Implementation of a Brazilian Cardioprotective Nutritional (BALANCE) Program for improvement on quality of diet and secondary prevention of cardiovascular events: A randomized, multicenter trial

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Abstract Background Appropriate dietary recommendations represent a key part of secondary prevention in cardiovascular disease (CVD). We evaluated the effectiveness of the implementation of a nutritional program on quality of diet, cardiovascular events, and death in patients with established CVD.

Methods In this open-label, multicenter trial conducted in 35 sites in Brazil, we randomly assigned (1:1) patients aged 45 years or older to receive either the BALANCE Program (experimental group) or conventional nutrition advice (control group). The BALANCE Program included a unique nutritional education strategy to implement recommendations from guidelines, adapted to the use of affordable and regional foods. Adherence to diet was evaluated by the modified Alternative Healthy Eating Index. The primary end point was a composite of all-cause mortality, cardiovascular death, cardiac arrest, myocardial infarction, stroke, myocardial revascularization, amputation, or hospitalization for unstable angina. Secondary end points included biochemical and anthropometric data, and blood pressure levels.

Results From March 5, 2013, to Abril 7, 2015, a total of 2534 eligible patients were randomly assigned to either the BALANCE Program group (n = 1,266) or the control group (n = 1,268) and were followed up for a median of 3.5 years. In total, 235 (9.3%) participants had been lost to follow-up. After 3 years of follow-up, mean modified Alternative Healthy Eating Index (scale 0-70) was only slightly higher in the BALANCE group versus the control group (26.2 ± 8.4 vs 24.7 ± 8.6, $P < .01$), mainly due to a 0.5-serving/d greater intake of fruits and of vegetables in the BALANCE group. Primary end point events occurred in 236 participants (18.8%) in the BALANCE group and in 207 participants (16.4%) in the control group (hazard ratio, 1.15; 95% CI 0.95-1.38; $P = .15$). Secondary end points did not differ between groups after follow-up.

Conclusions The BALANCE Program only slightly improved adherence to a healthy diet in patients with established CVD and had no significant effect on the incidence of cardiovascular events or death. (Am Heart J 2019;215:187-97.)

Unhealthy dietary patterns are important triggers in the development of chronic diseases.[1] Epidemiological studies have shown a lower risk of cardiovascular disease (CVD) incidence and mortality associated with healthy diets in individuals both with and without prior CVD.[2-6] Therefore, dietary guidelines recommend a combination of nutrient-based advice and healthy dietary patterns for the treatment and prevention of CVD and its risk factors.[7]

Efficacy of any dietary intervention is strongly influenced by degree of adherence which, in turn, is influenced by a number of factors[8] such as access to food and local culture that may determine dietary choices.[7,9] Diet quality may also vary across the socioeconomic spectrum, in which individuals with a lower social position tend to have worse dietary patterns.[10] Thus, strategies for dietary compliance that benefit those with low income are important given that higher-quality diets are associated with lower risk of cardiovascular events in these individuals as compared to those with the highest income.[6]

Guidelines have emphasized the need to adjust dietary recommendations according to personal preferences; regional foods; and cultural, ethnic, and economic aspects to improve adherence.[11] However, dietary

guidelines rarely discuss strategies for implementing nutritional recommendations in clinical practice.[12] In addition, it has been shown that the effect of dietary advice results in only modest beneficial changes in diet and in cardiovascular risk factors.[13]

Considering this context, a Brazilian Cardioprotective Nutritional (BALANCE) Program was developed, essentially composed of (*a*) a dietary prescription guided by nutritional content recommendations as per guidelines; (*b*) nutritional education program-based tools and suggestions of affordable foods; and (*c*) an intensive follow-up through one-on-one visits, group sessions, and phone calls.[14] The Program was shown to be feasible in patients with established CVD in a single-center pilot study in which it was more effective in reducing blood pressures, fasting glucose levels, weight, and body mass index (BMI) as compared with the diet proposed by the dietary guidelines valid at the time.[15] However, patients' adherence to diet and the effect on recurrence of cardiovascular events were not evaluated between groups.

Thus, we conducted a multicenter randomized trial to evaluate the effects of the implementation of BALANCE Program in improving adherence to recommendations in patients with established CVD, and its relationship with cardiovascular events and death.

Methods

Study design and oversight

A detailed description of the study design has been published previously.[14] Briefly, this was an open-label, multicenter, randomized (concealed) trial conducted in 35 sites in Brazil. The trial was designed and coordinated by the Research Institute at the Heart Hospital (HCor). The protocol was approved by the local research ethics boards from all sites, and all participants provided written informed consent.

Patients

We included patients aged 45 years or older with 1 or more of the following indicators of established CVD: (*a*) *coronary artery disease* (defined by previous acute myocardial infarction; stable or unstable angina; history of atherosclerotic stenosis ≥70% of the diameter of any coronary artery on conventional or computed tomography coronary angiography; or history of angioplasty, stenting, or coronary artery bypass surgery); (*b*) previous stroke; and (*c*) peripheral vascular disease (ankle to arm ratio <0.9 of systolic blood pressure in either leg at rest, angiography or Doppler demonstrating >70% stenosis in a noncardiac artery, intermittent claudication, vascular surgery for atherosclerotic disease, amputation due to atherosclerotic disease, or aortic aneurysm). The exclusion criteria were as follows: neurocognitive or psychiatric conditions that may hinder collection of reliable clinical data (defined at the investigator's discretion), life expectancy less than 6 months (eg, metastatic malignancy or other factor defined at the investigators' discretion), pregnancy or lactation, liver failure with a history of encephalopathy or anasarca, renal failure with indication for dialysis, congestive heart failure, previous organ transplantation, wheelchair use, or any restrictions to receiving an oral diet.

Randomization

Eligible participants were randomly assigned (1:1) to either the BALANCE Program group or the control group. The randomization was performed in blocks with stratification by study site. Allocation concealment was guaranteed through a 24-hour central Web-based automated system. Because of the nature of the intervention, participants, dieticians, and research assistants who collected data were aware of group allocation. Conversely, outcome adjudicators and statisticians were blinded to the assigned interventions.

Treatments

An experienced team of dieticians belonging to the coordinating team provided structured training for all researchers at the study sites. All site investigators followed a standard protocol to minimize variability and maintain fidelity across all sites. Support to the sites was provided by the coordinating team during all stages of the interventions, with feedback being provided as required.

Participants in both groups continued to receive usual medical care. The nutritional counseling for both BALANCE Program and control groups followed guidelines for the treatment of CVD.[16-19] The main differences between both dietary advices were the approach and intensity in implementing the nutritional approach.

BALANCE Program group

Beyond a dietary prescription guided by nutritional content recommendations as per guidelines, the BALANCE Program was composed by nutritional education program-based tools and suggestions of affordable foods. As previously described,[14] to implement the guideline recommendations and suggested menus, a list of cardioprotective foods was compiled based on a set of qualitative criteria: (*a*) no added sugar, (*b*) low energy content, (*c*) lack of nutrients that increase cardiovascular risk (cholesterol, saturated fatty acids [SFA], and sodium), and (*d*) presence of cardioprotective nutrients (antioxidants and dietary fiber). Then, a food-group strategy according to nutrient densities of the various foods was developed. All foods with an energy density of ≤4.64 kj/g, SFA density of ≤0.01 g/g, cholesterol density of ≤0.04 mg/g, and sodium density of ≤2.01 mg/g were assigned to the "green" group. The remaining foods were classified into 3 groups: those with 1 or 2 nutrient densities above the established cutoff points were assigned to a "yellow" group, whereas those with 3 or 4 nutrient densities above the established cutoff

points were categorized into the "blue" group. The "red" group was composed of foods known to be sources of *trans* fatty acids, refined sugar, artificial sweeteners, and preservatives—that is, ultraprocessed foods.[20] As a strategy to facilitate patient adherence to the BALANCE Program, heart symbols of different colors were used. An example of this food classification typology is shown in Supplemental Figure 1.

The pattern of colors (green, yellow, and blue) used in the BALANCE Program was those of the Brazilian flag, and it was chosen to facilitate patients' understanding and reminding of a proper healthy diet composition.[14] The largest field on the flag is green, suggesting that foods of green group should be consumed more frequently. The second largest portion of the flag is yellow, suggesting that these foods should be less consumed. Finally, blue is present only on a small part of the flag, suggesting that these foods should be restricted (Supplemental Figure 2). In allusion to the absence of red in the Brazilian flag, foods from the red group should not be consumed at all.

To facilitate adherence to the BALANCE Program prescription, 1,400- to 2.400-cal menus were elaborated, stipulating the amount of green, yellow, and blue food servings, as previously described.[14] The following recommendations were used to calculate the total daily energy: to weight management: 25 kcal/kg/d, to weight loss: 20 kcal/kg/d, and to weight gain: >30 kcal/d. Regarding macronutrients distribution, these menus were calculated as follows: 50%-60% of energy from carbohydrates, 10%-15% from proteins, 25%-35% from total fat, <7% from SFA, <10% polyunsaturated fatty acids, <20% monounsaturated fatty acids, <1% *trans* fatty acids, <200 mg/d of dietary cholesterol, 20-30 g/d dietary fiber, and <2400 mg/d sodium. A cookbook of regional Brazilian modified recipes (o reduce SFA, dietary cholesterol, and sodium concentration) was also devised and given to the participants as an educational tool.

With the objective of encouraging the subject's adherence to the Program, an intensive dietician-led follow-up was instituted as the third concept of BALANCE Program. Participants attend individual sessions with a registered dietitian every 6 months for 2 years. Also, in the first 2 years of the implementation of the program, participants received monthly telephone calls to evaluate their understanding of the Program diet and to reinforce nutritional advice. During the years 3 and 4 of the trial, participants took part in 2 annual group sessions (where topics such as "How important is food in your life?," "Is nutrition a part of health care?," "What are cardioprotective foods?," "How to improve my diet quality?," and others were addressed) and in 1 annual individual session, and received phone calls every 4 months. In total, 8 individual sessions, 4 group sessions, and 19 phone calls were scheduled over the 4 years of the program.

Control group

Control group participants were encouraged to follow generic dietary advice elaborated by dieticians. All subjects received a folder containing lists of foods that should be preferred or avoided. A tailored prescribed diet was not provided to the control group (Supplemental Methods; dietary prescriptions was only qualitative). Any energy restriction was accomplished by switching from foods with a high-energy density to others with a low-energy density.

Data collection and assessment

A standardized case report form was used to obtain the research information at baseline and at the 12th, 18th, 24th, 36th, and 48th month in both groups. Data from demographic characteristics; smoking and physical activity status; anthropometric measures (BMI and waist circumference); previous comorbidities (diabetes, hypertension, and dyslipidemia); medications; blood pressure levels; and serum concentration of total cholesterol, low-density lipoprotein, high-density lipoprotein (HDL), fasting glucose, and serum triglyceride were reported at baseline and updated each visit. Additionally, dietary intake data were obtained by two 24-hour recall interviews conducted by trained interviewers. One year after the beginning of the study, a form was introduced to include socioeconomic and recent physical activity status data. The methodology of data collection and evaluations has been previously published.[14]

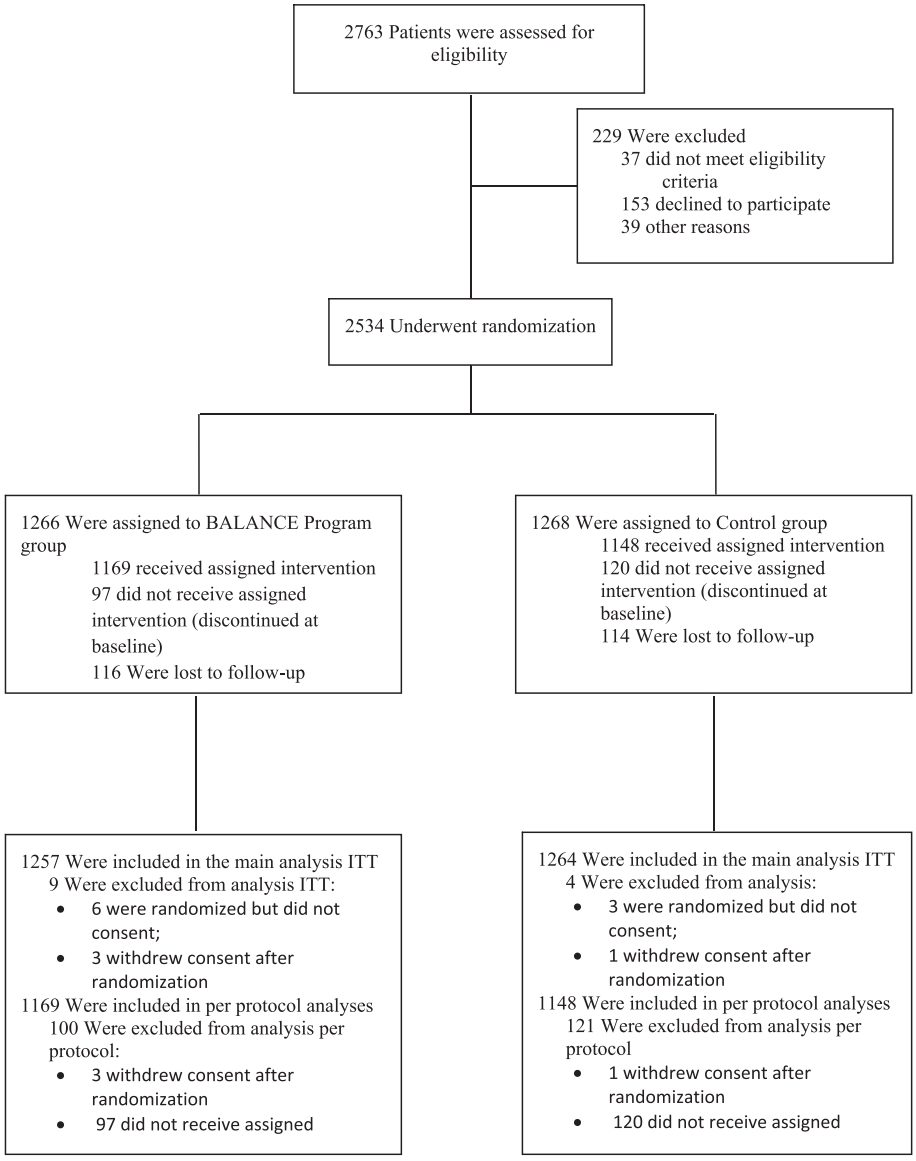
Diet compliance was defined based on an adaptation of the Alternative Healthy Eating Index (AHEI), which was highly predictive of cardiovascular disease risk.[21] The method of scoring in the modified AHEI (mAHEI) has been previously described, and it ranges from 0 to 70.[6]

End points

The primary composite end point was the occurrence of any of the following cardiovascular events: all-cause mortality, cardiovascular death, cardiac arrest, acute myocardial infarction, stroke, myocardial revascularization, amputation for peripheral arterial disease, or hospitalization for unstable angina. Secondary end points were the individual components of the composite end point and BMI; waist circumference; blood pressure levels; serum concentration of total cholesterol, low-density lipoprotein, HDL, and fasting glucose; and serum triglycerides.

All primary composite end point components were centrally assessed and entered into the Clinical End Points Committee (CEC) tracking database and independently adjudicated by 2 CEC physicians. If there was disagreement, the final decision was made by a third independent adjudicator. Only end points that were confirmed by the CEC were included in analyses. The detailed end point definitions and the adjudication process have been published previously.[14] Loss to follow-up was considered only in the absence of any presential, telephone, or correspondence contact to obtain information regarding primary end points. According to the characteristic of the interventions, adverse events were not collected.

Figure 1



Eligibility, randomization, and follow-up. *ITT*, intention to treat.

Statistical analysis

Assuming an incidence rate for primary end point of 20% in the control group, a relative risk reduction of 30% in the intervention group, a statistical power of 80%, and a type I error rate of 5%, the required sample size was determined to be 2,468 individuals.[22-25]

Baseline characteristics were reported as counts and percentages, mean and SD, or median and interquartile range, as appropriate. All analysis followed the intention-to-treat principle. The primary end point was presented using Kaplan-Meier survival curves and incidence per 1,000 person-years. The effect of the BALANCE Program versus control was assessed using a frailty Cox proportional-hazard model considering sites as random effects and expressed using hazard ratios (HRs) and 95% CIs. The *time to event* was defined as the number of days from the date of randomization to the date of the event confirmed by adjudication. Patients without confirmed event were censored at the time of the last follow-up contact.

We prespecified a sensitivity analysis with a model adjusted by sex, age, income and educational status, BMI, cardiovascular risk factors, baseline CVD, medication, physical activity, and alcohol consumption.[14] However, we removed income and educational status, physical

activity, and alcohol consumption from the models because of missing data. Additionally, a post hoc sensitivity analysis for the primary end point was performed, considering nonadjudicated events (29 events that were reported by the site investigator were not confirmed with appropriated documents). Patients who did not receive intervention and/or withdrew consent were excluded (per-protocol analyses).

Continuous secondary end points were analyzed over time by repeated measures using a mixed model. Variables that did not have a normal distribution were analyzed using generalized estimating equation models with a distribution that best fit the data.

Continuous secondary end points and the mAHEI score were analyzed over time by repeated measures using a mixed model. Variables that did not have a normal distribution were analyzed using generalized estimating equation models with a distribution that best fit the data.

We performed prespecified subgroup analyses according to sex, age, BMI, cardiovascular risk factors, and previously diagnosed CVD using interaction terms in the frailty Cox regression. In addition, a post hoc subgroup analysis was made to evaluate the effect of BALANCE Program on primary end point according to baseline diet adherence score. The significance level was .05. Assessment of treatment effect on secondary end points was not adjusted for multiple comparisons. Secondary end point and other analyses should be interpreted as exploratory. Analyses were performed using R software for Windows, version 3.3.3 (R Foundation for Statistical Computing).

Results

Participant characteristics

Between March 5, 2013, and April 7, 2015, a total of 2,534 participants (from 2,763 screened) were randomly assigned to either the BALANCE Program group (n = 1,266) or the control group (n = 1,268) (Figure 1). After assignment, 13 patients were excluded from analyses (4 individuals withdrew consent after randomization and 9 did not consent before randomization, characterizing deviation of protocol); thus, 1,257 patients in the intervention group and 1,264 in the control group were included in the intention-to-treat analyses.

Baseline characteristics were well balanced between groups (Table I). The mean age of the patients was 63.3 (SD 9.1) years, and 58.2% were men. Drug-treatment regimens were similar in both groups and continued to be balanced during follow-up (Supplemental Table I). Median duration of follow-up was 3.5 years (interquartile range 2.91-3.87 years). After the initial assessment, 217 (8.6%) participants (97 from the BALANCE Program group and 120 from the control group) chose not to attend subsequent visits, and their follow-up was based on medical records and phone calls. By December 20, 2017, a total of 235 (9.3%) participants had been lost to follow-up. Rates of loss to follow-up were similar in both groups, 9.5% in the BALANCE Program group and 9% in the control group, with no significant difference in time to dropout between groups. In comparison to those who remained in the study, patients who were lost to follow-up were poorer and had a lower BMI (Supplemental Table II, *A* and *B*).

The initial mAHEI scores were similar for both groups at baseline: 25.8 ± 8.5 points in BALANCE Program group and 25.3 ± 7.9 points in control group (Table II). After 1 year of intervention, the mAHEI score was significantly higher in the BALANCE group when compared to control group (28.2 ± 8.7 vs 26 ± 8.4 points; $P < .01$), and after 3 years, this difference remained, despite lower magnitude (26.2 ± 8.4 vs 24.7 ± 8.6 points; $P < .01$).

Dietary intake was similar in both groups at baseline. According to the proposed dietary guidelines,[16-19] both groups showed optimal nutrients intake at the beginning, except for SFA, dietary cholesterol, and sodium which remained above the recommended levels over time in both groups, and for dietary fiber, which remained lower than those recommended (Supplemental Table III).

Regarding components of mAHEI, the BALANCE group showed improvement of vegetables, fruits, whole grains, and alcohol intake after 1 year of intervention when compared to the control group. After 3 years, only vegetables and fruits intake remained significantly higher in the BALANCE group when compared to the control group (for vegetables: 3.09 ± 2.91 vs 2.53 ± 2.68, $P < .001$; for fruits: 3.78 ± 3.19 vs 3.43 ± 3.15, $P = .043$) (Supplemental Table IV).

After 3 years, in comparison to the control group, the BALANCE Program group showed reduction in the following: energy (−77.68 kcal, 95% CI −139.51 to −15.85, $P = .009$), % of energy from fat (−1.17%, 95% CI −2.16 to −0.17, $P = .016$), % of energy from SFA (−0.48%, 95% CI −0.92 to −0.05, $P = .025$), % of energy from monounsaturated fatty acids (−0.5%, 95% CI −0.9 to −0.09, $P = .01$), and dietary cholesterol intake (−27.95 mg, 95% CI −48.29 to −7.62, $P = .007$). On the other hand, the BALANCE group showed increase in % of energy from carbohydrates intake (1.67%, 95% CI 0.39-2.94, $P = .005$) (Supplemental Table III).

Primary and secondary end points

A total of 443 adjudicated primary end points events were included in the analysis: primary end point events were observed in 236 participants (18.8%) from the BALANCE Program group and in 207 participants (16.4%) from the control group and did not differ between groups (HR 1.15, 95% CI 0.95-1.38, $P = .15$) (Table III and Figure 2). In sensitivity analyses in which the primary end point was excluded, patients who did not receive intervention and/or withdrew consent (per-protocol analysis), or those adjusted for specific variables, including both adjudicated and nonadjudicated outcome,

Table I. Baseline characteristics of study participants

Characteristic	BALANCE Program group (n = 1257)	Control group (n = 1264)
Age, y	63.3 ± 9.2	63.3 ± 8.9
Sex, male	738/1257 (59)	728/1264 (58)
Current smokers	95/1237 (8)	96/1240 (8)
Physical activity		
Sedentary	819/1206 (68)	801/1214 (66)
Active	387/1206 (32)	413/1214 (34)
Education level		
None/primary school	677/1155 (59)	702/1107 (63)
Secondary school	384/1155 (33)	323/1107 (29)
College or university	94/1155 (8)	82/1107 (7)
Social position*		
Low	133/1147 (12)	187/1110 (17)
Medium	662/1147 (58)	631/1110 (57)
High	352/1147 (30)	292/1110 (26)
BMI, kg/m^2		
<25	237/1230 (19)	265/1229 (22)
25-30	519/1230 (42)	510/1229 (41)
>30	474/1230 (39)	454/1229 (37)
Hypertension	1127/1241 (91)	1113/1245 (89)
Diabetes mellitus	537/1241 (43)	558/1245 (45)
Dyslipidemia	960/1240 (77)	967/1244 (78)
Family history of coronary disease	818/1235 (66)	786/1242 (63)
Previous coronary disease	1163/1257 (93)	1161/1264 (92)
Previous stroke	154/1257 (12)	149/1264 (12)
Previous peripheral vascular disease	144/1257 (12)	146/1264 (12)
Drugs in use		
Blood pressure–lowering drugs	1183/1239 (96)	1181/1247 (95)
Lipid-lowering agents	1063/1239 (86)	1073/1247 (86)
Oral antidiabetic agents	461/1238 (37)	467/1247 (37)
Insulin	155/1238 (13)	167/1247 (13)
Antiplatelet therapy	1117/1239 (90)	1126/1247 (90)

Values indicate n/N (%); plus-minus values are means ± SD. Not all participants answered questions about education level and social position because those items were included after randomization begins.
*Lower social position means a mean family income of R$1,700.00 per month or U$425.00; medium social position means a mean family income of R$7,000.00 per month or U $1763.25; higher social position means a mean family income of R$20,888.00 per month or U$5,222.00.

Table II. Modified AHEI, mean score by treatment arm during follow-up

mAHEI	BALANCE Program group	Control group	Between-group difference, mean (95% CI)	*P* value
Baseline	25.8 ± 8.5 (n = 1188)	25.3 ± 7.9 (n = 1167)	0.48 (–0.19 to 1.16)	.39
1 y	28.2 ± 8.7 (n = 985)	26.0 ± 8 (n = 955)	2.16 (1.43-2.9)	<.01
3 y	26.2 ± 8.4 (n = 666)	24.7 ± 8.6 (n = 624)	1.67 (0.79-2.54)	<.01

Plus-minus values are means ± SD. Mean differences between groups, 95% CI, and *P* values were estimated by mixed model.

the results were similar to those observed in the intention-to-treat analyses (Supplemental Table V). In subgroup analyses, there were no differences in treatment effects across all subgroups (Supplemental Figure 3). At 3-year follow-up, there were no significant changes between groups in any secondary end point (Supplemental Table VI).

Discussion

In this study, implementing a culturally adapted nutritional program based on guidelines slightly improved adherence to diet recommendation in patients with established CVD in a middle-income country, but it failed to demonstrate effect on cardiovascular events and death after a median of 3.5 years of follow-up. The same occurred for surrogate outcomes such as blood pressure, lipid profile, and anthropometric variables.

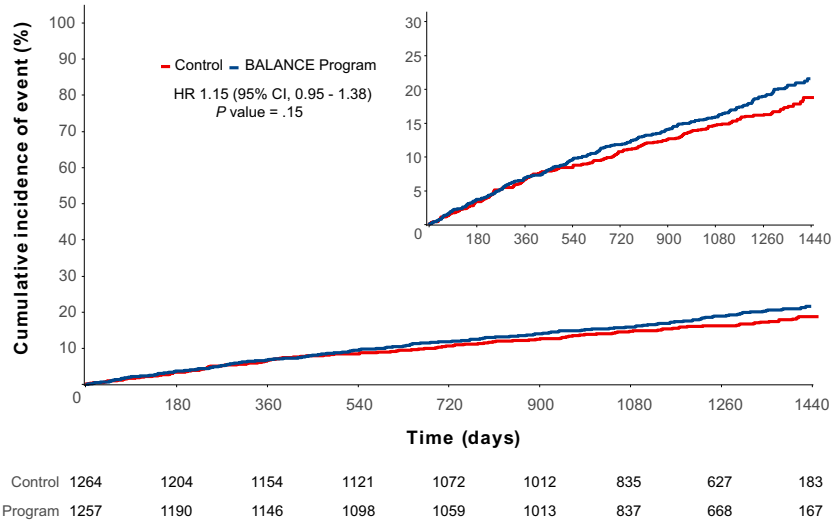
The higher dietary adherence compared to the control group according to mAHEI was observed mainly in the first year of the program; however, this difference may not be clinically relevant. Epidemiological studies in secondary cardiovascular prevention showed a 22% risk

Table III. Primary and secondary end point

End Point	BALANCE Program Group (n = 1257)	Control Group (n = 1264)	Hazard ratio (95% CI)	*P value*
Primary end point				
Events per person-years	236/3851	207/3872	1.15 (0.95-1.38)	.15
Crude rate per 1000 person-years (95% CI)	61.3 (53.5-69.1)	53.5 (46.2-60.7)		
Secondary end point				
Death from cardiovascular causes				
Events per person-years	52/4120	45/4103	1.15 (0.77-1.72)	.48
Crude rate per 1000 person-years (95% CI)	12.6 (9.2-16.1)	11 (7.8-14.2)		
Death from any cause				
Events per person-years	98/4120	97/4103	1.01 (0.77-1.34)	.93
Crude rate per 1000 person-years (95% CI)	23.8 (19.1-28.5)	23.6 (18.9-28.3)		
Amputation				
Events per person-years	4/4113	4/4099	0.99 (0.25-3.94)	098
Crude rate per 1000 person-years (95% CI)	1.0 (0-1.9)	1.0 (0-1.9)		
Unstable angina				
Events per person-years	29/4065	32/4039	0.89 (0.54-1.48)	.66
Crude rate per 1000 person-years (95% CI)	7.1 (4.5-9.7)	7.9 (5.2-10.7)		
Stroke				
Events per person-years	13/4100	22/4069	0.59 (0.30-1.16)	.13
Crude rate per 1000 person-years (95% CI)	3.2 (1.4-4.9)	5.4 (3.1-7.7)		
Not fatal myocardial infarction				
Events per person-years	36/4064	22/4065	1.64 (0.96-2.79)	.07
Crude rate per 1000 person-years (95% CI)	8.9 (6.0-11.8)	5.4 (3.2-7.7)		
Cardiac arrest				
Events per person-years	3/4114	1/4102	2.99 (0.31-28.73)	.34
Crude rate per 1000 person-years (95% CI)	0.7 (0 -1.6)	0.2 (0-0.7)		
Myocardial revascularization				
Events per person-years	87/3949	66/3972	1.33 (0.97-1.83)	.08
Crude rate per 1000 person-years (95% CI)	22.0 (17.4-26.7)	16.6 (12.6-20.6)		

The primary composite end point was the occurrence of any of the following cardiovascular events: all-cause death, cardiovascular death, cardiac arrest, acute myocardial infarction, stroke, myocardial revascularization, amputation for peripheral arterial disease, or hospitalization for unstable angina. CI and *P* values were estimated using the frailty Cox proportional-hazard model considering the recruiting centers as random effects.

Figure 2



Cumulative incidence of primary end point events.The primary composite end point was the occurrence of any of the following cardiovascular events: all-cause death, cardiovascular death, cardiac arrest, acute myocardial infarction, stroke, myocardial revascularization, amputation for peripheral arterial disease, or hospitalization for unstable angina.

reduction in composite outcome for individuals with high adherence to a healthy diet (mAHEI ≥28.7 points) compared to individuals with low adherence (mAHEI <16 points); however, the mean follow-up of these studies were 5 years.[6] Besides, it is known that individuals with profiles similar to those of participants of the BALANCE study—sedentary and overweight, or with multiple comorbidities, or reporting low energy intake—may be less adherent to dietary treatments.[26]

Up to 90% of the population in low- and middle-income countries show lower consumption of fruits, vegetables, and milk than is recommended.[27] In the BALANCE Program group, we showed small improvement in fruits and vegetables intake. Despite all efforts, achieving dietary change is difficult and usually involves long-term cultural change. Our nutritional strategy provided an attempt to increase the accessibility to the diet, adapting the menu to cultural specifications, and to incentivize the consumption of local foods. Beyond fruits and vegetables, it was recommended that higher quantities of other cardioprotective foods should be consumed; although locally produced foods were recommended, some participants may have considered such a recommendation as leading to an increase in spending exclusively for the diet—contributing to dropout or low adherence.[28]

Despite a significant number of evidence-based guidelines for dietary prevention and treatment of CVD and its risk factors, important gaps between the scientific data and its implementation still remain.[12,29,30] The BALANCE Program used a unique strategy with an objective to translate current guidelines and nutritional recommendations into clinical practice while respecting local culture and using a simple approach. However, it is known that long-term adherence to modified diets (which mainly include reduced SFA and sodium contents) is poor even with intensive counseling,[31,32] and the effectiveness of some nutrients and certain foods traditionally described as "beneficial or harmful" for primary and secondary cardiovascular prevention has been questioned.[1,33,34] Even with several strategies to improve adherence to the BALANCE Program, our results were not different from other studies which have reported low adherence to dietary guidelines.[29,30] Noteworthy is the fact that, additionally to dietary practices, other lifestyle modification strategies such as regular exercise, smoking cessation, and mental disorders should be incorporated to our Program to improve cardiovascular outcomes (all lifestyle changes may add some additional beneficial effect beyond diet intervention alone).

Beyond low diet adherence, another factor that may influence the lack of a positive effect was the high medicalization of the population. Brazil may be considered an example of a successful policy approach to reducing inequality in preventive and primary care because most common medications are free at the point of service for all citizens. Levels of total cholesterol, blood pressure, and HDL were fine from the baseline of the study. Therefore, adherence to medications may have overshadowed any additional dietary effect on risk factors.

Randomized clinical trials that have evaluated the effect of nutritional interventions on secondary prevention of cardiovascular disease are rare.[4,35] Therefore, we believe that our trial not only contributes with data on adherence to culturally adapted nutritional guidelines but also complements the findings from available evidences.

Our study has limitations. Although rates of loss to follow-up were similar between groups, participants in the control group who left the study had a worse cardiovascular risk profile, which may indicate benefit bias for the control group. Another limitation is that we have not used a specific dietary compliance index, although we used the mAHEI. However, the results form mAHEI and the nutrient intake are not in accordance—probably because we used the 24-hour recall for dietary intake data, which is an instrument known to underestimate dietary intake. Besides, mAHEI was developed from a nonquantitative food frequency questionnaire, although it could be overestimating its score. Additionally, we did not evaluate symptoms of feeding and eating disorders such as binge-eating disorder in our study, which are important features that may impair the patient's adherence to treatment.[36] However, we aimed to evaluate the effectiveness of our intervention in a "real-life" setting, which could be highlighted as a strength of this trial. Another limitation of this study is that it was only 3.5 years long, although going further would not have been useful because of lack of dietary adherence.

In conclusion, the BALANCE Program may slightly improve the diet quality in patients with established CVD when compared to the control intervention, but it was not able to reduce the incidence of death and cardiovascular events. Besides, it did not improve cardiovascular risk factors such as blood pressure, serum lipids, fasting glucose, and excess of body weight. Further work on ways to improve long-term diet quality in patients with established CVD should be developed in the context of a middle-income country.

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The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents. The author's responsibilities were as follows: B. W., A. P. G., A. B. C., A. C. B. F., C. R. T., E. S. L., R. P. C.. and O. B. designed research; A. C. B. F. and C. R. T. trained and mentored researches; C. K., F. C. A., P. M., R. A. S., K. G. S., A. S. M., C. C. J. P., C. D. M., A. S. B. M., D. O. P., K. C. S. M., L. S. P., D. M., P. S., P. R. T. M., E. M. S., M. R. S., L. P. S., R. S. T., S. N. A. A. B., P. M. P., S. H. A. A., A. O. L. V., A. S. G., A. F. R. C., M. M. P., B. R. B. A., L. P. S. C., H. A. M., C. B. P. A., H. M. S. C., R. O. M., A. C. C. , C. H. M., C. B., C. M. S., M. O., R. T. A. B., L. R. B., E. G. B., A. L., B. L. P. R., F. D., A. D. B. P., N. P. B., A. G., R. N., G. C. S., P. Z., B. M. F., S. B., T. D. S., J. S., L. M. G., G. S. S., M. L. P. S., V. M. S. B., C. P. S., G. C. M. B., C. L. A., S. B. L., J. S., A. S. N., J. L. B., F. E. Z. N., P. V. G. M., N. M. C., C. F., L. F. S., F. S. F., M. E. M. R., S. S. R., M. C. S. L., B. G. M., K. B. R., J. R. B., C. E. N., R. L. R., M. D., M. B., S. P., I. V., D. S. R., J. A. R., M. A. P. M., L. M. C., M. B., R. M. E. K., E. F. A., J. M. T., E. P. T., F. L. C., C. T. T., L. A. P., L. F. R., R. G. M. C., V. E. C., N. H. F., N. F. S., N. E. S., E. S. D., M. K. I., M. E. P. L., A. P. P. F. C., M. I. S. T., M. M. A. M., M. M. D., D. G. S. J., C. D., V. C. F. O. F., R. M. U., S. S., J. S. O. V., B. A. S. O., J. L. P., I. G. R., C. P. S. P., A. C. S. S., A. S. A., M. T. J., G. B. S., L. V. S. A., V. O. G. N., S. A. V., A. G. L. C., C. F. D., N. M. F. S. L., A. L. M., A. C. L. A., J. M. F. P., L. S. S., L. R. M. L., C. V. S. S., S. M. L. V., F. A. C., R. C. F., I. B. C., L. N. P. N., R. B. F., A. E. S. J., M. B. G. S., K. M. M. A., A. M. P., A. P. O. Q., G. M. N. F., D. M. O. C., C. G. N. C. C., V. B. V., E. M. V. M. C. A., V. S., C. S. A. R., G. A. A., L. B. G., C. S. T., L. M. A. J. S., L. B. C., T. S. S., S. O. J., A. B. L., B. R. S. R., M. A. S., J. A. F. N., L. P. P. D., R. C. A. C., J. M. M., R. C. L. D., E. C. B. B., J. M. A. B., R. M. L. S., A. F. S., A. F. T., E. H. M., N. M. B., J. K., L. V., W. C., M. S., M. C. O. I., M. T. A., J. T. K., C. M. M., V. A. M., C. R. O. B., T. T. F., V. A. R. S. A., J. D. L., S. C. P. M. F., S. L. P., K. C. S., L. H. A. G., L. C. H., L. M. B., M. P. R., K. L. A. L. D., M. C., V. M. B., D. R., J. B., H. H. M. H., A. P. S. C., M. B. F., C. R. H., A. S., S. R. S., P. A. R., T. M. X. M., M. C. C. K., and A. L. B. conducted the research in each site, contributing to the acquisition of data; A. C. B. F., C. R. T., and J. T. S. managed the study data; RHNS performed statistical analysis; B. W., A. B. C., A. C. B. F., A. M., C. R. T., S. A. S., F. Z., and R. H. N. S. wrote the paper. B. W. had primary responsibility for final content. All authors read and approved the final manuscript.

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Appendix. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2019.06.010.

References

1. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies. Am J Clin Nutr 2017;105 (6):1462-73, https://doi.org/10.3945/ajcn.117.153148.
2. Sotos-Prieto M, Bhupathiraju SN, Mattei J, et al. Association of changes in diet quality with total and cause-specific mortality. N Engl J Med 2017;377(2):143-53, https://doi.org/10.1056/NEJMoa1613502.
3. Schwingshackl L, Bogensberger B, Hoffmann G. Diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, Dietary Approaches to Stop Hypertension Score, and Health Outcomes: an updated systematic reviewand meta-analysis of cohort studies. J Acad Nutr Diet. 2018;118(1):74–100.e11. doi: https://doi.org/10.1016/j.jand.2017.08.024. Epub 2017 Oct 27.
4. Barzi F, Woodward M, Marfisi RM, et al. Mediterranean diet and all-causes mortality after myocardial infarction: results from the GISSI-Prevenzione trial. Eur J Clin Nutr 2003;57:604-11, https://doi.org/10.1038/sj.ejcn.1601575.
5. Trichopoulou A, Bamia C, Trichopoulos D. Mediterranean diet and survival among patients with coronary heart disease in Greece. Arch Intern Med 2005;165:929-35, https://doi.org/10.1001/archinte.165.8.929.
6. Dehghan M, Mente A, Teo KK, et al. Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial (ONTARGET)/Telmisartan Randomized Assessment Study in ACEI Intolerant Subjects With Cardiovascular Disease(TRANSCEND) Trial Investigators. Relationship between healthy diet and risk of cardiovascular disease among patients on drug therapies for secondary prevention: a prospective cohort study of 31 546 high-risk individuals from 40 countries. Circulation 2012;126(23):2705-12, https://doi.org/10.1161/CIRCULATIONAHA.112.103234.
7. Yu E, Malik VS, Hu FB. Cardiovascular disease prevention by diet modification. JACC Health Promotion Series J Am Coll Cardiol 2018;72(8):914-26, https://doi.org/10.1016/j.jacc.2018.02.085.
8. Alhassan S, Kim S, Bersamin A, et al. Dietary adherence and weight loss success among overweight women: results from the A TO Z weight loss study. Int J Obes 2008;32:985-91, https://doi.org/10.1038/ijo.2008.8.
9. Mahdavi R, Bagheri asl A, Abadi MAJ, et al. Perceived barriers to following dietary recommendations in hypertensive patients. J Am Coll Nutr 2017;36:193-9, https://doi.org/10.1080/07315724.2014.966176.
10. Miller V, Yusuf S, Chow CK, et al. Availability, affordability, and consumption of fruits and vegetables in 18 countries across income levels: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet Glob Heal 2016;4: e695-703, https://doi.org/10.1016/S2214-109X(16)30186-3.
11. Van Horn L, Carson JAS, Appel LJ, et al. American Heart Association Nutrition Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Stroke Council. Recommended dietary pattern to achieve adherence to the American Heart Association/American College of Cardiology (AHA/ACC) guidelines: a scientific statement from the American Heart Association. Circulation 2016;134:e505-29, https://doi.org/10.1161/CIR.0000000000000462.
12. Nieuwlaat R, Schwalm J-D, Khatib R, et al. Why are we failing to implement effective therapies in cardiovascular disease? Eur Heart J 2013;34:1262-9, https://doi.org/10.1093/eurheartj/ehs481.
13. Rees K, Dyakova M, Wilson N, Ward K, Thorogood M, Brunner E. Dietary advice for reducing cardiovascular risk. Cochrane Database Syst Rev. 2013 6;(12):CD002128. doi: 10.1002/14651858.CD002128.

14. Weber B, Bersch-Ferreira ÂC, Torreglosa CR, et al. The Brazilian Cardioprotective Nutritional Program to reduce events and risk factors in secondary prevention for cardiovascular disease: study protocol (The BALANCE Program Trial). Am Heart J 2016;171 (e1–2):73-81, https://doi.org/10.1016/j.ahj.2015.08.010.
15. Weber B, Galante AP, Bersch-Ferreira AC, et al. Effects of Brazilian Cardioprotective Diet Program on risk factors in patients with coronary heart disease: a Brazilian Cardioprotective Diet randomized pilot trial. Clinics (Sao Paulo) 2012;67:1407-14.
16. Xavier HT, Izar MC, Faria Neto JR, et al. V Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose. Arq Bras Cardiol 2013;101:01-22, https://doi.org/10.5935/abc.2013S010.
17. Sociedade Brasileira de Cardiologia; Sociedade Brasileira de Hipertensão; Sociedade Brasileira de Nefrologia. VI Brazilian Guidelines on Hypertension. Arq Bras Cardiol 2010;95:1-51.
18. Sociedade Brasileira de Diabetes. Diretrizes da Sociedade Brasileira de Diabetes 2009. Diabetes 2009;1:1-168.
19. Sociedade Brasileira de Hipertensão; Sociedade Brasileira de Cardiologia; Sociedade Brasileira de Endocrinologia e Metabologia; Sociedade Brasileira de Diabetes; Sociedade Brasileira de Estudos da Obesidade I Diretriz Brasileira de diagnóstico e tratamento da síndrome metabólicaArq Bras Cardiol 2005;84:1-28.
20. Monteiro CA, Levy RB. A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica 2010;26:2039-49.
21. McCullough ML1, Feskanich D, Stampfer MJ, Giovannucci EL, Rimm EB, Hu FB, Spiegelman D, Hunter DJ, Colditz GA, Willett WC. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. Am J Clin Nutr 2002 Dec;76(6):1261–71. https://doi.org/10.1093/ajcn/76.6.1261
22. de Lorgeril M, Renaud S, Salen P, Monjaud I, Mamelle N, Martin JL, Guidollet J, Touboul P, Delaye J. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. Lancet 1994;343:1454–19.
23. Burr ML. Secondary prevention of CHD in UK men: the diet and reinfarction trial and its sequel. Proc Nutr Soc 2007;66(1):9-15, https://doi.org/10.1017/S0029665107005241.
24. Afilalo J, Duque G, Steele R, et al. Statins for Secondary prevention in elderly patients. A hierarchical Bayesian meta-analysis J Am Coll Cardiol 2008;51:37-45, https://doi.org/10.1016/j.jacc.2007.06.063.
25. Heart protection Study Collaborative group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7-22, https://doi.org/10.1016/S0140-6736(02)09327-3.
26. Downer MK, Gea A, Stampfer M, et al. Predictors of short- and long-term adherence with a Mediterranean-type diet intervention: the PREDIMED randomized trial. Int J Behav Nutr Phys Act 2016;13, 67, https://doi.org/10.1186/s12966-016-0394-6.
27. Msambichaka B, Eze IC, Abdul R, et al. Insufficient fruit and vegetable intake in a low- and middle-income setting: a population-based survey in semi-urban Tanzania. Nutrients 2018;10:222, https://doi.org/10.3390/nu10020222.
28. Tong TYN, Imamura F, Monsivais P, et al. Dietary cost associated with adherence to the Mediterranean diet, and its variation by socio-economic factors in the UK Fenland Study. Br J Nutr 2018;119:685-94, https://doi.org/10.1017/S0007114517003993.
29. Rodríguez-Rodríguez E, Aparicio A, Aranceta-Bartrina J, et al. Low adherence to dietary guidelines in Spain, especially in the overweight/obese population: the ANIBES Study. J Am Coll Nutr 2017;36:240-7, https://doi.org/10.1080/07315724.2016.1248246.
30. Gant C, Binnenmars S, Berg E, et al. Integrated assessment of pharmacological and nutritional cardiovascular risk management: blood pressure control in the DIAbetes and LifEstyle Cohort Twente (DIALECT). Nutrients 2017;9:709, https://doi.org/10.3390/nu9070709.
31. Kwan MW-M, Wong MC-S, Wang HH-X, Liu KQ-L, Lee CL-S, Yan BP-Y, Yu C-M, Griffiths SM. Compliance with the Dietary Approaches to Stop Hypertension (DASH) diet: a systematic review. PLoS One 2013;8:e78412. https://doi.org/10.1371/journal.pone.0078412.
32. Basuray A, Dolansky M, Josephson R, et al. Dietary sodium adherence is poor in chronic heart failure patients. J Card Fail 2015;21:323-9, https://doi.org/10.1016/j.cardfail.2014.12.016.
33. Hartley L, May MD, Loveman E, et al. Dietary fibre for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev 2016, CD011472, https://doi.org/10.1002/14651858.CD011472.pub2.
34. Hooper L, Martin N, Abdelhamid A, Davey Smith G. Reduction in saturated fat intake for cardiovascular disease. Cochrane Database Syst Rev 2015;CD011737. doi: 10.1002/14651858.CD011737
35. de Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999;99:779-85.
36. Pogosova N, Kotseva K, De Bacquer D, et al. Psychosocial risk factors in relation to other cardiovascular risk factors in coronary heart disease: results from the EUROASPIRE IV survey. A registry from the European Society of Cardiology. Eur J Prev Cardiol 2017;24:1371-80, https://doi.org/10.1177/2047487317711334.