based on the results of the self-administered questionnaire survey carried out within the period between August and October 2014, the presence/absence of type 2 diabetes and time of onset were ascertained. The question of diabetes was "Do you have diabetes? If 'yes', then fill in the year and the month of onset of diabetes."

Statistical Analysis

The numbers of structured combined exercise training sessions during three periods – between day of enrollment to day 90, between days 151 and 180, and between days 241 and 270 – were totaled for each participant to classify these numbers using quartiles for comparison of the physical characteristics. This was followed by the calculation of multivariable-adjusted hazard ratios and 95% confidence intervals (CI) to examine the relationship between the combined exercise training frequency and the incidence of type 2 diabetes; for the former, potential confounders were adjusted using the Cox proportional hazards model. The lowest training frequency (1st quartile) was used as a reference to calculate the hazard ratio and 95% CI of the other groups. The hazard ratio when carrying out training four times/month was also calculated. To be specific, we calculated the hazard ratio of training 20 times, because four times/month is approximately 20 days of 150 days. As the first step, the age-adjusted hazard ratio was calculated only with the age (years, continuous) entered in the model as a potential confounder, and, second, the multivariable-adjusted hazard ratio was calculated with multiple potential confounders entered in the model. In the present study, two fatness indices, the BMI and waist circumference, were measured, as they were likely to be potential confounders. The Pearson correlation coefficient between them was 0.84. Therefore, the BMI (kg/m^2, continuous), which has been used as a fatness index for a large number of models in previous studies, was entered in the multivariable-adjusted model. Similarly, the thigh circumference as a muscle mass index (cm, continuous)[10] was entered in the model, considering the possibility of this also being a potential confounder. The Pearson correlation coefficient of BMI and thigh circumference was 0.66. Also, variance inflation factors of BMI and thigh circumference were 2.0 and 2.1, respectively. Hence, there was no multicollinearity in both models we examined. To ensure proportional hazards assumption, the log–log plot was visually confirmed and found no evidence of violation.

With a view to clarifying the presence/absence of potential modification effects, the product terms between the combined exercise training frequency (times/5 months, continuous) and potential confounders (all continuous variable) were entered in the model to confirm such interactions, and stratified analyses were carried out with factors showing them. On overall and stratified analyses, linearity testing was also carried out to examine the linear relationship between the combined exercise training frequency and incidence of type 2 diabetes, with the continuous variable, representing the former, entered in the Cox proportional hazards model. As sensitivity analysis, the training frequencies during five periods – between the day of enrollment to day 30, between days 31 and 60, between days 61 and 90, between days 151 and 180, and between days 241 and 270 – were classified using quartiles to examine the relationship between the combined exercise training frequency and the incidence of type 2 diabetes during each period. It was also confirmed whether or not similar results were obtained when entering the waist circumference, instead of the BMI in the model. As the number of admissions to the fitness facilities until day 270 after enrollment was defined as the combined exercise training frequency, it was necessary to consider the possibility of the presence of diabetes influencing such a number, if the disease had developed by this period. Therefore, analysis was also carried out on excluding participants in whom type 2 diabetes had developed within 1 year after enrollment. For all statistical analyses, Stata version 14.2 (StataCorp LP, College Station, Texas, USA) was used, with the significance level set at $P < 0.05$ on both sides.

RESULTS

Baseline Characteristics of Participants

The median (range) follow-up period was 5 years (1–9 years). Type 2 diabetes developed in 166 participants during the follow-up period (59,851 women-years). Table 1 shows the participants' baseline physical characteristics according to the frequency of combined exercise training. The average BMI of all participants was 23.2 kg/m^2, which is in the normal range of the World Health Organization BMI classification[11]. Those showing higher training frequencies were older, with higher fatness index values. The thigh circumference was also greater when the training frequency was higher.

Relationship Between the Frequency of Combined Training and Diabetes

Table 2 shows the hazard ratios, reflecting the participants' combined exercise training frequencies classified using quartiles, as well as the incidence of type 2 diabetes when carrying out training four times every month. The incidence of type 2 diabetes was lower among those showing higher training

Table 1 | Baseline characteristics (2005–2010) of the study participants by frequency of combined training

Characteristic†	Total (n = 10,680)	Q_1 (Lowest) (n = 2,716)	Q_2 (n = 2,812)	Q_3 (n = 2,610)	Q_4 (Highest) (n = 2,542)
Frequency of training, times/5 month (range)	54.5 (1–125)	31.3 (1–41)	48.3 (42–54)	60.2 (55–66)	80.5 (67–125)
Age (years)	57.8 (9.8)	56.9 (10.5)	57.6 (9.5)	58.1 (9.5)	58.5 (9.5)
Height (cm)	154.8 (5.6)	155.1 (5.6)	154.8 (5.6)	154.9 (5.6)	154.5 (5.5)
Weight (kg)	55.5 (8.4)	54.7 (8.3)	55.2 (8.2)	55.9 (8.3)	56.3 (8.7)
Body mass index (kg/m^2)	23.2 (3.3)	22.8 (3.3)	23.1 (3.2)	23.3 (3.3)	23.6 (3.4)
Waist circumference (cm)	76.0 (9.1)	75.0 (9.0)	75.8 (8.7)	76.3 (8.9)	77.1 (9.5)
Thigh circumference (cm)	52.6 (4.8)	52.2 (4.8)	52.4 (4.7)	52.8 (4.7)	52.8 (5.0)

†Values are presented as mean (standard deviation), unless otherwise specified. Q, quartile.

frequencies. Both the age-adjusted hazard and multivariable-adjusted hazard ratios were lower when the training frequency was higher. On examining each hazard ratio, the multivariable-adjusted hazard ratio of the fourth quartile (representing participants showing the highest training frequency) was significantly lower. The multivariable-adjusted hazard ratio when carrying out training at a four times/month increment was 0.84 (95% CI 0.72–0.99). Regarding the dose–response relationship between the training frequency and the incidence of type 2 diabetes, a significant negative linear relationship was observed in the multivariable-adjusted model (P for linearity = 0.040).

Interactions

The thigh circumference showed significant interactions (P for interaction = 0.018), whereas the BMI suggested the presence of interactions (P for interaction = 0.052). In line with this, the participants were divided into two categories based on their median BMI values and thigh circumferences to carry out stratified analysis (Table 3). On comparison between those showing higher and lower BMI values groups, the latter showed a more significant negative linear dose–response relationship. On comparison between those showing greater and lesser thigh circumferences, the latter showed a stronger negative linear dose–response relationship, whereas clear dose–response relationships were not observed in the former.

Sensitivity Analysis

On sensitivity analysis to confirm the relationship between the combined exercise training frequency and incidence of type 2 diabetes during each period, the training frequencies during five periods – between the day of enrollment to day 30, between days 31 and 60, between days 61 and 90, between days 151 and 180, and between days 241 and 270 – were classified using quartiles. The results during all periods were similar to those of analysis of the numbers of admissions to the fitness facilities until day 270 after enrollment, classified using quartiles, and the multivariable-adjusted hazard ratio at each point when carrying out training at a four times/month increment was 0.98 (95% CI 0.86–1.12), 0.82 (95% CI 0.71–0.93), 0.88 (95% CI 0.77–1.00), 0.90 (95% CI 0.79–1.03) and 0.91 (95% CI 0.80–1.03), respectively. Furthermore, when entering the waist circumference, instead of the BMI, in the model, the multivariable-adjusted hazard ratio when carrying out training at a four times/month increment was 0.83 (95% CI 0.71–0.98), being similar to the results when entering the BMI. When excluding participants in whom type 2 diabetes had developed within 1 year after enrollment (n = 19), this ratio was 0.82 (95% CI 0.69–0.97), being similar to the results when including them.

DISCUSSION

We observed a negative linear dose–response relationship between the frequency of structured combined aerobic and resistance training and the incidence of type 2 diabetes in Japanese women practicing a combined training program of fixed intensity and duration. We further analyzed these results after stratification by BMI and circumference of the thigh (indicator of muscle mass), which have been suggested as possible modifications of the relationship. A similar negative linear relationship between the frequency of combined exercise training and incidence of type 2 diabetes was observed in the lower BMI and thigh circumference groups. Therefore, it is likely that the preventive effect on type 2 diabetes of the combined exercise training is to some extent mediated through increases in muscle mass.

The results of the present study support the results of previous observational studies. Grøntved *et al.* reported that resistance training might delay and/or prevent the incidence of type 2 diabetes based on their studies involving American health professionals as study participants, and it was increased in both studies if the training included aerobic exercise in addition to resistance training[6,7]. In their first study following male American medical professionals, the group that practiced resistance training for longer duration per week had a lower risk of developing type 2 diabetes[7]. In addition, they reported that a group practicing an aerobic activity for ≥150 min/week had a lower relative risk than a group practicing only resistance training. In their second study following female American nurses, they also reported that a group practicing aerobic activity for ≥150 min/week had a lower relative risk of developing diabetes than a group practicing only resistance training[6].

Table 2 | Hazard ratios of the incidence of type 2 diabetes by the frequency of combined training from the Curves Japan Study (2005–2014)

Variable	Q_1 (lowest) (n = 2,716)	Q_2 (n = 2,812)	Q_3 (n = 2,610)	Q_4 (highest) (n = 2,542)	Per 4 times/month Increase	P linearity
No. cases (n)	48	49	36	33		
Women-years of follow up	15,117	15,813	14,711	14,210		
Case per 10,000 women-years (n)	32	31	24	23		
Age-adjusted HR (95% CI)	1.00 (reference)	0.95 (0.64–1.41)	0.73 (0.48–1.13)	0.69 (0.44–1.07)	0.88 (0.75–1.03)	0.116
Multivariable-adjusted HR (95% CI)†	1.00 (reference)	0.84 (0.56–1.26)	0.69 (0.45–1.06)	0.61 (0.39–0.95)	0.84 (0.72–0.99)	0.040

†Adjusted for age, body mass index and thigh circumference. CI, confidence interval; HR, hazard ratio; Q, quartile.

Table 3 | Hazard ratios of the incidence of type 2 diabetes by frequency of combined training in analysis stratified by body mass index and thigh circumference from the Curves Japan Study (2005–2014)

Variable	Q_1 (lowest)	Q_2	Q_3	Q_4 (highest)	Per 4 times/month Increase	P linearity
Lower body mass index (median <22.7 kg/m²)	(n = 1,390)	(n = 1,343)	(n = 1,290)	(n = 1,317)		
Case per 10,000 women-years (n)	21	18	10	7		
Multivariable-adjusted HR (95% CI)†	1.00 (Reference)	0.80 (0.39–1.65)	0.45 (0.18–1.09)	0.29 (0.10–0.79)	0.59 (0.41–0.84)	0.003
Higher body mass index (median ≥22.7 kg/m²)	(n = 1,368)	(n = 1,321)	(n = 1,326)	(n = 1,325)		
Case per 10,000 women-years (n)	45	45	39	38		
Multivariable-adjusted HR (95% CI)†	1.00 (Reference)	0.88 (0.54–1.44)	0.83 (0.50–1.36)	0.77 (0.47–1.27)	0.93 (0.77–1.11)	0.412
Lower thigh circumference (<median 52.3 cm)	(n = 1,339)	(n = 1,440)	(n = 1,270)	(n = 1,291)		
Case per 10,000 women-years (n)	34	33	24	19		
Multivariable-adjusted HR (95% CI)†	1.00 (Reference)	0.85 (0.49–1.47)	0.52 (0.28–1.00)	0.44 (0.23–0.87)	0.73 (0.57–0.94)	0.013
Higher thigh circumference (median ≥52.3 cm)	(n = 1,421)	(n = 1,330)	(n = 1,261)	(n = 1,328)		
Case per 10,000 women-years (n)	27	31	26	26		
Multivariable-adjusted HR (95% CI)†	1.00 (Reference)	1.04 (0.58–1.86)	0.88 (0.47–1.62)	0.81 (0.44–1.49)	0.95 (0.76–1.18)	0.630

†Adjusted for age, body mass index and thigh circumference. CI, confidence interval; HR, hazard ratio; Q, quartile.

It is likely that combined aerobic and resistance training simultaneously provides the individual effects unique to aerobic exercise and resistance training, respectively. Insulin-mediated blood glucose uptake occurs mainly in skeletal muscles[12]. Resistance training facilitates glycemic control by increasing muscle mass, which incorporates blood glucose and thus might delay and/or prevent development of type 2 diabetes[13]. The magnitude of the negative dose–response relationship between the frequency of combined exercise training and incidence of type 2 diabetes was greater in the lower BMI group (median <22.7 kg/m²) than in the higher BMI group (median ≥22.7 kg/m²).

The present study measured the circumference of the thigh as an index for muscle mass. Similar to the observation in the lower BMI group at the start of the training, the magnitude of the negative dose–response relationship was greater in the lower thigh circumference group (median <52.3 cm) as well. However, the training had no clear effect on the higher thigh circumference groups (median ≥52.3 cm). On the basis of the more pronounced negative dose–response relationships observed in the lower thigh circumference and BMI groups, it is possible that the structured combined aerobic and resistance training increased muscle mass to a greater extent in the group with less muscle mass at baseline as compared with the group with greater muscle mass at baseline, which might consequently delay and/or prevent development of type 2 diabetes.

Aerobic exercise might delay and/or prevent the development of type 2 diabetes by improving insulin resistance through modification of muscle quality, including reduction of adiposity and increase of glucose transporter type 4 in muscle cells[13–15]. In the present study, we observed a negative dose–response relationship between the frequency of combined exercise training and the incidence of type 2 diabetes in the higher BMI group; however, this dose–response relationship was much stronger in the lower BMI group (Table 3). This indicates that the influence of the insulin resistance effect, in terms of adiposity reduction, might be relatively low, because the study participants were originally a group with lower BMI (23.2 kg/m^2). Alternatively, it might have been difficult to obtain the desired effect from the aerobic exercise in the combined exercise training used by the fitness facility to which the study participants belonged, because this aerobic exercise, stepping on a step board practiced between resistance training, is a low-volume aerobic exercise.

To our knowledge, this is the first study that assessed the relationship between combined aerobic and resistance training and the incidence of type 2 diabetes. The present study is unique in that all study participants practiced the same supervised structured combined aerobic and resistance training. In addition, data regarding the frequency of the combined exercise training were objectively and accurately obtained, which makes information bias unlikely. The present study had several limitations. First, no adjustment for smoking, drinking, family history of diabetes and diet, which have been reported to be risk factors for the development of type 2 diabetes in previous studies, was carried out in the present study. Therefore, these factors might have confounded the results of this study. However, previous similar cohort studies showed the impact of these potential confounding factors, such as smoking, drinking and family history of diabetes, on the relationship between physical activity and incidence of diabetes as constrictive[16,17]. Hence, these potential confounding factors do not dramatically change the present study results.

Second, assessment of diabetes was based on a self-administered questionnaire. We did not confirm the validity of the questionnaire regarding diabetes status. However, a previous study showed that 94% of self-reported diabetes in participants sampled from Japanese middle-aged men and women were consistent with medical records[18].

Third, the frequency of combined exercise carried out in facilities other than the study facility was not considered, because exercise frequency in the present study was defined as the frequency of use of the study fitness facility. Although the study participants might be practicing leisure-time physical activities in other places than the study fitness facility, this definition allowed accurate reporting on their practice frequency and activity level.

Fourth, because this was a retrospective cohort study carried out with Japanese women who belonged to a specific fitness facility, they might be of high socioeconomic status, good compliance and a high level of cultural education. Hence, generalization of the results of the present study requires care. In addition, it is unclear how generalizable this study is to other ethnic groups, as these Japanese women had lower BMI compared with Western populations. Similarly, we were not able to consider the influence of dropout during the follow-up period, and had the limitation of representativeness.

Fifth, we did not have information on whether participants had a medical check-up periodically during the follow-up period. However, we speculate that there is no strong relationship between training frequency and the chance of hospital diagnosis. If there is a bias, the bias results in the underestimation of the relationship between the frequency of training and the incidence of diabetes. This is due to the point that women who have a high frequency of training tend to have a high frequency of visiting a hospital.

Finally, this was an observational study. It is necessary to carry out randomized controlled trials involving participants without diabetes to clarify whether a combined aerobic and resistance training reduces the risk of development of type 2 diabetes.

In conclusion, we observed a negative linear dose–response relationship between the frequency of combined exercise training and the incidence of type 2 diabetes in Japanese women, which included just a few individuals with BMIs in the obese range. However, no clear negative relationship was observed in individuals who at baseline were retaining muscle mass to some extent. Thus, habitual combined exercises are likely to be an effective primary preventive measure for type 2 diabetes among those with a relatively lower muscle mass. Additional studies regarding combined aerobic and resistance training should be carried out for the prevention of type 2 diabetes, the incidence of which is greatly increasing in the world.

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DISCLOSURE

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