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Brief report

Phosphorus ingestion with a high-carbohydrate meal increased the postprandial energy expenditure of obese and lean individuals

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ABSTRACT

Objectives: Phosphorus ingestion with glucose was reported to stimulate the postprandial peripheral uptake of both phosphorus and glucose, a process that favors energy production. The aim of this study was to determine whether phosphorus ingestion with a meal can affect energy metabolism.
Methods: Overnight fasted men (eight lean and seven obese) consumed a high-carbohydrate meal (648 kcal) with either placebo or phosphorus (500 mg) tablets in a random order. Energy expenditure and substrate oxidation were monitored for 240 min using ventilated hood indirect calorimetry.
Results: Phosphorus ingestion with a meal increased the postprandial energy expenditure of both lean and obese individuals ($P < 0.001$), although in different patterns. Alterations in postprandial substrate oxidation was highly noticeable from time 120 min onward, where phosphorus-treated lean participants exhibited a significant decrease in respiratory quotient.
Conclusion: Phosphorus ingestion with a high-carbohydrate meal alters postprandial energy metabolism mainly by enhancing postprandial energy expenditure that may ultimatly favor weight loss.

Introduction

Obesity is associated with the consumption of refined carbohydrates [1] that are depleted of micronutrients [2], especially phosphorus. Phosphorus is essential for the phosphorylation and synthesis of many compounds, including adenosine triphosphate. Intracellular trapping of glucose, which is required for energy production, is attained through its phosphorylation and this was clearly evident after phosphorus coingestion with glucose [3]. Intake of phosphorus-containing supplements after a meal [4] or with orange juice [5] was reported to increase the resting metabolic rate of obese women. In addition, we recently found that phosphorus supplementation (3 mo) was able to improve body weight and waist circumference of individuals who were overweight and obese [6].

Postprandial energy metabolism that comprises energy expenditure and substrate oxidation is a vital component of energy balance especially because ~50% of a normal person's time is spent in postprandial condition [7]. The contribution of postprandial energy expenditure (PEE), also known as thermic effect of feeding, to total energy expenditure fluctuates between 2% and 20% [8], and this was reported to be affected by several factors including type of macronutrients, micronutrients, obesity, and insulin sensitivity [9]. However, differences in PEE between lean and obese individuals are not well established, alhough obesity was frequently shown to blunt PEE, an effect that seems to be reversed by weight loss [9].

The fact that phosphorus content of a meal affects postprandial phosphorus status [3] has incited us to examine the effect that phosphorus ingestion with a meal has on postprandial energy metabolism. Thus, the aim of the present study was to determine the effect phosphorus ingestion with a refined carbohydrate meal has on postprandial energy metabolism of both lean and obese individuals.

Materials and methods

A randomized, blinded crossover study with eight lean and seven obese men aged between 20 and 29 y was conducted. The study was approved by the University Institutional Review Board and registered at ClinicalTrial.gov. Participants were asked to stop all nutritional supplements, avoid intense exercise for 3 d before providing fasting blood samples for baseline characteristics, or attending experimental sessions that were 1 wk apart. During each experimental session (placebo or phosphorus), overnight-fasted participants arrived at the laboratory at 0800, anthropometric measurements were taken and the men were asked to relax for 30 min in a semiupright sitting position (45 degrees). Energy metabolism

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measurements (PEE; percentages of carbohydrate and fat oxidations [%CO and %FO, respectively]) were then taken for 30 min before meal ingestion and for 4 h after meal ingestion, covering the main absorptive state of metabolism. Measurement was done using indirect calorimetric unit with canopy [10] (Cosmed Quark CPET Unit, Cosmed Group, Erie, PA, USA), which is known to be of high reability [11] and was calibrated according to that of Carrière et al. [10]. Oxidation of carbohydrate and fat was calculated based on the following equations of Frayn [12]:

$$C = 4.55\ VCO_2(L/min) - 3.21\ VO_2 - 2.87\ n;$$

$$f = 1.67\ VO_2(L/min) - 1.67\ VCO_2 - 1.92\ n$$

where c and f are the amounts (g) of carbohydrate and fat oxidized per minute, respectively, and n, the amount (g) of urinary nitrogen excreted per minute was assumed to be 13 g/min as per Carrière et al. Respiratory quotient (RQ) was calculated according to the Weir [13] equation

$$RQ = VCO_2/VO_2$$

A 648 kcal meal composed of white bread, strawberry jam, butter, and orange juice (energy: 59.3% carbohydrate, 36.7% fat, 2.2% protein, and 131 mg phosphorus; ~0.2 mg/kcal phosphorus) with either four placebo or four phosphorus tablets (125 mg of phosphorus/tablet as potassium phosphate; ~1 mg/kcal phosphorus) consumed within 15 min and measurements were recorded at intervals of 15 min with a 15-min break between each measurement. The tablets (phosphorus and placebo) were manufactured and analyzed by NutraScience (New York, NY, USA).

Statistical analysis

A sample size of seven men was determined by the application of power analysis to detect a 5% difference in the mean, with SD of 3.3% for the population, at 0.05 significance level and a desired statistical power of 80% [10]. Data were presented as mean ± SE and metabolic measurements were expressed as the changes from baseline values. General linear model (GLM) with time as random effect was performed to determine the effect of time, phosphorus, adiposity (lean of body mass index [BMI] between 20 and 24.9 kg/m^2 or obese of BMI of ≥30 kg/m^2), and their interactions. The level of statistical significance was set at $P < 0.05$.

Results

Participants in both experimental groups were of similar age and all had normal and similar fasting blood glucose, creatinine, and glomerular filtration rate values. In addition, baseline values of %CO and %FO and RQ were similar between the groups. As expected BMI, waist circumference, and baseline energy expenditure were significantly greater in obese than in lean individuals (Table 1).

In both groups, PEE increased after meal consumption, achieved its peak at 60 to 120 min, and then progressively decreased without returning to baseline levels within the experimental time, whereas obese participants showed a ramp at 150 min postconsumption. Changes in PEE were statistically significant according to time ($P < 0.05$) and phosphorus ingestion with meals was found to significantly increase PEE ($P < 0.01$). Changes in PEE were significantly different according to adiposity ($P < 0.05$); changes of phosphorus-treated obese individuals were slightly higher than those of lean participants before the 120 min mark (Fig. 1A).

The magnitude of changes in %CO (Fig. 1B) and %FO (Fig. 1C) was small during the first 120 min postconsumption and gradually amplified thereafter. During this period, %CO increased ($P < 0.001$) and %FO decreased ($P < 0.001$) with time. In addition, phosphorus ingestion with the meal was found to significantly increase %CO ($P < 0.01$) and decrease in %FO ($P < 0.05$), and %FO showed significance according to adiposity; lean men had higher %FO than their obese counterparts ($P < 0.05$). It is worth noting that changes in %CO and %FO were highly evident in the phosphorus-treated lean participants from the 150 min mark onward compared with other groups.

Changes in RQ (Fig. 1D), the ratio of carbon dioxide produced to oxygen consumed, were almost stable in the first 120 min and decreased gradually thereafter, indicating an increase in the contribution of %FO to total energy expenditure. The changes in RQ were statistically significant according to time ($P < 0.01$), interaction between time and adiposity ($P < 0.01$), and interaction between phosphorus and adiposity ($P < 0.001$), which further shows that only lean participants were highly affected by phosphorus ingestion.

Table 1
Baseline characteristics of lean and obese participants

Characteristics	Lean (n = 8)	Obese (n = 7)
Age (y)	23.50 ± 1.38	22.71 ± 1.19
BMI (kg/m^2)	23.23 ± 0.51	35.18 ± 0.97*
Waist circumference (cm)	93.88 ± 2.04	118.93 ± 3.54*
Fasting blood glucose (mg/dL)[a]	94.25 ± 2.70	93.57 ± 3.77
Creatinine (mg/dL)[b]	0.925 ± 0.059	0.914 ± 0.034
Glomerular filtration rate (mL/min/1.73 m^2)[c]	111.38 ± 5.90	115.86 ± 3.79
Baseline resting energy expenditure (kcal/d)[†]	1668.4 ± 132.8	2138.1 ± 95.6*
Baseline carbohydrate oxidation (%)[†]	30.74 ± 6.48	33.21 ± 6.11
Baseline fat oxidation (%)[†]	52.74 ± 6.72	54.29 ± 6.92
Respiratory quotient[†]	0.821 ± 0.030	0.810 ± 0.025

BMI, boy mass index.
*Shows significant difference between lean and obese participants.
[†]Baseline metabolic measurements are the average of the two visits. Variables are expressed as mean ± SE
[a]: Roche hexokinase assay using Cobas C501 analyzer.
[b]: Roche enzymatic assay using Cobas C501 analyzer.
[a]: Using Levey *et al.* (2009) equation. Ann Intern Med. 150(9):604–12.

Discussion

The findings from the present study confirm that exogenous phosphorus is involved in PEE [4,5,14] of both lean and obese individuals. The mechanism(s) by which phosphorus ingestion with meal increased or extended PEE may relate to improved availability of bodily phosphorus [3]. The observed varied pattern of changes in PEE between lean and obese participants implies that a prolonged period of metabolic measurements is required to better understand the effects of phosphorus. According to Jaedig et al. (1994), the short PEE monitoring (60 min only) of phosphorus-supplemented orange juice (100 mL, 10 g carbohydrate) consumption may explain the reported difference between lean and obese individuals [5].

Postprandial energy metabolism appears to be comprised of two phases (phase 1: 0–120 min and phase 2: 120–240 min) that seem to coincide with the absorptive and postabsorptive states, respectively. In phase 1, the changes in substrate oxidation were modest and were similar between groups and treatments. In contrast, large changes in PEE were identified and phosphorus-treated obese participants maintained higher PEE values. Such increases may have been partially attributed to an increase in intestinal protein synthesis, especially as phosphorus was reported to increase the levels of ApoB48 level [15].

In phase 2, PEE was associated with a gradual decrease in RQ indicating a shift toward an increase in fat utilization that was highest among the phosphorus-treated lean participants. The mechanism(s) behind this observation may relate to the capacity of phosphorus to enhance insulin sensitivity, from the mid-postprandial time [3], which is known to stimulate the energy-requiring processes [16,17] of glycogen [18] and protein syntheses. The inability of phosphorus to alter substrate oxidation or RQ of obese individuals may be due to its incapability to substantially affect insulin sensitivity especially as obese individuals are known to have high levels of insulin (insulin resistance) [8] that favors lipogenesis rather than %FO. This condition may have been aggravated by the extensive utilization of phosphorus in phase 1.

Although small, the increment of PEE with phosphorus supplemetation has a tremedous long-term physiological relevance. Phosphorus was able to increase PEE on average by 0.06 kcal/min, which is equivalent to ~50 kcal/d (1500 kcal/mo), assuming that

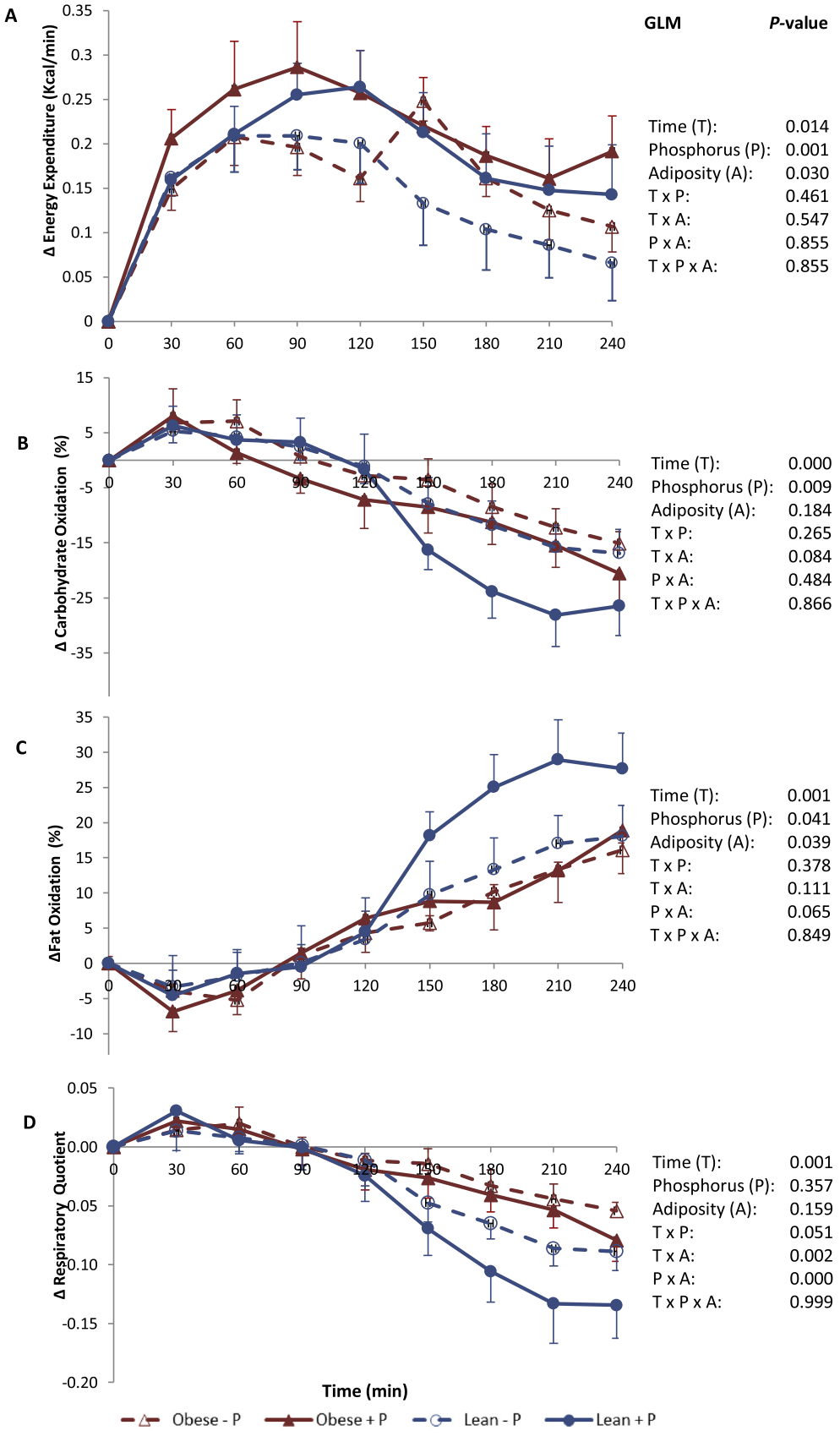

Fig. 1. Changes in postprandial energy expenditure (**A**), carbohydrate oxidation (%) (**B**), fFat oxidation (%) (**C**) and respiratory quotient (**D**) of lean and obese men. Empty circles and dashed lines (): lean participants consumed meal with placebo. Full circles with full lines: lean participants consumed meal with phosphorus. Empty triangles and dashed lines: obese participants consumed meal with placebo. Full triangles and full lines: obese participants consumed meal with phosphorus.

the individual stays in the postprandial phase 50% of the day. This concept was supported by a recent case–control study in which participants suppplemented with phosphorus had lower BMI and waist circumference than a control group [6].

Findings from the present study implicated phosphorus in energy metabolism due to its ability to alter substrate oxidation and amplify PEE. Furthermore, phosphorus may contribute to satiation and appetite suppression, which were reported to be positively associated with PEE [4,5,14,19,20]. Previous empirical results showed that consumption of phosphorus-rich foods, including dairy products [21] and meats, are associated with an increase in PEE [19,22] and a decrease in body weight [23]. In contrast, consumption of refined carbohydrates [1] that are poor sources of micronutrients [2] such as phosphorus are associated with obesity.

We believe that these findings are of potential importance as phosphorus intake has been shown to have been dramatically decreased over the past few decades as a result of "food modernization." Data in the literature reporting high phosphorus intake among populations [24,25] build their interpretations on the recommended daily allowances (RDA) that require scrutiny as they are based on the lower edge of the normal adult serum inorganic phosphate and not on the median [26,27]. In addition, plasma phosphorus, which was reported to be associated with morbidity and mortality, is shown to be a poor indicator of phosphorus intake [28,29]; thus health problems may be related to a defect in phosphorus handling. However, association of diseases with intake [29,30] are affected by many factors including dietary patterns, energy intake, and source of phosphorus. For example, association outcomes of meat intake are likely to be confounded by the fact that meat is a good source of both phosphorus and heme iron and the latter was reported to be associated with risk for cardiovascular diseases [31].

On the other hand, the ability of phosphorus to affect postprandial energy metabolism, especially energy expenditure, may help in elucidating the inconsistencies in diet-induced thermogenesis among various experiments [5,14].

The study was performed on men to limit the possible hormonal effects on energy metabolism. The meal was designed to mimic typical a breakfast. Hormones and metabolites were not simultaneously monitored to avoid the stress effect of blood sampling. Measurements of certain metabolic changes were limited to 4 h postmeal consumption; a clearer picture would have been provided if participants were followed for a longer period of time.

Conclusion

The addition of phosphorus to a meal led to an increase of PEE in both lean and obese individuals and to a decrease in RQ of lean participants. This reveals a potential role for dietary phosphorus in energy balance, which contributes to better weight management.

References

[1] Drewnowski A, Specter S. Poverty and obesity: the role of energy density and energy costs. Am J Clin Nutr 2004;79:6–16.
[2] Reddy MB, Love M. The impact of food processing on the nutritional quality of vitamins and minerals. Impact of processing on food safety. 1999: 99–106.
[3] Khattab M, Abi-Rashed C, Ghattas H, Hlais S, Obeid O. Phosphorus ingestion improves oral glucose tolerance of healthy male subjects: Aa crossover experiment. Nutr J 2015;14:1.
[4] Kaciuba-Uściłko H, Nazar K, Chwalbińska-Moneta J, Ziemba A, Kruk B, Szczepanik J, et al. Effect of phosphate supplementation on metabolic and neuroendocrine responses to exercise and oral glucose load in obese women during weight reduction. Journal of J Physiol Pharmacol 1993;44:425–40.
[5] Jaedig S, Lindgärde F, Arborelius M. Increased postprandial energy expenditure in obese women after peroral K-and Mg-phosphate. Miner Electrolyte Metab 1994;20:147–52.
[6] Ayoub J, Samra M, Hlais S, Bassil M, Obeid O. Effect of phosphorus supplementation on weight gain and waist circumference of overweight/obese adults: a randomized clinical trial. Nutr Diabetes 2015;5:e189.
[7] Freckmann G, Hagenlocher S, Baumstark A, Jendrike N, Gillen RC, Rössner K, et al. Continuous glucose profiles in healthy subjects under everyday life conditions and after different meals. J Diabetes Sci Tech 2007;1:695–703.
[8] Tentolouris N, Pavlatos S, Kokkinos A, Perrea D, Pagoni S, Katsilambros N. Diet-induced thermogenesis and substrate oxidation are not different between lean and obese women after two different isocaloric meals, one rich in protein and one rich in fat. Metabolism 2008;57:313–20.
[9] Thörne A, Hallberg D, Wahren J. Meal–induced thermogenesis in obese patients before and after weight reduction. Clin Physiol 1989;9:481–98.
[10] Charrière N, Montani J-P, Dulloo AG. Postprandial thermogenesis and respiratory quotient in response to galactose: comparison with glucose and fructose in healthy young adults. J Nutr Sci 2016;5.
[11] Ashcraft CM, Frankenfield DC. Validity test of a new open-circuit indirect calorimeter. JPEN J Parenter Enteral Nutr 2015;39:738–42.
[12] Frayn K. Calculation of substrate oxidation rates in vivo from gaseous exchange. J Appl Physiol 1983;55:628–34.
[13] JdV Weir. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949;109:1–9.
[14] Jaedig S, Henningsen N. Increased metabolic rate in obese women after ingestion of potassium, magnesium-and phosphate-enriched orange juice or injection of ephedrine. Int J Obes 1991;15:429–36.
[15] Hazim J, Hlais S, Ghattas H, Shatila D, Bassil M, Obeid O. Phosphorus supplement alters postprandial lipemia of healthy male subjects: a pilot cross-over trial. Lipids Health Dis 2014;13:109.
[16] Hettleman B, Sabina R, Drezner M, Holmes E, Swain J. Defective adenosine triphosphate synthesis. An explanation for skeletal muscle dysfunction in phosphate-deficient mice. J Clin Invest 1983;72:582.
[17] Fischbeck KH. Effects of ATP depletion and protein synthesis inhibition on muscle plasma membrane orthogonal arrays. Exper Neurol 1984;83:577–88.
[18] Wensheng X, Tran TL, Finegood DT, Van De Werve G. Dietary Pi deprivation in rats affects liver CAMP, glycogen, key steps of gluconeogenesis and glucose production. Biochem J 2000;352:227–32.
[19] Crovetti R, Porrini M, Santangelo A, Testolin G. The influence of thermic effect of food on satiety. Eur J Clin Nutr 1998;52:482–8.
[20] Obeid O, Dimachkie S, Hlais S. Increased phosphorus content of preload suppresses ad libitum energy intake at subsequent meal. Int J Obes 2010;34:1446–8.
[21] Mirmiran P, Esmaillzadeh A, Azizi F. Dairy consumption and body mass index: an inverse relationship. Int J Obes 2005;29:115–21.
[22] Westerterp KR. Diet induced thermogenesis. Nutr Metab 2004;1:1.
[23] Halton TL, Hu FB. The effects of high protein diets on thermogenesis, satiety and weight loss: A critical review. J Am Coll Nutr 2004;23:373–85.
[24] Anderson JJ. Potential health concerns of dietary phosphorus: Cancer, obesity, and hypertension. Ann N Y Acad Sci 2013;1301:1–8.
[25] Calvo MS, Uribarri J. Public health impact of dietary phosphorus excess on bone and cardiovascular health in the general population. Am J Clin Nutr 2013. ajcn. 053934.
[26] National Institutes of Health. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D and fluoride. Washington DC: National Academies Press; 1997.
[27] Obeid O. Low phosphorus status might contribute to the onset of obesity. Obes Rev 2013;14:659–64.
[28] de Boer IH RueTC, Kestenbaum B. Serum phosphorus concentrations in the third National Health and Nutrition Examination Survey (NHANES III). Am J Kidney Dis 2009;53:399–407.
[29] Chang AR, Lazo M, Appel LJ, Gutiérrez OM, Grams ME. High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III. Am J Clin Nutr 2014;99:320–7.
[30] Mancini FR, Affret A, Dow C, Balkau B, Clavel-Chapelon F, Bonnet F, et al. High dietary phosphorus intake is associated with an increased risk of type 2 diabetes in the large prospective E3 N cohort study. Clin Nutr 2017.
[31] Fang X, An P, Wang H, Wang X, Shen X, Li X, et al. Dietary intake of heme iron and risk of cardiovascular disease: a dose–response meta-analysis of prospective cohort studies. Nutr Metab Cardiovasc Dis 2015;25:24–35.