Whole Grain Compared with Refined Wheat Decreases the Percentage of Body Fat Following a 12-Week, Energy-Restricted Dietary Intervention in Postmenopausal Women1–4

Mette Kristensen,5,6 Søren Toubro,6 Morten Georg Jensen,5 Alastair B. Ross,8 Giancarlo Riboldi,9 Michela Petronio,7 Susanne Bügel,5 Inge Tetens,7 and Arne Astrup5

5Department of Human Nutrition, University of Copenhagen, Denmark; 6Reduce-Research Clinic of Human Nutrition, Roskilde, Denmark; 7Department of Nutrition, National Food Institute, Danish Technical University, Lyngby, Denmark; 8Department of Bioanalytical Sciences, Nestle Research Centre, Lausanne, Switzerland; and 9Barilla, Parma, Italy

Abstract

Observational studies show inverse associations between intake of whole grain and adiposity and cardiovascular risk; however, only a few dietary intervention trials have investigated the effect of whole-grain consumption on health outcomes. We studied the effect of replacing refined wheat (RW) with whole-grain wheat (WW) for 12 wk on body weight and composition after a 2-wk run-in period of consumption of RW-containing food intake. In this open-label randomized trial, 79 overweight or obese postmenopausal women were randomized to an energy-restricted diet (deficit of $\sim$1250 kJ/d) with RW or WW foods providing 2 MJ/d. Body weight and composition, blood pressure, and concentration of circulating risk markers were measured at wk 0, 6, and 12. Fecal output and energy excretion were assessed during run-in and wk 12. Plasma alkyresorcinol analysis indicated good compliance with the intervention diets. Body weight decreased significantly from baseline in both the RW ($-2.7 \pm 1.9$ kg) and WW ($-3.6 \pm 3.2$ kg) groups, but the decreases did not differ between the groups ($P = 0.11$). The reduction in body fat percentage was greater in the WW group ($-3.0\%$) than in the RW group ($-2.1\%$) ($P = 0.04$). Serum total and LDL cholesterol increased by $-5\%$ ($P < 0.01$) in the RW group but did not change in the WW group; hence, the changes differed between the groups ($P = 0.02$). In conclusion, consumption of whole-grain products resulted in a greater reduction in the percentage fat mass, whereas body weight changes did not differ between the RW and WW groups. Serum total and LDL cholesterol, two important risk factors of cardiovascular disease, increased with RW but not WW consumption, which may suggest a cardioprotective role for whole grain. J. Nutr. 142: 710–716, 2012.

Introduction

Observational studies strongly indicate an inverse association between a high intake of whole-grain products and adiposity (1) or risk of body weight gain (2–4) as well as comorbidities such as CVD11 (5). Whole-grain cereals consist of the intact, ground, cracked, or flaked caryopsis, where the starchy endosperm, germ, and bran are present in the same relative proportions as in the intact caryopsis (6). In contrast to refined grain products comprising mainly the endosperm, whole-grain foods are rich in a number of vitamins, minerals, dietary fibers, and phytochemicals, which are proposed to be responsible for the health-promoting effects (7,8). In some studies, a beneficial effect of whole grain has been found on LDL cholesterol, but not HDL cholesterol or TG, an effect often attributed to viscous dietary fibers, such as oat β-glucans (9,10). Also, the higher concentration of dietary fiber and lower energy density of whole-grain foods are hypothesized to lead to reduced energy intake and loss of weight and FM. WW, the primary source of whole grain in many Western countries, is high in nonviscous dietary fibers. These are known to exert physiological effects in the large intestine where they are partly fermented and induce bulking (11). Some, although not all (14), single meal studies have also demonstrated that intake of WW products and wheat bran induce satiety (12,13), an effect often attributed to soluble viscous dietary fibers (15). Furthermore, dietary fibers, including wheat dietary fibers, may increase
fetal losses of fat and energy (16), which may also contribute to a negative energy balance. Only a few dietary interventions studied the effect of consuming high amounts of either mixed or WW foods on body weight and composition and reported conflicting results, possibly related to variations in study design, the population, and intervention foods investigated (10,17–22). Three studies focused on the role of whole grain as part of an energy-restricted diet (21–23); none reported a significantly greater body weight loss compared to control, but Katcher et al. (22) found an effect on abdominal FM independent of weight loss after 4–7 daily servings of mixed whole-grain foods for 12 wk compared to control. This study was carried out in the US, where the average consumption of whole-grain foods is low, i.e., 0.75 servings or ~12 g/d (4). Whole grain is more frequently consumed in Denmark, where the median intake is estimated to be ~30 g/d (24), and the efficacy of a whole-grain intervention may depend on habitual consumption. Thus, our objective was to compare the effect of a high intake of WW vs. RW foods on body weight and composition in Danish postmenopausal women. Secondary endpoints were cardiovascular risk markers, insulin sensitivity, dietary intake, and fecal energy excretion. Finally, AR was included as a marker of compliance.

Participants and Methods

Study design. This study was an open-label parallel intervention of 14-wk duration in which the participants were randomly allocated to intake of RW or WW foods for 12 wk after a 2-wk run-in period, during which all participants were provided with RW foods.

Participants. A total of 153 women were assessed for eligibility following advertising in the local papers in the Copenhagen area. Of these, 85 overweight and obese women were enrolled in the study; 79 were randomized after the run-in period, and a total of 72 women completed the study (38 in the WW and 34 in the RW group) (Supplemental Fig. 1). There was no difference in any of the baseline characteristics. Inclusion criteria were: BMI, 27–37 kg/m², age, 45–70 y, and >1 y postmenopausal (self-reported). Exclusion criteria were: smoking, chronic illnesses (diabetes or CVD), untreated hypertension (>160/100 mm Hg), elevated fasting total cholesterol (>6.5 mmol/L) or glucose (>7.0 mmol/L), use of dietary supplements, food dislikes or intolerances relevant to the study, and use of medications (except antihypertensives). All participants attended a screening visit before enrollment, where weight, height, waist circumference, blood pressure, and fasting glucose and total cholesterol concentrations were measured. Also, they were interviewed to assess eligibility for enrollment. All participants gave written consent after receiving verbal and written information about the study, which was approved by the Ethical Committee of the Capital Region of Denmark in accordance with the Declaration of Helsinki (KF 01 290502).

Intervention foods. The intervention foods were intended to replace ~2 Mj of the study participants’ habitual diet. All participants received the same amount of foods per day independent of ER and were instructed to consume 62 g of bread (fresh weight, 66% DM), 60 g pasta (uncooked, 89% DM), and 28 g biscuits (fresh weight, 98% DM) daily (Table 1). Breads and biscuits were made from common wheat specifically for this project, whereas both pastas were the commercially available type made from durum wheat. The whole-grain foods used were defined as containing a minimum of 50% of whole grain per DM, including the starchy endosperm, germ, and bran, in milled form. The WW foods provided 105 g of whole grains daily. There was no restriction on consumption of other cereal products. The participants collected their intervention foods biweekly.

Weight loss program. The participants followed a slightly energy-restricted diet based on their habitual choice of food items (apart from the intervention foods) to aid weight loss. The weight loss program was based on an educational system consisting of five color-coded, isoenergetic interchangeable units of 250 kJ representing different nutrients (protein-rich, complex carbohydrate-rich, simple carbohydrate-rich, fat-rich, and alcohol). The participants were instructed to adhere to a diet with a deficit of at least 1250 kJ/d, but not less than 3500 kJ/d. Also, they were instructed to have a minimum intake of protein of 60 g/d. ER was calculated as follows (25):

For participants ≤60 y: ER = 1.3 × (0.0364 × weight + 3.47).
For participants >60 y: ER = 1.3 × (0.0364 × weight + 2.88).

The participants met with a dietician five times during the study and were instructed to keep a food diary that included count of total units, number of color-coded units, and units of intervention foods consumed on a daily basis throughout the study. The ER was recalculated by the dietician at each visit and the recommended number of units adjusted accordingly.

Anthropometric measures. All measurements were performed in the morning after ≥10 h fasting. Body weight was measured on an electronic scale while the participants were wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm by using a wall-mounted stadiometer without shoes. Waist circumference was measured to the nearest 0.5 cm at the narrowest point between the iliac crest and the lowest rib. Body composition was measured by DXA scanning (Lunar Radiation) and FFM was calculated as total body mass – FM.

Laboratory procedures. Blood pressure was measured twice with the use of a fully automatic blood pressure monitor (Omron M4-I; Omron Healthcare Europe). Participants who used antihypertensive medication were instructed to take their medication as usual even when fasting. Fasted blood samples were collected at wk 0, 6, and 12 and stored at –20°C until analyzed in one batch. All fecal samples were collected in preweighed plastic containers for 48 h during wk 2 of the run-in period and during wk 12 of the intervention period. Participants kept the plastic containers in a cooled box and brought them to the department daily. Samples were weighed and homogenized 1:1 with distilled water, the pH was measured (Lutron PH-208, Heatmister), and 20 g of each sample was freeze-dried and homogenized and samples from each participants’ 48 h collection were pooled.

Analytical procedures. Plasma concentrations of glucose and serum concentrations of TG, and total, HDL, and LDL cholesterol and insulin were measured as described elsewhere (26). HOMA index of insulin resistance and β cell function were calculated (27). Serum hsCRP was measured by a solid-phase chemiluminescent immunometric assay using an IMMULITE 1000 Automated Immunoassay Analyzer. Plasma IL-6 was measured as described elsewhere (26). IL-6 concentration was determined by using a solid-phase chemiluminescent method using the IMMULITE 1000 automated analyzer (Diagnostic Products). Plasma concentrations of serum IL-6 were measured by using a solid-phase chemiluminescent immunometric assay (Lumo-Tracks Chemiluminescent Immunoassay System, Diagnostic Products). Plasma concentrations of serum IL-6 were measured by using a solid-phase chemiluminescent immunometric assay (Lumo-Tracks Chemiluminescent Immunoassay System, Diagnostic Products).

### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>RW</th>
<th>WW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole grain, g/d</td>
<td>0</td>
<td>105</td>
</tr>
<tr>
<td>Energy, MJ/d</td>
<td>2.07</td>
<td>1.99</td>
</tr>
<tr>
<td>Carbohydrates, g/d</td>
<td>95.8</td>
<td>86.8</td>
</tr>
<tr>
<td>Sugars, g/d</td>
<td>11.5</td>
<td>11.8</td>
</tr>
<tr>
<td>Fat, g/d</td>
<td>6.6</td>
<td>6.8</td>
</tr>
<tr>
<td>Protein, g/d</td>
<td>16.0</td>
<td>16.6</td>
</tr>
<tr>
<td>Dietary fibers, g/d</td>
<td>4.5</td>
<td>11.0</td>
</tr>
<tr>
<td>Fiber, g/d</td>
<td>22.8</td>
<td>28.5</td>
</tr>
<tr>
<td>Total tocots, mg/d</td>
<td>3.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Folic acid, mg/d</td>
<td>11.4</td>
<td>34.0</td>
</tr>
<tr>
<td>AR, mg/d</td>
<td>3.1</td>
<td>25.5</td>
</tr>
</tbody>
</table>

1. AR, alkalizesorcinol; RW, refined wheat; WW, whole-grain wheat.
2. Calculated value.

Whole-grain, weight loss, and cardiovascular risk
measured by sandwich ELISA (R&D Systems). HbA1c was measured by ion-exchange HPLC (normal reference range 4.1–6.4%). Fecal energy excretion was measured by bomb calorimetry (Ika-calorimeter system C4000). Plasma AR were analyzed by normal-phase liquid chromatography coupled to a tandem mass spectrometer, after liquid-liquid extraction (28). Results are given as the sum of all 5 main homologs quantified. Based on previously published data for intake of either whole-grain or refined-grain foods under controlled circumstances (10), conservative thresholds based on fasting concentrations of <80 nmol total AR/L for intake of only RW foods, and >100 nmol total AR/L for intake of WW foods were set as criteria for compliance. Participants who were outside of the limits at both 6 and 12 wk were considered noncompliant. The within- and between day/ batch CV was <10% for all analyses.

Total tocols were extracted from the intervention foods using n-hexane ethyl acetate after saponification with potassium hydroxide and analyzed by HPLC. The total folate content of the intervention foods was microbiologically determined and the ferulic acid content was measured after ethyl acetate extraction following sodium hydroxide hydrolysis. All food analyses were done as described elsewhere (29), except for AR, which were estimated from literature values (30) (Table 1).

**Statistical methods.** Based on a weight loss study of a low- or high-glycemic diet (31), it was necessary to include 36 participants in each group to detect a difference in weight loss of 1.0 kg with an estimated weighted SD of 1.3 (α = 0.05; β = 1–0.8). Thus, 85 women were recruited to allow for a 15% dropout rate. All statistical analyses were performed in SAS System for Windows (release 9.2, SAS Institute). Homogeneity of variances were tested by Levene test. For normally distributed data, Student’s t tests, ANCOVA, or repeated measures ANOVA (RM ANOVA) were applied. ANOVA was carried out to examine the effect of diet (RW and WW) and time (wk 1–12) and their interaction on food intake. ANCOVA was carried out to examine the effect of diet (RW and WW) and time (wk 1–12) and their interaction on anthropometric and biochemical variables. For anthropometric variables, participant was modeled as a random variable and corresponding baseline values, baseline BMI, and age were modeled as covariates. For analyses on biochemical variables, body weight change from baseline was also included as covariate. ANCOVA was used to examine the effect of diet (RW and WW) and time (wk 1–12) and their interaction on food intake. For anthropometric variables, ITT analyses was performed (last measurement carried forward). Post hoc pairwise comparisons were made using Tukey-Kramer’s adjustment when main effects reached significance. All data are presented as means ± SEM unless otherwise indicated. Differences were considered significant at P < 0.05 and as tendencies when P < 0.10.

**Results**

A total of 72 women completed the study. Age did not differ between the RW (60.3 ± 5.3 y) and WW (59.1 ± 5.6 y) groups. Ten women in each group used antihypertensive medication.

**Body weight and composition.** During the 12-wk parallel intervention, the groups did not differ in the reduction in body weight (P = 0.11), whereas the percentage of initial weight loss tended to be greater in the WW group than in the RW group (P = 0.09) (Table 2; Fig. 1). There were significant time × diet interactions for total and central FM percentages, whereby both decreased in both groups (P < 0.01), and the change in total FM percentage tended to be greater (P = 0.07) in the WW group than in the RW group at wk 12 (Fig. 1). FM did not change in either group; BMI and waist circumference decreased in both groups (P < 0.01), but the decreases did not differ. ITT analyses using baseline measurements carried forward for seven participants who dropped out before wk 6 resulted in greater P values, but similar tendencies were observed for differences between the two groups with regard to decreased FM percentage (P = 0.06) and central FM percentage (P = 0.09); body weight loss between the two groups still did not differ (P = 0.11).

**Cardiovascular risk markers.** After 12 wk, changes in serum total and LDL cholesterol differed significantly between groups, as they increased in the RW group by 5.6 and 5.3%, respectively, whereas neither changed in the WW group (Table 3). IL-6 increased by ~10% in the WW group (P < 0.05), whereas there was no change in the RW group; the changes tended to differ between the groups (P = 0.09). Changes in blood pressure and serum concentrations of TG, HDL cholesterol, hsCRP, HbA1c, insulin, and glucose, and HOMA-IR did not differ between groups (Table 3).

**Dietary intake and compliance.** Of the 72 women who completed the study, 57 kept daily food diaries eligible for data analysis. Daily intake of the intervention foods was recorded and mean daily energy intake from intervention bread, pasta, and biscuits did not differ between the groups, indicating good compliance in both the RW (91.5% of foods provided) and WW (94.2% of foods provided) groups (Supplemental Table 1). Total energy intake did not differ between the groups. Plasma total AR did not differ between groups at baseline and increased only in the WW group (P < 0.001 at wk 6 and 12 compared to baseline and the RW group), objectively confirming that, overall, participants had complied well with the diet (Fig. 2A). The ratio between AR homologs C17:0 and C21:0, an indicator of either rye or wheat intake, was similar in the RW and WW groups at baseline and indicated some intake of rye-based products. The ratio decreased from 0.13 to 0.06–0.07 for the WW group at 6 and 12 wk (P < 0.001 compared to baseline and the RW group), whereas this was steady at 0.13–0.15 in the RW

**Table 2** Body weight and composition in postmenopausal women who consumed energy-restricted diets containing RW or WW foods for 12 wk

<table>
<thead>
<tr>
<th></th>
<th>RW (n = 34)</th>
<th></th>
<th>WW (n = 38)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>wk 0</td>
<td>wk 6</td>
<td>wk 12</td>
<td>wk 0</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>83.5 ± 1.9</td>
<td>81.7 ± 1.8</td>
<td>80.8 ± 1.3**</td>
<td>81.3 ± 1.3</td>
</tr>
<tr>
<td>BMI, kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>30.4 ± 0.6</td>
<td>29.7 ± 0.6</td>
<td>29.4 ± 1.7**</td>
<td>30.0 ± 0.4</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>90.0 ± 1.5</td>
<td>96.3 ± 1.5</td>
<td>94.9 ± 1.4*</td>
<td>97.3 ± 1.2</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>44.0 ± 0.7</td>
<td>44.0 ± 0.8</td>
<td>44.2 ± 0.7</td>
<td>42.9 ± 0.8</td>
</tr>
</tbody>
</table>

<sup>1</sup> Values are means ± SEM. Asterisks indicate different from wk 0: * P < 0.05, ** P < 0.01. CO, completers only; FFM, fat free mass; ITT, intention to treat; RW, refined wheat; WW, whole-grain wheat.

<sup>2</sup> P values refer to comparison between values in RW and WW groups in a CO analysis and in an ITT analysis (ANCOVA analysis adjusted for time (wk 6 and 12), age, baseline BMI, and corresponding baseline value).
group (Fig. 2B), confirming that the RW group was consuming some rye products and that the plasma C17:0: C21:0 ratio does respond to a change in the source of AR.

We reanalyzed data excluding individuals with plasma AR concentrations outside the expected thresholds for compliance as defined above, which reduced the sample size from 72 to 43. This did not change the conclusions for anthropometric measures or analyzed biomarkers; however, a greater difference in the decrease in FM percentage was observed compared to the complete sample (−3.3 ± 0.5% vs. −2.2 ± 0.4%; P = 0.02; WW, n = 21 and RW, n = 22) despite the smaller sample. This suggests that the incorporation of a large amount of intervention foods against a background of a free-living, energy-restricted diet is challenging for participants. Importantly, noncompliance in the RW group did not reflect a lack of intake of refined intervention foods but rather a high intake of whole-grain products aside from the foods provided.

**TABLE 3** Cardiovascular risk markers in postmenopausal women who consumed an energy-restricted diet containing RW or WW foods for 12 wk

<table>
<thead>
<tr>
<th>Blood pressure, mm Hg</th>
<th>RW (n = 34)</th>
<th></th>
<th>WW (n = 38)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>wk 0</td>
<td>wk 6</td>
<td>wk 12</td>
<td>wk 0</td>
</tr>
<tr>
<td>Systolic</td>
<td>138 ± 4</td>
<td>131 ± 2</td>
<td>132 ± 3</td>
<td>133 ± 2</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.61 ± 0.14</td>
<td>5.80 ± 0.11</td>
<td>5.91 ± 0.17***</td>
<td>5.57 ± 0.16</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.75 ± 0.13</td>
<td>3.97 ± 0.12</td>
<td>3.96 ± 0.15**</td>
<td>3.75 ± 0.16</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.63 ± 0.07</td>
<td>5.64 ± 0.07</td>
<td>5.55 ± 0.07</td>
<td>5.73 ± 0.09</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>7.45 ± 0.26</td>
<td>7.59 ± 0.26</td>
<td>7.20 ± 0.29</td>
<td>7.62 ± 0.24</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.01 ± 0.21</td>
<td>1.98 ± 0.22</td>
<td>1.80 ± 0.17</td>
<td>1.91 ± 0.15</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.62 ± 0.03</td>
<td>5.59 ± 0.03</td>
<td>5.71 ± 0.03</td>
<td>5.63 ± 0.04</td>
</tr>
<tr>
<td>hsCRP, mg/L</td>
<td>1.00 (0.42; 1.58)</td>
<td>1.06 (0.44; 1.76)</td>
<td>1.07 (0.49; 1.65)</td>
<td>0.95 (0.35; 1.55)</td>
</tr>
<tr>
<td>IL-6, ng/L</td>
<td>1.70 (1.30; 2.00)</td>
<td>1.84 (1.54; 2.14)</td>
<td>1.83 (1.51; 2.15)</td>
<td>2.45 (2.13; 2.78)</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM or geometric means (95% CI). Asterisks indicate different from wk 0. * P < 0.05, ** P < 0.1. HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high sensitivity CRP; RW, refined wheat; WW, whole-grain wheat.

2 P values refer to comparison between absolute values in RW and WW groups in a compliers-only analysis (ANCOVA analysis for time (wk 6 and 12), age, baseline BMI, change in body weight from baseline, and corresponding baseline value.

3 hsCRP >10 mg/L not included in analysis; RW: n = 30; WW: n = 35.

**Fecal output, excretion of DM, and energy and pH.** Daily fecal volume did not differ between groups at baseline, nor was there a difference between the groups after 12 wk (Supplemental Table 2). Fecal energy excretion and pH did not change from baseline in either group or differ between groups at any time point.

**Discussion**

We hypothesized that participants consuming whole-grain foods as part of an energy-restricted diet would experience a greater reduction in body weight and fat than participants consuming refined-grain foods. The FM percentage decreased more in the group of participants consuming whole-grain foods compared to those consuming refined foods (−3.0 vs. −2.1%; P = 0.04), and a tendency was observed for central FM percentage (−3.9 vs. −2.8%; P = 0.07), whereas the difference in weight loss between groups was not significant (P = 0.11). A total of 72 participants, nearly equally distributed in the 2 groups, completed the study, which is the sample size required to observe a difference in weight loss of 1.0 ± 1.5 kg according to the power calculation. The observed difference in weight loss of 0.9 kg was only slightly smaller than this; thus, the main explanations for the lack of difference in weight loss between groups are likely a smaller effect than anticipated as well as a larger variation in the weight loss than predicted. Although none of the cardiovascular risk markers improved in either group, a 5–6% increase from baseline in both total and LDL cholesterol occurred in the RW group but not the WW group.

Whole-grain foods as part of a weight loss diet may have a beneficial effect on body weight and composition, primarily due to the greater fiber content compared to their refined counterparts, which in turn dilutes energy density and may reduce hunger between meals, both of which affect energy balance (8). However, results from clinical intervention trials show conflicting results. Katcher et al. (22) found a decrease in abdominal FM percentage in the group consuming 5–daily servings of whole-grain foods for 12 wk (−2.2%) compared to the group consuming refined-grain foods (−0.9%; P = 0.03 for difference

---

**FIGURE 1** Percentage changes in body weight, total FM, and central FM in postmenopausal women who consumed an energy-restricted diet containing RW or WW products for 12 wk. Values are means ± SEM, n = 34 (RW) or 38 (WW). Asterisks indicate different from RW, *P < 0.05, **P < 0.01. HbA1c, glycated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high sensitivity CRP; RW, refined wheat; WW, whole-grain wheat.
between the groups). Similarly, Shimizu et al. (34) found that both waist circumference and visceral fat area in Japanese men decreased more after whole-grain rice/barley consumption compared to rice alone for 12 wk. In a different study in overweight and obese South Korean women, body weight and FM percentage decreased more in the group consuming whole-grain rice compared to the group consuming white rice (35) and 80 g/d of whole-grain oat cereal for 12 wk was found to lead to a decreased waist circumference compared to refined cereal products, even without difference in weight loss between the groups (44). Thus, consistent with our findings, FM can be reduced by consumption of whole grain, even when body weight changes do not differ. However, not all studies reported a lack of benefits on anthropometric variables (17–19,36,37). Theories have been put forward that the mechanisms behind these effects could be due to lower postprandial insulin and glucose responses that favor lipolysis and lipid oxidation rather than fat storage (38–40). However, the loss of FM in the present study was not accompanied by improved insulin sensitivity (assessed as homeostatic model assessment of insulin resistance), nor was this the case in the study by Katcher et al. (22). The authors suggested that decreased abdominal FM was related to inflammation. In contrast to this, we found that the increase in the plasma IL-6 concentration tended to be greater in the WW group compared to the RW group (P = 0.09), whereas hsCRP did not change from baseline in either group or differ between groups at any time. Although usually interpreted as a negative finding, an increase in IL-6 can occur after increased physical activity, for instance, but an inflammatory response induced by whole grain cannot be ruled out.

We previously found that the WW breads used in this study induced greater satiety compared to RW breads, whereas the pastas did not differ in their ability to suppress hunger (41), which indicates that participants consuming whole-grain foods, especially bread, may have experienced less hunger than those consuming refined-grain foods. Contrary to this, self-reported energy intake and fecal energy excretion did not differ between groups in the present study; however, it cannot be ruled out that there may be a small contribution from these to a negative energy balance.

The prevalence of women with features of metabolic syndrome increases after the onset of menopause, which is linked with substantial metabolic changes emerging with estrogen deficiency. Thus, there is increased risk of developing CVD among postmenopausal women (42). Hence, a key finding in the present study is that changes from baseline in serum total and LDL cholesterol differed between groups due to an increase from baseline in the RW group by ~5%. We anticipated a decrease in serum total and LDL cholesterol concentrations in both groups due to decreased dietary fat and energy intake, but also that the decrease in the WW group would be larger due to an increased intake of dietary fiber, which would be in accordance with other studies (23,43–45), although not all (17–19). Several reasons why this was not observed may exist. Hypcholesterolemic effects differ depending on the types of whole-grain foods tested; specifically, oat and barley foods, rich in soluble β-glucans, often exhibit cholesterol-lowering properties, whereas wheat and rice most often do not, although this is not always the case (10,46). Also, nonfiber components such as phenolic compounds and glycine betaine may also play a role in lipoprotein metabolism (47). It has been suggested that durum wheat may be superior to common wheat with regard to lipi-lowering properties (46), and a large proportion of the whole grain consumed in the present study was indeed durum.

However, the most likely confounder in the present study is the habitual intake of rye bread among our participants, which is assumed to be relatively high, because rye bread consumption among Danes is common and the main contributor to whole-grain intake (24). Participants in the RW group may have reduced their whole-grain intake overall, resulting in increased total and LDL cholesterol, although some still managed to include whole-grain (rye) foods in their diet, because this was not restricted. Plasma AR increased in the WW group as has been reported in other intervention studies with whole-grain foods of wheat and rye (10,33). The ratio of AR homologs C17:0:C21:0 decreased markedly in the WW group from baseline to wk 6 and 12, which indicates that at baseline and in the RW group, whole-grain rye foods were a part of the diet and that this changed with the WW intervention.

Using plasma AR to measure compliance with the WW or RW diets did not lead to any changes in the results, but the decrease in FM percentage in the WW group was more pronounced. However, the small effect modification by AR may be due to the fact that compliance was close to 100% in the present study. Plasma AR concentrations are useful as a validation of self-reported compliance and may prove to be even more useful in less compliant populations and population-based studies. Noncompliant participants in the WW group had a greater reduction in FM compared to participants who complied with the WW diet. Likely, the large amount of intervention foods provided made it difficult to adhere to the energy restriction, thus compromising weight loss, particularly among those with the smallest ER. Contrary to this, non-

**FIGURE 2** Plasma total AR concentrations (A) and the AR C17:0:C21:0 ratio (B) in postmenopausal women who consumed an energy-restricted diet containing RW or WW products for 12 wk. An AR C17:0:C21:0 ratio > 0.15 indicates intake of whole-grain rye, whereas a ratio <0.1 indicates that most AR are derived from WW (32,33). Values are geometric means with 95% CI limits, n = 34 (RW) or 38 (WW). Asterisks indicate different from RW and from wk 0. *P < 0.001. AR, alkylresorcinol; RW, refined wheat; WW, whole-grain wheat.
compliant participants in the RW group lost less FM despite a high whole-grain intake (AR > 100 mmol/L). However, because they consumed both refined-grain and whole-grain foods, their overall energy intake increased. Another explanation may be that consumption of refined grains may offset the potential benefits of whole-grain consumption, as recently suggested after an inverse association between whole-grain intake and visceral adipose tissue volume was diminished in people consuming ≥4 servings/d of refined grain (48).

A shortcoming of whole-grain interventions is the difficulty associated with blinding. We used an open-labeled design; thus, the participants may have responded better when allocated to the WW group (or worse when allocated to the RW group), whereby effect size may be overestimated. This is a common confounder, because no studies to our knowledge that compare whole grains to refined grains have been able to successfully blind treatments to date. It is not known to what extent the effects observed in the present study will persist in a longer-term perspective. It is generally difficult to ensure good adherence to one specific diet composition for a longer period of time, as highlighted by others (8), but combining evidence from observational and intervention studies may provide insight.

In conclusion, we found that FM percentage decreased significantly more in participants consuming whole-grain foods compared to those consuming refined foods. Furthermore, refined-grain consumption increased serum total and LDL cholesterol concentrations. With the increasing number of well-controlled clinical intervention studies over recent years, there is emerging evidence for a beneficial role of whole grain in terms of reduced FM percentage but still, no firm conclusions can be drawn. Further studies elucidating the role of particle size and comparing different grains side by side are lacking and the use of plasma AR as a biomarker of whole-grain intake is encouraged.

Acknowledgments
The authors thank Jane Jørgensen, Lone Agerskov, Charlotte H. Andersen, and John Lind for their excellent technical assistance, and students Anne Møller Petersen, Anna Klocker Jepsen, Sisse Ebbesen, and Louise Mathiesen for their assistance with data collection. M.K., S.T., I.T., S.B., M.P., G.R., and A.A. designed the clinical study; M.K. and M. G.J conducted the clinical study; A.B.R. performed AR measurements and statistical analyses of these; M.K. analyzed data and wrote the paper; and M.K. and A.A. had primary responsibility for final content. All authors read and approved the final manuscript.

Literature Cited


