

ORIGINAL RESEARCH

## A randomized study of raisins versus alternative snacks on glycemic control and other cardiovascular risk factors in patients with type 2 diabetes mellitus

Harold Bays<sup>1</sup>, Kathy Weiter<sup>1</sup> & James Anderson<sup>2</sup>

<sup>1</sup>Louisville Metabolic and Atherosclerotic Research Center, 3288 Illinois Ave, Louisville, KY 40213, USA, and <sup>2</sup>Medicine and Clinical Nutrition, University of Kentucky, 506 Knapp Farm Drive, Hermitage, TN 37076, USA

### Abstract

Just as the type and duration of physical activity can have variable effects on the glucose levels and other cardiometabolic parameters among patients with type 2 diabetes mellitus (T2DM), so can the types of foods have variable effects as well. This 12-week randomized study of 51 study participants evaluated the impact of routine consumption of dark raisins versus alternative processed snacks on glucose levels and other cardiovascular risk factors among patients with type T2DM. In this study, compared to alternative processed snacks, those who consumed raisins had a significant 23% reduction in postprandial glucose levels ( $P = 0.024$ ). Also compared to snacks, those who consumed raisins had a 19% reduction in fasting glucose and 0.12% reduction in hemoglobin A1c, although these latter findings did not achieve statistical significance. Regarding blood pressure, compared to alternative processed snacks, those who consumed raisins had a significant 8.7 mmHg reduction in systolic blood pressure ( $P = 0.035$ ) (7.5% [ $P = 0.031$ ]) but did not experience a significant reduction in diastolic blood pressure. Compared to alternative processed snacks, those who consumed raisins did not have a significant improvement in body weight, body mass index, waist circumference, fasting insulin, homeostatic model assessment of insulin resistance, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol (HDL), triglyceride, or non-HDL cholesterol levels. Overall, these data support raisins as a healthy alternative compare to processed snacks in patients with T2DM.

### Keywords:

adiposopathy, blood pressure, diabetes mellitus, dry fruit, obesity, raisins

### History

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### Introduction

Many factors can influence glucose levels and cardiovascular disease (CVD) risk factors among patients with type 2 diabetes mellitus (T2DM). Nutritional quality is one such important factor. Raisins are dry fruits that have satiating effects and a low-to-moderate glycemic index. Raisins are relatively high in fiber, fructose, polyphenols, phenolic acid, tannins, antioxidants, flavonoids (such as quercetin), resveratrol constituents, and potassium. Individually or collectively, these properties have the potential to affect glucose metabolism, as well as have effects on other CVD risk factors such as blood pressure [1,2]. Consumption of proteins, unsaturated fats, fish, nuts, fruit, vegetables, and whole grains may reduce CVD risk, especially when compared with consumption of saturated fats and processed foods with high glycemic index [3]. The glycemic index of foods is a metric that reflects a consumed food's effect on glucose blood levels, wherein 100 represents an equivalent amount of ingested pure glucose.

Consumption of foods with higher glycemic index may increase glucose blood levels, triglyceride blood levels, and CVD risk [4].

When compared to white bread, acute consumption of raisins may significantly blunt postprandial glucose in healthy individuals [5]. In a study of patients with well-controlled T2DM who were instructed to eat less fruits and vegetables than the recommended five servings per day, two servings of Corinthian raisins versus snacks of similar energy density for 24 weeks significantly lowered diastolic blood pressure and increased total antioxidant potential compared to baseline. Corinthian raisins did not affect body weight, glycemic control, lipid profile, and C-reactive protein [6].

A study of similar design to this current study found that, compared to alternative processed snacks among patients with prehypertension and mild hyperglycemia (not diabetes mellitus), those who consumed dark California raisins 3 times per day for 12 weeks experienced significantly decreased mean postprandial glucose and significantly reduced systolic blood pressure [1]. Whereas this prior Raisin study (ClinicalTrials.com Identifier Number: NCT01260272) evaluated raisins versus snacks in a generally healthy population, the purpose of this current, follow up, randomized, comparator study was to evaluate raisins versus alternative snacks on cardiovascular risk factors among patients with T2DM.

Correspondence: Harold Bays, MD, Louisville Metabolic and Atherosclerotic Research Center, 3288 Illinois Ave, Louisville, KY 40213, USA. E-mail: hbaysmd@aol.com

## Materials and methods

This was a randomized, unblinded, single-site, active-controlled study in patients with T2DM having inadequate glycemic control (NCT01677936). Expected participation for each study subject was 14 to 16 weeks in total: 2–4 weeks for screening, followed by study visits at weeks 4, 8 and 12, with a total of 12 weeks of dosing with assigned study product. At each visit, subjects underwent a general clinical assessment, vital sign measurements, and study product accountability. Laboratory obtained at randomization included fasting blood testing of lipid levels, glucose, insulin, hemoglobin A1c (HbA1c), and 2-hour glucose and insulin levels after liquid meal. Laboratory evaluation at week 8 included fasting glucose, insulin, HbA1c, and 2-hour glucose and insulin levels after liquid meal. At week 12, laboratory evaluation included fasting lipid levels, glucose, insulin, HbA1c, and 2-hour glucose and insulin levels after liquid meal. Figure 1 displays the flow diagram for this 5-visit study.

Prior to initiation of the study, and prior to any protocol-directed procedures, study participants underwent the informed consent process that included review of an Institutional Review Board-approved informed consent document/agreement explaining the procedures of the study and the potential risks. Each study subject (or representative) was required to sign and received a dated copy of the informed consent document.

The hypothesis of this study was that routine consumption of raisins over 12 weeks by patients with inadequately controlled T2DM would improve glycemic control, and improve other cardiovascular risk factors compared to the routine consumption of generally equal calorie alternative snacks. The primary efficacy end points included 2-hour postprandial glucose levels and HbA1c at week 12 compared to baseline. Secondary efficacy end points included fasting glucose levels, systolic and diastolic blood pressure, and waist circumference. Tertiary efficacy end points (exploratory analyses) included insulin levels, homeostatic model assessment (HOMA), lipid levels (total cholesterol, triglycerides, low-density lipoprotein [LDL] cholesterol, high-density lipoprotein [HDL] cholesterol, non-HDL cholesterol, body weight [kilograms], and body mass index [BMI]).

Main inclusion criteria included men or women > 18 years of age with T2DM, HbA1c 6.5–10%, and BMI 25.0–50 kg/m<sup>2</sup>. Another inclusion criterion included planned or anticipated changes in lifestyle health practices. Main exclusion criteria included intolerance, dislike, or unwillingness to consume raisins or any of the comparator snacks and affiliated ingredients, change in anti-diabetes mellitus medication within 3 months prior to screening visit and/or anticipated change in anti-diabetes medications throughout the course of the trial, change in blood pressure and/or lipid-altering medications within 1 month of screening visit, significant CVD within 3 months of screening, history of gastrointestinal malabsorption (eg, uncontrolled Crohn's disease, etc.) or history of bariatric surgery, blood pressure > 180 mmHg systolic or > 100 mmHg diastolic, weight change (increase or decrease) of > 5 pounds in 2 months (by history) prior to visit 1, bradycardia defined as pulse < 50 beats/minute, history of clinically significant anemia, fasting serum lipoprotein values of: LDL-cholesterol > 160 mg/dL, or triglycerides > 500 mg/dL (exclusionary during screening only), creatinine level on screening > 1.5 times the upper range of normal, liver enzymes on screening > 2 times the upper limits of normal, or potassium level above the upper range of normal on screening (one repeat laboratory was permitted if the initial elevated potassium level was thought to be possibly due to laboratory error). Insulin use was permitted as long as: (1) the daily dose of insulin was stable for at least 1 month prior to screening; (2) no plans existed to change insulin dose during the study; and (3) fasting and postprandial insulin levels were not obtained on insulin-treated subjects. Systemic corticosteroids (intravenous, subcutaneous, intra-articular) were excluded, but inhaled and intranasal corticosteroids were allowed. Other excluded medications included anti-obesity/weight maintenance drug therapies within 2 months of the initial study visit, use of digoxin or other cardiac antidysrhythmic drugs, and anticoagulants (such as warfarin, Coumadin). Miscellaneous exclusion criteria included blood donation within 2 months prior to study entry or plans to donate blood during the course of this study.

Dark, dry Californian raisins were provided as 1 oz (28 g) prepackaged serving of raisins (90 kcal/serving). Alternative prepackaged comparator process snacks were provided as 100 kcal/serving packages that did not contain raisins or

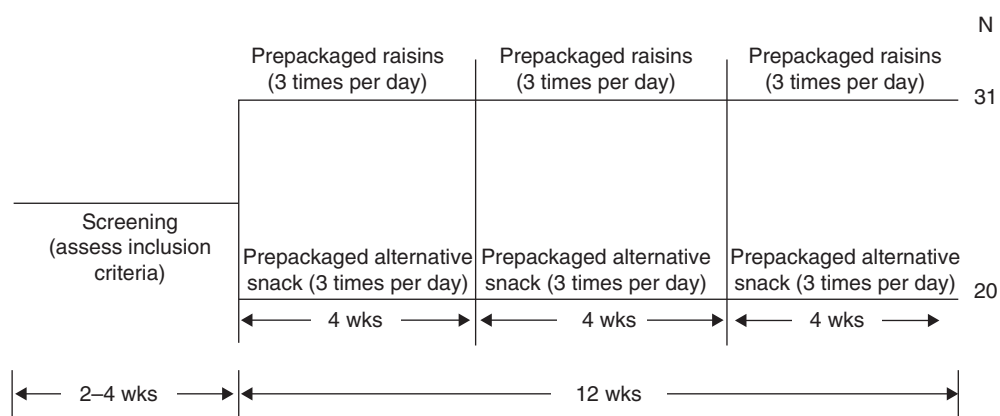


Figure 1. Study flow diagram. Abbreviation: N = Number randomized to each group; wks = Weeks.

predominantly fruits or vegetables, and must not have contained over 10 g of sugar per serving. Both treatments were administered orally three times daily before breakfast, lunch, and dinner, with 8 oz of non-caloric fluid (preferably water but non-caloric soft drinks or hot beverage were acceptable). Some illustrative comparator snack examples included Keebler® Cheez-It® Crackers, Nabisco Honey Maid Cinnamon Roll Thin Crisps, and Pepperidge Farm® Goldfish® Baked Snack Crackers. Nutritional information of the pre-packaged raisins used in this trial, as well as the example alternative snacks, is listed in Table I. Two hour postprandial glucose levels were obtained at baseline, and at weeks 8 and 12, after consumption of a liquid meal [7] consisting of Boost Original® containing 240 cal, 4 g of fat, 41 g of carbohydrates, 28 g of sugar, and 10 g of protein. Although dietary diaries were not collected, all subjects were instructed on the National Cholesterol Education Program, Adult Treatment Panel III Therapeutic Lifestyle Change diet [8].

Primary, secondary, and special interest end point datasets included the intent-to-treat (ITT) population, defined as all subjects who were randomized and received at least one dose of test product after obtaining a baseline value at the baseline visit. The safety population was defined as all randomized subjects who received at least one dose of study therapy and assessed by treatment-emergent adverse experiences, clinical laboratory test results, and physical examinations in the safety sample. For the ITT analysis, the last observation carried forward (LOCF) method was used to impute missing data points for subjects who discontinued without completing the entire treatment period. If a study participant did not have baseline values and/or did not complete any post-intervention comparative values, then this study subject no longer met the definition of ITT, and the subject was removed from the efficacy analysis. If a study participant met the ITT population and had post-intervention comparative values, but the LOCF was unavailable due to missing isolated data points after obtaining the baseline value, then the baseline values for the isolated data points were omitted for this study participant, as is reflected in the reported *n* values. For comparative datasets of parametric (normal) distribution, unpaired *t*-test was utilized for between-group comparisons from baseline to end-of-study (week 12). The  $\alpha$  for statistical significance was  $\leq 0.05$ , two-sided. The confidence interval for statistical testing was set at 95%.

Table I. Table of nutrition values for raisins and illustrative snacks.

Measure	Raisins	Illustrative snack*	Range for illustrative snacks
Calories (kcal)	90	100	100
Total fat, g	0	3.0	2.0–3.5
Cholesterol, mg	0	1.7	0–5.0
Sodium, mg	5	180	170–200
Potassium, mg	220	0	N/A
Total carbohydrate, g	22	16.0	14–19
Dietary fiber, g	2	0.7	0–1.0
Sugars, g	20	2.0	0–6.0
Protein, g	< 1	2.0	1.0–3.0

\*Values are average of the three representative snack packs listed in the Materials and Methods section.

Abbreviations: N/A = Not applicable.

Software used in these analyses included GraphPad Prism 5 for Windows (version 5.04, 2010) and Microsoft Excel 2013.

## Results

Figure 2 describes the study participant disposition during the course of this randomized trial. Table II describes the demographics and baseline vital signs and laboratory data. In general, the patient population included men and women with T2DM having a mean age of  $\sim 58$  years. Study participants were generally overweight or obese and had increased waist circumference. Demographically, the raisin and processed alternative snack groups were generally comparable at baseline. Compared to the processed alternative snack group at baseline, the raisin group did have somewhat of a higher BMI, waist circumference, postprandial glucose level, HbA1c, and higher fasting insulin levels. Although this was a small study, minorities were well represented, constituting 35% of the study participants. Compliance with raisins and snacks administration was  $> 90\%$ .

Table III describes the sentinel outcomes of the trial. Regarding glucose-related end points, compared to snacks, those who consumed raisins had significantly reduced postprandial glucose levels by 23% ( $P = 0.024$ ). Also compared to snacks, those who consumed raisins had reduced postprandial glucose levels by 36 mg/dL ( $P = 0.072$ ), reduced fasting glucose levels by 32 mg/dL ( $P = 0.066$ ), reduced fasting glucose levels by 19% ( $P = 0.062$ ), and reduced HbA1c by 0.12%, although statistical significance was not achieved. Regarding HbA1c, this difference included one raisin subject who had no substantial change in fasting or postprandial glucose levels from the beginning to end of trial, yet had an inexplicable increase in HbA1c of 2% at end of study. If this potential outlier value was removed, then compared to snacks, raisins would have reduced HbA1c by 0.22%.

Regarding blood pressure, those who consumed raisins had significantly reduced systolic blood pressure by 8.7 mmHg ( $P = 0.035$ ), and reduced systolic blood pressure by 7.5% ( $P = 0.31$ ) but did not reduce diastolic blood pressure.

Otherwise, compared to snacks, raisins did not significantly change body weight, BMI, waist circumference, fasting insulin, HOMA-estimated insulin resistance (HOMA-IR), total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, or non-HDL cholesterol.

Regarding safety, only one serious adverse experience occurred in a raisin-administered subject who experienced a pulmonary embolus after a surgical procedure of hip replacement. The number of subjects with adverse experiences (irrespective of causality) was similar, with 40% of snack subjects reporting one or more adverse experiences, compared to 48% of raisin subjects reporting one or more adverse experiences. The most common adverse experiences in the raisin group were gastrointestinal in nature (ie, diarrhea, nausea, etc.); adverse experiences occurred in which occurred in 8 raisin subjects compared to 1 snack subject. No laboratory adverse experiences were reported. Regarding tolerance, 1 of 20 randomized snack subjects (5%) withdrew due to intolerance to snacks; 3 of 31 randomized raisin subjects (10%) withdrew due to intolerance to raisins.

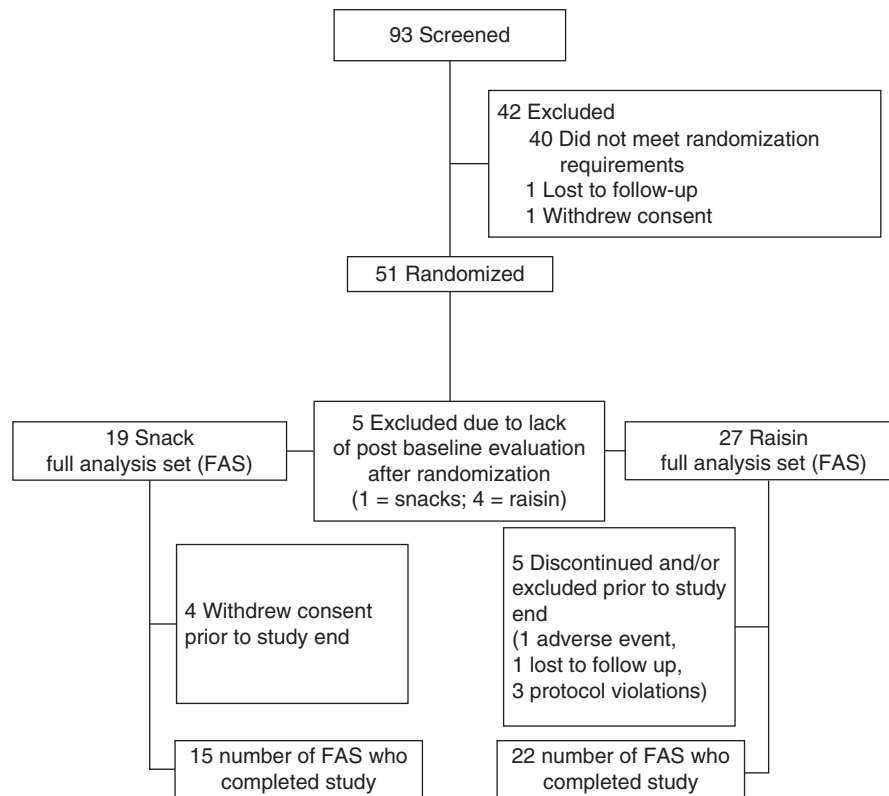


Figure 2. Flow diagram showing study participant disposition. FAS which was a portion of the ITT population including randomized patients with baseline and at least one valid post-baseline evaluation. Abbreviations: FAS = Full Analysis Set; ITT = Intent to treat.

## Discussion

This study evaluated the cardiometabolic effects of the routine consumption of raisins versus processed snacks over 12 weeks, which was similar in study design to a prior 2011 study [PN001] titled: “A Randomized, Un-blinded, Single Research Site, Comparator Study of Raisins Versus Alternative Snacks on Cardiovascular Risk Factors in Generally Healthy Subjects” [2]”. At the time of this 2011 study,

almost no information existed regarding the effects of raisins (or any dried fruit) on cardiometabolic risk factors. In this follow-up study among patients with T2DM, compared to alternative processed snacks, those who consumed raisins had significantly reduced postprandial glucose levels and systolic blood pressure, to a statistical and clinically relevant degree. Also compared to snacks, those who consumed raisins had reduced fasting glucose and HbA1c, although these latter findings were not of statistical significance. Regarding other

Table II. Baseline demographic, mean vital signs, and mean laboratory data in full analysis set.

Demographics	Snack n = 19	Raisin n = 27	Total N = 46
Mean age in years	59	58	58
Gender n (%)			
Men	9 (47%)	10 (37%)	19 (41%)
Women	10 (53%)	17 (63%)	27 (59%)
Race n (%)			
White American or Caucasian	15 (79%)	15 (56%)	30 (65%)
Black or African-American	4 (21%)	9 (33%)	13 (28%)
American-Indian/Alaska-Native	0 (0.0%)	2 (7%)	2 (4%)
Multiracial/ more than one race	0 (0.0%)	1 (4%)	1 (2%)
<i>Vital signs (mean)</i>			
Body mass index in kg/m <sup>2</sup> (SD)	34 (5)	37 (7)	36 (6)
Waist circumference in cm (SD)	113 (12)	120 (14)	117 (13)
Systolic blood pressure in mmHg (SD)	130 (13)	129 (16)	130 (15)
Diastolic blood pressure in mmHg (SD)	75 (9)	74 (10)	74 (10)
<i>Laboratory</i>			
2-hour postprandial glucose in mg/dL (SD)	155 (60)	208 (63)	185 (66)
Fasting glucose in mg/dL (SD)	140 (35)	162 (47)	153 (43)
Hemoglobin A1c % (SD)	7.08 (0.62)	7.62 (1.0)	7.39 (0.90)
Fasting insulin in mIU/L (SD)	11 (9)	14 (16)	13 (13)
Two hour postprandial insulin in mIU/L (SD)	36 (31)	34 (38)	35 (35)

Abbreviation: SD = Standard deviation.



Table III. Raisins and alternative snacks in patients with type 2 diabetes mellitus: mean baseline glucose and blood pressure measures to week 12.

	Raisins change from baseline	Snacks change from baseline	Between-group differences: raisins versus snacks	95% confidence interval in between-group differences	<i>P</i> value for raisins versus snacks
Postprandial glucose (%)	-5.7 (SD = 24)	17 (SD = 36)	-23	-43 to -3.2	0.024
Postprandial glucose (mg/dL)	-17 (SD = 64)	19 (SD = 51)	-36	-75 to 3.4	0.072
Fasting glucose (%)	-3 (SD = 29)	16 (SD = 34)	-19	-40 to 0.99	0.062
Fasting glucose (mg/dL)	-13 (SD = 57)	19 (SD = 44)	-32	-66 to 2.3	0.066
Hemoglobin A1c (%)	0.00 (SD = 0.76)	0.12 (SD = 0.70)	-0.12	-0.61 to 0.37	0.619
Systolic blood pressure (mmHg)	-4.2 (SD = 13)	4.5 (SD = 14)	-8.7	-17 to -0.66	0.035
Systolic blood pressure (%)	-3.7 (SD = 12)	3.8 (SD = 11)	-7.5	-14 to -0.72	0.031
Diastolic blood pressure (mmHg)	0.63 (SD = 7.3)	0.63 (SD = 6.3)	0.0	-4.2 to 4.2	0.999
Diastolic blood pressure (%)	1.3 (SD = 9)	1.3 (SD = 8)	0.1	-5.1 to 5.2	0.981

Abbreviation: SD = Standard deviation.

cardiovascular and metabolic parameters, compared to snacks, administration of raisins did not significantly improve diastolic blood pressure, body weight, BMI, waist circumference, fasting insulin, HOMA-IR, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, or non-HDL cholesterol levels.

Despite a different patient population, among the most striking findings of this study were the similarities between the cardiometabolic effects of raisins versus alternative processed snacks in this study involving patients with T2DM, versus a similar study of raisins in individuals selected for having hyperglycemia (but not diabetes mellitus) and some elevation in blood pressure (but not hypertension), as reported in the relative Clinical Study Reports and data postings on ClinicalTrials.gov (NCT01260272) [1]. Table II describes the comparative metabolic similarities regarding these two different patient groups. This may not be surprising in that overweight and obese patients with prehypertension and pre-diabetes mellitus may simply represent an earlier stage of the disease of obesity, or more specifically, the disease of adiposopathy [9,10]. Patients with overweight and obesity with prehypertension and pre-diabetes mellitus often progress to hypertension and diabetes mellitus over time, especially with greater increases in body fat over time and/or lack of appropriate nutritional intervention and increased physical activity [11]. Regarding lifetime risk of atherosclerotic CVD (ASCVD) among individuals with overweight and obesity, perhaps the most effective timing of intervention to reduce ASCVD risk is before the onset of major ASCVD risk factors (eg, diabetes mellitus and hypertension) [12]. Such an early intervention strategy might best be achieved via implementing more healthy food choices and more active physical activities. However, healthy nutrition choices still have an important role among patients with overweight or obesity who progress to metabolic diseases, such as diabetes mellitus. Determining which choices are healthiest is best supported by comparative clinical trial evidence – as was done in this trial.

With specific regard to findings of this study, at baseline, mean HbA1c was > 7%, which is above glycemic treatment goal recommended by the American Diabetes Association [13]. The American Diabetes Association has also recommended postprandial glucose levels of < 180 mg/dL (< 10.0 mmol/L) [13]. In addition to the well-established

contribution of hyperglycemia to microvascular disease, elevations of postprandial glucose levels may be associated with increased ASCVD risk and may contribute to endothelial dysfunction [11,14]. In this study, compared to alternative processed snacks, consumption of raisins significantly reduced postprandial glucose levels. Regarding the clinical implications of the degree of glucose lowering in this study, Table III (and Table IV) describes the degree of glycemic improvement that might be expected with a nutritional intervention strategy that employs routine consumption of raisins versus process snacks. This degree of glycemic improvement among patient with T2DM is roughly the same as the degree of glycemic worsening as might occur with implementation of high-intensity statin (eg, increase in HbA1c of 0.12%) [15]. This study did not specifically evaluate the effect of raisin consumption on statin-promoted hyperglycemia; however, statins are generally recommended to patients with T2DM to reduce macrovascular disease [16]. Given that nutritional intervention is among the preferred treatments of choice to manage potential statin-promoted hyperglycemia [17], then this provides just one illustrative example of how this study provides support for a nutritional strategy wherein raisins might be preferred as a snack choice compared to processed snacks. Also compared to alternative processed snacks, administration of raisins reduced systolic blood pressure. Regarding clinical significance, cardiovascular outcome studies support the substantial potential benefits of modest blood pressure reduction, even among patients with ASCVD having “normal” blood pressure [18].

Regarding limitations, this study is potentially limited by being an unblinded, single-site study of modest size. This study made no attempt to assess CVD clinical outcomes. The raisins used in this study were dark seedless raisins, which constitute ~ 95% of California raisins [19]. It is unclear if the same findings in this study would apply to other types of raisins. Finally, compared to the alternative processed snack group at baseline, the raisin group did have somewhat of a higher BMI, waist circumference, postprandial glucose level, HbA1c, and higher fasting insulin levels. The implications of this are unclear. One might suppose this population would be at increased risk of worsening glucose control after meals and over time. It is, therefore, possible that the chance imbalance in this randomized clinical trial may have diminished the relative effectiveness of raisins in this patient population.

Table IV. Cardiometabolic effects of raisins compared to processed snacks when consumed for 12 weeks in two similarly designed studies involving: (a) a prior study among patients with baseline hyperglycemia (fasting glucose > 90 mg/dL) but not diabetes mellitus [1] and (b) this study of patients with T2DM.

Metabolic parameter	Patients with hyperglycemia but no diabetes mellitus	Patients with T2DM
Postprandial glucose (%)	Raisins significantly reduced postprandial glucose levels by 16% ( $P = 0.033$ )	Raisins significantly reduced postprandial glucose levels by 23% ( $P = 0.024$ )
Postprandial glucose (mg/dL)	Raisins reduced postprandial glucose levels by 13.5 mg/dL ( $P = 0.09$ )	Raisins reduced postprandial glucose levels by 36 mg/dL ( $P = 0.072$ )
Fasting glucose (%)*	Raisins reduced fasting glucose levels by 0.8% ( $P = 0.750$ )	Raisins reduced fasting glucose levels by 19% ( $P = 0.062$ )
Fasting glucose (mg/dL)*	Raisins reduced fasting glucose levels by 0.5 mg/dL ( $P = 0.835$ )	Raisins reduced fasting glucose levels by 32 mg/dL ( $P = 0.066$ )
HbA1c (%)	Raisins reduced HbA1c by 0.08% ( $P = 0.173$ )	Raisins reduced HbA1c by 0.12%, ( $P = 0.619$ )
Systolic blood pressure (%)	Raisins significantly reduced systolic blood pressure by 4.8% ( $P = 0.0497$ )	Raisins significantly reduced systolic blood pressure by 7.5% ( $P = 0.031$ )
Systolic blood pressure (mmHg)	Raisins significantly reduced systolic blood pressure by 6.5 mmHg ( $P = 0.0468$ )	Raisins significantly reduced systolic blood pressure by 8.7 mmHg ( $P = 0.035$ )
Other metabolic parameters	Raisins did not significantly improve diastolic blood pressure, body weight, body mass index, waist circumference, fasting insulin, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, or non-HDL cholesterol	Raisins did not significantly improve diastolic blood pressure, body weight, body mass index, waist circumference, fasting insulin, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, or non-HDL cholesterol

\*Although neither demonstrated statistical difference on fasting glucose levels in the studies of this size, raisins numerically reduced the absolute and percentage reduction in fasting glucose more in the diabetes mellitus group than in the patients without diabetes mellitus group – possibly because of the higher baseline glucose levels in the patients with T2DM.

Abbreviations: HbA1c = Hemoglobin A1c; HDL = High-density lipoprotein; LDL = Low-density lipoprotein; T2DM: Type 2 diabetes mellitus.

Conversely, it is also possible that the imbalance might have had other relative effects on cardiometabolic parameters. Concerns of the potential implications either way may be somewhat mitigated by the strikingly consistent findings of this trial in a different patient population, with a previous similarly designed trial, demonstrating similar findings. (Table IV).

Overall, the relative improvement in the CVD risk factors of glucose and blood pressure with raisins found in this randomized trial would be consistent with, and supportive of, the findings of a meta-analysis of 16 prospective cohort studies of 56,423 deaths among 833,234 participants. In this meta-analysis, a higher consumption of fruits and vegetables was associated with a lower risk of cardiovascular and overall mortality [20].

### Conclusion and clinical implications

In this study of patients with T2DM, compared to alternative processed snacks, administration of raisins significantly reduced postprandial glucose levels and systolic blood pressure, and non-significantly reduced fasting glucose and HbA1c. Compared to snacks, administration of raisins did not significantly improve diastolic blood pressure, body weight, BMI, waist circumference, fasting insulin, HOMA-IR, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, or non-HDL cholesterol levels. These findings were consistent with a similar study of raisins in individuals having hyperglycemia (but not diabetes mellitus) and some elevation in blood pressure (but not hypertension). Thus, raisins may be a healthy alternative to processed snacks not only in generally healthy individuals with evidence of early metabolic abnormalities but also among patients with T2DM.

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